P-ISSN: 0216-504X E-ISSN: 2620-536X

JURNAL INFO KESEHATAN

Published by:
Research and Community Service Unit, Poltekkes Kemenkes Kupang

JURNAL INFO KESEHATAN	VOLUME 21	NUMBER 4	PAGE 610-895	MONTH DECEMBER	YEAR 2023

JURNAL INFO KESEHATAN

Editorial Team

Editorial Address
Piet A.Tallo Street, Liliba-Kupang, East Nusa Tenggara, Indonesia
Phone/fax: (0380) 8800256
Email: jurnalinfokesehatan@gmail.com
Website: http://jurnal.poltekeskupang.ac.id/index.php/infokes

Accredited by:
Ministry of Research, Technology and Higher Education of the Republic of Indonesia (Kemenristekdikti) Number: 105/E/KPT/2022, April 7, 2022

This journal is indexed on:

Published by:
Research and Community Services Unit, Poltekkes Kemenkes Kupang

Published Every 3 Months
March, June, September and December

JURNAL INFO KESEHATAN

p-ISSN 0216-504X I e-ISSN 2620-536X
Volume 21 Number 4, December 2023

TABLE OF CONTENTS

GUIDELINES FOR AUTHORS
JURNAL INFO KESEHATAN

MANUSCRIPT PREPARATION AND SUBMISSION

Initial submission

The article is the result of a research study in health. The article should be written in English and Indonesian. The initial submission should be clean and complete but does not have to comply with all Jurnal Info Kesehatan (Journal of Health Info) specifications yet.

Manuscripts of insufficient priority or quality are promptly rejected. Manuscripts retained to undergo a review process for potential publication in the Journal will be submitted to a technical check. Authors will be informed immediately if their manuscripts need reformatting and will be given 14 days to make specific changes.

Visit http://jurnal.poltekeskupang.ac.id/index.php/infokes for online manuscript submission.

Questions? Write jurnalinfokesehatan@gmail.com or call M. Ibraar Ayatullah at (+62) 813-1411-9647).

Manuscript File Formats

All manuscripts should be submitted in Word document format. Jurnal Info Kesehatan submission system is located at http://jurnal.poltekeskupang.ac.id/index.php/infokes

Manuscript Components

Research result article consists of: Title, author's name, abstract in English, keywords, introductions, research methods, results and discussions, conclusions, and References.

Review article consists of: Title, author's name, abstract in English, Keywords, Introductions, research methods, results and discussions, Conclusion, and References.

Author mush attach a plagiarism checking document (can use Turnitin, iThenticket or something else). The maximum similarity tolerated is 25%.

WRITING GUIDE

Title

a) The title is written in English and informative, concise, and not too long or short (10- 25 words).
b) Consists of the variables under study and describes the content of the manuscript.
c) A title does not contain abbreviations or formulas.
d) The title page should include the title of the manuscript only. The names of authors should be deleted to ensure the double-blinding of the paper during the peer review process.

Abstract and Keyword

a) The abstract is concisely written, about the most important ideas, and contain theproblems or research objectives, research method, and research results.
b) Written in English language with 300-350 words maximum.
c) Keywords contain main words.

Introduction

An introduction is presented in an integrated manner without subtitles. It is written in theform of paragraphs with a contains:

a) Background or research rational.
b) Theoretical basis (literature review in brief).
c) Research objective.

Research Method

The method is written with a containing:

a) The study design.
b) Data collection techniques and data sources.
c) Method of data analysis.

Results and Discussion

The results represent a major part of scientific articles containing:

a) Results of data analysis.
b) Results of hypothesis testing.
c) It can be presented with a table or graph to clarify results verbally.
d) Discussion is an important part of the entire scientific article. The purposes of the discussion are: answer the research problem, interpret the findings, integrate the findings of research into the existing knowledge, and formulate a new theory or modify the existing theories.
e) A serial number that is used is number 1, 2, 3, and so on, do not need to use a composite number. Hyphens should not change the serial number.

Conclusion

a) Contain conclusions and recommendations.
b) Conclusions contain answers to the research questions.
c) Recommendations refer to the results of research and practical form of action, specify to whom and for what recommendation intended.
d) Written in essay form, not in numerical form.

References

The main references are national journal, international journals and proceeding. All references should be to the most pertinent and up-to-date sources:

a) Contain literature that is referenced in the content, arranged alphabetically, and written in the APA (*American Psychological Association*) 6th Edition system.
b) Fully written, appropriate with the references in the content.
c) Only load literature referenced in the content.
d) Source of reference are at least 80% from literature published last 10 years
e) References are least 80% from research article in journal or research reports.
f) Reference format is APA (*American Psychological Association*) 6th Edition style better to use Reference Manager (Mendeley, Zotero or Endnote, etc).

Example:

Journal:

Author1A, Author2 B. (Year).Title of Manuscript.*Name of Journal or its Abbreviation*. *Vol.(Issue),pages*. doi:…….

Casadei, D., Serra, G., Tani, K. (2007). Implementation of a Direct Control Algorithm for Induction Motors Based on Discrete Space Vector Modulation. *IEEE Transactions on Power Electronics,15(4), 769-77.*

Casadei, D., Serra, G., Tani, K. (2007). Implementation of a Direct Control Algorithm for Induction Motors Based on Discrete Space Vector Modulation. *IEEE Transactions on Power Electronics,15(4), 769-77.* doi: http://doi.org/10.1109/63.849048

Proceeding:

If the proceedings consists of several volumes

Author1 A, Author2 B.(Year).*Title of Manuscript*. Name of Conference of Seminar. City.Volume: pages. doi:…….

Calero C, Piatiini M, Pascual C, Serrano MA. (2009). Towards Data Warehouse Quality Metrics. Proceedings of the 3rd Intl. Workshop on Design and Management of Data Warehouses (DMDW). *Interlaken. 39, 2-11*. doi: http://doi.org/10.1109/63.849048

Texbooks:

If the references are refer to specific page range in a book

Author1 A, Author2 B. (Year). *The Title of the Book. Edition*. City: Publisher. pages.

De Vaus, D. A. (2014). *Surveys in social research.* Sydney, Australia: Allen & Unwin.

Book chapter:

If the references are refer to specific page range in a book chapter

Author1 A, Author2 B. (Year). The Title of the Book. Edition. City: Publisher. pages.

McKenzie, H., Boughton, M., Hayes, L., & Forsyth, S. (2008). Explaining the complexities and value of nursing practice and knowledge. In I. Morley & M. Crouch (Eds.), *Knowledge as value: Illumination through critical prisms* (pp.209-224). Amsterdam, Netherlands: Rodopi.

Newspaper article:

Author1 A, Author2 B. (Year, Month date). *The Title of the Newspaper Article*. Publisher. Retrieved from……..

Fellner, C. (2019, April 7). Time bomb: Two new cases as NSW faces worst measles outbreak in years. *The Sydney Morning Herald*. Retrieved from https://www.smh.com.au.

The editor would like to give a great acknowledgment to all of the reviewers. Without their contribution and expertise, it would be difficult to maintain the high standards of a peer-reviewed journal.

Dr. Helen Bradely
Dr. Smathi Chong
Dr. Gillian Mashman
Israfil, S. Kep, M. Kes
Setiawan, SKM, M.Kes
Norzawani Jaffar, Ph.D
Mohd Razif Shahril, Ph.D
Azmahani Abdullah, Ph.D
Dr. Kusmiyati, SKM, MPH
Prof. Sakinah Harith, Ph.D
Solikhah, SKM, M.Kes, PhD
Abbe Maleyki Mhd Jalil Ph.D
Dr. Sabina Gero, S.Kp., M. Sc
Dr. R.H. Kristina, SKM, M.Kes
Dr. Drs. Abdul Wahab, M. Kes
Dr. Fathmawati, S.Si.T, M.Kes
Prof. Dr. Khayan, SKM, M.Kes
Priska E. Tenda, SF, Apt., MSc
Dr. drg. Jusuf Kristianto, M.Kes
Dr.drg. Christina Ngadilah, MPH
Marichatul Jannah, S.ST, M.Kes
Dr. drg. Wiworo Haryani, M. Kes
Dr. drg. Christina Ngadilah, MPH
Dr. Linda Suwarni, SKM., M. Kes
Ermi Ndoen, S.KM, MSc.PH, Ph.D
Dr. Drs. Jefrin Sambara, Apt, M.Si
Kholisotul Hikmah, S.S.T., M. Epid
Dr. Indah Budiastutik, SKM, M.Kes
Agus Hendra Al Rahmad, SKM, MPH
Dr. Mareta Bakale Bakoil, S.ST, MPH
Mariana Ngunju Awang, SST, M. Kes
Alfiyana Yuliasari, S.Keb., Bd. M.K.M
Adam Astrada, Ns., MHS, CNS, DHSc
Dr. Yessi Dessy Arna, M. Kep., Sp. Kom
Norma Tiku Kambuno, S.Si., Apt, M. Kes
Dr. Arif Setyo Upoyo, S.Kp, Ners, M. Kep
Kraichat Tantrakarnapa, B.S., M.Sc., Ph.D.
Dr. Yuanita Clara Luhi Rogaleli, S.Si, M.Kes
Dr. Brahmaputra Marjadi, MPH, PhD, SFHEA
Prof. Dr. Ridwan Amiruddin, SKM, M.Kes, M.Sc, PH
Dr. Ns. Ni Luh Putu Inca Buntari Agustini, S.Kep., MNS
Prof. Nelson Martins, B. Med, MD, GCERT PH, MHM, PhD

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 610-625
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1222*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Single Nucleotide Variation in the Promoter Region of the APOA1 Gene as a Candidate Biomarker for Dyslipidemia

Toeti Rahajoe[1,4a], Kartika Nugraheni[2b], Pinda Ayu Widiyani[3,5c], Balqis Aureola Putri Asihanto[1d], Aprilia Indra Kartika[1e*]

[1] Department of Medical Laboratory Technology, Faculty of Nursing and Health Sciences, Universitas Muhammadiyah Semarang, Semarang, Central Java, Indonesia
[2] Department of Nutrition, Faculty of Nursing and Health Science, Universitas Muhammadiyah Semarang, Semarang, Central Java, Indonesia
[3] Master of Public Health, Universitas Negeri Semarang, Semarang, Central Java, Indonesia
[4] Central Java Provincial Health Laboratory, Semarang, Central Java, Indonesia
[5] Public Health Center Limbangan, Semarang, Central Java, Indonesia

[a] Email address: toeti.rahajoe@unimus.ac.id
[b] Email address: kn.nugraheni@unimus.ac.id
[c] Email address: pinda.ayu.wd@gmail.com
[d] Email address: balqisasihanto@gmail.com
[e] Email address: kartika.biotech@unimus.ac.id

Received: 13 June 2023 Revised: 26 September 2023 Accepted: 26 September 2023

Abstract
Dyslipidemia is a lipid profile abnormality that can escalate the risk of cardiovascular disease. The rate of cardiovascular events in Indonesia is very high. One of the causes of dyslipidemia is due to polymorphisms in genes associated with lipid metabolism. The APOA-1 gene encodes the APOA-1 protein which functions to regulate HDL protein synthesis. The objective of this study is to determine APOA1 gene polymorphisms in patients with dyslipidemia. Samples of healthy controls and dyslipidemia patients were used in this investigation. The lipid profiles of the patients and normal controls are determined at the onset of the study. Following DNA extraction, the APOA-1 gene was amplified and sequenced using the serum sample. MEGA X and BLAST were used to analyze the sequencing results. The study's findings demonstrated that the APOA-1 gene length in samples of dyslipidemic patients and normal controls was 433 bp. While the normal control samples have the same sequence as the database, the dyslipidemic patient samples have an APOA-1 gene polymorphism in the promoter region. APOA-1 gene polymorphism results in disturbances in lipid profiles, particularly HDL which is at risk of developing dyslipidemia. The APOA-1 gene has the potential to be developed as a biomarker for diagnosing dyslipidemia involving a larger number of samples.

Keywords: APOA-1gene, Dyslipidemia, Polymorphism.

Corresponding Author:

Aprilia Indra Kartika
Department of Medical Laboratory Technology, Faculty of Nursing and Health Sciences, Universitas Muhammadiyah Semarang, Semarang, Central Java, Indonesia
Email: kartika.biotech@unimus.ac.id

1. INTRODUCTION

Dyslipidemia is a disorder of lipid metabolism characterized by abnormal lipid profiles (triglycerides, LDL (low-density lipoprotein), HDL (high-density lipoprotein), and cholesterol) (Xu, Song, Mao, & Xu, 2022). Dyslipidemia patients possess total cholesterol ≥ 200 mg/dL, LDL ≥ 160mg/dL, HDL cholesterol <40 mg/dL, or triglycerides ≥200 mg/dL (Rojas et al., 2018). One of the potential factors for cardiovascular disease is dyslipidemia. Approximately, 17.9 million people die from cardiovascular disease each year, accounting for 32% of all deaths worldwide (WHO, 2019). The cardiovascular event rate is evaluated to be 15 out of 1,000 people, or around 2,8 million individuals in Indonesia (Kementerian Kesehatan Republik Indonesia, 2018).

Dyslipidemia is affected by genetic, lifestyle, diet, and environmental factors (Kopin & Lowenstein, 2017). An imbalance in the genes involved in lipid metabolism leads to genetic factors. Polymorphisms in genes cause variations in the expression of proteins related to lipid metabolism. Genome-wide association Studies have discovered over a hundred genes that affect lipid levels and have correlated dyslipidemia to a genetic component (Asselbergs et al., 2012). The genes that play a role in influencing HDL lipid levels are the APOA-1, ABCA1, LCAT, SAR1B, and ABCG1 genes. These genes are identified to influence the risk of early atherosclerotic cardiovascular disease (García-Giustiniani & Stein, 2016).

One of the genes that codes for the production of the APOA-1 protein is APOA-1 (Apolipoprotein A-I), promotes cholesterol efflux from tissues and serves as a cofactor for the enzyme lecithin cholesterol acyltransferase (LCAT), which is involved in the reverse transport of cholesterol from tissues to the liver for excretion. One of the main proteins discovered in plasma HDL, APOA-1, is crucial for moving extra cholesterol from the peripheral blood to the liver. Furthermore, APOA-1 functions as an antioxidant and an anti-inflammatory (Georgila, Vyrla, & Drakos, 2019). APOA-1-related studies have illustrated that APOA-1 levels can be employed as a predictor and prognostic tool in ischemic stroke patients (Eldeeb et al., 2020).

The expression of proteins involved in HDL formation is disrupted by the polymorphism in the APOA-1 gene. The amounts of HDLC and APOA-1 proteins in a serum drop as a result of variations in the APOA-1 gene sequence on the gene promoter (Al-bustan, et. al., 2013). Several single-nucleotide polymorphisms (SNPs) have been identified in the APOA-1 gene which is situated on the long arm of chromosome 11. The transition from G to A which is located at -75 bp upstream from the transcription start site of the APOA-1 gene predisposes a person to coronary artery disease (Xu et al., 2017). Individuals with the APOA1-75A allele possess a low risk of suffering from coronary artery disease and T2DM as the serum contains high concentrations of APOA-1 and HDL-C (Hedayatnia et al., 2020; Liao, et. al., 2015; Rashad et al., 2021).

The Indonesian population has a high incidence and mortality rate from cardiovascular disease. Dyslipidemia-related APOA-1 gene polymorphisms can be uncovered to monitor cardiovascular events. Since dyslipidemia can cause other comorbidities involving atherosclerotic cardiovascular disease, stroke, and subcortical infarction if it is not detected early, the APOA-1 gene polymorphism has the potential to be used as an initial screening in patients with dyslipidemia (de Grooth et al., 2004; Liu, et al., 2019; Smach et al., 2012; Wang et al., 2016; Westfall et al., 2012; Xu et al., 2017). This study aims to identify variations in the apoA1 gene sequence in the promoter region, 5'UTR, introns, exon 1, and exon 2.

2. RESEARCH METHOD

The materials required are 5 whole blood samples of dyslipidemia patients, Merck lysis buffer, proteinase K Promega, phenol Smart Lab, Merck 96% ethanol, Merck 70% ethanol, Vivantis TE buffer, fluorvue Promega 500 µL, PCR Kit (Green Taq Promega) , running buffer,

Agarose Gene Direx, NFW Promega, loading dye Promega, isolate DNA from PCR sample, Smobio DNA Marker 100 bp, primer forward 5'- AGG GAC AGA GCT GAT CCT TGA ACT CTT AAG-3' dan primer reverse 5' - TTA GGG GAC ACC TAC CCG TCA GGA AGA GCA - 3'.

This type of study is referred to as exploratory design. Patients at the Semarang City Health Center who were dyslipidemic provided the research sample. For the dyslipidemia group, there were 25 patients whose samples fulfilled the criteria of having triglycerides ≥200 mg/dL, HDL cholesterol <40 mg/dL, LDL cholesterol <160 mg/dL, or cholesterol ≥ 200 mg/dL to be tested for the APOA-1 gene. Five individuals without a history of abnormal lipid profiles served as controls.

Each group (dyslipidemia and control) received 4 mL of venous blood. A nurse at the Puskesmas (Primary Health Unit) utilized the venous blood of patients with dyslipidemia and controls. Through research licensing procedures, specifically ethical clearance and approval of research subjects with informed consent number: 320/KEPK/EC/2021, the retrieval process was performed.

Peripheral blood is drawn from 25 dyslipidemic patients and 5 controls, and 3 mL of each is put into a 15 mL conical tube to begin the DNA isolation process. Proteinase K was added in an amount of 20µL and buffer lysis in a ratio of 1:1. For sixty minutes, the solution was vigorously shaken. After adding phenol up to a 1:1 ratio, homogenize for ten to fifteen minutes. The samples were centrifuged for 20 minutes at 3000 rpm. Using a micropipette, the supernatant was extracted and then placed into a microtube. The supernatant was gradually stirred with a 1:1 addition of cold 96% ethanol. After being removed, the DNA threads were placed in a different microtube. Three 500µL 70% ethanol washes were performed on the DNA threads. Washing was performed by centrifugation for 10 min at 14000 rpm. The supernatant was discarded the pellet was air-dried. The pellet was added with 50µL of TE buffer.

DNA purity was evaluated using the MaestroGen MN-913A Nanodrop Spectrophotometer with a wavelength of 260nm to assess DNA double bands and a wavelength of 280nm to measure protein or phenol contaminants. 2µL of DNA sample was inserted into the sample well on the tool.

DNA amplification using PCR must be use sterile materials. The PCR components to be reacted were Master Mix Green Taq Promega 12.5µL, template DNA adjusted for DNA concentration (total concentration 120ng), primer APOA-1 forward 5'- AGG GAC AGA GCT GAT CCT TGA ACT CTT AAG-3' 2µL , primer APOA-1 reverse 5'-TTA GGG GAC ACC TAC CCG TCA GGA AGA GCA-3' (Al-bustan et al., 2013) in the amount of 2µL and Nuclease Free Water to adjust the volume of the DNA template. The APOA-1 gene primer owns a product length of 433bp.

The next step was DNA amplification utilizing the PCR BIO-RAD T100™ Thermal Cycler. The PCR cycle was generated for 35 cycles, then the hot start temperature was set at 95°C for 4 min, denaturation at 95°C for 30 sec, annealing at 60°C for 30 sec, extension at 72°C for 4 min and extension finally at 72°C for 10 min, and cooling down at 12°C for ∞.

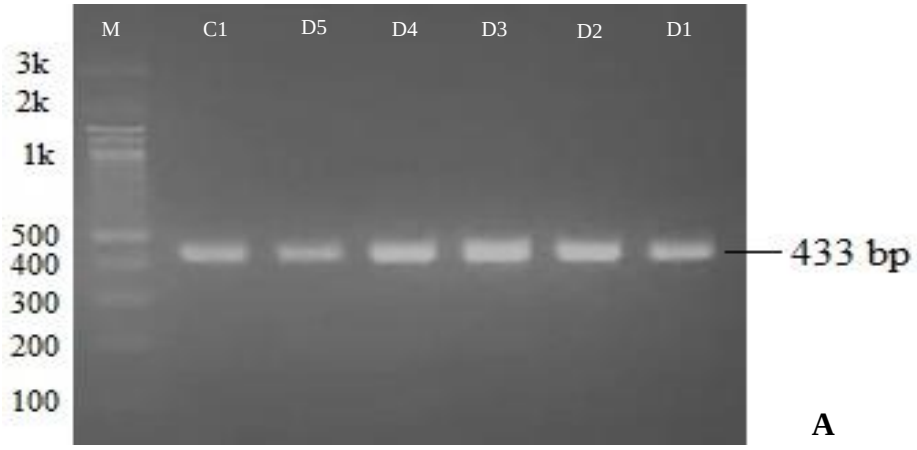
Using DNA gel electrophoresis, the outcomes of DNA amplification of patient samples with dyslipidemia were observed. Utilizing a set of Mupid electrophoresis instruments for DNA electrophoresis. Weighing 2.5 grams of agarose is the first step in making agarose gel. Erlenmeyer was filled with a solution of agarose powder and 100 milliliters of 1x TAE buffer. The temperature and duration were adjusted before the Erlenmeyer containing the solution was placed inside the microwave. After adding up to 4µL of Flurovue via pipette to the agarose solution, homogenize the mixture. A comb is installed after the solution is poured into a gel mold. The gel is moved to the electrophoresis chamber once it has solidified, and 1x TBE buffer is added until the gel sinks. Pipette 2µL of loading dye and add 10µL of PCR product. The

mixture was put into the electrophoretic gel wells. Samples were run at 50 volts for 60 min. The sample was read in the MUV21-312 UV transilluminator and then the DNA bands formed were detected.

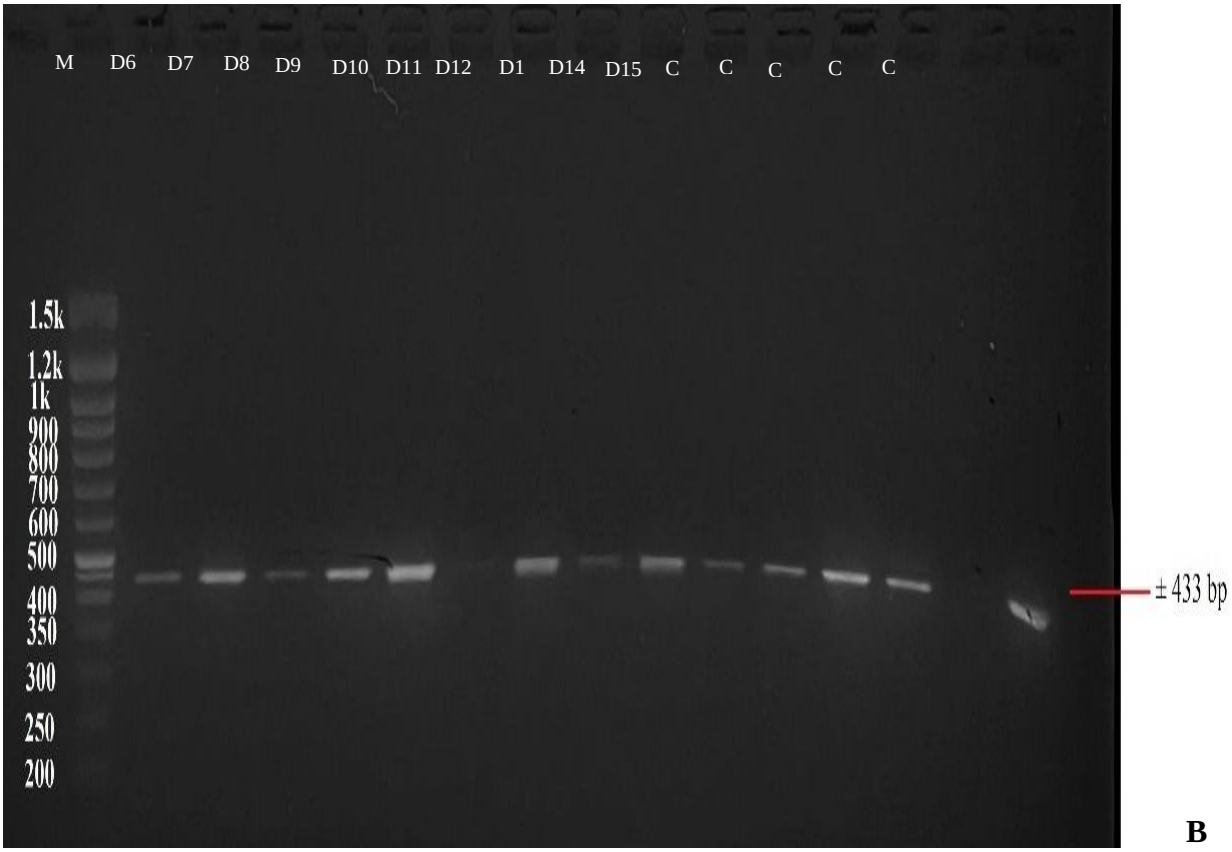
PT. Indonesian Science Genetics will be sequencing the amplified sample. The DNA baser application was used to sequence the DNA and produce a consensus fasta file or contig analysis. The BLAST NCBI application was subsequently utilized to align the results, and changes in the nucleotide base sequence and amino acid composition of the sample were examined. Using the BLAST (Basic Local Alignment Search Tool) online bioinformatics tool, the analysis results validated their presence and degree of similarity with the gene database.

3. RESULTS AND DISCUSSION

ApoA1 gene amplification in dyslipidemic patients and controls.



A



B

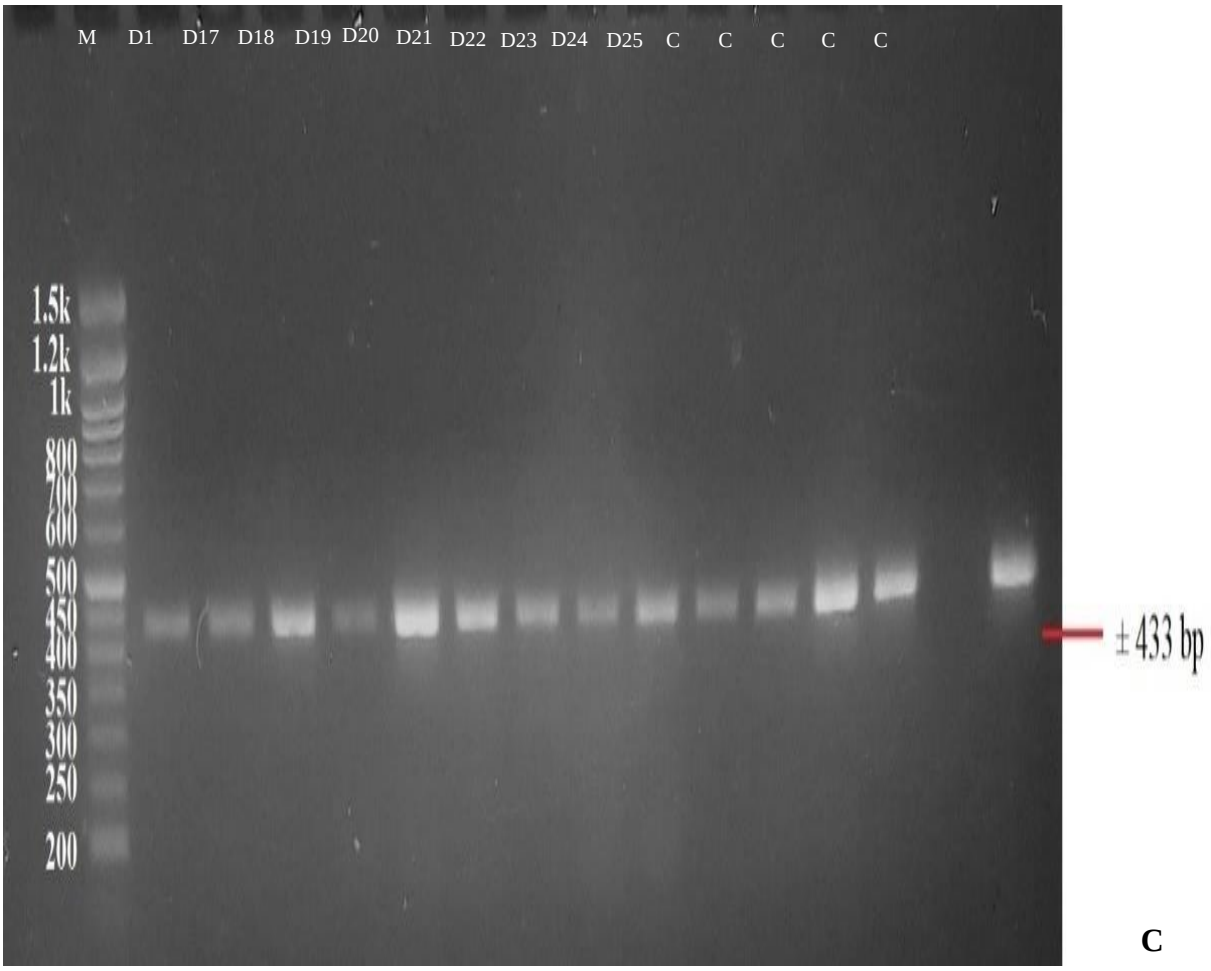


Figure 1. Products of APOA-1 gene amplification in dyslipidemic patients and controls. A single DNA band was formed which displayed a size of about 433 bp, this indicated a specific apoA1 gene amplification product. Figures A, B, C show M (Ladder Smobio DNA Marker 100 bp), C (Control), D1-25 (Dyslipidemia)

The APOA-1 gene amplification results revealed a single, parallel band with a marker measuring 433 bp between the dyslipidemic samples (D1 to D25) and control samples (C1 to C6) (Figure 1). APOA-1 gene amplification with a 435 bp product length in the promoter region, 5'UTR, introns, exon 1, and exon 2 (Al-bustan et al., 2013). The APOA-1 promoter region is located at nucleotides 1-142. APOA-1 is part of the APOA1/CIII/IV/V cluster gene located on chromosome 11q23-24 functioning to encode a protein component of HDL which is responsible for regulating the amount of serum lipids.

B. Sequencing of the APOA-1 gene in the dyslipidemia and control groups

The APOA-1 gene amplification results can be sequenced to perform a polymorphism analysis. Using BLAST NCBI, the acquired APOA-1 sequences were examined for similarities with the APOA-1 gene in the database. The homo sapiens apolipoprotein A1 gene, promoter region, exons 1, 2, and partial CDS accession number JX438706.1 are similar to the sequence data for samples D1–D5 and C1 (Figure 2).

Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
Homo sapiens apolipoprotein A1 gene, promote...	Homo s...	773	773	99%	0.0	98.85%	435	JX438706.1
Homo sapiens apolipoprotein A1 (APOA1), Ref...	Homo s...	773	773	99%	0.0	98.85%	8870	NG_012021.1
Homo sapiens apolipoprotein A-I precursor (AP...	Homo s...	773	773	99%	0.0	98.85%	7870	EF444948.1
Homo sapiens genomic sequence	Homo s...	773	773	99%	0.0	98.85%	7635	EF444947.1
Homo sapiens apolipoprotein A-V (APOA5), apo...	Homo s...	773	773	99%	0.0	98.85%	49331	AY555191.1

Source: https://blast.ncbi.nlm.nih.gov/Blast.cgi

Figure 2. BLAST results of APOA-1 samples.

The process of ascertaining a gene's specific nucleotide base order is referred to as DNA sequencing. The degree of similarity between the DNA sequencing results and the genes in the GenBank BLAST NCBI database was initially determined. The E-Value, or expected value, which demonstrates how many sequences are anticipated to be found in the database using Bit Score, indicates the degree of similarity. It is simpler to determine the degree of similarity when the e-value is lower because it indicates a higher likelihood of similarity with the previously identified gene(Stover & Cavalcanti, 2017). The degree of similarity between the sample sequences and the previous gene sequences can be perceived from the e-value (figure 2). E value which demonstrates a low value (0.0) so that the sample can be identified to be similar to the NCBI database gene sequence (figure 2).

Alignment analysis of the APOA-1 gene with the database available at NCBI. Sequences of samples D1-D5 and C1 were aligned with the database available at NCBI to see differences in nucleotides that lead to polymorphism.

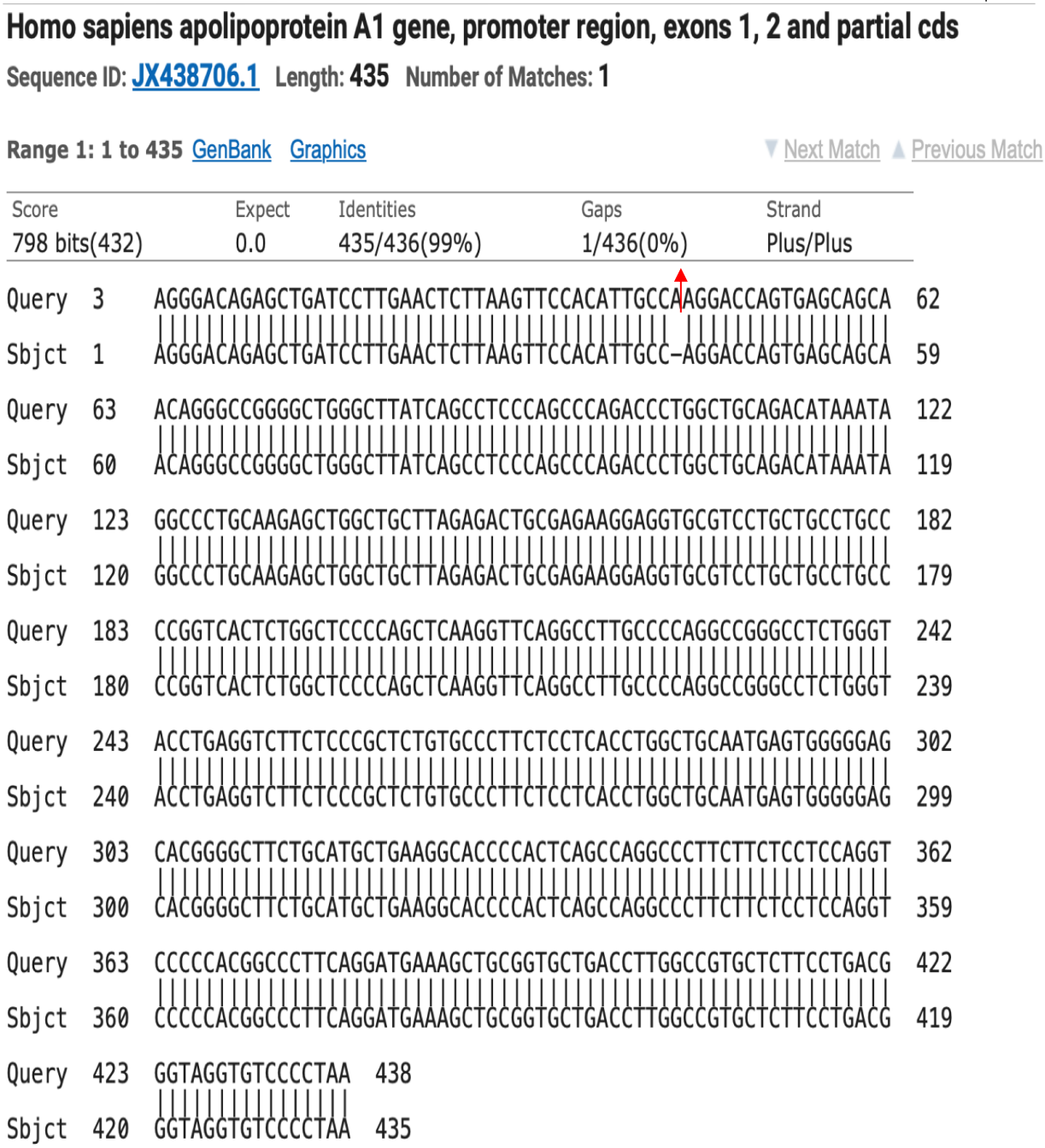


Figure 3. Alignment Results of the NCBI BLAST Program Sample D1.

The D1 sample's alignment results correspond to the APOA-1 gene JX438706.1, which has a 435 bp total molecular length and a 433 bp specific target sample. Nucleotide bases in Sample D1 differed from those in the database. The APOA-1 gene database indicates adenine in Sample D1, which has a deletion at nucleotide 42 (Figure 3). The promoter region of sample D1 contains the sequence variation. Nucleotides 1-142 in the targeted sequence contain the APOA-1 promoter region.

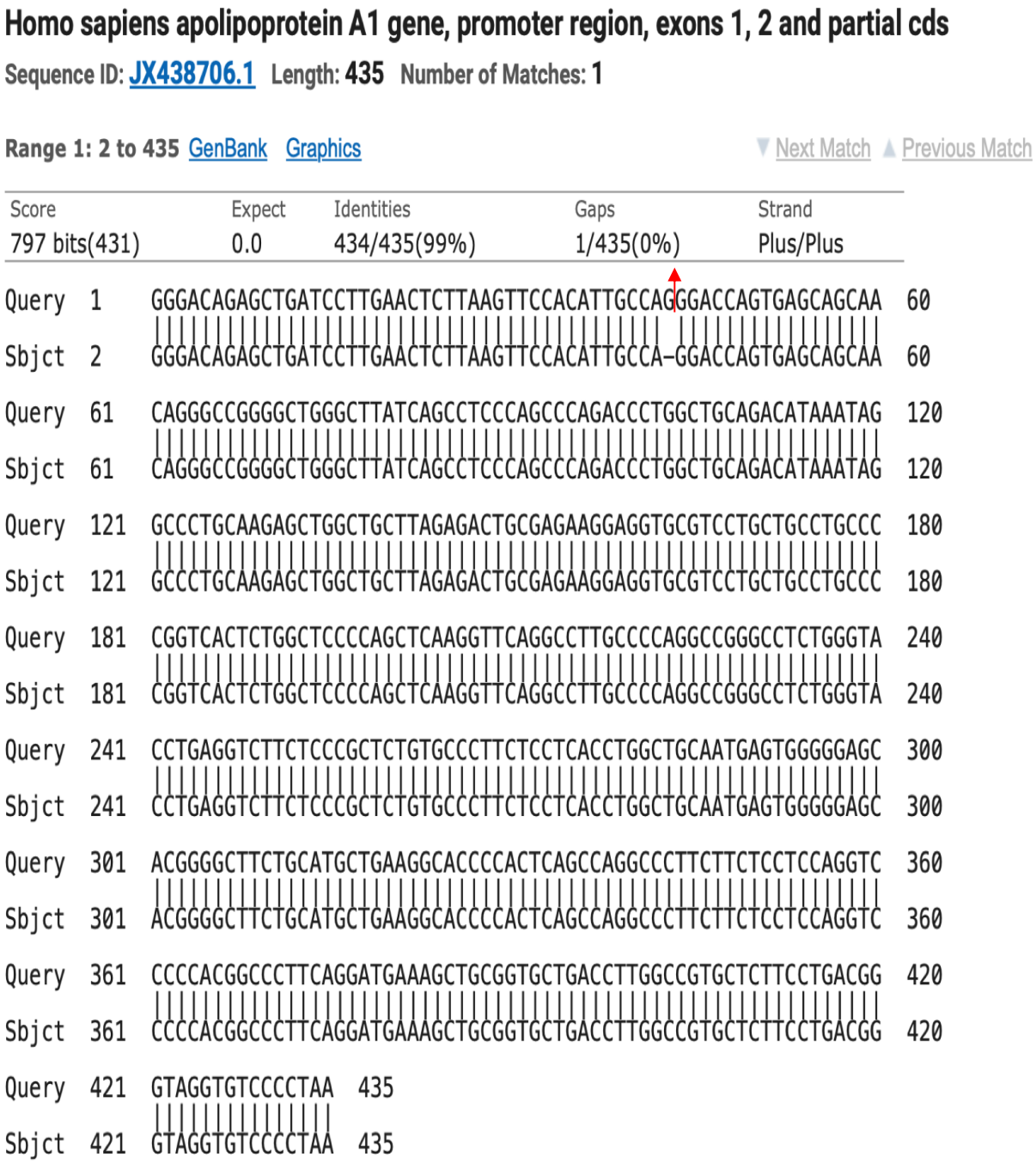


Figure 4. Alignment Results of the NCBI BLAST Program Sample D2.

The APOA-1 gene JX438706.1, which has a total molecular length of 435 bp and a specific target sample of 433 bp, is aligned with the alignment results of the D2 sample. Nucleotide bases in Sample D2 differed from those in the database. In the APOA-1 gene database, adenine is the 43rd nucleotide; sample D2 contains a deletion (Figure 4). Sample D2's sequence variation is located in the promoter region.

Homo sapiens apolipoprotein A1 gene, promoter region, exons 1, 2 and partial cds

Sequence ID: JX438706.1 Length: 435 Number of Matches: 1

Range 1: 2 to 435 GenBank Graphics ▼ Next Match ▲ Previous Match

Score	Expect	Identities	Gaps	Strand
793 bits(429)	0.0	434/436(99%)	2/436(0%)	Plus/Plus

```
Query  1    GGGACAGAGCTGATCCTTGAACTCTTAAGTTCCACATTGCCAGGACCAGTGGAGCAGCAA  60
            ||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||
Sbjct  2    GGGACAGAGCTGATCCTTGAACTCTTAAGTTCCACATTGCCAGGACCAGT-GAGCAGCAA  60

Query  61   CAGGGCCGGGGCTGGGCTTATCAGCCTCCCAGCCCAGACCCTGGGCTGCAGACATAAATA  120
            |||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||
Sbjct  61   CAGGGCCGGGGCTGGGCTTATCAGCCTCCCAGCCCAGACCCT-GGCTGCAGACATAAATA  119

Query  121  GGCCCTGCAAGAGCTGGCTGCTTAGAGACTGCGAGAAGGAGGTGCGTCCTGCTGCCTGCC  180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  120  GGCCCTGCAAGAGCTGGCTGCTTAGAGACTGCGAGAAGGAGGTGCGTCCTGCTGCCTGCC  179

Query  181  CCGGTCACTCTGGCTCCCCAGCTCAAGGTTCAGGCCTTGCCCCAGGCCGGGCCTCTGGGT  240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  180  CCGGTCACTCTGGCTCCCCAGCTCAAGGTTCAGGCCTTGCCCCAGGCCGGGCCTCTGGGT  239

Query  241  ACCTGAGGTCTTCTCCCGCTCTGTGCCCTTCTCCTCACCTGGCTGCAATGAGTGGGGGAG  300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  240  ACCTGAGGTCTTCTCCCGCTCTGTGCCCTTCTCCTCACCTGGCTGCAATGAGTGGGGGAG  299

Query  301  CACGGGGCTTCTGCATGCTGAAGGCACCCCACTCAGCCAGGCCCTTCTTCTCCTCCAGGT  360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  300  CACGGGGCTTCTGCATGCTGAAGGCACCCCACTCAGCCAGGCCCTTCTTCTCCTCCAGGT  359

Query  361  CCCCCACGGCCCTTCAGGATGAAAGCTGCGGTGCTGACCTTGGCCGTGCTCTTCCTGACG  420
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  360  CCCCCACGGCCCTTCAGGATGAAAGCTGCGGTGCTGACCTTGGCCGTGCTCTTCCTGACG  419

Query  421  GGTAGGTGTCCCCTAA  436
            ||||||||||||||||
Sbjct  420  GGTAGGTGTCCCCTAA  435
```

Figure 5. Alignment Results of the NCBI BLAST Program Sample D3.

The APOA-1 gene JX438706.1, which has a total molecular length of 435 bp and a specific target sample of 433 bp, is aligned with the alignment results of the D3 sample. Nucleotide bases in Sample D3 differed from those in the database. Nucleotides 51 and 103nt in the APOA-1 gene database are guanine, but sample D3 has a deletion (Figure 5). The promoter region of the D3 sample contains the sequence variation.

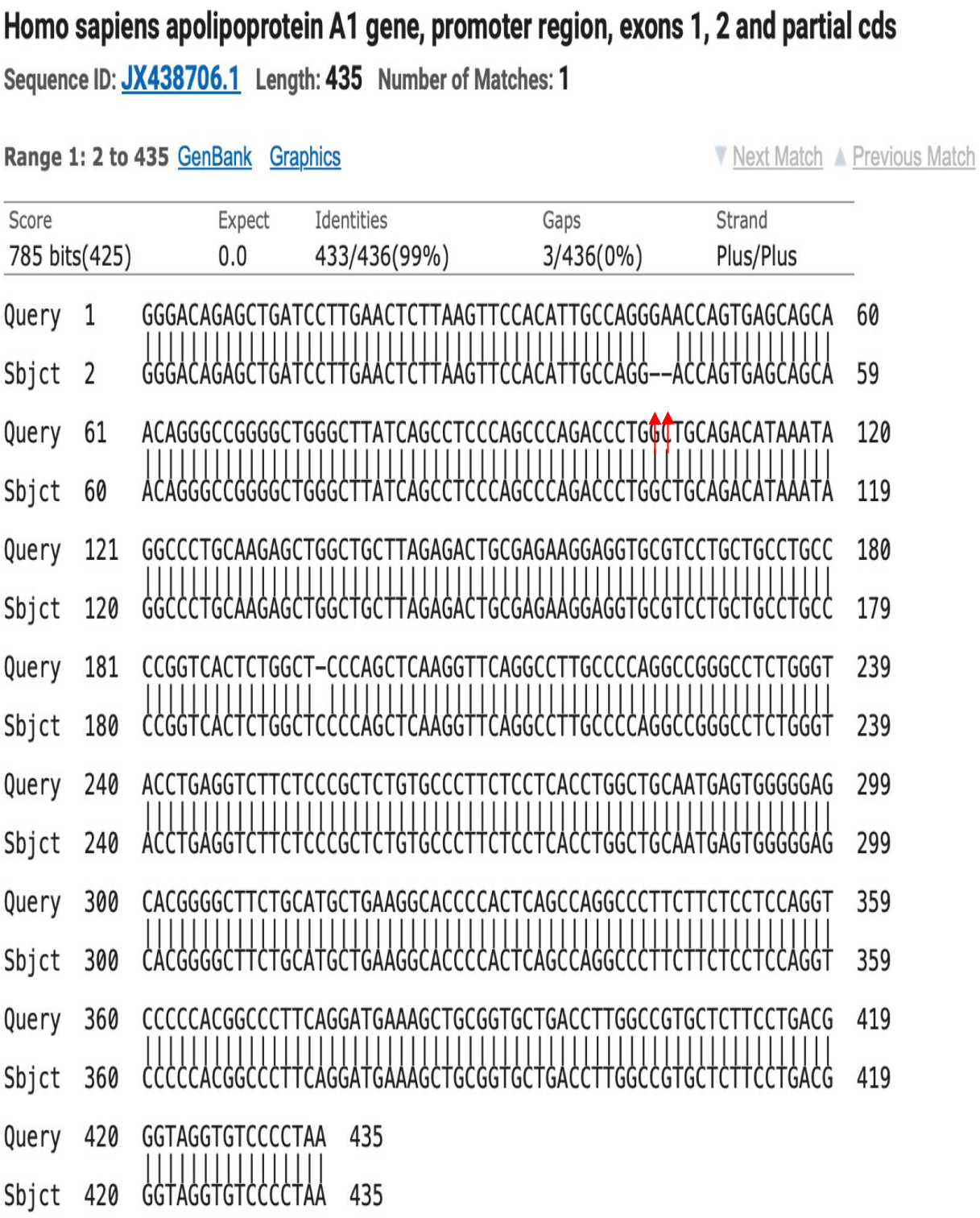


Figure 6. Alignment Results of the NCBI BLAST Program Sample D5

The APOA-1 gene JX438706.1, which has a total molecular length of 435 bp and a specific target sample of 433 bp, is aligned with the alignment results of the D5 sample. Positions 55 and 56nt of the apoA1 gene contain the nucleotides guanine and adenine in the database, but sample D5 has a deletion (Figure 6). The nucleotide bases of the APOA-1 gene varied between Sample D5 and the database.

Homo sapiens apolipoprotein A1 gene, promoter region, exons 1, 2 and partial cds

Sequence ID: JX438706.1 Length: 435 Number of Matches: 1

Range 1: 1 to 435 GenBank Graphics ▼ Next Match ▲ Previous Match

Score	Expect	Identities	Gaps	Strand
804 bits(435)	0.0	435/435(100%)	0/435(0%)	Plus/Plus

```
Query  3    AGGGACAGAGCTGATCCTTGAACTCTTAAGTTCCACATTGCCAGGACCAGTGAGCAGCAA  62
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  1    AGGGACAGAGCTGATCCTTGAACTCTTAAGTTCCACATTGCCAGGACCAGTGAGCAGCAA  60

Query  63   CAGGGCCGGGGCTGGGCTTATCAGCCTCCCAGCCCAGACCCTGGCTGCAGACATAAATAG  122
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  61   CAGGGCCGGGGCTGGGCTTATCAGCCTCCCAGCCCAGACCCTGGCTGCAGACATAAATAG  120

Query  123  GCCCTGCAAGAGCTGGCTGCTTAGAGACTGCGAGAAGGAGGTGCGTCCTGCTGCCTGCCC  182
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  121  GCCCTGCAAGAGCTGGCTGCTTAGAGACTGCGAGAAGGAGGTGCGTCCTGCTGCCTGCCC  180

Query  183  CGGTCACTCTGGCTCCCCAGCTCAAGGTTCAGGCCTTGCCCCAGGCCGGGCCTCTGGGTA  242
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  181  CGGTCACTCTGGCTCCCCAGCTCAAGGTTCAGGCCTTGCCCCAGGCCGGGCCTCTGGGTA  240

Query  243  CCTGAGGTCTTCTCCCGCTCTGTGCCCTTCTCCTCACCTGGCTGCAATGAGTGGGGGAGC  302
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  241  CCTGAGGTCTTCTCCCGCTCTGTGCCCTTCTCCTCACCTGGCTGCAATGAGTGGGGGAGC  300

Query  303  ACGGGGCTTCTGCATGCTGAAGGCACCCCACTCAGCCAGGCCCTTCTTCTCCTCCAGGTC  362
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  301  ACGGGGCTTCTGCATGCTGAAGGCACCCCACTCAGCCAGGCCCTTCTTCTCCTCCAGGTC  360

Query  363  CCCCACGGCCCTTCAGGATGAAAGCTGCGGTGCTGACCTTGGCCGTGCTCTTCCTGACGG  422
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct  361  CCCCACGGCCCTTCAGGATGAAAGCTGCGGTGCTGACCTTGGCCGTGCTCTTCCTGACGG  420

Query  423  GTAGGTGTCCCCTAA  437
            |||||||||||||||
Sbjct  421  GTAGGTGTCCCCTAA  435
```

Figure 7. NCBI BLAST Program Alignment Results Sample DA6 (normal).

The alignment results of sample C are aligned with the APOA-1 gene JX438706.1 which posses a total molecular length of 435 bp with a specific target sample of 433 bp. Sample C and did not experience changes in nucleotide bases compared to the APOA-1 gene database contained in NCBI (Figure 7).

The bands of DNA that are visible on the band vary in thickness (figure 1). This results from varying sample DNA concentrations during the PCR mixing procedure. Adding the DNA template concentration, which needs to be the same for every PCR reaction, is a crucial first step in optimizing the PCR reaction. While excessive DNA concentrations can result in DNA

bands that smear and non-specific amplification results, low template DNA concentrations can cause DNA bands to become faint, not clearly visible, and even amplification may not occur (Asif et al., 2021). The thickness of DNA bands in this study cannot be utilized as a reference for individuals with dyslipidemia or not because the control sample has the same band thickness as the sample. Thus, to determine more specifically the differences in APOA-1 gene polymorphism in the sample, a further process was performed, which is DNA sequencing.

After analyzing the level of similarity, the analysis process is continued by perceiving the DNA sequence alignment utilizing the BLAST program (Figure 3 to figure 7). It is presented that the APOA-1 gene with accession number JX438706.1 had specifically targeted dyslipidemia and control samples at 433 bp in length. Al bustan's research targeting the APOA-1 gene illustrated a PCR product with a length of 435 bp. A 433 bp molecule was discovered in a Chinese study that employed PCR to examine the connection between the G75A polymorphism of the APOA-1 gene and lipid regulation in hyperlipidemic patients implementing pravastatin. The study's findings suggest that in hyperlipidemic patients, the presence of different APOA-1 SNP G75A genotypes may have an impact on how well pravastatin and policosanol regulate lipid levels (Liu et al., 2016).

Variations in the APOA-1 gene sequence in samples D1 to D5 are located in the promoter area. Variations of Rs670 has been reported to enhance promoter function with minor A alleles associated with abnormal variations in serum lipid levels in some populations (Al-bustan et al., 2013). Variations in the upstream region on the transcriptional side have also been reported to be essential for regulating APOA-1 expression. Variations in the promoter region result in reduced APOA-1 expression in serum proteins. The promoter region that undergoes polymorphism is in accordance with low HDL-C concentrations (Al-bustan et al., 2013). Sequence integrity of the upstream region on the transcription site is also identified to influence APOA-1 expression. Various mutations in the promoter region result in decreased expression of the APOA-1 gene and the amount of APOA-1 protein in serum (Pagani et al., 1990; Smith, Brinton, & Breslow, 1992) demonstrated a heterozygosity component in mutations in the promoter region (-27 and -5) affecting the reduction of the amount of APOA-1 expression, hence, it would reduce the APOA-1 protein and HDLC in serum. Sequence variations and allelic frequencies in the APOA-1 promoter region can influence variations in APOA-1 expression (França, Alves, & Hutz, 2005; Haase, et al., 2010; Wang, et al., 2017) which will affect the amount of lipids in serum

The change in amino acid sequence from guanine to adenine at base pairs at the onset of transcription (-75G/A) indicates that variations in the APOA-1 gene polymorphism occur and play a role in the occurrence of lipid regulation (Liao et al., 2015). Point mutations are alterations in one or more nucleotide base pairs. Proteins may change slightly as a result of certain mutations. If the new amino acid is similar to the one being replaced in terms of properties or if it is still present in a protein region where the amino acid sequence serves no functional objective, then the amino acid change may not be significant (Urry et al., 2021).The APOA-1 gene polymorphism is believed to have an essential role in a number of other diseases such as Alzheimer's diabetes, breast cancer, and schizophrenia and others (Jian et al., 2013; Pandith et al., 2021; Smach et al., 2012).

Dyslipidemia is a disorder of lipid metabolism characterized by increased LDL, cholesterol, and triglycerides, and decreased HDL (Rojas et al., 2018). relationship between dyslipidemia in the family and CVD risk. Both genetics and epigenetics have an impact on CVD. The identification of novel molecules, gene mutations, and polymorphisms in the synthesis, transport, and metabolism of lipoproteins provides therapeutic targets and enables treatment. Genetic abnormalities have been associated with a higher risk of CVD and low HDL-c. Low HDL-c and early CVD have been associated with APOA-1-4 deletions,

inversions, and substitutions. Reduced HDLC and familial hypoalphalipoproteinemia are caused by polygenic defects in a variety of genetic variants, including deletions, inversions, and substitutions in the apolipoprotein gene associated with CAD, accounting for roughly 50% of HDLC alterations (Gene et al., 2016).

It has been possible to identify polymorphisms in the APOA-1 gene that influence the risk of developing DM through prior research. Due to their high serum HDL-C counts, people with APOA1 -75 G/A genotypes AA and allele A have a low risk of T2DM and CAD (Rashad et al., 2021). Mutations at the locus (G-75A) were also consistent in previous studies involved in dyslipidemia, but (C83T), resulted in differences in the hyperlipidemic group. In the hyperlipidemic group, genotype allele frequencies, APOA1 concentrations were significantly different (Pakdel, et al., 2018).

There are several mutations in specific sequences of the APOA-1 gene. One is that in Chinese women, the rs662799 polymorphism is significantly correlated with dyslipidemia and coronary heart disease; however, larger sample sizes and multi-ethnic validation are required for these findings to be validated (APOA5) (Wang et al., 2016). Furthermore, the APOA-1 gene mutations rs670, rs5069, and rs2070665 affect the incidence of dyslipidemia in the Kazakh population. The frequency of the CC genotype at rs1321085 was discovered in 7.2% of the obese group, 4.4% of the overweight group, 5.6% in the control group. The APOA-1 rs5070 A/G genetic polymorphism plays an essential role in the susceptibility of large arterial sclerosis in diabetic patients (Hsu & Lee, 2017).

APOA-1 rs5072 variant is associated with dysregulation of triglyceride metabolism in schizophrenic patients treated with APD Antipsychotic Drug-Induced Dyslipidemia allowing for a higher risk of dyslipidemia (Fan, et al., 2021). Mutations of APOA-1 and ApoB are presented to predict the development of cardiovascular disease and patients with schizophrenia have lower expression of APOA-1 than healthy subjects (refs 39, 40)

Analysis of the relationship between APOA-1 polymorphism and high-density lipoprotein (HDL) cholesterol level and myocardial infarction in Japan (Shioji et al., 2004). The findings revealed that the three APOE genotype polymorphisms, ABCA1 G (-273)C, APOA-1 T84C, and APOA-1 independently correlate with HDL-C levels. Hepatic lipase, phospholipid transfer protein, and cholesterol ester transferase protein are some of the substances that have been utilized to control HDL-C levels. The APOA1 T84C polymorphism is a risk factor for myocardial infarction in Japan and has a significant impact on HDL-C levels in the general Japanese population.

While normal controls did not experience any variation in the APOA-1 sequence, four dyslipidemic patients who had the APOA-1 gene amplified had a sequence with a single nucleotide variation in the promoter area. The polymorphism is located in the APOA-1 gene's promoter region, with base positions ranging from base 41 to base 55.

4. CONCLUSION

Approximately, 433 bp of APOA1 gene amplification products were produced by all dyslipidemia samples and the normal control sample. In the promoter region of the APOA1 gene, single nucleotide sequence variations were detected in the four dyslipidemia samples that underwent successful sequencing; no such variations were detected in the normal control samples.

REFERENCES

Al-bustan, S. A., Al-serri, A. E., Annice, B. G., Alnaqeeb, M. A., & Ebrahim, G. A. (2013). Re-sequencing of the APOAI promoter region and the genetic association of the -75G > A polymorphism with increased cholesterol and low density lipoprotein levels among a

sample of the Kuwaiti population. *BMC Medical Genetics*, *14*(1), 1. https://doi.org/10.1186/1471-2350-14-90

Asif, S., Khan, M., Waqar Arshad, M., & Shabbir, M. I. (2021). PCR Optimization for Beginners: A Step by Step Guide. *Research in Molecular Medicine*, *9*(2), 81–102. https://doi.org/10.32598/rmm.9.2.1189.1

Asselbergs, F. W., Guo, Y., Van Iperen, E. P. A., Sivapalaratnam, S., Tragante, V., Lanktree, M. B., … Drenos, F. (2012). Large-Scale Gene-Centric Meta-analysis Across 32 Studies Identifies Multiple Lipid Loci. *American Journal of Human Genetics*, *91*(5), 823–838. https://doi.org/10.1016/j.ajhg.2012.08.032

de Grooth, G. J., Klerkx, A. H. E. ., Stroes, E. S. G., Stalenhoef, A. F. H., Kastelein, J. J. P., & Kuivenhoven, J. A. (2004). A review of CETP and its relation to atherosclerosis. *Journal Lipid Research*, *45*(11), 1967–1974. https://doi.org/10.1194/jlr.R400007-JLR200

Eldeeb, M. A., Zaki, A. S., Ashour, S., Abdel Nasser, A., El Bassiouny, A., & Abdulghani, K. O. (2020). Serum Apolipoprotein A1: a Predictor and Prognostic Biomarker in Acute Ischemic Stroke. *Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, *56*(3). https://doi.org/10.1186/s41983-019-0138-z

Fan, L., You, Y., Fan, Y., Shen, C., & Xue, Y. (2021). Association Between ApoA1 Gene Polymorphisms and Antipsychotic Drug-Induced Dyslipidemia in Schizophrenia. *Neuropsychiatric Disease and Treatment*, *17*, 1289–1297. https://doi.org/10.2147/NDT.S305200

França, E. De, Alves, J. G. ., & Hutz, M. . (2005). APOA1 / C3 / A4 gene cluster variability and lipid levels in Brazilian children. *Brazillian Journal of Medical and Biological Research*, *38*(4), 535–541. https://doi.org/10.1590/S0100-879X2005000400006

García-Giustiniani, D., & Stein, R. (2016). Genetics of dyslipidemia. *Arquivos Brasileiros de Cardiologia*, *106*(5), 434–438. https://doi.org/10.5935/abc.20160074

Gene, M., Bora, K., Saikia, M., Borah, P., Hussain, I., & Das, D. (2016). Single nucleotide polymorphisms of APOA1 gene and their relationship with serum apolipoprotein A-I concentrations in the native population of Assam. *Meta Gene*, *7*, 20–27. https://doi.org/10.1016/j.mgene.2015.10.005

Georgila, K., Vyrla, D., & Drakos, E. (2019). Apolipoprotein A-I (ApoA-I), Immunity, Inflammation and Cancer. *Cancers*, *11*(8), 1–26. https://doi.org/10.3390/cancers11081097

Haase, C. L., Tybjærg-hansen, A., Grande, P., & Frikke-schmidt, R. (2010). Genetically Elevated Apolipoprotein A-I, High-Density Lipoprotein Cholesterol Levels, and Risk of Ischemic Heart Disease. *J Clin Endocrinol Metab*, *95*(12), 500–510. https://doi.org/10.1210/jc.2010-0450

Hedayatnia, M., Asadi, Z., Zare-feyzabadi, R., Yaghooti-khorasani, M., Ghazizadeh, H., Ghaffarian-zirak, R., … Ghayour-mobarhan, M. (2020). Dyslipidemia and cardiovascular disease risk among the MASHAD study population. *Lipids in Health and Disease*, *19*(42), 1–11. https://doi.org/10.1186/s12944-020-01204-y

Hsu, L., & Lee, T. (2017). ScienceDirect Apolipoprotein A1 rs5070 A / G polymorphism with stroke subtypes in Taiwan. *Journal of the Chinese Medical Association*, *80*(6), 360–365. https://doi.org/10.1016/j.jcma.2017.01.002

Jian, Z., Lung, C., Ko, P., Sun, Y., Huang, J., Ho, C., … Liaw, Y. (2013). The association between the apolipoprotein A1 / high density lipoprotein -cholesterol and diabetes in Taiwan — a cross-sectional study. *BMC Endocrine Disorder*, *13*(42), 1–8. https://doi.org/10.1186/1472-6823-13-42

Kementerian Kesehatan Republik Indonesia. (2018). *Hasil Riset Kesehatan Dasar Tahun 2018*. Kementerian Kesehatan Republik Indonesia.

Kopin, L., & Lowenstein, C. (2017). In the Clinic Dyslipidemia. *Annals of Internal Medicine*, *167*(11), ITC81–ITC95. https://doi.org/10.7326/AITC201712050

Liao, B. H., Cheng, K. Q., Dong, S. H., Liu, H. D., & Xu, Z. L. (2015). Effect of apolipoprotein A1 genetic polymorphisms on lipid profiles and the risk of coronary artery disease. *Diagnostic Pathology*, *10*(1), 1–5. https://doi.org/10.1186/s13000-015-0328-7

Liu, S., Liu, J., Weng, R., Gu, X., & Zhong, Z. (2019). Apolipoprotein E gene polymorphism and the risk of cardiovascular disease and type 2 diabetes. *BMC Cardiovascular Disorders*, *19*(213), 1–6. https://doi.org/10.1186/s12872-019-1194-0

Liu, T. N., Wu, C. T., He, F., Yuan, W., Li, S. X., Li, H. W., … Wu, M. (2016). Relationship between the G75A polymorphism in the apolipoprotein A1 (ApoA1) gene and the lipid regulatory effects of pravastatin in patients with hyperlipidemia. *Genetics and Molecular Research*, *15*(2). https://doi.org/10.4238/gmr.15028216

Pagani, F., Sidoli, A., Giudici, G. A., Barenghi, L., Vergani, C., & Baralle, F. E. (1990). Human apolipoprotein A-I gene promoter polymorphism : association with hyperalp ha1 i poproteinemia. *Journal Lipid Research*, *31*(8), 1371–1377. https://doi.org/10.1016/S0022-2275(20)42608-2

Pakdel, A., Reza, M., Eidgahi, A., & Bandegi, A. R. (2018). Association Between MspI Polymorphisms of the Apolipoprotein A-I Gene and Hyperlipidemia in an Iranian Population. *Middle East J Rehabil Helath Stud*, *5*(1), 26–29. https://doi.org/10.5812/mejrh.60496.Research

Pandith, A. A., Bhat, I. A., Niyaz, I., Qasim, I., Bhat, I. A., Manzoor, U., & Koul, A. M. (2021). Association of APOA1-75G/A and+ 83C/T polymorphic variation with acute coronary syndrome patients in Kashmir (India). *Journal of Cardiovascular and Thoracic Research*, *13*(2), 109.–115. https://doi.org/10.34172/jcvtr.2021.09

Rashad, N. M., Ebrahem, G. A., El-shal, A. S., Zenar, M. R. H. A.-, Ahmed, I. G., & Hamed, M. G. (2021). Association of Apolipoprotein A1 Gene Polymorphism and Coronary Heart Diseases in Patients with Type 2 Diabetes Mellitus. *The Eguptian Journal of Hospital Medicine*, *82*(2), 289–295. https://doi.org/10.21608/ejhm.2021.143897

Rojas, M. P., Prieto, C., Bermúdez, V., Garicano, C., Nava, T. N., Martínez, M. S., ... & Rojas, J. (2017). Dyslipidemia: Genetics, lipoprotein lipase and HindIII polymorphism. *F1000Research*, *6*. https://doi.org/10.12688/f1000research.12938.1

Shioji, K., Mannami, Æ. T., Kokubo, Æ. Y., Goto, Y., Nonogi, H., & Iwai, N. (2004). An association analysis between ApoA1 polymorphisms and the high-density lipoprotein (HDL) cholesterol level and myocardial infarction (MI) in Japanese. *J Hum Genet*, *49*, 433–439. https://doi.org/10.1007/s10038-004-0172-1

Smach, M. A., Edziri, H., Charfeddine, B., Othman, L. Ben, Lammouchi, T., Ltaief, A., … Limem, K. (2012). Polymorphism in apoA1 Influences High-Density Lipoprotein Cholesterol Levels but Is Not a Major Risk Factor of Alzheimer ' s Disease. *Dement Geriatr Cogn Disord Extra*, *1*, 249–257. https://doi.org/10.1159/000329910

Smith, J. D., Brinton, E. A., & Breslow, J. L. (1992). Polymorphism in the human apolipoprotein AI gene promoter region. Association of the minor allele with decreased production rate in vivo and promoter activity in vitro. *The Journal of clinical investigation*, *89*(6), 1796-1800. https://doi.org/ 10.1172/JCI115783

Stover, N. A., & Cavalcanti, A. R. O. (2017). Using NCBI BLAST. *Current Protocols in Essential Laboratory Techniques*, *2017*(May), 11.1.1-11.1.34. https://doi.org/10.1002/cpet.8

Urry, L. A., Meyers, N., Cain, M. L., Wasserman, S. A., Minorsky, P. V., Orr, R., ... & Campbell, N. A. (2021). *Campbell biology: Australian and New Zealand version*. Pearson Australia.

Wang, Yanmei, Lu, Z., Zhang, J., Yang, Y., Shen, J., Zhang, X., & Song, Y. (2016). The APOA5 rs662799 polymorphism is associated with dyslipidemia and the severity of coronary heart disease in Chinese women. *Lipids in Health and Disease*, *15*(170), 1–9. https://doi.org/10.1186/s12944-016-0343-z

Wang, Yanzhe, Liu, F., Li, L., Deng, S., & He, Z. (2017). The association between apolipoprotein A1-C3-A5 gene cluster promoter polymorphisms and risk of ischemic stroke in the northern Chinese Han population. *Journal of International Medical Research*, *45*(6), 2042–2052. https://doi.org/10.1177/0300060517713517

Westfall, P. J., Pitera, D. J., Lenihan, J. R., Eng, D., Woolard, F. X., & Regentin, R. (2012). Production of amorphadiene in yeast , and its conversion to dihydroartemisinic acid , precursor to the antimalarial agent artemisinin. *PNAS*, *109*(3), 111–118. https://doi.org/10.1073/pnas.1110740109

WHO. (2019). *WHO Updates Cardiovascular Risk Charts*. WHO

Xu, L., Zhou, Y., Yao, J., Sun, S., Rui, Q., Yang, X., & Li, X. (2017). Apolipoprotein A1 polymorphisms and risk of coronary artery disease : a meta-analysis. *Arch Med Sci*, *4*, 813–819.

Xu, X., Song, Z., Mao, B., & Xu, G. (2022). Review Article Apolipoprotein A1-Related Proteins and Reverse Cholesterol Transport in Antiatherosclerosis Therapy : Recent Progress and Future Perspectives. *Cardiovascular Therapeutics*. https://doi.org/10.1155/2022/4610834

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 626-635
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1153*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Behavior of Providing Additional Recovery Food to Increase Weight of Malnourished Toddlers Aged 24-59 Months at Magetan District Health Center

Agung Suharto[1a*], Berliana Septy Harviandani[1b]

[1] Department of Midwifery, Politeknik Kesehatan Kementerian Kesehatan Surabaya, Surabaya, East Java, Indonesia

[a] Email address: agungsuharto14@gmail.com
[b] Email address: berlianasepty17@gmail.com

Received: 11 April 2023 Revised: 25 June 2023 Accepted: 28 September 2023

Abstract
The percentage of under-five malnutrition problems in Indonesia was 17.8%, with 3.8% and 14% of under-five cases being malnutrition. The Magetan Health Service reports that as of 2021, there were 332 cases of undernourished toddlers; however, the Panekan Health Center reported 116 cases of undernourished toddlers in 2020 based on weight/body length data. The undernourished toddlers was defined as those who were between the ages of 24 and 59 months. This kind of study employs secondary data sources, an analytical approach, a quasi-experimental design, and a non-equivalent control group design. This study included 73 toddlers as subjects: 31 toddlers who did not receive any nutrition, 42 toddlers who did receive nutrition, and malnourished toddlers aged 24-59 months. Data collection uses data collection sheets. The Independent and Paired t-tests are the analysis methods employed. The average difference in body weight between the two groups was found to be 0.594 with a range of 0.0324 kilograms – 1.156 kilograms. The study's results were obtained using the Paired t-test with a p-value = 0.000 with a significance level of 0.05 and the independent t-test with a p-value = 0.038 with a significance level of 0.05. The study concludes that supplementary feeding has an impact on the weight of undernourished toddlers at the Panekan Health Center who are between the ages of 24 and 59 months. It is hoped that by continuing to supplement food, the recovery program may decrease the number of undernourished children under five.

Keywords: Toddlers, Supplementary Food, Weight, Malnutrition.

Corresponding Author:

Agung Suharto
Department of Midwifery, Politeknik Kesehatan Kementerian Kesehatan Surabaya, Surabaya, East Java, Indonesia
Email: agungsuharto14@gmail.com

1. INTRODUCTION

Toddler nutrition is an indicator that demonstrates the level of community welfare because children under the age of five are a group that is vulnerable to health and nutrition (Hadi & Rahayu, 2022). To ensure that children have a healthy nutritional status, nutritional intake is crucial for their growth and development. Malnutrition is one of the main nutritional problems in Indonesia, so the government emphasizes the Healthy Indonesia (Umar et al., 2021). Initiative designed to enhance community health and nutrition, backed by equity in health service delivery and financial protection for the years 2015–2019. The National Medium-Term Development Plan for 2015–2020 includes enhancing mothers' and children's nutritional status as one of its primary goals. One health issue that adds to Indonesia's poor human resource (HR) quality is malnutrition (Kementerian Kesehatan Republik Indonesia, 2022).

Toddlers are a nutritionally vulnerable group; they easily suffer from nutritional disorders due to a lack of the food. The nutritional problems that must be faced in Indonesia at this time are the problem of undernutrition and overnutrition (Nurazizah et al., 2022). Overnutrition problems arise from societal economic progress combined with a lack of knowledge about nutrition and health. Undernutrition problems are caused by poverty, a lack of food supplies, unsanitary environments, and a lack of public awareness about nutrition and health (Kementerian Kesehatan Republik Indonesia, 2018).

According to the Ministry of Health's 2020 Nutritional Status Monitoring, the percentage of toddlers (those under five years old) who had nutritional issues in 2020 was 17.8%, which was unchanged from the previous year (Kementerian Kesehatan Republik Indonesia, 2020). This number incorporates 3.8% Malnourished Toddlers and 14% Undernourished (Kementerian Kesehatan Republik Indonesia, 2018). Whereas in East Java Province in 2017 the incidence of malnutrition was around 9.40%. Based on data from 2017, the Magetan District Health Office reported 332 cases of under-five malnutrition. According to Panekan Health Center weight-for-height (weight/height) data from 2020, there were 116 cases of undernourished toddlers (Dinas Kesehatan Magetan, 2022).

Malnutrition in children can have two main causes: underlying causes, indirect causes, and direct causes. Malnutrition has two primary causes: insufficient dietary intake and infectious diseases. Food that does not contain the necessary nutrients or insufficient amounts of food can lead to a lack of intake of nutrients. While infections impair the ability of various organs to properly absorb nutrients from food (Suharto et al., 2020).

Malnutrition in children under five can affect children's intelligence, decrease children's productivity, and low cognitive abilities. Toddlers are one of the groups that are vulnerable to health problems, the problem of malnutrition. Malnutrition in toddlers that is not immediately addressed will develop into severe malnutrition (Akombi et al., 2017). Low body resistance, which leaves the body vulnerable to infectious diseases, a lack of energy and protein that stunts toddlers' growth and development, an acute lack of energy and protein that can result in marasmus and kwashiorkor, physical and cognitive impairments, reduced IQ, iron deficiency anemia, and disorders resulting from iodine and vitamin A deficiency are consequences of malnutrition. This is due to the extremely rapid growth and development that occurs during the toddler stage (Teja, 2022).

The East Java Health Office initiated efforts in 2020 to enhance feeding practices for nutritional issues. nutrient-dense food assistance, supplemental food assistance for breast milk, patient care for malnourished toddlers, and referral nutrition are provided through the Recovery Supplementary Feeding Program. Furthermore, the East Java Health Office increased cross-sectoral support, convened with the food and nutrition team, and established a malnutrition recovery center and counseling at Posyandu or primary health unit (Dinas Kesehatan Jawa Timur, 2021). Likewise, Magetan Regency also provides Recovery to improve nutrition for

undernourished toddlers. The research aims to identify the effect of providing recovery supplementary food on undernourished toddlers at the Panekan Health Center in 2020.

2. RESEARCH METHOD

This research utilizes experimental research with secondary data sources (Suharto, Nugroho & Santosa, 2022). Following the research objectives, this research is a type of research that examines the effect of providing additional recovery food on the weight of toddlers aged 24-59 months (Heryana, 2019). This study employed a quasi-experimental design with a non-equivalent control group design (Ichsan, 2022).

Table 1. Research design non-equivalent control group.

	Pretest	Intervention	Post test
Experiment Group	O1	X	O2
Control Group	O1		O2

Information:
Experiment Group:
O1 : Pretest, which is weighing undernourished toddlers aged 24-59 months before being given Recovery Supplementary Food.
X : Treatment is provided Recovery Supplementary Food.
O2 : Posttest, which is weighing undernourished toddlers aged 24-59 months after being given Recovery Supplementary Food.

Control Group:
O1 : Pretest, which is weighing the weight of malnourished toddlers aged 24-59 months before.
O2 : Posttest, which is weighing the weight of malnourished toddlers aged 24-59 months after.

This research was conducted at the Panekan Magetan Health Center. When: The research was performed from February to May 2020. Research Population The population in this study was data on malnourished toddlers aged 24-59 as many as 89 toddlers for August 2020. The sample in this study were toddlers aged 24-59 months, totaling 73 toddlers. Sample criteria encompass: 1. Inclusion Criteria: These are the general qualities of research participants established from a reachable target population that will be the subject of the study. The following were the study's inclusion criteria: 1) Malnourished toddlers (ages 24-59 months) for August 2020. 2. Exclusion Criteria: For a variety of reasons, subjects who satisfy the inclusion criteria are eliminated from the study based on the exclusion criteria. Undernourished toddlers younger than 24 months and older than 59 months were the study's exclusion criteria. A total of seventy-three malnourished toddlers were used as study samples. Probability sampling combined with the Simple Random Sampling technique was the sampling method employed in this investigation (Nursalam, 2008; Nursalam, 2020). Sampling in this study was by making lots of 89 lots, and then 16 lots were shuffled to get a sample size of 73 toddlers.

Providing Supplemental Food for Recovery was the study's independent variable. The weight of toddlers between the ages of 24 and 59 months served as the study's dependent variable. Data collection techniques refer to the methods used to approach subjects to gather the necessary subject characteristics for a study (Worotitjan, Mintjelungan & Gunawan, 2013). The data collection technique for this research is secondary data obtained from the medical records of toddlers aged 24-59 months at Panekan Health Center in 2020. The research procedures implemented were: 1. Arrange for permits to Baskebangpol Magetan Regency. 2. Take care of permits in the field by submitting a permit letter and research approval to the

Panekan Health Center. Instruments are the tools employed for data collection (Elisanti & Ardianto, 2020). The instrument in this study was a data collection sheet.

Research Data Processing and Analysis Techniques. After the data is collected, data processing is conducted, (Nursalam, 2020). This study incorporated data on malnourished toddlers aged 24-59 months at the Panekan Health Center and selected which data to employ and not use. In this study, variables that received recovery were coded 2 and those that did not receive. Finding meaning or significance from study results in the form of broad research conclusions is the objective of analysis. To aid in the making of conclusions, the impact of additional recovery feeding on the weight of malnourished toddlers between the ages of 24 and 59 months was analyzed in this study. With the assistance of a computer program, a Paired t-test with a significance of 0.000 ($p < 0.05$) was conducted to examine the impact of Recovery on the weight of malnourished toddlers aged 24-59 months (Suharto, Nugroho & Santosa, 2022). This research has received ethical permission from the Ethics Commission for Health Polytechnic, Ministry of Health Surabaya with a number: No.EA/0350/KEPK-Poltekkes_Sby/V/2020.

3. RESULTS AND DISCUSSION

Description of Research Locations. The Magetan Regency Government maintains the Panekan Health Center, which is situated on Panekan No. 8 in Magetan Regency, East Java Province. BPJS Kesehatan First Level Medical Facilities, encompassing inpatient health centers, are located in Magetan Regency. With a population of 57,338 and an area of 64.2 km², Panekan is composed of 17 villages and sub-districts. It is located 6 km to the northwest of Magetan Regency's capital city, and Ngawi Regency borders the Panekan area on the north. The districts of Magetan and Sidoejo, which are located west of Mount Lawu in the Central Java Province, encircle the southern portion. The districts of Karas, Sukomoro, and Magetan encircle the eastern portion (Dinas Kesehatan Magetan, 2022).

The health program to reduce the number of undernourished children under five at the Panekan Community Health Center is a Recovery Supplementary Food Program in the form of local food and biscuits which are provided to undernourished and severely malnourished children aged 6-59 months (Suriani, et al., 2022).

Table 2. Weight of Malnourished Toddlers Aged 24-59 months before and after in the group that received and those who did not receive recovery food supplementation.

Toddler Group		Weight		N
		Before	After	
Get recovery food supplementation	Mean	10,540	11,098	42
	SD	1,3395	1,4105	42
No get recovery food supplementation	Mean	10,471	10,503	31
	SD	0,9606	0,9968	31
Total				73

It is clear from the table 2 show that there are 73 samples of malnourished toddlers between the ages of 24 and 59. With an SD before 1.3395 and an SD after 1.4105, 42 of the toddlers who were received had average weights before 10.540 and after 11.098. In contrast, 31 toddlers who did not receive recovery food supplementation had average weights before and after 10.471 and 10.503, respectively, with SDs before and after 0.9968.

Table 3. Paired t-test in the group of toddlers who received recovery food supplementation and did not receive recovery food supplementation.

Toddler Group	Weight	Mean	SD	*p-value*
Get recovery food supplementation	before – after	0.5571	0.4789	0.000
No Get recovery food supplementation	before – after	0.0323	0.1423	0.217

Table 3 show that it is identified, data analysis using the Paired t-test statistic in the group of toddlers who received possessed an average weight before and after 0.5571 with an SD of 0.4789 with a significance level of 0.05 obtained a p value 0.000 which means ($p < 0.05$). Therefore, it can be concluded that there is an effect on nutritional toddler weight at the Panekan Public Health Center for toddlers aged 24-59 months. H0 is then rejected and H1 is accepted. It can be stated that there is a significant difference between the weight of toddlers who received the first measurement (before weight) and the second measurement (after weight). On the other hand, the average weight of the toddlers in the non-PMT-P group was 0.0323 before and after, with an SD of 0.1423 at a significance level of 0.05. A p-value of 0.217 was determined, indicating that the data was significant ($p > 0.05$). Then H0 is accepted and H1 is rejected, thus it can be said that there is no significant difference between the weight of toddlers who did not receive in the first measurement (before weight) and the second measurement (after weight).

Table 4. Weight gain in the group of toddlers who received and did not receive Get recovery food supplementation.

	Toddler Group	Sum	Mean	SD
Weight	Get recovery food supplementation	42	11.098	1,4105
	No recovery food supplementation	31	10,503	0,9968

Table 4 illustrates that the sample of toddlers who received recovery food supplementation was 42 children, with an average weight of 11.098 kg. This demonstrates that children who received recovery food supplementation had an average weight that was higher than that of children who did not (11.098 > 10.503). In the meantime, 31 children, weighing an average of 10.503 kg, did not receive recovery food supplements.

Table 5. Independent t-test on toddlers who get recovery food supplementation and do not get recovery food supplementation

	Mean	Range		SD	p-value
		Maximum	Minimum		
Weight	0.5944	0.0324	1.1563	0.2818	0.038

Table 5 show that data analysis using the independent t-test statistical test with a significance level of 0.05 obtained a p-value of 0.038 which means ($p < 0.05$), thus, H0 is rejected and H1 is accepted so that it can be said that there is a difference in weight significant difference between toddlers who did not receive recovery food supplementation and those who received recovery food supplementation. The difference in average weight between the two groups was 0.594 kilograms, with a difference range between 0.0324 – 1.156 kilograms.

The previous body weight in the group of toddlers who received and did not receive recovery food supplementation. The number of undernourished toddlers aged 24-59 months was identified to be 73, with 42 toddlers in the group of toddlers who received recovery food supplementation and 31 in the group that did not. These findings were derived from tests that

were utilized to determine the average weight before and after in the group of toddlers who received recovery food supplementation and those who did not. Toddlers receiving recovery food supplements weigh on average less than 10.540 and have standard deviations of less than 1.3395. Toddlers without recovery food supplementation, on the other hand, had an average weight of 10.471 and a standard deviation before 0.9606. It can be concluded that the average weight before the toddler group who received P was higher, which is 10.540 (Suharto, Wildan & Handayani., 2020).

Weight before and after in the group of toddlers who received and did not receive recovery food supplementation. According to the results of tests implemented to determine the average weight before and after in the groups of toddlers who received and those who did not receive recovery food supplementation, there were 73 undernourished toddlers between the ages of 24 and 59 months. Of these, 42 toddlers received recovery food supplementation, and 31 toddlers did not receive it. The average weight and standard deviation of toddlers who received recovery food supplements were 11.098 and 1.4015, respectively. In contrast, toddlers who did not receive weighted averages after 10.503 and standard deviation after 0.9968. Hence, it can be concluded that the weight after the toddler group who received recovery food supplementation was higher, namely 11.098 (Suharto, & Santosa, 2023). The supplementary feeding program is still not utilized by a large number of families (PMT). Providing additional recovery food (PMT-P), whose nutritional value has been measured so that nutritional needs can be met, is one method to combat malnutrition. There is an effect of supplemental feeding on the growth of children under the red line, indicating that the growth of children under the red line influences the supplementary feeding intervention (Zakaria & Astuti, 2022).

Effect of Providing Recovery Supplementary Food on the weight of malnourished toddlers aged 24-59 months at the Panekan Health Center. Based on the Paired T-Test statistical test results, the toddler group that did not receive it had an average body weight before and after of 0.0323 with an SD of 0.1423 at a significance level of 0.05. A p-value of 0.217 was determined, indicating that the data are significant ($p>0.05$). It can be concluded that there is no significant difference in the weight of toddlers who did not receive the first measurement (before weight) and the second measurement (after weight) since H0 is accepted and H1 is rejected. However, the average weight of the toddlers in the receiving group was 0.5571 before and after, with a standard deviation of 0.4789 at a significance level of 0.05. This resulted in a p-value of 0.000, meaning that the difference was less than 0.05. After that, H0 is rejected and H1 is accepted. It is therefore possible to conclude that there is an effect of recovery food supplementation on nutritional toddler weight for toddlers aged 24-59 months because there is a significant difference between the weight of the toddlers who received the first measurement (before weight) and the second measurement (after weight) (Erlinawati, Apriza & Parmin, 2022).

This is consistent with the research, which indicates that a large amount of balanced nutrition is necessary to produce energy or power. Sources of calories stored from excess carbohydrates or carbohydrates (glycogen and fat) can affect body weight. In his research, toddlers' average weight after receiving food was 8629.41, with a p-value of 0.001, meaning that the weight of undernourished toddlers was affected by additional food ($p <0.05$) (Aty et al., 2021).

According to Edvina's research, malnourished toddlers between the ages of 6 and 48 months who underwent PMT displayed a range in body weight between 7.57 kg and 8.67 kg. Toddlers' nutritional status before receiving extra food was, at most, in the very poor category, according to 33 respondents (94.30%), and after receiving additional food, it was in the less category, in accordance with 22 respondents (62.90%). Body weight before and after PMT was different; the weight after PMT was 6.81% higher than the initial weight. The Wilcoxon test

yielded a significance value of 0.0001 (p <0.05), indicating that supplemental feeding has an impact on the nutritional status of malnourished toddlers between the ages of 6 and 48 months (Tat et al., 2020).

Toddler's weight after giving recovery food supplementation minimum weight is 6.5 kg while the maximum is 16 kg and the average is 8.8796 kg with a p-value of 0.000 while the significance of 0.05 which means there is an effective recovery food supplementation program for weight gain in toddlers in Banyumas Regency (Marlina et al., 2022).

The same is true of studies that discovered toddlers' average body weight was 9.0 kg, with the lowest body weight being 4.1 kg, before receiving recovery food supplements. The average toddler weight increased to 9.9 kg after receiving recovery food supplementation, with the lowest weight being 5.3 kg and the highest weight being 12.1 kg. A significance value of 0.000 with a p-value of less than 0.05 was obtained from the paired t-test results, indicating that recovery food supplementation has an impact on changes in toddler weight (Manurung et al., 2022).

A program of intervention for malnourished toddlers is supplemental feeding. Providing supplementary food to malnourished children in the nutritionally vulnerable group is generally intended to improve their nutritional status. This is performed based on the weight of children under five who have not gained weight in three consecutive months and whose weight on the KMS is below the red line (Mugianti et al., 2022). The objective of supplemental feeding is also to increase vital nutrients and energy. Meanwhile, the aim of feeding additional food to malnourished infants and toddlers is to attain optimal nutritional status by progressively introducing high-energy, high-protein, and adequate vitamin and mineral food in stages (Kementerian Kesehatan Republik Indonesia, 2020).

One way to overcome malnutrition that occurs in the toddler age group is to organize recovery food supplements. Food supplementation recovery for children aged 6-59 months is intended as a supplement, not as a substitute for the main daily food. PMT Recovery is intended to be based on local food ingredients with regional specialties adapted to local conditions. As was performed by the Panekan Health Center, they provide local food ingredients such as rice, eggs, green beans, and fruits (Latuihamallo et al., 2022).

The average weight of undernourished children aged 24-59 months between those who received and those who did not receive recovery food supplementation. Data analysis was performed using the Independent T-Test statistic test with a significance level of 0, 05 obtained a p-value of 0.038 which means (p <0.05) based on research that has been conducted to determine the average weight of undernourished toddlers aged 24-59 months between those who receive and those who do not receive recovery food supplementation. This implies that H0 is rejected and H1 is accepted, indicating that there is a significant weight difference between toddlers who receive recovery food supplementation and those who do not. The two groups' weight differences range from 0.0324 kg to 1.156 kg, with an average difference of 0.594 kg (Mawaddah & Tiyawati, 2021). Exclusive breastfeeding is the behavior of giving breast milk only to babies until the age of six months without other food and/or drinks. The best food for babies is breast milk in sufficient amounts, which can satisfy their nutritional needs for the first six months of life. A significant, long-lasting, and economical intervention to lower toddler morbidity and death is exclusive breastfeeding. However, most babies are not exclusively breastfed as recommended by the World Health Organization (Nazli & Erlinda, 2020).

4. CONCLUSION

The results of the research that has been done, conclusions are obtained about the effect of supplementary recovery feeding on the weight of undernourished toddlers aged 24-59 months at the Panekan Health Center, namely as follows: The average weight of

undernourished toddlers before toddlers who did not receive was 10.471, and for toddlers who received was 10.540. After recovery food supplementation, the average weight of undernourished toddlers is 10.503 for those who do not receive it and 11.098 for those who do. At the Panekan Health Center, the weight of malnourished toddlers between the ages of 24 and 59 months has an impact. The Panekan Health Center is anticipated to benefit from the research's findings. Education: It is hoped that the results of this study will inform obstetrics teaching materials about nutrition for children under five. If undernourished toddlers do not receive proper care, they will grow into malnourished toddlers, which can impede their development and growth as well as cause death. For researchers: For further research, the result of this study can be utilized as reference material. Moreover, it is hoped that further research will be able to monitor PMT-P which has been provided only for consumption by toddlers or their families, as well as processing methods and can identify other factors that can affect malnutrition in toddlers.

REFERENCES

Akombi, B. J., Agho, K. E., Hall, J. J., Merom, D., Astell-Burt, T., & Renzaho, A. M. N. (2017). Stunting and severe stunting among children under-5 years in Nigeria: A multilevel analysis. *BMC Pediatrics*, *17*(1), 1–16. https://doi.org/10.1186/s12887-016-0770-z

Aty, Y. M. V. B., Herwanti, E., & Mochsen, R. (2021). Simultaneous Factors Affecting Toddler Nutritional Status. *Jurnal Info Kesehatan*, *19*(1), 64–76. https://doi.org/10.31965/infokes.vol19.iss1.514

Dinas Kesehatan Jawa Timur. (2021). *Profil Kesehatan Dinas Kesehatan Provinsi Jawa Timur 2021*. *Dinas Kesehatan Provinsi Jawa Timur*.

Dinas Kesehatan Magetan. (2022). *Profil Kesehatan Kabupaten Magetan 2021*. Dinas Kesehatan Magetan.

Elisanti, A. D., & Ardianto, E. T. (2020). Dasar-dasar Metodologi Penelitian Kuantitatif Bidang Kesehatan. Jember: Polije Press

Erlinawati, E., Apriza, A., & Parmin, J. (2022). Toddler Growth in the Working Area of Kuok Public Health Center, Kampar Regency. *Jurnal Info Kesehatan*, *20*(2), 117–126. https://doi.org/10.31965/infokes.vol20.iss2.628

Hadi, S. P. I., & Rahayu, T. B. (2022). Pengembangan Aplikasi Sahabat Bunda | Cegah Stunting Berbasis Android Sebagai Upaya Pencegahan Dini Stunting. *Embrio*, *14*(1), 84–96. https://doi.org/10.36456/embrio.v14i1.4503

Heryana, A. (2019). *Buku Ajar Metodologi Penelitian pada Kesehatan Masyarakat*. Jakarta: e-book tidak di publikasikan.

Ichsan, B. (2022). *Pengantar Metodologi Penelitian Kedokteran dan Kesehatan Masyarakat*. Muhammadiyah University Press.

Kementerian Kesehatan Republik Indonesia. (2020). *Profil Kesehatan Indonesia Tahun 2019*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Kementerian Kesehatan Republik Indonesia. (2022). *Profil Kesehatan Indonesia 2021*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Kementerian Kesehatan Republik Indonesia. (2018). *Hasil Utama RISKESDAS 2018*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Latuihamallo, A., Margawati, A., Mexitalia, M., Ediati, A., & Syauqy, A. (2022). Differences in Development and Diet of Stunting and Non-Stunting Children in the Rowosari Health Center Work Area, Semarang, Indonesia. *Jurnal Gizi Indonesia (The Indonesian Journal of Nutrition)*, *10*(2), 161–167. https://doi.org/10.14710/jgi.10.2.161-167

Manurung, S., Suratun, S., Wartonah, W., Ekarini, N. L. P., & Maryam, R. S. (2022). The Effect of Multimedia-Based Education on Knowledge, Attitudes, and Behavior Hypertension Patients in Stroke Prevention. *Jurnal Info Kesehatan*, *20*(2), 166–175. https://doi.org/10.31965/infokes.vol20.iss2.822

Marlina, H., Triana, A., & Fanora, E. (2022). Causes of Stunting in Toddlers: Literature Review. *International Journal of Multidisciplinary Research and Growth Evaluation*, *February*, 138–142. https://doi.org/10.54660/anfo.2021.3.1.11

Mawaddah, S., & Tiyawati, S. (2021). Passive Smokers Pregnant Women with Low Birth Weight. *Jurnal Info Kesehatan*, *19*(1), 47–54. https://doi.org/10.31965/infokes.vol19.iss1.299

Mugianti, S., Riyadi, B. D., Suyitno, J. H., & Suprajitno, S. (2022). Comparison of Body Mass Index and Behavior of CERDIK of Individuals as Risk Factors of Suffering from Non-Communicable Diseases. *Jurnal Info Kesehatan*, *20*(2), 135–142. https://doi.org/10.31965/infokes.vol20.iss2.805

Nazli, R., & Erlinda, E. (2020). Pemodelan Aplikasi Pendukung Keputusan Makanan Pendamping Air Susu Ibu (Mpasi) Berbasis Android. *Jurnal Teknologi Dan Open Source*, *3*(2), 272–283. https://doi.org/10.36378/jtos.v3i2.900

Nurazizah, Y. I., Nugroho, A., Nugroho, A., Noviani, N. E., & Noviani, N. E. (2022). Hubungan Status Gizi Dengan Kejadian Anemia Pada Remaja Putri. *Journal Health and Nutritions*, *8*(2), 44. https://doi.org/10.52365/jhn.v8i2.545

Nursalam. (2020). *Metodologi Penelitian Ilmu Keperawatan.* Edisi 5. Jakarta: Salemba Medika.

Nursalam. (2008). *Konsep dan Penerapan Metodologi Penelitian Ilmu Keperawatan.* Edisi 2. Jakarta: Salemba Medika

Suharto, A., Nugroho, H. S. W., & Santosa, B. J. (2022). *Metode Penelitian dan Statistika Dasar (Suatu Pendekatan Praktis)*. Bandung: Media Sains Indonesia.

Suharto, A., & Santosa, B. J. (2023). *Buku Monograf Pemberdayaan Masyarakat dalam Mewujudkan Keluarga Sehat Bebas Stunting Berbasis Health Belief Model dan Theory of Planned Behavior*. Bandung: Media Sains Indonesia.

Suharto, A., Wildan, M., & Handayani, T. E. (2020). Development of Stunting Prevention Behavior Model Based on Health Promotion Model and Social Capital in The Magetan District. *Health Notions*, *4*(2), 48–56. https://doi.org/10.33846/hn40204

Suriani, B., Nurfatimah, N., Saadong, D., Subriah, S., & Ramadhan, K. (2022). The Relationship of Mother's Role in Stimulation with Motor Development in Toddler. *Jurnal Info Kesehatan*, *20*(1), 20-28. https://doi.org/10.31965/infokes.vol20.iss1.618

Tat, F., Romana, A. B. Y. ., & Shafie, Z. B. M. (2020). The Sunrise Model Approach to the Nutritional Status of Toddlers at the Kupang District Primary Health Center. *Jurnal Info Kesehatan*, *18*(2), 96–104. https://doi.org/10.31965/infokes.vol18.iss2.321

Teja, M. (2022). *Percepatan Penurunan Prevalensi Stunting 14 %. Info Singkat, 14(3),25-30.*

Umar, F., Nurhaeda, & Juwita. (2021). Analisis Faktor-Faktor Risiko Stunting Anak Balita pada Masa Pandemi Covid-19 di Puskesmas Tawaeli Kota Palu Tahun 2020. *Media Publikasi Promosi Kesehatan Indonesia (MPPKI)*, *4*(3), 413–418. https://doi.org/10.56338/mppki.v4i3.1612

Worotitjan, I., Mintjelungan, C. N., & Gunawan, P. (2013). Pengalaman Karies Gigi Serta Pola Makan Dan Minum Pada Anak Sekolah Dasar Di Desa Kiawa Kecamatan Kawangkoan Utara. *E-GIGI*, *1*(1), 59–68. https://doi.org/10.35790/eg.1.1.2013.1931

Zakaria, R., & Astuti, S. C. D. (2022). The Effect of Black Cumin (Nigella Sativa) on Breastfeeding Mothers. *Jurnal Info Kesehatan*, *20*(1), 29–40. https://doi.org/10.31965/infokes.vol20.iss1.627

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 636-642
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1174*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

The Effect of Smartphone-Based Nursing Therapy to Reducing Post Cardiac Surgery

Sidik Awaludin[1a*], Elly Nurachmah[2b], Dwi Novitasari[3c]

[1] School of Nursing, Faculty of Health Sciences, Jenderal Soedirman University, Purwokerto, Central Java, Indonesia
[2] Faculty of Nursing, University of Indonesia, Depok, West Java, Indonesia
[3] Faculty of Health, Harapan Bangsa University, Purwokerto, Central Java, Indonesia

[a] Email address: abifayza@yahoo.co.id
[b] Email address: ellynur08@yahoo.co.id
[c] Email address: dwinovitasari@uhb.ac.id

Received: 9 May 2023 Revised: 29 September 2023 Accepted: 29 September 2023

Abstract

The disease that is the number one cause of death in the world today is heart disease. Actions to overcome the problem of coronary heart disease, one of them with surgery. Pain is a significant issue at all stages of surgery. Post-cardiac surgery discomfort should be manageable with smartphone-based nursing care. The goal of this study was to determine if smartphone-based nursing care may help heart surgery patients feel less pain. The research design used a quasi-experimental pre- and post-control group design. The sample size in this study was 46 respondents, which were divided into 23 respondents in the intervention group and 23 respondents in the control group. The inclusion criteria of this study were cardiac surgery patients on the first day, adult patients receiving paracetamol drip therapy and 1000 mg tablets, and hemodynamic stability. Nursing interventions to deal with pain in this study were carried out using hypnosis and music videos in smartphone-based applications. Research results showed a post-treatment pain score of 2.04 in the intervention group and 4.60 in the control group. Nursing interventions carried out using videos in smartphone-based applications are able to overcome post-cardiac surgery pain, so pain management using smartphones can be an intervention choice to deal with post-cardiac surgery pain. Hypnosis and music nursing interventions using videos on smartphone-based applications can be used as nursing therapy to treat pain after cardiac surgery.

Keywords: Cardiac Surgery, Pain, Smartphone, Nursing Therapy.

Corresponding Author:

Sidik Awaludin
School of Nursing, Faculty of Health Sciences, Jenderal Soedirman University, Purwokerto, Central Java, Indonesia
Email: agungsuharto14@gmail.com

1. INTRODUCTION

Heart disease remains the world's number-one killer and a major public health concern. The WHO estimates that 17.9 million deaths from cardiovascular disease occurred in 2016, which represents 31% of all deaths worldwide. Heart failure is the leading cause of mortality when compared to other medical diagnoses, and it accounts for the majority of heart disease diagnoses, along with coronary heart disease, hypertensive heart disease, and heart failure (Virani et al., 2021).

One of the management options for coronary heart disease is surgery (Zipes, 2018). Both elective and cito surgery are stressful events that require special nursing care (Chandrababu et al., 2017; Smeltzer et al., 2015). Each stage of cardiac surgery has a major problem, namely pain. The surgical nurse has a role in dealing with every patient's pain complaint so that the patient is free from pain. Various types of nursing therapy can treat pain, such as hypnosis and music.

Hypnosis nursing therapy is a technique or practice of influencing someone who intentionally enters into a sleep-like state. In this condition, the hypnotized person can follow orders and accept suggestions without resistance. Hypnosis is a brief cognitive-behavioral technique without specific side effects. Hypnosis involves being introduced to procedures that the subject is told to experience imaginatively. Hypnotic procedures are used to encourage and evaluate responses to suggestions. In the process of hypnosis, one is guided by a hypnotist to receive suggestions from subjective experience and changes in perception, taste, emotion, thought, and behavior (Awaludin et al., 2022). Hypnosis is used by the surgeon to see himself or herself through each of the different parts of the procedure, from start to finish, very easily and pain-free (Awaludin, Nurachmah, & Novitasari, 2020). Hypnosis affects a person's perception and behavior by means of the suggestibility principles, entering a condition known as transhipnosis. There is a significant degree of suggestibility in trance, an altered state of consciousness that differs from regular sleep, unconsciousness, and coma. In 1996, 20 kids were hypnotized by Andrew and Welbury, and they found that in 16 of them who were both hypnotized and under anesthesia at the same time, their sense of pain decreased (Abdeshahi et al., 2013; Eren et al., 2015). Since a long time ago, hypnosis has been successfully applied during eye surgery in a number of instances. Overall, our findings indicate that even though hypnosis in combination with topical anesthetics could not be completely eradicated, patients in the hypnosis group had much better outcomes. Given the individual variances in hypnotic efficacy and pain sensitivity, pain for all patients may make sense. In general, a lot of patients in the hypnosis group showed less pain, less fear, and more cooperation (Chen et al., 2018).

Music therapy is a therapy that uses music or musical elements by a therapist to improve, maintain, or restore physical, mental, emotional, and spiritual health. Music therapy is a complementary therapy (Comeaux & Steele-Moses, 2013). Music that can be used for the healing process is music that is tailored to your wishes, such as classical music, instrumental music (DevarePhadke & HadiyaParkar, 2014), and slow music (Amiri et al., 2017). Listening to music can affect the physiological functions of a person's body, such as breathing, heart rate, and blood pressure (Awaludin, et al., 2020; Heidari et al., 2015). Music relaxes the body, stabilizes the metabolic rate, and fulfills the body's oxygen needs, which affect vital signs such as heart rate, respiratory rate, and blood pressure that are within acceptable ranges (Berman, Snyder & Frandsen, 2016; Peate & Evans, 2020). The release of noradrenaline and adrenaline can be decreased by being relaxed. Reduced levels of the hormone noradrenaline result in lower blood pressure, whereas reduced levels of the hormone adrenaline have the opposite impact on the cardiovascular system, resulting in a reduction in heart rate (Jiménez-Jiménez et al., 2013). Listening to therapeutic music for 30–35 minutes can reduce anxiety and pain and maintain

hemodynamics within normal limits (Ciğerci & Özbayır, 2016; DevarePhadke & HadiyaParkar, 2014).

Providing nursing therapy can be done through smartphone media. The smartphone app provides useful functions that can be integrated into both conventional and modern maintenance manuals. Smartphone applications can also be programmed to respond to critical items in self-assessments to automatically detect significant problems (Bauer et al., 2020; Kim et al., 2016).

Based on this description, to provide nursing services to patients with cardiac surgery in the form of post-cardiac surgery pain management, it is necessary to conduct research on pain interventions in cardiac surgery patients by utilizing the development of smartphone technology. The purpose of this research is to determine the effect of smartphone-based nursing therapy on the pain of cardiac surgery patients.

2. RESEARCH METHOD

This research is a type of experimental research that used a quasi-experimental pre and post control group design. The sample size 46 participants; 23 of them were in the intervention group, and 23 of them were in the control group. The sampling technique used was consecutive sampling. The inclusion criteria of this study were first-day cardiac surgery patients, adult patients receiving paracetamol drip therapy and 1000 mg tablets, and hemodynamically stable patients. The nursing therapy provided in this study is hypnosis and music in smartphone applications. Instruments for measuring pain using the Visual Analogue Scale (VAS). Statistical analysis used the Mann Whitney test.

3. RESULTS AND DISCUSSION

Table 1. Distribution of respondents by age.

Group	n	Mean	SD
Control	23	60	5,7
Intervention	23	58	6,3

Table 1 shows the average age of respondents in the intervention group was 58 years and the control group was 60 years.

Table 2. Distribution of respondents by gender.

Group	Male		Female	
	n	%	n	%
Control	13	56.5	10	43,4
Intervention	15	65,2	8	34,7

Table 2 shows the majority of the gender of the respondents in this study were male.

Table 3. Results of the Pain Scale Mean Difference Test Respondents Between Post-Treatment Groups.

Variable	Intervention Group (Mean)	Control Group (Mean)	p-value
Pain Scale	2.04	4.60	<0.001*

**= p-value < 0.05*

Table 3 shows that the pain scale data between the treatment and control groups after the smartphone-based nursing intervention showed a significant difference (p-value <0.001 (0.05)

The results of the study based on the characteristics of the respondents, according to Table 1 show that the age range in this study was late adulthood and the elderly. With the increasing age of the elderly, degenerative diseases will arise, increasing the risk factors for coronary heart disease (Noale et al., 2020). A similar issue arises with valvular heart disease as well. According to the findings of research conducted in Brazil, individuals with valvular heart disease were 45.3 years old on average. Rheumatic heart disease (RHD) and degenerative valve disease are the most frequent causes; however, they can happen at any age, depending on the reason (Coffey et al., 2021; Tarasoutchi et al., 2020). Increasing age also increases the risk of calcification of the heart valves, causing heart valve dysfunction (Bhatt et al., 2015).

The majority of respondents in this study were male (table 2). Compared to women, men are more likely to have coronary heart disease; contrast this with coronary heart disease in women (Virani et al., 2021). Men who have unhealthy lifestyles, such as smoking, drinking, and unhealthy diets, are more likely to get heart disease (Khalili et al., 2014; Virani et al., 2021). Additionally, it is believed that hormones have a significant role in the prevalence of coronary heart disease. Estrogen and progesterone, which have an impact on the menstrual cycle and menopause, are the hormones that are involved. In addition, it is believed that the use of hormonal contraception may have an impact on the prevalence of coronary heart disease (Khan et al., 2017).

The results of this study showed that the postoperative pain scale on the first day between the treatment and control groups was in the moderate pain category. On the first day of surgery, the patient received morphine analgesic therapy after regaining consciousness, then was extubated, and the morphine therapy was replaced with paracetamol 1000 mg drip up to H on the second day of operation. When the patient was moved to the usual treatment room, the paracetamol 1000 mg drip therapy was replaced with tablets, and the dose was reduced to 500 mg. The analgesic therapy given is in accordance with the theoretical concept. Analgesic therapy given to cardiac surgery patients is in the form of opioid and non-opioid analgesics. The non-opioid type most often used is paracetamol. Non-steroidal anti-inflammatory drugs (NSAIDs), metamizole N-methyl-D-aspartate (NMDA) antagonists, alpha-2 agonists, local anesthetics, and gabapentinoids (Yu et al., 2019).

The analgesic effect is very good when combined with opioid analgesics. This enables an approximate 40%–50% dosage decrease of the opioid, which can lessen the likelihood of side effects from usage. Opioid analgesics are frequently used to relieve postoperative pain, but they have undesirable side effects such as sleepiness and respiratory depression that can prolong the patient's stay in intensive care and postpone extubation. Due to the possibility of renal damage and bleeding in patients undergoing heart surgery, the use of NSAIDs may be restricted (Bigeleisen & Goehner, 2015; Keawnantawat et al., 2017; Zubrzycki et al., 2018).

In this study, video-based smartphone applications were used to deliver nursing interventions for pain management. The findings of this study are consistent with the idea that smartphones are cellular technologies that offer advantages in the medical field, including standardizing therapy, boosting motivation and adherence to therapeutic programs, providing education, and facilitating quick decisions (Soangra & Lockhart, 2021), and observing the interventions provided. Nursing interventions are given to patients according to predetermined programs; nursing therapy videos can be easily accessed and followed by patients via their smartphones (Xu et al., 2019). The limitation of this study is that it only combines two nursing interventions to relieve pain post cardiac surgery.

4. CONCLUSION

Hypnosis and music nursing therapy using videos in smartphone-based applications can significantly overcome post-cardiac surgery pain. The study's findings are consistent with the

idea that smartphones are cellular technologies with advantages in the medical field, including standardizing therapy, boosting motivation and adherence to treatment plans, offering education, and facilitating early decision-making. Patients using cellphones can readily obtain and follow smartphone-based nursing interventions.

REFERENCES

Abdeshahi, S. K., Hashemipour, M. A., Mesgarzadeh, V., Payam, A. S., & Monfared, A. H. (2013). Effect of hypnosis on induction of local anaesthesia, pain perception, control of haemorrhage and anxiety during extraction of third molars: a case–control study. *Journal of Cranio-Maxillofacial Surgery*, *41*(4), 310–315. https://doi.org/10.1016/j.jcms.2012.10.009

Amiri, M. J., Sadeghi, T., & Negahban Bonabi, T. (2017). The effect of natural sounds on the anxiety of patients undergoing coronary artery bypass graft surgery. *Perioperative Medicine*, *6*, 17. https://doi.org/10.1186/s13741-017-0074-3

Awaludin, S., Nurachmah, E., & Novitasari, D. (2020). Hypnosis is a surgical pain intervention: a systematic review. *1st International Conference on Community Health (ICCH 2019)*, 276–284. https:doi.org/ 10.2991/ahsr.k.200204.059

Awaludin, S., Nurachmah, E., Soetisna, T. W., & Umar, J. (2022). The effect of a smartphone-based perioperative nursing intervention: Prayer, education, exercise therapy, hypnosis, and music toward pain, anxiety, and early mobilization on cardiac surgery. *Journal of Public Health Research*, *11*(2), jphr-2021. https://doi.org/10.4081/jphr.2021.2742

Awaludin, S., Sumeru, A., Alivian, G. N., & Novitasari, D. (2020). The Effect of Sikkomodo (Combination of Music, Humor, and Prayer) Formulation Toward Blood Pressure of Hypertension Patient on The Elderly Group in Banyumas Regency. *SHS Web of Conferences*, *86*, 1002. https://doi.org/10.1051/shsconf/20208601002

Bauer, M., Glenn, T., Geddes, J., Gitlin, M., Grof, P., Kessing, L. V, Monteith, S., Faurholt-Jepsen, M., Severus, E., & Whybrow, P. C. (2020). Smartphones in mental health: a critical review of background issues, current status and future concerns. *International Journal of Bipolar Disorders*, *8*, 2. https://doi.org/10.1186/s40345-019-0164-x

Berman, A., Snyder, S. J., & Frandsen, G. (2016). *Kozier & Erb's. of Fundamentals Nursing Concepts, Process, and Practice* (10th ed.). England: Pearson Education, Inc.

Bhatt, H., Sanghani, D., Julliard, K., & Fernaine, G. (2015). Is mitral annular calcification associated with atherosclerotic risk factors and severity and complexity of coronary artery disease? *Angiology*, *66*(7), 659–666. https://doi.org/10.1177/0003319714550239

Bigeleisen, P. E., & Goehner, N. (2015). Novel approaches in pain management in cardiac surgery. *Current Opinion in Anesthesiology*, *28*(1), 89–94. https://doi.org/10.1097/ACO.0000000000000147

Chandrababu, R., Nayak, B. S., Pai, V. B., Patil, N. T., George, A., George, L. S., & Devi, E. S. (2017). Effect of complementary therapies in patients following cardiac surgery. *Holistic Nursing Practice*, *31*(5), 315–324. https://doi.org/10.1097/HNP.0000000000000226

Chen, X., Yuan, R., Chen, X., Sun, M., Lin, S., Ye, J., & Chen, C. (2018). Hypnosis intervention for the management of pain perception during cataract surgery. *Journal of Pain Research*, 1921–1926. https://doi.org/10.2147/JPR.S174490

Ciğerci, Y., & Özbayır, T. (2016). The effects of music therapy on anxiety, pain and the amount of analgesics following coronary artery surgery. *Turkish Journal of Thoracic and Cardiovascular Surgery*, *24*(1), 44-50. https://doi.org/10.5606/tgkdc.dergisi.2016.12136

Coffey, S., Roberts-Thomson, R., Brown, A., Carapetis, J., Chen, M., Enriquez-Sarano, M., Zühlke, L., & Prendergast, B. D. (2021). Global epidemiology of valvular heart disease.

Nature Reviews Cardiology, *18*(12), 853–864. https://doi.org/10.1038/s41569-021-00570-z

Comeaux, T., & Steele-Moses, S. (2013). The effect of complementary music therapy on the patient's postoperative state anxiety, pain control, and environmental noise satisfaction. *Medsurg Nursing*, *22*(5),313-318.

DevarePhadke, S., & HadiyaParkar, S. (2014). Effect of music intervention on immediate post operative coronary artery bypass graft surgery (CABG) patients. *Indian Journal of Physiotherapy & Occupational Therapy*, *8*(4), 106-111.

Eren, G., Dogan, Y., Demir, G., Tulubas, E., Hergunsel, O., Tekdos, Y., Dogan, M., Bilgi, D., & Abut, Y. (2015). Hypnosis for sedation in transesophageal echocardiography: a comparison with midazolam. *Annals of Saudi Medicine*, *35*(1), 58–63. https://doi.org/10.5144/0256-4947.2015.58

Heidari, S., Babaii, A., Abbasinia, M., Shamali, M., Abbasi, M., & Rezaei, M. (2015). The effect of music on anxiety and cardiovascular indices in patients undergoing coronary artery bypass graft: a randomized controlled trial. *Nursing and Midwifery Studies*, *4*(4), e31157. https://doi.org/10.17795/nmsjournal31157

Jiménez-Jiménez, M., García-Escalona, A., Martín-López, A., De Vera-Vera, R., & De Haro, J. (2013). Intraoperative stress and anxiety reduction with music therapy: A controlled randomized clinical trial of efficacy and safety. *Journal of Vascular Nursing*, *31*(3), 101–106. https://doi.org/10.1016/j.jvn.2012.10.002

Keawnantawat, P., Thanasilp, S., & Preechawong, S. (2017). Translation and validation of the Thai version of a modified brief pain inventory: a concise instrument for pain assessment in postoperative cardiac surgery. *Pain Practice*, *17*(6), 763–773. https://doi.org/10.1111/papr.12524

Khalili, D., Haj Sheikholeslami, F., Bakhtiyari, M., Azizi, F., Momenan, A. A., & Hadaegh, F. (2014). The incidence of coronary heart disease and the population attributable fraction of its risk factors in Tehran: a 10-year population-based cohort study. *PloS One*, *9*(8), e105804. https://doi.org/10.1371/journal.pone.0105804

Khan, N. S., Shehnaz, S. I., Guruswami, G. K., Ibrahim, S. A. M., & Mustafa, S. A. J. (2017). Knowledge of warning signs, presenting symptoms and risk factors of coronary heart disease among the population of Dubai and Northern Emirates in UAE: a cross-sectional study. *Nepal Journal of Epidemiology*, *7*(2), 670-680. https://doi.org/10.3126/nje.v7i2.17973

Kim, K., Pham, D., & Schwarzkopf, R. (2016). Mobile Application Use in Monitoring Patient Adherence to Perioperative Total Knee Arthroplasty Protocols. *Surgical Technology International*, *28*, 253–260.

Noale, M., Limongi, F., & Maggi, S. (2020). Epidemiology of cardiovascular diseases in the elderly. *Frailty and Cardiovascular Diseases: Research into an Elderly Population*, 29–38. https://doi.org/10.1007/978-3-030-33330-0_4

Peate, I., & Evans, S. (2020). *Fundamentals of anatomy and physiology: For nursing and healthcare students*. John Wiley & Sons.

Smeltzer, S. ., Bare, B. ., Hinkle, J. L., & Cheever, K. . (2015). Handbook for Brunner and Suddarth's Textbook of Medical-Surgical Nursing. *Lippincott Williams & Wilkins*.

Soangra, R., & Lockhart, T. (2021). Smartphone-based prediction model for postoperative cardiac surgery outcomes using preoperative gait and posture measures. *Sensors*, *21*(5), 1704. https://doi.org/10.3390/s21051704

Tarasoutchi, F., Montera, M. W., Ramos, A. I. de O., Sampaio, R. O., Rosa, V. E. E., Accorsi, T. A. D., Santis, A. de, Fernandes, J. R. C., Pires, L. J. T., & Spina, G. S. (2020). Update of the Brazilian Guidelines for Valvular Heart Disease–2020. *Arquivos Brasileiros de*

Cardiologia, *115*, 720–775. https://doi.org/10.36660/abc.20201047

Virani, S. S., Alonso, A., Aparicio, H. J., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Cheng, S., Delling, F. N., Elkind, M. S. V., Evenson, K. R., Ferguson, J. F., Gupta, D. K., Khan, S. S., Kissela, B. M., Knutson, K. L., Lee, C. D., Lewis, T. T., Liu, J., … American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee (2021). Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. *Circulation*, *143*(8), e254–e743. https://doi.org/10.1161/CIR.0000000000000950

Xu, L., Li, F., Zhou, C., Li, J., Hong, C., & Tong, Q. (2019). The effect of mobile applications for improving adherence in cardiac rehabilitation: a systematic review and meta-analysis. *BMC Cardiovascular Disorders*, *19*, 166. https://doi.org/10.1186/s12872-019-1149-5

Yu, H., Zheng, J.-Q., Hua, Y.-S., Ren, S.-F., & Yu, H. (2019). Influence of volatile anesthesia versus total intravenous anesthesia on chronic postsurgical pain after cardiac surgery using the initiative on methods, measurement, and pain assessment in clinical trials criteria: study protocol for a prospective randomized controlled trial. *Trials*, *20*, 645. https://doi.org/10.1186/s13063-019-3742-4

Zipes, D. P. (2018). Braunwald's heart disease: a textbook of cardiovascular medicine. *BMH Medical Journal*, *5*(2), 63.

Zubrzycki, M., Liebold, A., Skrabal, C., Reinelt, H., Ziegler, M., Perdas, E., & Zubrzycka, M. (2018). Assessment and pathophysiology of pain in cardiac surgery. *Journal of Pain Research*, 1599–1611. https://doi.org/10.2147/JPR.S162067

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 643-651
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1110*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

HBsAg Status, Molecular Detection and Therapy Evaluation of Hepatitis B Patient

Agustina W. Djuma[1a], Sherly Dewu[1b], Ayorince Herlinalt Gloria Banunu[2c], Norma T. Kambuno[1d], Aldiana Astuti[1e*]

[1] Department of Medical Laboratory Technology, Poltekkes Kemenkes Kupang, Kupang City, East Nusa Tenggara, Indonesia
[2] Prof. Dr. W.Z Johannes Hospital Kupang, Kupang City, East Nusa Tenggara, Indonesia

[a] Email address: hdhelmydj@gmail.com
[b] Email address: dewusherly@gmail.com
[c] Email address: ino5layauw@yahoo.com
[d] Email address: norma.kambuno@gmail.com
[e] Email address: aldiana.astuti@mail.ugm.ac.id

Received: 13 March 2023 Revised: 4 October 2023 Accepted: 17 October 2023

Abstract
The management of chronic hepatitis B involves various therapeutic approaches, including nucleotide analogs (NUCs) and pegylated-interferon alpha (peg-IFN), either in isolation or in combination. Reverse transcriptase enzyme is competitively inhibited by NUCs, which effectively suppresses HBV replication and lowers viral load. Concerning their cost-effectiveness, high response rates, low side effects, and oral administration, NUCs are recommended. Prolonged use, particularly of NUCs with a low genetic barrier or as monotherapy, can, however, lead to resistance, long-term safety issues, and the need for ongoing treatment. Physicians and other healthcare professionals are extremely concerned about the emergence of resistance and possible safety concerns related to the long-term use of NUCs. Moreover, the requirement for continuous therapy presents notable obstacles concerning patient adherence, distribution of healthcare resources, and overall economic viability. To clarify these problems and direct the creation of more potent and long-lasting treatment plans for chronic hepatitis B, urgent research is required. Hepatitis B surface antigen (HBsAg) detection is frequently accomplished via the use of the Chemiluminescent Microparticle Immunoassay (CMIA), which is a crucial early serologic marker for screening and diagnosis. Polymerase chain reaction (PCR) molecular testing is employed to confirm the presence of HBsAg. Polymerase Chain Reaction (PCR) was the technique we utilized to verify the outcomes. Twenty-eight of the HBsAg-positive patients at W.Z. Johannes Kupang Hospital had positive PCR results, highlighting the significance of molecular confirmation. The results of this study emphasize the value of precise HBsAg testing and the supplementary function of molecular confirmation in the treatment of patients with chronic hepatitis B. Furthermore, it clarifies the current therapeutic approaches applied to this patient population, highlighting the necessity of customized therapeutic approaches based on each patient's unique profile and potential complications.

Keywords: Hepatitis B Virus, HBsAg, PCR, Treatment.

Corresponding Author:

Aldiana Astuti
Department of Medical Laboratory Technology, Poltekkes Kemenkes Kupang, Kupang City, East Nusa Tenggara, Indonesia
Email: aldiana.astuti@mail.ugm.ac.id

1. INTRODUCTION

Chronic hepatitis B, stemming from the hepatitis B virus (HBV) infection, stands as a pressing global health concern, notably in developing nations (World Health Organization, 2016a; World Health Organization, 2016b). Muljono, (2017) estimated that 257 million people worldwide suffer from chronic HBV infection. With a population of more than 250 million, Indonesia changed HBsAg prevalence from 9.4% in 2007 (based on data from Basic Health Research) to 7.1% in 2013, indicating a change from a high-endemic to a moderate-endemic nation (Kementerian Kesehatan Republik Indonesia, 2018; Wijayadi et al., 2018). Notably, Kambuno et al., (2017) discovered that among blood donors in East Nusa Tenggara, Indonesia, the prevalence of hepatitis B and hepatitis C was 3.5% and 0.5%, respectively.

Recently, the management of chronic hepatitis B hinges on nucleoside(s) analogs (NUCs) and pegylated-interferon alpha (peg-IFN), which can be administered independently or in combination (Jefferies, et al., 2018; Kim & Kim, 2018; Khairani, 2022). According to Hindarto, Rostinawati, and Retnoningrum, (2011), NUCs effectively suppress HBV replication and lower the amount of the virus in the host's system by acting as competitive inhibitors of the reverse transcriptase enzyme. Treatment regimens have incorporated a variety of NUCs, such as emtricitabine, telbivudine (LdT), entecavir monohydrate (ETV), adefovir dipivoxil (ADV), lamivudine (LAM), and tenofovir disoproxil fumarate (TDF) (Wibowo et al., 2020). With ETV or TDF achieving undetectable HBV DNA levels in 94-98% of cases and HBeAg seroconversion in 40-41% of HBeAg-positive patients, long-term NUC administration has demonstrated the ability to suppress HBV DNA, achieve HBeAg seroconversion, induce HBsAg loss, and reduce ALT levels (Fahira & Hasan, 2020).

The attractiveness of NUCs lies in their oral administration, minimal side effects, high response rates, and cost-effectiveness (Bedre, 2016). Extended use, however, particularly with low-genotypic barrier NUCs or as monotherapy, may lead to drug resistance, long-term safety issues, and an ongoing need for treatment to maintain suppression of viral replication. Combination therapy using nucleoside and nucleotide analogs is advised to combat drug resistance. Treatment for NUC is complicated by genetic variations, particularly in the polymerase gene's reverse transcriptase domain (Nugraha et al., 2022).

Remarkably, genetic mutation patterns of hepatitis B patients receiving NUC treatment at Prof. Dr. W. Z. Johannes Kupang Hospital have never been studied before. Obtaining data on mutation patterns has substantial clinical significance, enabling medical professionals to make more knowledgeable treatment choices. Consequently, there may be a decrease in the viral load and an interruption to the progression of the disease (Trisnaningtyas, Sari, & Setyaningrum, 2017).

Due to these considerations, this study undertakes an exploration of the mutation patterns among hepatitis B patients undergoing NUC treatment, intending to provide invaluable insights to enhance treatment precision and ultimately contribute to more effective disease management.

2. RESEARCH METHOD

This study is a descriptive observational study with a cross-sectional design, which received ethical clearance from the Health Research Ethics Committee of Poltekkes Kemenkes Kupang, under the reference number LB.02.03/1/0112/2022. The study encompassed a cohort of 28 outpatients receiving therapy at Prof. W. Z. Johannes Hospital who had all previously undergone PCR testing to confirm that they were positive for the hepatitis B surface antigen (HBsAg). Using particular primers, the P and S genes of the Hepatitis B Virus (HBV) were generated for the PCR analysis.

In this study, we utilized advanced diagnostic techniques to comprehensively assess the presence and characteristics of Hepatitis B surface antigen (HBsAg) (Winata, 2017). Our evaluation employed the Abbott Architect HBsAg Qualitative II reagent, a highly sensitive automated assay designed for the detection of HBsAg in human serum or plasma. With the Chemiflex protocol, the diagnostic technique known as Chemiluminescent Microparticle Immunoassay (CMIA) demonstrated exceptional sensitivity and 100% accuracy in identifying positive samples. This assay's analytical sensitivity ranged from 0.017 to 0.022 IU/ml, guaranteeing accurate and consistent results (Yulia, 2020).

Furthermore, the Molecular Biology Laboratory in the Hematology-Oncology Division of the Department of Internal Medicine at Cipto Mangunkusumo Hospital managed the molecular examination portion of our study. In this phase, we utilized the QIAamp DNA Mini Kit from QIAGEN (CA, USA) to carefully extract VHB DNA from serum samples that were obtained from each research subject. The DNA that had been extracted was then dissolved in a 60 µL solution. To investigate further the genetic aspects of the virus, we used particular primers following the protocol that Hindarto, Rostinawati, & Retnoningrum, (2011) established. In particular, we employed the Polymerase Chain Reaction (PCR) technique to amplify the polymerase gene (P gene) and the S gene, which encode the envelope proteins of the VHB, including HBsAg and two other essential proteins.

The research encompassed a two-phase approach. Firstly, a qualitative serological examination for HBsAg was conducted at the Clinical Pathology Laboratory of Prof. Dr. W. Z. Johannes Kupang Hospital. The P and S genes on the HBV were then identified by molecular PCR analysis at the Molecular Biology Laboratory of the Hematology-Oncology Division at RS. Cipto Mangunkusumo Jakarta. Patient-related data, including demographic data like age and gender, were gathered retrospectively from the medical records of outpatients at Prof. Dr. W. Z. Johannes Hospital who had previously received a hepatitis B diagnosis. The medical records offered valuable insights into treatment data, involving information on prescribed medications, including type, dosage, and duration, as well as details regarding any coexisting conditions the patients may have had. Antiviral therapy and supportive therapy were both included in the treatment profile data. The Indonesian Liver Research Association (PPHI) Guidelines' criteria were utilized to evaluate treatment compliance.

3. RESULTS AND DISCUSSION

To validate the outcomes of our molecular examination, we introduced a positive control sample of VHB DNA, sourced from a hepatitis B patient through the Eijkman laboratory. If the VHB sample from a research subject produced the same product size (249 bp) as the previously mentioned positive control, it was considered positive. Through PCR molecular analysis, our thorough investigation produced an 82.1% confirmation rate for positive serology results. Of the 28 samples that were analyzed, 23 demonstrated evidence of VHB, as indicated by the presence of the P gene or both ORFs, the P gene and the S gene, which developed an electrophoresis product that regularly measured 249 bp, which was consistent with the positive control (refer to Figure 1).

The VHB PCR examination involved the targeted amplification of both the P gene and the S gene, representing two of the four overlapping open reading frame (ORF) regions that collectively constitute the compact genome and protein structure of the virus. The hepatitis B surface antigen (HBsAg) is encoded by the Surface gene (Gen S), and the largest ORF is the Polymerase gene (Gen P), which is located between nucleotides 2357 and 1621 (Winata, 2017; Tiollais, Pourcel, & Dejean, 1985). Particularly, there is some overlap between the Gen P and Gen S sequences, as well as some between Gen C and Gen X. Gene alterations in Gen S, C, or X, can significantly affect the polymerase's ability to function. It should be understood that

mutations resulting in drug resistance frequently occur in the polymerase gene. Genetic variations in this gene, specifically in the reverse transcriptase domain, can present a significant obstacle to the administration of Nucleos(t)ide analogues (NUCs).

The Surface gene (Gen S) encodes a polypeptide which constructs the virus's outer envelope. It is situated in an ORF between nucleotides 2848 and 833, as described by Hindarto, Rostinawati, and Retnoningrum, (2011). 226 amino acids constituents of the fundamental protein of the virus envelope, which is produced when transcription begins at the Gen S region. The determinant, which is the principal antigen of HBsAg and is located between amino acids 124 and 149, remains a crucial component. This determinant is universally present in all VHB variants and is consistently present in the three protein types (large, medium, and small) synthesized by Gen S. Importantly, any alterations in the amino acids within the determinant region hold the potential to induce changes in the double loop conformation, thereby resulting in modifications to the antigenicity of HBsAg. According to Zampino (2015), these changes prevent antibodies produced after vaccination or infection from attaching to this antigen. Our investigation encompassed a thorough analysis of HBsAg using molecular and serological tests. These findings possess significant ramifications for how treatment plans are developed and how the illness is managed.

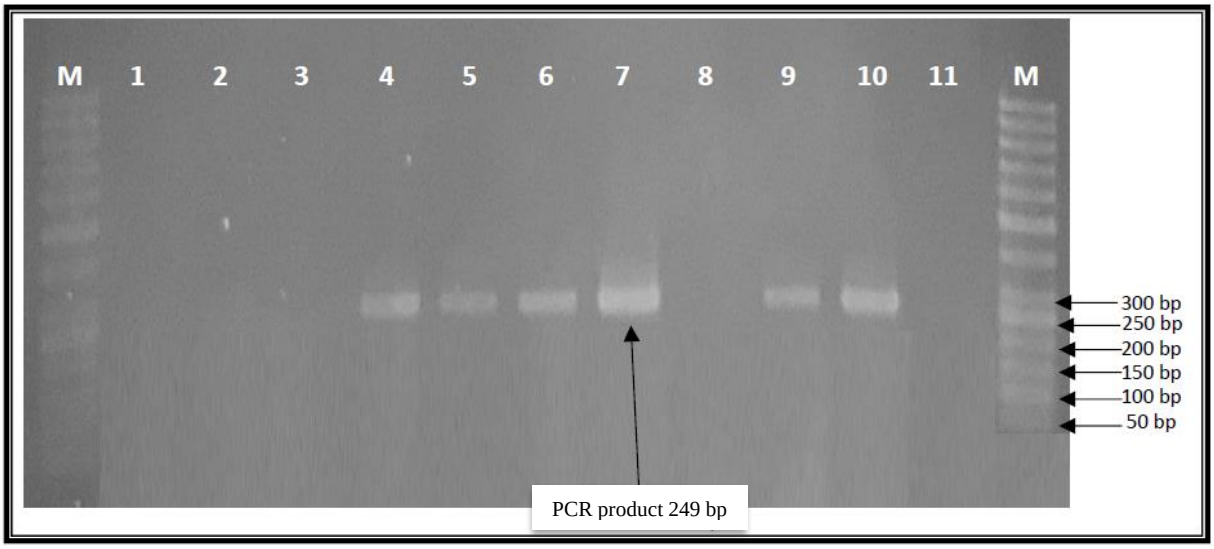


Figure 1. The result of electrophoresis of patient samples with positive HBsAg.

M= DNA Marker at 50 bp	6=sample	32	(positive)
1= sample 27	7=sample	33	(positive)
2= sample 28	8=sample	34	
3= sample 29	9=sample	14	(positive)
4= sample 30 (positive)	10=positive		control
5=sample 31 (positive)	11=NTC		

Figure 1 demonstrates that 5 samples was found to be a positive match with number 10, which was positive control.

Description of Hepatitis B Patient Therapy. Antiviral therapy in hepatitis B patients is applied after confirming positive HBsAg for morethan 6 months (chronic hepatitis B).

Therapy aims to enhance liver function and clinical status while impeding the progression of cirrhosis and hepatocellular carcinoma (Borgia et al., 2012). The disease phase must be introduced to carry out the management of hepatitis B. According to the Indonesian Liver

Research Association's (PPHI) guidelines, serum HBV DNA, HBeAg status, ALT, and liver histology parameters are required to determine when to begin treatment. Antiviral resistance is one of the crucial factors to take into consideration when delivering therapy; the prevalence of resistance will increase if therapy is administered at the incorrect time, type, or dose (Trisnaningtyas & Setyaningrum, 2017).

Initially, lamivudine, an oral nucleotide analog (NA), was the new class of treatment for hepatitis B. Interferon was the first therapy used to treat the disease. Adefovir, entecavir, Peg-IFN, telbivudine, and tenofovir were approved for use as Hepatitis B therapies as a result of later developments (Zoulim & Perrillo, 2008). It is widely acknowledged that the presence of covalently closed circular DNA (cccDNA) in the nucleus of infected hepatocytes means that hepatitis B treatment cannot eradicate the hepatitis B virus (Nurainy & Muljono, 2018; Robinson, Wong, & Gish, 2023; Seto, 2019). The two types of medications employed for chronic hepatitis B therapy up to this point are nucleoside/nucleotide analogs and pegylated interferon (PEG-IFN).

To the best of our knowledge, entecavir and tenofovir are the recommended therapies due to their high barrier resistance and good efficacy. Almost every region in Indonesia encounters challenges associated with drug availability, particularly concerning the categories of drugs covered by the BPJS. Second-line treatments like lamivudine, adefovir, and telbivudine can be utilized in situations where tenofovir and entecavir are not available. However, prolonged use of the medication can lead to the issue of high resistance. As a result, the patient began taking tenofovir as a government program medication (Borgia et al, 2012).

Sulaiman et al., (2020) reported a cohort study at RSCM presenting that the use of NA in hepatitis patientswas proven to enhance hepatitis B infection in liver disease, the degree of liver stiffness also decreasedsignificantly. Furthermore, following NA administration, there was a significant decrease in alanine aminotransferase (ALT) levels. The fact that HBV DNA had been identified in 34% of the study participants, however, demonstrated that NA was unable to provide a "hepatitis B cure". Nevertheless, administering NA still markedly enhances liver function, lowers the incidence of liver cancer, delays the development of liver cirrhosis, and lengthens the life expectancy of hepatitis B patients (. The 2017 EASL guidelines define lamivudine (LAM), adefovir dipivoxil (ADV), entecavir (ETV), telbivudine (TBV), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF) as nucleoside/nucleotide analogs for chronic hepatitis B therapy (World Health Organization, 2016; Conners et al., 2023; Jackson, Locarnini, & Gish, 2018). Clinical trials have displayed nucleoside/nucleotide analogs to have superior viral efficacy and better tolerance than PEG- IFN.

Table 1. Profile of antiviral therapy used by Hepatitis B patients.

Antiviral	**Amount**	**%**
Tenofovir	5	18,0
Lamivudine	4	14,0
Total	9	32, %

In Indonesia, tenofovir and lamivudine therapy is the most frequently used treatment. These two drug types are more widely accessible, less expensive, less likely to cause side effects, and safe for a wide age range (Fadrian, 2016). Likewise, at Prof. Dr. W.Z. Johannes. No additional drug classes, including entecavir (ETV), telbivudine (TBV), tenofovir disoproxil fumarate (TDF), adefovir dipivoxil (ADV), and tenofovir alafenamide (TAF), were discovered. The scarcity of the aforementioned medications is additionally connected to hospital stock levels, which restricts doctors' options for treatment (Abdul Basit, et al., 2017; Agarwal, et al., 2015).

Furthermore, not all hepatitis B patients have the results of the serum HBV DNA examination, HBeAg status, ALT, and liver histology, which should be available to select the appropriate therapy (Sulaiman et al., 2021). This limits the comprehensiveness of the examination of patients with hepatitis B. The treatment of hepatitis B patients at Prof. Dr. W.Z. Johannes provides more supportive therapy, as indicated in the table, due to the restricted availability of medications.

Table 2. Overview of Supportive Therapy in Hepatitis B patients.

Medicine	**Amount**	**%**
Livron B Plex	14	50
Curcuma	11	39
Ranitidine	1	4
Simvastatin	3	11
Atorvastatin	1	4
Folic acid	1	4
Metformin	1	1
Glibenclamide	2	7
Vitamin D	1	4
Dexamethasone zalf	1	4
Allopurinol	1	4
Cetirizine	1	4
Amlodipine	1	4
Sulfas Ferrous	1	4
Vitamin C	1	4
Aspilets	2	7
Cefixime	1	4
Aspar K	2	7
Omeprazole	1	4
Retaphyl	1	4
Lansoprazole	1	4
Meloxicam	1	4
Domperidone	1	4
Paracetamol	1	4
	52	100,0

We discovered that only 32 percent of the patients in our study received antiviral therapy. There are various reasons for the restricted application of antiviral therapy. Initially, it supports the results of a different study by Bedre et al. from 2016, which demonstrated a comparable pattern of low antiviral therapy utilization among patients with hepatitis B. The studies' consistent treatment patterns highlight a prevalent clinical strategy that favors supportive therapies for the management of hepatitis B, such as Curcuma and Livron B Plex.

There are probably several contributing factors to this comparatively low rate of antiviral therapy initiation. The clinical circumstances of the patients, such as their SGPT levels and HBeAg status, were critical in deciding the course of treatment. According to clinical guidelines for the management of hepatitis B, patients with positive HBeAg and elevated SGPT levels were primarily treated with antiviral therapy. On the other hand, patients with distinct clinical profiles frequently received supportive treatments like Livron B Plex and Curcuma, which enhance appetite and liver function without specifically addressing viral replication.

We discovered that 11 patients in our study cohort received Curcuma plus Livron as a combination therapy, and 3 patients received Livron as a supportive therapy. The range of patient management techniques among the participants in our study is demonstrated by these differences in treatment modalities.

Recognizing the limitations of our research is crucial. The presence of additional treatments, differences in treatment approaches, and the relatively low rate of antiviral therapy utilization introduce potential confounding factors that need to be taken into consideration when interpreting our findings. Furthermore, the reality that patients' treatment regimens vary from one another may affect how generalizable our findings are, underscoring the need for more investigation into the efficacy of various therapeutic modalities in the management of hepatitis B.

4. CONCLUSION

Based on the information we gathered, we advise the W.Z. Johannes Hospital administration to finish the examination criteria for hepatitis B patients before enforcing therapy to achieve the best possible therapeutic outcomes. Therapy selection cannot be made solely based on HBsAg and HBeAg status; liver histology, serum HBV DNA, and ALT/AST status must all be taken into consideration. Second, we recommend the completeness of line 1 and line 2 hepatitis drugs as standard treatment to obtain maximum therapeutic results and reduce antiviral resistance.

REFERENCES

Abdul Basit, S., Dawood, A., Ryan, J., & Gish, R. (2017). Tenofovir alafenamide for the treatment of chronic hepatitis B virus infection. *Expert review of clinical pharmacology*, *10*(7), 707-716. https://doi.org/10.1080/17512433.2017.1323633

Agarwal, K., Fung, S. K., Nguyen, T. T., Cheng, W., Sicard, E., Ryder, S. D., ... & Foster, G. R. (2015). Twenty-eight day safety, antiviral activity, and pharmacokinetics of tenofovir alafenamide for treatment of chronic hepatitis B infection. *Journal of hepatology*, *62*(3), 533-540. https://doi.org/10.1016/j.jhep.2014.10.035

Bedre, R. H., Raj, U., Misra, S. P., & Varadwaj, P. K. (2016). Antiviral therapy with nucleotide/nucleoside analogues in chronic hepatitis B: A meta-analysis of prospective randomized trials. *Indian Journal of Gastroenterology*, *35*, 75-82. https://doi.org/10.1007/s12664-016-0632-5

Borgia, G., Carleo, M. A., Gaeta, G. B., & Gentile, I. (2012). Hepatitis B in pregnancy. *World journal of gastroenterology: WJG*, *18*(34), 4677–4683. https://doi.org/10.3748/wjg.v18.i34.4677

Conners, E. E., Panagiotakopoulos, L., Hofmeister, M. G., Spradling, P. R., Hagan, L. M., Harris, A. M., ... & Wang, S. H. (2023). Screening and testing for hepatitis B virus infection: CDC recommendations—United States, 2023. MMWR Recommendations and Reports, 72(1): 1–25. https://doi.org/10.15585/mmwr.rr7201a1

Fadrian, F. (2016). Terapi Antiviral Pada Sirosis Hati Dekompensata Terkait Infeksi Virus Hepatitis B. *Majalah Kedokteran Andalas*, *39*(1), 35-41.

Fahira, A., & Hasan, I. (2020). Higher Risk of Hepatocellular Carcinoma Progression in the Population of Untreated Immune-Tolerant Phase Chronic Hepatitis B Patients: An Evidence Based. *The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy*, *21*(1), 68-78. https://doi.org/10.24871/211202068-78

Hindarto, C. K., Rostinawati, T., & Retnoningrum, D. S. (2011). Identifikasi Mutasi Pada Daerah Dna Polimerase Dan Hbsag Virus Hepatitis B. *Fitofarmaka: Jurnal Ilmiah Farmasi*, *1*(2), 22-30. https://doi.org/10.33751/jf.v1i2.161

Jackson, K., Locarnini, S., & Gish, R. (2018). Diagnostics of hepatitis B virus: standard of care and investigational. *Clinical liver disease*, *12*(1), 5. https://doi.org/10.1002/cld.729

Jefferies, M., Rauff, B., Rashid, H., Lam, T., & Rafiq, S. (2018). Update on global epidemiology of viral hepatitis and preventive strategies. *World journal of clinical cases*, *6*(13), 589. http://doi.org/10.12998/wjcc.v6.i13.589

Kambuno, N. T., Sari, A., Nurdin, K. E., Novicadlitha, Y., & Siregar, I. (2018, December). The relation of blood donors' characteristic toward prevalences of HBsAg and anti-HCV on Blood Transfussion Unit of PMI in Province of East Nusa Tenggara. In *Proceeding1st. International Conference Health Polytechnic of Kupang* , 303-310.

Kementerian Kesehatan Republik Indonesia. (2018). *Hasil Utama RISKESDAS 2018*. Kementerian Kesehatan Republik Indonesia.

Kim, B. H., & Kim, W. R. (2018). Epidemiology of hepatitis B virus infection in the United States. Clinical liver disease, 12(1), 1-4. https://doi.org/10.1002/cld.732

Khairani, N., Siregar, T. M., Frisnoiry, S., Manullang, S., & Hasibuan, N. I. (2022, December). SEIR Model in Spread Disease. *Proceedings of the 4th International Conference on Innovation in Education, Science and Culture, ICIESC 2022, 11 October 2022, Medan, Indonesia*.

Muljono, D. H. (2017). Epidemiology of hepatitis B and C in Republic of Indonesia. *Euroasian journal of hepato-gastroenterology*, *7*(1), 55. https://doi.org/10.5005/jp-journals-l0018-1212

Nugraha, E. S., Supriami, S. H., Atik, N., Agustanti, N., Wahyudi, Y., Girawan, D., ... & Abdurachman, S. A. (2022). Antiviral Treatment and One-Year Follow-Up of Chronic Hepatitis B Patients in Bandung: An Observational Study. *The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy*, *23*(2), 117-122. https://doi.org/10.24871/2322022217-222

Nurainy, N., & Muljono, D. H. (2018) Karakteristik Reverse Transcriptase Gen Polymerase Virus Hepatitis B Pada Penderita Hepatitis B Kronis Asimptomatik Pra-Pengobatan. *Ejki, 5(3),183-190.*

Robinson, A., Wong, R., & Gish, R. G. (2023). Chronic hepatitis B virus and hepatitis D virus: new developments. *Clinics in Liver Disease*, *27*(1), 17-25. https://doi.org/10.1016/j.cld.2022.08.001

Seto, A. R. (2019). *Hubungan Jumlah Dan Aktivitas Sel Nk Dengan Kekakuan Hati Pada Pasien Hepatitis B Kronik Penelitian Observasional Analitik Cross-Sectional diInstalasi Rawat Jalan Divisi Gasteroenterologi–Hepatologi Departemen Ilmu Penyakit Dalam RSUD Dr. Soetomo Surabaya.* Thesis. Universitas Airlangga.

Sulaiman, A. S., Hasan, I., Lesmana, C. R. A., Jasirwan, C. O. M., Nababan, S. H. H., Kalista, K. F., ... & Gani, R. A. (2021). Analog nukleosida/nukleotida sebagai terapi hepatitisB kronis: studi kohort 3 tahun. *Jurnal Penyakit Dalam Indonesia*, *8*(3), 139-145.

Tiollais, P., Pourcel, C., & Dejean, A. (1985). The hepatitis B virus. *Nature*, *317*(6037), 489-495.

Trisnaningtyas, R. W., Sari, C. P., & Setyaningrum, N. (2017). Evaluasi Terapi Pada Pasien Hepatitis B di RSUP Dr. Sardjito Yogyakarta. *Jurnal Ilmiah Farmasi*, *13*(1), 29-34.

Wibowo, B. P., Susanto, E., Supriono, S., & Mustika, S. (2020). Perbandingan Potensi Telbivudin Dan Tenofovir Dalam Menurunkan Skor Aspartate Transaminase To Platelet Ratio Index (Apri) Pada Pasien Hepatitis B. *Majalah Kesehatan Fkub*, *7*(1), 41-47. https://doi.org/10.21776/ub.majalahkesehatan.2020.007.01.5

Winata, A. (2017). Identifikasi hasil Hepatitis B Surface Antigen (HBsAg) Pada Perawat yang Bekerja Di Ruang Infeksi Rumah Sakit Umum Bahteramas Provinsi Sulawesi Tenggara. *Karya Tulis Ilmiah*. Poltekkes Kemenkes Kendari.

Wijayadi, T., Sjahril, R., Ie, S. I., Wahyuni, R., Pattelongi, I., Massi, M. N., ... & Muljono, D.H. (2018). Seroepidemiology of HBV infection among health-care workers in South Sulawesi, Indonesia. *BMC Infectious Diseases, 18*, 279. https://doi.org/10.1186/s12879-018-3190-x

World Health Organization (2016a). *Global health sector strategy on viral hepatitis: Towards Ending Viral Hepatitis 2016-2021 [Internet]*. Geneva: World Health Organization.

World Health Organization. (2016b). *Guidelines for the screening care and treatment of persons with chronic hepatitis C infection*. Geneva: World Health Organization.

Yulia, D. (2020). Virus Hepatitis B Ditinjau dari Aspek Laboratorium. *Jurnal Kesehatan Andalas, 8*(4). https://doi.org/10.25077/jka.v8i4.1108

Zampino, R., Boemio, A., Sagnelli, C., Alessio, L., Adinolfi, L. E., Sagnelli, E., & Coppola, N. (2015). Hepatitis B virus burden in developing countries. *World journal of gastroenterology, 21*(42), 11941–11953. https://doi.org/10.3748/wjg.v21.i42.11941

Zoulim, F., & Perrillo, R. (2008). Hepatitis B: reflections on the current approach to antiviral therapy. *Journal of hepatology, 48* (Supplement 1), S1-S19. https://doi.org/10.1016/j.jhep.2008.01.011

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 652-670
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1105*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

Use of Artificial Intelligence in Early Warning Score in Critical ill Patients: Scoping Review

Suhartini Ismail[1a], Zahrotul Wardah[2b]*, Adi Wibowo[3c]

[1] Department of Nursing, Faculty of Medicine, Unversitas Diponegoro, Semarang, Central Java, Indonesia
[2] Master of Nursing Program, Unversitas Diponegoro, Semarang, Central Java, Indonesia
[3.] Department of Computer Science, Universitas Diponegoro, Semarang, Central Java, Indonesia

[a] Email address: suhartini.ismail@fk.undip.ac.id
[b] Email address: zahrawardah44@gmail.com
[c] Email address: bowo.adi@live.undip.ac.id

Received: 6 March 2023 Revised: 2 October 2023 Accepted: 30 October 2023

Abstract

Early Warning Score (EWS) systems can identify critical patients through the application of artificial intelligence (AI). Physiological parameters like blood pressure, body temperature, heart rate, and respiration rate are encompassed in the EWS. One of AI's advantages is its capacity to recognize high-risk individuals who need emergency medical attention because they are at risk of organ failure, heart attack, or even death. The objective of this study is to review the body of research on the use of AI in EWS to accurately predict patients who will become critical. The analysis model of Arksey and O'Malley is employed in this study. Electronic databases such as ScienceDirect, Scopus, PubMed, and SpringerLink were utilized in a methodical search. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA SR) guidelines were utilized in the creation and selection of the literature. This analysis included a total of 14 articles. This article summarizes the findings on several aspects: the usefulness of AI algorithms in EWS for critical patients, types of AI algorithm models, and the accuracy of AI in predicting the quality of life of patients in EWS. The results of this review show that the integration of AI into EWS can increase accuracy in predicting patients in critical condition, including cardiac arrest, sepsis, and ARDS events that cause inhalation until the patient dies. The AI models that are often used are machine learning and deep learning models because they are considered to perform better and achieve high accuracy. The importance of further research is to identify the application of AI with EWS in critical care patients by adding laboratory result parameters and pain scales to increase prediction accuracy to obtain optimal results.

Keywords: Early Warning Score, Artificial Intelligence, Machine Learning, Computational Intelligence, Critical Patients.

Corresponding Author:

Zahrotul Wardah
Master of Nursing Program, Unversitas Diponegoro, Semarang, Central Java, Indonesia
Email: zahrawardah44@gmail.com

1. INTRODUCTION

Critical patients require precise and timely care when receiving home health care. Until a patient passes away, the Early Warning Score (EWS) is a tool employed to predict their condition (Abbott et al., 2018). To predict the patient's clinical condition based on vital sign data, complex learning models must be applied in a transparent and explanatory manner to critical patient conditions (Chiew et al., 2019). Several physiological data parameters in EWS have developed, such as the National Early Warning Score (NEWS) and Modified Early Warning Score (MEWS), which have demonstrated less stable accuracy of results (Smith et al., 2008). This can cause the patient to fall into critical condition.

By using a clinical multicenter research model, it is possible to predict a patient's critical condition before they pass away, which can help delay the need for intervention until the patient is admitted to the intensive care unit (Dziadzko et al., 2018; Nielsen et al., 2022). Artificial Intelligence (AI) models provide a new discourse for predicting acute critical patients earlier with a higher degree of precision than EWS (Barton et al., 2019; Shickel et al., 2019). This is consistent with Kang's, et al., (2020) research, which demonstrates that AI algorithms outperform traditional triage tools and EWS in accurately predicting critical patient care needs using EMS information (Kang, et al., 2020).

Artificial Intelligence (AI) is a product of technological advancements that have contributed to the development of new applications in the medical and nursing fields. These applications aid medical professionals in diagnosing patients and conducting clinical follow-ups, which can enhance the quality of care for critically ill patients. Another example of AI is the Early Warning Score (EWS), which is currently being implemented into practice (Lei, 2017; Tang et al., 2021). The physiological parameters monitored in EWS indicators considered EWS systems are the patient's respiratory rate, oxygen saturation, systolic blood pressure, pulse rate, level of consciousness, and temperature (Royal College of Physicians, 2017; Royal College of Physicians, 2019)**.** In hospital clinical practice, physicians will administer clinical interventions that result in high EWS if they notice elevated EWS values or high EWS results. The primary rationale behind utilizing AI-based EWS for forecasting the deterioration in the clinical state of critical patients is the utilization of machine learning, which decreases errors in diagnosis prediction and aids in decision-making for critical patients (Lauritsen, et al., 2020; Lee et al., 2020). The use of artificial intelligence (AI) technology in the Early Warning System (EWS) for patients with life-threatening illnesses is indicative of the technology's expanding application in Indonesia's healthcare industry. When it comes to supporting medical service providers and helping the medical team reach a final decision, technology is crucial (Romero-Brufau et al., 2021).

Several previous studies have demonstrated the advantages of implementing EWS-related AI for hospitalized critical patients. Thus, a scoping review is required to conduct a comprehensive analysis of the application of artificial intelligence (AI) in Early Warning Scores (EWS) for critical patients. The scoping review provides a thorough understanding of how EWS-related AI is applied to predict the deterioration in critical patients' clinical status, which lowers hospital mortality.

2. RESEARCH METHOD

A scoping review is a specific method that aims to ‘map the literature’ on a topic of interest to identify gaps in knowledge (Arksey & O’Malley, 2005; Armstrong et al., 2011). This approach was an appropriate approach for this review as it allowed for the inclusion of variety of studies. Design, especially when there is new information being discovered. It is distinct from a systematic review in that it does not entail evaluating the caliber of the literature. Instead, of reporting on the breadth and depth of a particular subject, these reports summarize a variety

of evidence. The review was guided by the five stages identified by Arksey and O'Malley (18): (1) defining the objectives and search questions; (2) identifying relevant research; (3) selecting a study; (4) displaying data as graphs and qualitative themes; and (5) collecting data and composing a report (Arksey & O'Malley, 2005). The question for this study is "What are the comprehensive images of the application of AI related to EWS in identifying clinical changes in critical patients?"

A literature search associated with the full text of this article employs databases, including PubMed, ScienceDirect, Scopus, and SpringerLink. Boolean literature search operators "OR/AND". We utilized a range of search terms such as "early warning score" AND "artificial intelligence" OR "machine learning" OR "computational intelligence" AND "critical patients. intelligence" AND "critical patients". Additionally, we expanded our search to include government websites associated with the Department of Health and investigated graduate theses that were accessible. Examining the references listed in the studies that were included enhanced our search. We employ specific filters to improve the accuracy of our results, even though our searches are limited to the year of publication. The researcher considers each study's scope and ability to address the research questions when selecting relevant research. Publications discussing AI models for EWS in critical patients—particularly adult patients, as pediatric patients have different EWS parameters than adult patients—are encompassed if they adhere to certain inclusion criteria. Critical patients who were hospitalized participated in the reviewed articles. Reports, editorials, and non-English articles are not accepted.

Iterative steps are employed in determining which studies to include in the scoping review; team discussions are utilized to add clarity at this stage and are primarily led by the lead author. To conduct this scoping review, pertinent information about the objectives and methods of relevant publications was compiled and arranged, and the literature was independently searched through dependable databases. The obtained articles were examined for similarities and differences. Figure 1: An explanation of the PRISMA-SR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Review) guidelines' search and selection process for articles to be utilized as literature (McGowan et al., 2020).

3. RESULTS AND DISCUSSION

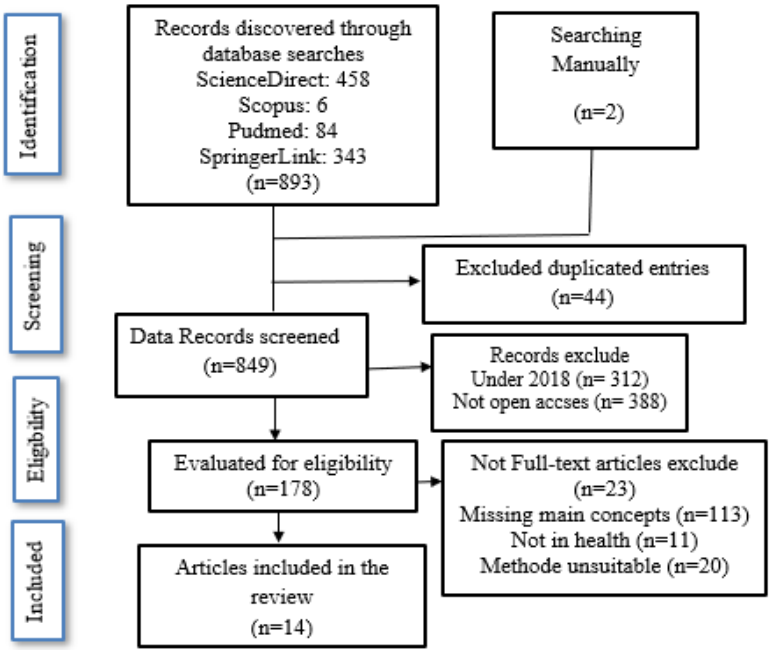


Figure 1. PRISMA SR flow diagram of studies search

The database search results of 893 articles, with details from ScienceDirek 458 articles, Scopus 6 articles, PubMed 84 articles, Springerlink 343 articles, duplicate screening of 44 articles, in accordance with the year of publication ≤ 2018 318, Not open access 388, so the remaining 178 articles are evaluated for feasibility, not full text 23 articles, missing main concept 113 pieces, unhealthy 11, unsuitable method 20 articles thus, the remaining 14 articles were reviewed. Extraction results of 14 journals were analyzed and summarized based on author, year of publication, purpose, method, setting, findings, and recommendations.

Of the selected studies, 10 performed a retrospective analysis of vital sign data, while two trials and two studies used prospective cohort study design and two productive observational studies. Only twelve studies underwent continuous analysis. One article was evaluated using the EMT, and vital sign measurements were conducted using a tool that was examined using the EWS score. By contrast, those vital signs were subjected to triage analysis in the one remaining study. These investigations were performed in medical facilities, but the study by (Spangler et al., 2019) was conducted in a prehospital setting.

Data extraction from selected literature. The articles obtained were extracted from data in the form of a matrix in Microsoft Word. The domains used in data extraction include the name of the researcher, year, purpose, method, setting, findings, recommendations, and findings, see Table 1.

Table 1. Matrix of analysis in the literature

No	Author Year, Country	Aim	Method	Findings	Recommendation
1	(Kang et al., 2020) Korea	To develop and validate related Artificial Intelligence (AI) algorithms in predicting the critical care needs of patients	The multicenter retrospective cohort study	Compared with conventional triage and EWS assessments, the Artificial Intelligence (AI) algorithm can predict the clinical status needs of critical patients with 95% accuracy utilizing EMS data.	Deep learning algorithms require model development, and the addition of a larger population than in other countries would be great.
2	(Lauritsen, et al., 2020) Denmark	To detect acute critical illnesses and more complex clinical conditions at an early stage.	CROSS-TRACKS retrospective cohort record database	Two models summarize the predictive power of xAI-EWS. The first model is the individual xAI-EWS model, which indicates an elevated probability of developing an acute critical illness. The second population-based xAI-EWS model can forecast more advanced clinical outcomes (sepsis, AKI, ALI).	Other techniques that increase the number of respondents in the database can perform its development with more varied parameters.
3	(Lee et al., 2021) South Korea	To validate DEWS in a large multicenter cohort and compare the predictive performance of IHCA DEWS with MEWS	Retrospective cohort study	MEWS 0.754 has a lower internal AUROC predictive performance than DEWS 0.860. When assessing the incidence of cardiac arrest, DEWS outperforms traditional MEWS in terms of specificity and sensitivity.	To replace other trigger scoring systems in the RS with DEWS in clinical practice, more research and carefully planned prospective clinical trials are required.

				DEWS can predict more cardiac arrest events (30 minutes to 24 hours) and reduce false alarms by nearly ½ of MEWS.	
4	(Soudan et al., 2022) United Arab Emirates	To identify the predictive model that correlates with the patient's vital signs, leading to the most precise predictions for the likelihood of cardiac arrest.	Experimentation	Several trials were conducted by employing six AI algorithms regarding the results of vital signs from 1 hour to 12 hours, the highest result being the Random Forest model more than 80%.	None
5	(Pirneskoski et al., 2020) Finlandia	To compare the accuracy of conventional NEWS prediction performance with Random Forest machine learning using vital signs the addition of glucose parameters	Retrospective registry studies such as this	Machine learning techniques generate better prediction results than EWS and traditional triage. It has been demonstrated that incorporating variables to the EWS that are not part of the TTV parameters—like blood sugar—increases the likelihood of death.	Prospective studies can be employed by future researchers, as more work is required to validate this new risk stratification model. Considering the challenges with generalizability, comparable research in various pre-hospital. Additional research could be performed particularly on diverse populations, on other variables that can be developed in machine learning.
6	(da Silva et al. 2021) Brazil	To predict clinical changes during critical conditions using the calculation of the prognostic index in the hospital utilizing the	Experiments with the deep-signs model	Experiments demonstrate that vital signs with DeepSign incorporation have been applied to predict critically ill patients (accuracy > 80%)	To conduct experiments with the DeepSign model using real data collected from ICU patients, and to compare the results of the DeepSign model with another model that predicts the prognostic index by

		DeepSign algorithm model that associates with the results of vital signs		than a prediction of RS prognostic vital signs index	using deep learning techniques while accounting for previous data.
7	(Kuan-Han et al., 2021) Taiwan	To build a machine learning model that can anticipate the in-hospital death rate of non-traumatic adult patients who arrive at the emergency department during different stages of their stay, and to evaluate the effectiveness of other machine learning models and MEWS in comparison.	A Retrospective observational cohort study	Machine learning can predict the incidence of death in the hospital for 48 hours. MEWS's AUPRC performance fell below 0.1, while the machine learning model's AUPRC was 0.317 in 6 hours and 0.2150 in 168 hours, machine learning can predict hospital mortality more than MEWS in adult non-trauma emergency department patients.	Future research can enhance the effectiveness of other machine learning models to produce better clinical outcomes in emergency department patients.
8	(Rojas et al., 2018) Chicago	To develop machine learning to escalate the accuracy of scores in predicting patients who are readmitted to the ICU.	Observational cohort study	Patients who were readmitted to the ICU had an average time to re-admission of 65 hours, and patients who were readmitted to the ICU had the potential to be longer than those who were not readmitted (3.9 days vs 2.9). With 95% confidence, the machine learning derivative model has the highest AUC for predicting a patient's	The addition of research variables is tremendously essential in machine learning models hence, information is obtained about the reasons for entering the intensive care unit.

				return to the intensive care unit (76%).	
9	(Chiew et al., 2019) Singapore	To assess and contrast the effectiveness of machine learning models versus traditional risk stratification tools such as Rapid Sequence Organ Failure Assessment (qSOFA), National Early Warning Score (NEWS), modified early warning score (MEWS), and Singapore ED Sepsis (SED).	Observational study	The application of the machine learning model could enhance the accuracy of forecasting 30-day in-hospital mortality rates for patients displaying symptoms of sepsis in the emergency department, in comparison to utilizing conventional risk stratification methods.	Future research may employ electronic models to assess whether they are capable of helping predict improved clinical outcomes for patients with sepsis.
10	(Rangan et al., 2022) Israel	To create essential equipment with minimal requirements that can utilize lightweight sensors for quick and easy monitoring, automatic and regular running of a sepsis prediction engine, generation of early warnings, and an increased window of time for preventative therapeutic interventions	Retrospective Study	The results demonstrated that combining only heart rate and temperature predicts sepsis 6 hours earlier with greater accuracy, with an area under the curve of 0.94, sensitivity of 82%, and specificity of 85%. similar to alternative predictors of sepsis.	Future research should be conducted to verify the practicality of Vital-SEP in a clinical setting and evaluate the quality improvement and outcomes. A prospective study should be performed to accomplish this.

11	(Arnold et al., 2019) Amerika Serikat	To compare the predictive capabilities of commercially available AI-based EWS models to those of a doctor's clinical evaluation for detecting deterioration in patients admitted to the general internal medicine ward	Prospective observational study	The The combination of physician and EWS forecasts in a linear regression model produces an AUROC of 0.75, which is higher than the prognostic powers of EWS (p;0.05) and physicians (p;0.016). Regarding the ability of EWS and physicians to predict clinical deterioration in patients admitted to the general medicine ward within 24 hours, there is no discernible difference in performance.	Further research is to understand the differences between these predictions, to incorporate them into a risk prediction model together, and to employ them in clinical practice.
12	(Kia et al., 2020) New York	To compare RF models with Modified The early Warning Score (MEWS) uses sensitivity and specificity.	Cohort study single center retrospective	The study revealed that the mortality rate was 3.4%, and the RF model outperformed other models, achieving a sensitivity of 81.6%, specificity of 75.5%, AUC-ROC of 0.85, and AUC-PR of 0.37. The RF model displayed a 37% increase in sensitivity, an 11% increase in specificity, and a 14% increase in AUC-ROC when compared to the conventional MEWS. Furthermore, the RF model could predict mortality up to six hours in advance of	The future study is expected to generate predictions that are judged by discovering hidden patterns and adding even more data

				the event and identify indicators of clinical deterioration.	
13	(Spangler et al., 2019) Swedia	To authenticate the use of a machine learning-based method for creating risk scores that are following hospital outcomes, using a pre-hospital database.	Prospective cohort study	According to research findings, machine learning offers a viable way to enhance prehospital risk assessment accuracy beyond what currently occurs and beyond rule-based triage algorithms.	Further research is recommended to further investigate whether the inclusion of more regular data additions such as free text notes and delivery center call recordings, enhance the prognostic significance of the findings presented here.
14	(Wu et al., 2022) Cina	To create and authenticate a machine-learning algorithm for the early detection of moderate-to-severe cases of ARDS caused by inhalation.	Retrospective derivation cohort	The impact of predicting moderate to severe acute respiratory distress syndrome (ARDS) caused by inhalation six hours before its onset using the machine learning model in conjunction with the primary characteristics derived from three non-invasive vital sign assessments.	Future research is expected to increase the number of patients by expanding the cause of ARDS such as COVID-19.

This article summarizes the themes contained in the application of Artificial Intelligence (AI) models associated with EWS in determining changes in the clinical condition of patients, including the advantages of implementing AI in EWS compared to conventional (article numbers 1,2,3,4,5,6,7, 10, 12). AI classification, types of AI models related to EWS (article numbers 1,2,3,4,9), and accuracy of AI models in predicting patient Quality of Life (article numbers 1,4,6,8,13,14).

THEME 1: The usefulness of implementing AI in a conventional EWS. Reducing additional clinical damage and more serious complications in critical patients can be achieved by identifying AI-based EWS associated with physician prognosis in determining critical patient conditions and predicting clinical status changes earlier (Arnold et al., 2019; da Silva et al., 2021). Sepsis is a common complication in critically ill patients. By merging AI algorithms with vital sign data, it is possible to predict critical patients by calculating the probability of sepsis within six hours. When compared to traditional triage and EWS studies, the effectiveness of the Artificial Intelligence (AI) algorithm can accurately predict the clinical status needs of critical patients using EMS data (95% (Kang et al., 2020). The AI algorithm model with EWS developed into xAI-EWS is presented.

In summary, two individual-based xAI-EWS models were developed that can predict a high probability of developing an acute critical illness. The second population-based xAI-EWS model can predict clinically advanced (sepsis, AKI, and ALI) (Lauritsen, et al., 2020). AI-based alerts using the DeepLearning model with parameters of vital signs can predict more and faster cardiac arrest events with an accuracy of 80%, thereby reducing the incidence of false alarms in hospitals. Early detection of critical patients using EWS, both modified EWS (MEWS) and national EWS (NEWS), has less than optimal accuracy, increasing code blue calling activities in hospitals (Lee et al., 2021; Soudan et al., 2022). Cardiac arrest incidents will result in a rise in the mortality rate among critically ill patients. For this reason, the development of an AI algorithm related to EWS data combined with laboratory results can be employed in predicting the incidence of death in critical patients (Allen et al., 2020; Kia et al., 2020; Kuan-Han et al., 2021; Pirneskoski et al., 2020).

THEME 2: Types of AI Models Linked to Databased. Based on the anticipated outcomes, different types of algorithms can be employed to learn the mapping function between inputs and outputs. Regression and classification algorithms are two categories into which AI algorithms can be subdivided. The latter generates numerical outputs based on a given set of inputs, whereas the former generates a categorical result that indicates the category to which the input set belongs (Soudan et al., 2022).

Subtheme: Machine Learning (ML) Models. ML models originate from computational learning theory and work by constructing data-driven models through paired sample input/output training (Alam et al., 2019).

Random Forest (RF). Several decision trees are implemented by the Random Forest (RF) algorithm to generate predictions from input data. Among the many benefits of RF are its flexibility and resistance to overfitting. With just one hour's worth of input data, this model has proven to be highly accurate in predicting cardiac arrest events (Pirneskoski et al., 2020; Soudan et al., 2022). ML (machine learning) models can increase user intuition by finding hidden patterns in large data sets (Kia et al., 2020).

Subtheme: Deep Learning Model (DL). A deep learning model is heavily reliant on the amount of data that can be analyzed. The likelihood of attaining ideal outcomes increases with the amount of data available (Kang et al., 2020). DEWS, which incorporates three layers of long-term memory (LSTM) to reflect trends in patient vital signs, can be utilized to clarify the merging of DL with EWS (Lee et al., 2021). DL was developed into DEEPSOFA with the TCN model. The xAI-EWS model was designed as a variation of the convolutional neural network

(CNN) recognized as the Convolutional Network (TCN) score, as a predictive model for acute critical illness. The SOFA score is calculated every time one of the model components is updated with a new measurement (Lauritsen, et al., 2020).

Support Vector Machine (SVM). The most effective hyperplane for classifying new data has been identified using the training set of data. The SVM model's benefit is its capacity to manage non-linear classifications, which are employed in regression and clarification. This method's drawbacks encompass the difficulty of determining which machine learning technique is best for non-linear classification and the requirement for a sizable amount of data.

Naive Bayes (NB). A naive Bayes classifier is a statistical algorithm based on Bayes' Theorem that estimates the probability of an event occurring. A statistical method that calculates the likelihood of an event happening that is based on Bayes' Theorem is known as a naive Bayes classifier. According to the Naive Bayes model, predictor values' impact on a specific classification is independent of other predictor values. The basic idea behind the Naïve Bayes classifier is that each feature generates an equal and independent contribution to the result (Soudan et al., 2022).

K Nearest Neighbor (KNN). The KKN classifier attempts to identify samples that are not identified, and then these elements are included in the part of the data closest to the simple majority data (Zhang et al., 2018). The fundamental concept of the Naïve Bayes classifier is that every feature contributes equally and independently to the outcome

Multi-Layer Perceptron (MLP). To classify input vectors into output vectors, Multi-Layer Perceptron (MLP) is a Neural Networks (NNs) implementation that uses an input layer, a hidden layer, and an output layer (Soudan et al., 2022). However, this device does not develop widely and is rarely employed in attachment AI for EWS.

Convolutional Neural Network (CNN). Convolutional Neural Networks (CNNs) are a subset of Deep Learning (DL) algorithms that were developed specifically to automatically identify and extract relevant features for classification from input elements. It is frequently employed in the analysis of both organized and unorganized data. CNN's capacity to efficiently learn and extract features from massive data sets is one of its primary benefits. This is especially true in the healthcare industry, where CNN is frequently utilized to analyze unstructured medical data and put complex models into practice. CNN requires fewer data analyses than other AI algorithm techniques.

THEME 3: Accuracy of AI in EWS in Predicting patient quality of life. According to the study, the application of AI algorithms for predicting the likelihood of critical patient care is highly effective with a success rate of 0.867 (95% confidence interval). According to the study. Additionally, it can be employed to accurately predict prognosis and treatment (Kang et al., 2020). Critical patients frequently experience life-threatening acute respiratory distress syndrome (ARDS), which affects critical patient morbidity and mortality. The development of AI in predicting early ARDS conditions associated with EWS data can be identified quickly. It predicted the onset of moderate to severe ARDS in critically ill patients using AI algorithms. Who are being induced by inhalation (Wu et al., 2022). It was discovered that the most frequently employed AI algorithm in the medical literature is for disease prediction, specifically for conditions like cancer, disorders of the nervous system, heart problems, and cardiac arrest. The trained partition's AI prediction accuracy was 80%, while the test partition's accuracy was 20%. Within the next sixty minutes, the highest prediction accuracy was attained regarding the emergence of a critical CA. Therefore, it is essential to consistently check high-risk patients' vital signs and enter these values into predictive algorithms. This allows a CA to be predicted up to 60 minutes in advance of its occurrence. Medical personnel will therefore be in a better position to act quickly to prevent this from happening. Only one day of data is needed to produce a sufficiently accurate prediction. Therefore, prediction algorithms can start guiding

medical staff moderately quickly (Soudan et al., 2022). The trial results mentioned above clarify that internal signs that are connected to vital signs can be utilized. The objective is to predict the vital signs with a high degree of accuracy (above 80%) to predict the Prognostic Index before a significant decline in the patient's condition. Because of this, doctors can start treating patients earlier and achieve better results (da Silva et al., 2021).

The Machine learning algorithm model has significantly better performance accuracy with a receiving curve of 0.76 than MEWS with a receiving curve of 0.58, which can be concluded that the treatment of patients who will return to intensive care after being transferred is more accurate than utilizing machine learning than MEWS in indications of transfer patients from the ICU to the inpatient unit (Rojas et al., 2018). Furthermore, compared to the triage algorithms currently in use in hospitals, machine learning can be used to predict a patient's condition before hospital admission, increasing the accuracy of prehospital risk assessment (Spangler et al., 2019).

Based on this scoping review, the application of AI to EWS shows excellent potential. However, several important research areas need to be explored for these models to be effectively implemented in clinical practice. Potential for Improved Prediction Accuracy: Most of the studies in our review utilized a prediction window between 30 minutes to 72 hours before clinical changes occurred. The length of the model prediction window is essential because a prediction window that is too short will not produce real clinical benefits (it will not give the clinical team enough time to intervene) (Pirneskoski et al., 2020). The results of 14 articles indicate that the worsening of a patient's clinical condition to the point of death frequently results in vital signs changing for the worse before the patient becomes critical and cardiac arrest occurs. This allows predicting critical patients by observing vital signs. Research has also illustrated that abnormalities in these vital signs may begin to appear quite a long time, perhaps even hours before worsening occurs. However, health professionals might require assistance to quickly identify these changes in routine observations. Nevertheless, it is possible to create Artificial Intelligence (AI) systems that can identify these irregularities and estimate the probability of a decline in clinical status that could lead to cardiac arrest. According to Shang, (2021), there is a greater prevalence of literature on artificial intelligence (AI) in medicine than there is in nursing literature reviews. Because of this, artificial intelligence (AI) has many applications that are useful for medical professionals, such as nurses and doctors. Although it is widely recognized for its capacity to aid in the diagnosis and interpretation of medical imaging, nurses—who play a crucial role in the healthcare team's decision-making processes—can make use of additional technologies. However, nurses' adoption of these technologies has been slow, as noted by Pepito et al., (2019). For this reason, a more in-depth study is required regarding AI in EWS which is associated with the TTV results performed by nurses.

The implementation of AI in EWS has an enormous amount of promise to increase the precision of patient critical event prediction. This review's numerous studies demonstrate how AI algorithms, like decision trees and neural networks, can generate predictions that are more accurate in real-time. This implies that early warning systems for medical personnel can be more effectively utilized, enabling prompt and effective action (Barton et al., 2019). An AI algorithm with high accuracy in determining cardiac arrest based on the medical records results is Random Fores reaching 81% in 1 hour predicting cardiac arrest and CNN reaching 84% in 12 hours predicting cardiac arrest (Soudan et al., 2022). To predict early clinical changes and prevent additional clinical damage and more serious complications in critical patients, it is crucial that AI-based EWS identification, which employs machine learning algorithms related to the health prognosis of workers, including nurses, determine the condition of critical patients (Arnold et al., 2019; da Silva et al., 2021). The application of AI in EWS can be used to forecast changes in the clinical status of patients in critical condition before more clinical deterioration

and major complications—like sepsis, inhalation-induced ARDS, cardiac arrest, and death—occur. AI algorithms can be applied to help medical professionals identify illnesses and clinical changes in critically ill patients, allowing them to decide what additional interventions are necessary (Kim et al., 2019). Another benefit of using EWS is to help detect physiological abnormalities that cause heart attacks; it is hoped that the ML algorithm model can help reduce this by increasing the detection of patients at risk of heart attack (Rajkomar et al., 2019).

AI has a lot of advantages for the health industry, but because data is limited and subject to change, predictions may be biased. For AI algorithms to generate predictions based on input data, learning models must be used for training. The algorithm being used determines how the training continues. There are two primary categories of AI models: machine learning (ML) and classical AI. While Shallow Learning (SL) and Deep Learning (DL) use nested networks of decision elements to achieve accurate predictions, machine learning (ML) models use deep neural networks to enable decision-making without the need for training pairs (Ongsulee et al., 2018). Deep learning is a machine learning method capable of learning intricate data representations and transforming input data representations into results with a higher level of abstraction (Kapitanova & Son, 2012). Achievement Because the model-building process can eliminate the pre-possessing stage, deep learning techniques are thought to be superior. Deep learning is a type of machine learning that can recognize intricate patterns in data and produce outcomes based only on the data input, without the need for explicit predictors (Rajkomar et al., 2018). The variability in model usage can be attributed to the fact that the predictive performance of models derived solely from historical data is determined by the training dataset (Kong et al., 2016). The analysis of big data can be sampled and integrated with background knowledge employing data processing techniques such as decision trees, random forests, artificial neural networks (ANN), Bayesian networks, and support vector machines (SVM) (Awad et al., 2017).

Retrospective Versus Prospective Evaluation. Since the majority of the research in this review was retrospective, the algorithms' performance in a real-world clinical setting might not be as satisfactory as it would be in a controlled retrospective setting. Furthermore, the degree to which this Early Warning Score (EWS) can detect clinical deterioration that the treatment team has not yet noticed is still being investigated. Even when the risk of deterioration has been accurately identified, doctors frequently disregard warnings about potential clinical deterioration, particularly when they are fatigued. In two case studies, prospective research on artificial intelligence (AI)-based EWS (Arnold et al., 2019) discovered that the use of random forest classifiers in EWS predicted clinical worsening by 75% compared to predictions by physicians 70% Linear regression models combining physician and EWS predictions possessed an AUROC of 0.75, outperforming physicians (p=0.016) and EWS (p=0.05). Machine learning-based risk scores outperform widely used rule-based triage algorithms and human prioritization decisions in predicting outcomes (Spangler et al., 2019). The results are also similar to those identified by (Pirneskoski et al., 2019) who invented machine learning a value of 84% for the NEWS score in predicting 1-day mortality. Even though the machine learning models presented in the Spangler, 2019 study performed well in prospective validation, they might need to enhance their generalization when utilized in other contexts. If the model is directly applied in other settings, such as a hospital, hospital admissions and guidelines for intensive care may differ, which could lead to biased outcome predictions. These kinds of anomalies are probably also in the predictor variables.

Standardization of Performance Metrics. The primary finding of this review is that the research community does not have generally accepted guidelines for disclosing measurements of performance from different studies. When this happens, it becomes difficult to compare study results meaningfully and, if there is overlap, it is unclear if the most clinically relevant

metrics were selected. The majority of the research included in this review report employ Area Under the Receiver Operating Curve (AUROC) as the main performance metric, which is typical of the literature on artificial intelligence.

Strengths of the Review. Although the search strategy was extensive, it only partially addressed particular clinical outcomes, the frequency of sampling, or the screening schedule. The inclusion criteria in this review supported the examination of findings from studies conducted in a variety of clinical settings, including emergency care units and specialist units or wards. This made it possible to identify as many studies as possible examining the use of AI models and vital signs to predict the risk of patient deterioration. This contributes to defining the application of AI-driven prediction models across various patient care contexts with diverse clinical outcomes. Weighted aggregation was employed to compare the artificial intelligence (AI) model's performance with the Early Warning Score (EWS) in cases where the first study's data was available. It indicates the degree to which the accuracy of the models differs in predicting clinical deterioration. the application of AI in EWS is to corroborate detecting physiological abnormalities that cause heart attacks; It is hoped that the AI algorithm in the ML model can help reduce this by enhancing the detection of patients who are at risk of having a heart (Rajkomar et al., 2019). When the evaluation process can assist in analyzing Vital Signs (TTV) results to support decision-making in critical nursing diagnoses and gather crucial patient data efficiently and precisely in critical patient care, artificial intelligence (AI) is used in critical nursing services. Artificial intelligence (AI) is one of the latest technological developments in the healthcare industry and provides new opportunities for providers. Numerous advantages and opportunities are generated by AI integration, such as faster disease prognosis, better disease treatment, enhanced patient participation, and engagement, decreased medical errors and better service quality, reduced medical costs and operational efficiency, and higher productivity for better and maximum outcomes (Lee & Yoon, 2021)

The Limitations is it is essential to acknowledge the various limitations of the review's findings. Initially, a single author managed every step of the process, including the literature search, full-text article feasibility assessment, review inclusion and research data extraction. Second, because studies with positive results are more likely to be published, the results of this review may be influenced by publication bias, as only published studies are included. Third, even though this review included studies from a variety of backgrounds, the heterogeneity in patient populations, clinical practices, and research methodologies among the studies may limit the ability to generalize findings. The definition of clinical outcomes was based on different criteria or using EWS with different aggregate weights, and the sampling procedure and frequency varied between studies, ranging from one-time observations to repeated observations of patients' vital signs. Finally, differences in the Artificial Intelligence (AI) employed in these studies may also result in variations in prediction time windows and other parameters.

4. CONCLUSION

Through a scoping review approach, this study resulted in the application of AI to the Early Warning Score (EWS) system in hospitals that can be employed to enhance the accuracy of predicting changes in patients in critical condition, including cardiac arrest, sepsis, inhalation-induced ARDS events until the patient dies. Because AI models perform better and achieve high accuracy, they are frequently utilized in deep learning and machine learning applications. To achieve the best outcomes, more research must be employed on the application of AI with EWS in critical care patients. This research should include the addition of pain scales and laboratory result parameters to enhance prediction accuracy.

ACKNOWLEDGMENTS
Thank you for the scholarship fund support that has been provided by BKD East Kalimantan 2023.

REFERENCES

Abbott, T. E. F., Cron, N., Vaid, N., Ip, D., Torrance, H. D. T., & Emmanuel, J. (2018). Pre-hospital National Early Warning Score (NEWS) is associated with in-hospital mortality and critical care unit admission: A cohort study. *Annals of Medicine and Surgery*, *27*(December 2017), 17–21. https://doi.org/10.1016/j.amsu.2018.01.006

Alam, M. Z., Rahman, M. S., & Rahman, M. S. (2019). A Random Forest based predictor for medical data classification using feature ranking. *Informatics in Medicine Unlocked*, *15*(January), 100180. https://doi.org/10.1016/j.imu.2019.100180

Allen, A., Mataraso, S., Siefkas, A., Burdick, H., Braden, G., Dellinger, R. P., McCoy, A., Pellegrini, E., Hoffman, J., Green-Saxena, A., Barnes, G., Calvert, J., & Das, R. (2020). A Racially Unbiased, Machine Learning Approach to Prediction of Mortality: Algorithm Development Study. *JMIR Public Health and Surveillance*, *6*(4), e22400. https://doi.org/10.2196/22400

Arksey, H., & O'Malley, L. (2005). Scoping studies: towards a methodological framework. *International Journal of Social Research Methodology*, *8*(1), 19–32. https://doi.org/10.1080/1364557032000119616

Armstrong, R., Hall, B. J., Doyle, J., & Waters, E. (2011). "Scoping the scope" of a cochrane review. *Journal of Public Health*, *33*(1), 147–150. https://doi.org/10.1093/pubmed/fdr015

Arnold, J., Davis, A., Fischhoff, B., Yecies, E., Grace, J., Klobuka, A., Mohan, D., & Hanmer, J. (2019). Comparing the predictive ability of a commercial artificial intelligence early warning system with physician judgement for clinical deterioration in hospitalised general internal medicine patients: a prospective observational study. *BMJ Open*, *9*(10), e032187. https://doi.org/10.1136/bmjopen-2019-032187

Awad, A., Bader-El-Den, M., McNicholas, J., & Briggs, J. (2017). Early hospital mortality prediction of intensive care unit patients using an ensemble learning approach. *International Journal of Medical Informatics*, *108*, 185–195. https://doi.org/10.1016/j.ijmedinf.2017.10.002

Barton, C., Chettipally, U., Zhou, Y., Jiang, Z., Lynn-Palevsky, A., Le, S., Calvert, J., & Das, R. (2019). Evaluation of a machine learning algorithm for up to 48-hour advance prediction of sepsis using six vital signs. *Computers in Biology and Medicine*, *109*, 79–84. https://doi.org/10.1016/j.compbiomed.2019.04.027

Chiew, C. J., Liu, N., Tagami, T., Wong, T. H., Koh, Z. X., & Ong, M. E. H. (2019). Heart rate variability based machine learning models for risk prediction of suspected sepsis patients in the emergency department. *Medicine*, *98*(6), e14197. https://doi.org/10.1097/MD.0000000000014197

da Silva, D. B., Schmidt, D., da Costa, C. A., da Rosa Righi, R., & Eskofier, B. (2021). DeepSigns: A predictive model based on Deep Learning for the early detection of patient health deterioration. *Expert Systems with Applications*, *165*, 113905. https://doi.org/10.1016/j.eswa.2020.113905

Dziadzko, M. A., Novotny, P. J., Sloan, J., Gajic, O., Herasevich, V., Mirhaji, P., Wu, Y., & Gong, M. N. (2018). Multicenter derivation and validation of an early warning score for acute respiratory failure or death in the hospital. *Critical Care*, *22*(1), 1–12. https://doi.org/10.1186/s13054-018-2194-7

Kang, D.-Y., Cho, K.-J., Kwon, O., Kwon, J.-M., Jeon, K.-H., Park, H., Lee, Y., Park, J., &

Oh, B.-H. (2020). Artificial intelligence algorithm to predict the need for critical care in prehospital emergency medical services. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine*, *28*(1), 17. https://doi.org/10.1186/s13049-020-0713-4

Kapitanova, K., & Son, S. H. (2012). Machine learning basics. In *Intelligent Sensor Networks: The Integration of Sensor Networks, Signal Processing and Machine Learning*. CRC Press. https://doi.org/10.1201/b14300

Kia, A., Timsina, P., Joshi, H. N., Klang, E., Gupta, R. R., Freeman, R. M., ... & Levin, M. A. (2020). MEWS++: enhancing the prediction of clinical deterioration in admitted patients through a machine learning model. *Journal of clinical medicine*, *9*(2), 343. https://doi.org/10.3390/jcm9020343

Kim, S. Y., Kim, S., Cho, J., Kim, Y. S., Sol, I. S., Sung, Y., Cho, I., Park, M., Jang, H., Kim, Y. H., Kim, K. W., & Sohn, M. H. (2019). A deep learning model for real-time mortality prediction in critically ill children. *Critical Care*, *23*, 279. https://doi.org/10.1186/s13054-019-2561-z

Kong, G., Xu, D.-L., Yang, J.-B., Yin, X., Wang, T., Jiang, B., & Hu, Y. (2016). Belief rule-based inference for predicting trauma outcome. *Knowledge-Based Systems*, *95*, 35–44. https://doi.org/10.1016/j.knosys.2015.12.002

Kuan-Han, W., Fu-Jen, C., Hsiang-Ling, T., Jui-Cheng, W., Yii-Ting, H., Chih-Min, S., & Yun-Nan, C. (2021). Predicting in-hospital mortality in adult non-traumatic emergency department patients: A retrospective comparison of the modified early warning score (MEWS) and machine learning approach. *PeerJ*, *9*(11988), 14. https://doi.org/10.7717/peerj.11988

Lauritsen, S. M., Kristensen, M., Olsen, M. V., Larsen, M. S., Jørgensen, M. J., Lange, J., & Thiesson, B. (2020). Explainable artificial intelligence model to predict acute critical illness from electronic health records. *Nature Communications*, *2020*, 1–11. https://doi.org/10.1038/s41467-020-17431-x

Lauritsen, S. M., Kristensen, M., Olsen, M. V, Larsen, M. S., Lauritsen, K. M., Jørgensen, M. J., Lange, J., & Thiesson, B. (2020). Explainable artificial intelligence model to predict acute critical illness from electronic health records. *Nature Communications*, *11*(1), , 3852. https://doi.org/10.1038/s41467-020-17431-x

Lee, D. H., Yetisgen, M., Vanderwende, L., & Horvitz, E. (2020). Predicting severe clinical events by learning about life-saving actions and outcomes using distant supervision. *Journal of Biomedical Informatics*, *107*, 103425. https://doi.org/10.1016/j.jbi.2020.103425

Lee, Y. J., Cho, K.-J., Kwon, O., Park, H., Lee, Y., Kwon, J.-M., Park, J., Kim, J. S., Lee, M.-J., Kim, A. J., Ko, R.-E., Jeon, K., & Jo, Y. H. (2021). A multicentre validation study of the deep learning-based early warning score for predicting in-hospital cardiac arrest in patients admitted to general wards. *Resuscitation*, *163*, 78–85. https://doi.org/10.1016/j.resuscitation.2021.04.013

Lee, D., & Yoon, S. N. (2021). Application of artificial intelligence-based technologies in the healthcare industry: Opportunities and challenges. *International Journal of Environmental Research and Public Health*, 18(1), 271. https://doi.org/10.3390/ijerph18010271

Lei, Y. (2017). 3 - Individual intelligent method-based fault diagnosis. In Y. Lei (Ed.), *Intelligent Fault Diagnosis and Remaining Useful Life Prediction of Rotating Machinery* (pp. 67–174). Butterworth-Heinemann. https://doi.org/10.1016/B978-0-12-811534-3.00003-2

McGowan, J., Straus, S., Moher, D., Langlois, E. V, O'Brien, K. K., Horsley, T., Aldcroft, A., Zarin, W., Garitty, C. M., Hempel, S., Lillie, E., Tunçalp, Özge, & Tricco, A. C. (2020).

Reporting scoping reviews-PRISMA ScR extension. *Journal of Clinical Epidemiology*, *123*, 177–179. https://doi.org/10.1016/j.jclinepi.2020.03.016

Nielsen, P. B., Langkjær, C. S., Schultz, M., Kodal, A. M., Pedersen, N. E., Petersen, J. A., Lange, T., Arvig, M. D., Meyhoff, C. S., Bestle, M. H., Hølge-Hazelton, B., Bunkenborg, G., Lippert, A., Andersen, O., Rasmussen, L. S., & Iversen, K. K. (2022). Clinical assessment as a part of an early warning score—a Danish cluster-randomised, multicentre study of an individual early warning score. *The Lancet Digital Health*, *4*(7), e497–e506. https://doi.org/10.1016/S2589-7500(22)00067-X

Ongsulee, P., Chotchaung, V., Bamrungsi, E., & Rodcheewit, T. (2018). Big Data, Predictive Analytics and Machine Learning. *2018 16th International Conference on ICT and Knowledge Engineering (ICT&KE)*, 1–6. https://doi.org/10.1109/ICTKE.2018.8612393

Pepito, J. A., C. Locsin, R., & Constantino, R. E. (2019). Caring for Older Persons in a Technologically Advanced Nursing Future. *Health*, *11*(05), 439–463. https://doi.org/10.4236/health.2019.115039

Pirneskoski, J., Tamminen, J., Kallonen, A., Nurmi, J., Kuisma, M., Olkkola, K. T., & Hoppu, S. (2020). Random forest machine learning method outperforms prehospital National Early Warning Score for predicting one-day mortality: A retrospective study. *Resuscitation Plus*, *4*(October), 100046. https://doi.org/10.1016/j.resplu.2020.100046

Rajkomar, A., Dean, J., & Kohane, I. (2019). Machine Learning in Medicine. *New England Journal of Medicine*, *380*(14), 1347–1358. https://doi.org/10.1056/NEJMra1814259

Rajkomar, A., Oren, E., Chen, K., Dai, A. M., Hajaj, N., Hardt, M., ... & Dean, J. (2018). Scalable and accurate deep learning with electronic health records. *NPJ digital medicine*, *1*(1), 18. https://doi.org/10.1038/s41746-018-0029-1

Rangan, E. S., Pathinarupothi, R. K., Anand, K. J. S., & Snyder, M. P. (2022). Performance effectiveness of vital parameter combinations for early warning of sepsis-an exhaustive study using machine learning. *JAMIA Open*, *5*(4), ooac080. https://doi.org/10.1093/jamiaopen/ooac080

Rojas, J. C., Carey, K. A., Edelson, D. P., Venable, L. R., Howell, M. D., & Churpek, M. M. (2018). Predicting Intensive Care Unit Readmission with Machine Learning Using Electronic Health Record Data. *Annals of the American Thoracic Society*, *15*(7), 846–853. https://doi.org/10.1513/AnnalsATS.201710-787OC

Romero-Brufau, S., Whitford, D., Johnson, M. G., Hickman, J., Morlan, B. W., Therneau, T., Naessens, J., & Huddleston, J. M. (2021). Using machine learning to improve the accuracy of patient deterioration predictions: Mayo Clinic Early Warning Score (MC-EWS). *Journal of the American Medical Informatics Association*, *28*(6), 1207–1215. https://doi.org/10.1093/jamia/ocaa347

Royal College of Physicians. (2017). National Early Warning Score (NEWS) 2 Standardising the assessment of acute-illness severity in the NHS. *Updated report of a working party*. Royal College of Physicians.

Royal College of Physicians. (2019). *Resources to support the adoption of the National Early Warning Score*. Royal College of Physucians.

Shang, Z. (2021). A Concept Analysis on the Use of Artificial Intelligence in Nursing. *Cureus*, *13*(5). https://doi.org/10.7759/cureus.14857

Shickel, B., Loftus, T. J., Adhikari, L., Ozrazgat-Baslanti, T., Bihorac, A., & Rashidi, P. (2019). DeepSOFA: A Continuous Acuity Score for Critically Ill Patients using Clinically Interpretable Deep Learning. *Scientific Reports*, *9*(1), 1–12. https://doi.org/10.1038/s41598-019-38491-0

Smith, G. B., Prytherch, D. R., Schmidt, P. E., & Featherstone, P. I. (2008). Review and performance evaluation of aggregate weighted 'track and trigger' systems. *Resuscitation*,

77(2), 170–179. https://doi.org/10.1016/j.resuscitation.2007.12.004

Soudan, B., Dandachi, F. F., & Nassif, A. B. (2022). Smart Health Attempting cardiac arrest prediction using artificial intelligence on vital signs from Electronic Health Records. *Smart Health*, *25*(October 2021), 100294. https://doi.org/10.1016/j.smhl.2022.100294

Spangler, D., Hermansson, T., Smekal, D., & Blomberg, H. (2019). A validation of machine learning-based risk scores in the prehospital setting. *PLoS ONE*, *14*(12), 1–18. https://doi.org/10.1371/journal.pone.0226518

Tang, K. J. W., Ang, C. K. E., Constantinides, T., Rajinikanth, V., Acharya, U. R., & Cheong, K. H. (2021). Artificial Intelligence and Machine Learning in Emergency Medicine. *Biocybernetics and Biomedical Engineering*, *41*(1), 156–172. https://doi.org/10.1016/j.bbe.2020.12.002

Wu, J., Liu, C., Xie, L., Li, X., Xiao, K., Xie, G., & Xie, F. (2022). Early prediction of moderate-to-severe condition of inhalation-induced acute respiratory distress syndrome via interpretable machine learning. *BMC Pulmonary Medicine*, *22*(1), 1–9. https://doi.org/10.1186/s12890-022-01963-7

Zhang, S., Li, X., Zong, M., Zhu, X., & Wang, R. (2018). Efficient KNN Classification with Different Numbers of Nearest Neighbors. *IEEE Transactions on Neural Networks and Learning Systems*, *29*(5), 1774–1785. https://doi.org/10.1109/TNNLS.2017.2673241

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 671-680
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1244*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

Evaluating the Usability of the AKUDia Mobile App for Blood Sugar Monitoring: A Feasibility Study

Siti Badriah[1a*], Yanyan Bahtiar[1b], Henri Setiawan[2c]

[1] Department of Nursing, Poltekkes Kemenkes Tasikmalaya, Tasikmalaya, West Java, Indonesia
[2] Department of Nursing, STIKes Muhammadiyah Ciamis, Ciamis, West Java, Indonesia

[a] Email address: siti.badriah@dosen.poltekkestasikmalaya.ac.id
[b] Email address: yanyan.bahtiar@dosen.poltekkestasikmalaya.ac.id
[c] Email address: henrisetiawan1989@gmail.com

Received: 27 June 2023 Revised: 18 October 2023 Accepted: 8 December 2023

Abstract

A variety of ultra-invasive portable blood sugar test kits have been available on the market; these kits require drawing blood from capillaries, which can still be painful and uncomfortable and even enhance the risk of infection. To develop a non-invasive blood sugar meter that is painless and comfortable to use, innovation is required. AKUDia, a mobile application for monitoring blood sugar, was developed as a smart wearable device to help older adults with diabetes stay healthy. This study aimed to measure the usability of the AKUDia application using a usage questionnaire. In terms of a feasibility study, this was quantitative. USE Questionnaire contains a list of questions encompassing 30 questions divided into four dimensions: Usefulness, Ease to use, Ease of learning, and Satisfaction. 50 respondents were recruited for this study, meeting the inclusion criteria of DM patients who had completed a week-long training program on using the AKUDia application. Samples were selected by simple random sampling, and descriptive and univariate data analyses were performed. The AKUDia feasibility test results demonstrated a usability value of 83%, which was classified as very feasible; an ease of use value of 74 percent, which was classified as feasible; an ease of learning value of 83%, which was classified as very feasible; and a satisfaction aspect of 71% at the feasible level. The average usability value of the four categories (usability, ease of use, ease of learning, and satisfaction), which was obtained at 78 percent, indicates that the AKUDia application's usability is at a practicable level. The usability of the AKUDia application is feasible. Governments should support the use and implementation of this innovation in addition to healthcare professionals like doctors and nurses. Information technology systems have the potential to serve as an instrument for illness prevention, treatment, and rehabilitation in addition to promoting health. Future studies should be enhanced to investigate, through experimental research, how the AKUDia application supports nursing care and health management for individuals with diabetes mellitus and the general population.

Keywords: AKUDia, Diabetes Mellitus, Mobile Application, Usability.

Corresponding Author:

Siti Badriah
Department of Nursing, Poltekkes Kemenkes Tasikmalaya, Tasikmalaya, West Java, Indonesia
Email: siti.badriah@dosen.poltekkestasikmalaya.ac.id

1. INTRODUCTION

The prevalence of diabetes mellitus (DM), a chronic illness, is rising (Pannu et al., 2022). Globally, the number of people with diabetes mellitus aged 20 to 79 years increased from 151 million (4.6%) in 2000 to 537 million (10.5%) in 2021. It is projected that this trend will continue, with 637 million (11.3%) expected in 2030 and 783 million (12.2%) anticipated in 2045 (Mehra et al., 2023). Recently, DM affects over 16 million people in Indonesia, accounting for 33% of the nation's health spending (Badriah, Bahtiar, & Andang, 2022). Several initiatives have been contributed in place by the government, such as the Healthy Community Movement, which aims to prevent and promote disease by encouraging regular health screenings, increased physical activity, and the five pillars of diabetes management: meal planning, physiotherapy, activity, medication administration, and blood sugar monitoring (Setiawan et al., 2021).

Comprehensive government programs have not had the best effect on reducing cases of diabetes, according to the findings of Basic Health Research, which showed that the prevalence of diabetes increased significantly in Indonesia from 6.9 percent in 2013 to 8.5 percent in 2018, and cases in West Java DM increased from 1.3 percent to 1.7 percent (Ariyanto, et al., 2021). Cipto National Referral Hospital Mangunkusmo Hospital in Indonesia reports that the condition has complications in addition to its increasing prevalence. These complications encompass 33.40 percent diabetic retinopathy, 34 percent neuropathy, 1.3 percent amputations, 13.3 percent heart disease (including angina, MCI, and heart failure), 5.3 percent stroke, and 10.9 percent peripheral arterial disease (Kementerian Kesehatan Republik Indonesia, 2017).

Many precautions have been taken to avoid complications, which comprises monitoring blood sugar levels, which serve as crucial indicators of blood sugar control, and controlling diabetes mellitus (DM). They haven't exactly been very successful thus far, nevertheless, as evidenced by the low behavior for DM prevention and the continuing increasing DM prevalence. Residents of Tasikmalaya City report having a sweet tooth in 55.77 percent of cases, and 53.59 percent report consuming sweets more than once a day. 30.07 percent smoke, 43.89 percent participate in less physical activity, and 62.23 percent of people regularly eat fatty foods. All these figures are higher than the national average (Badan Penelitian dan Pengembangan Kesehatan Kemenkes Republik Indonesia, 2019). Due to the condition of the elderly, the majority of whom have diminished physical abilities, phenomena in society demonstrate that families who care for older adults with diabetes desire to avoid visiting primary healthcare facilities for their safety and comfort (Badriah et al., 2019).

Since family empowerment has been identified in other studies to be effective in enhancing family behavior and support in controlling blood sugar levels, it is hoped that a non-invasive blood sugar level check tool can be used at home under family supervision (Badriah et al., 2021). A plethora of highly intrusive portable blood sugar test kits have arrived on the market; these kits take blood samples from capillaries, which are still painful and uncomfortable and may potentially pose a risk for infection (Abidin et al., 2015). Even with disposable strips, they remain expensive (Bruen et al., 2017; Prawiroredjo & Julian, 2019). Thus, the development of a non-invasive blood sugar meter—a convenient and painless device for monitoring blood sugar levels—is imperative. Previous studies have established the sensitivity level of NIR LEDs at the fingertips. Due to its highest correlation score for the sensitivity of the non-invasive NIR LED blood sugar sensor, the thumb was selected (Badriah et al., 2022). The next step requires developing a smart wearable device that can access blood sugar levels in real-time in order to monitor and detect blood sugar levels.

Currently, on the market, various smartwatches have the function of detecting health conditions in the form of heart rate, body temperature, and even Body Mass Index (BMI), encompassing the watch (Apple Inc., 2021), Fitbit (Fitbit, 2019), and Galaxy watch (Samsung,

2019). Because of its closed operating system, the smartwatch is unable to optimize the data on board. The project will develop a wearable smart device called AKUDia, a mobile application for monitoring blood sugar, to help older adults with diabetes maintain their health. The usefulness of AKUDia must first be assessed using a use questionnaire to ascertain whether the program is beneficial, simple to use, easy to learn, and provides user satisfaction.

The AKUDia application can monitor the blood sugar levels of diabetics in real-time using data from non-invasive blood sugar tests employing NIR LED sensors that are connected to a smartwatch. This is the way this study differs from the previous one. Interested parties, involving medical professionals (physicians, nurses, dietitians, and pharmacists), as well as families, may examine these results at any time and from any location using smartphones. As of right now, the products available only display blood sugar test results on the Smart Watch; other people cannot access the results in real-time via their smartphones. This study aimed to measure the usability of the AKUDia application using a usage questionnaire.

2. RESEARCH METHOD

This study employed a quantitative descriptive design to examine the usability level of is AKUDia Application. The AKUDia application is a system administered to compile the results of evaluating blood sugar levels from a blood sugar measuring sensor. Figure 1 illustrates the AKUDia application.

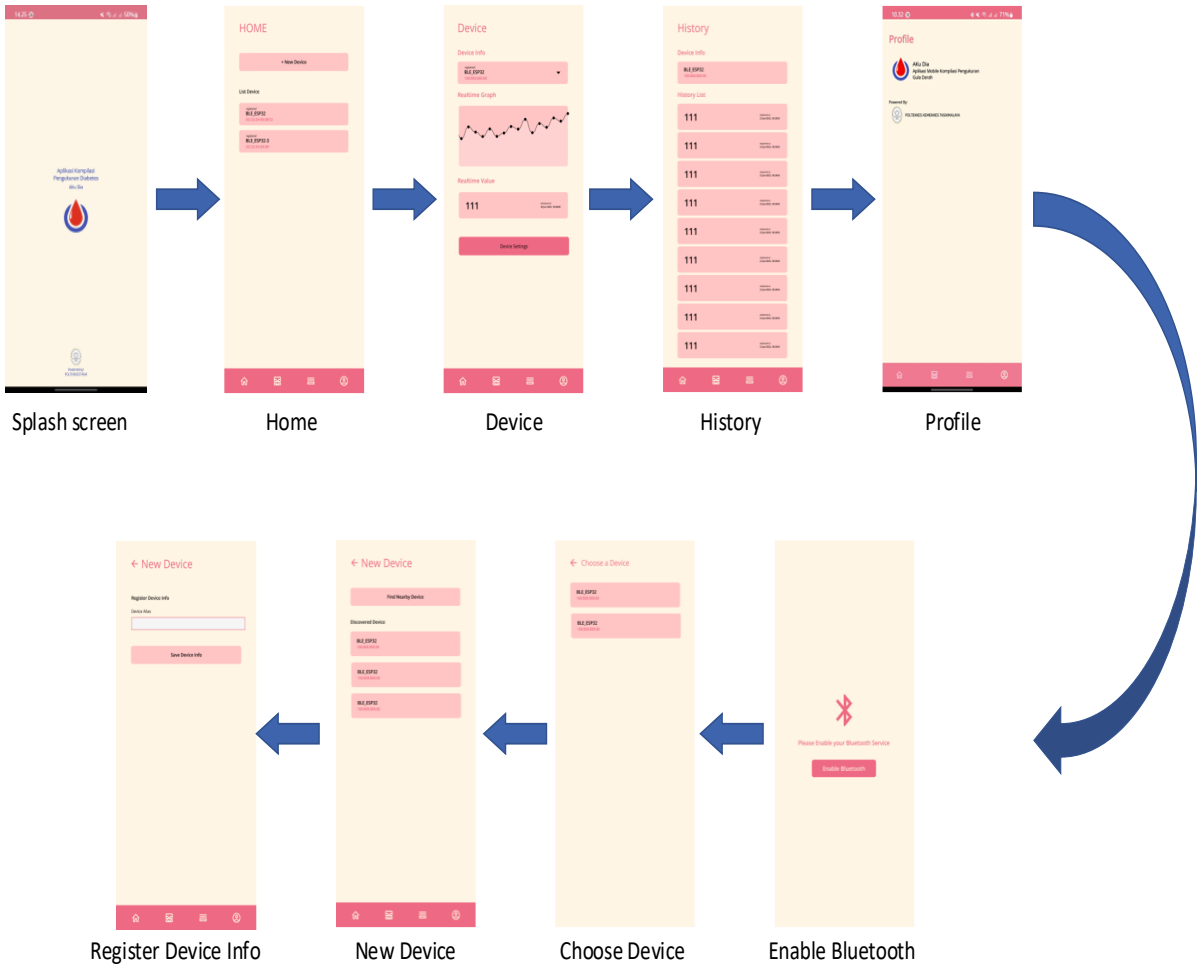


Figure 1. AKUDia Application Design.

The Kahuripan Primary Health Center in Tasikmalaya's diabetic population was the study's subject. The sample size determined by the Slovin formula for population 49 and e, or 10% sampling error, ranged from 29 to 36 samples. With the inclusion criteria of DM patients who had received one week of instruction on using the AKUDia application, a sample of fifty respondents was obtained for this study. To select participants for the study from the entire population and calculate the number of respondents, a straightforward random sampling technique was employed.

A questionnaire that was employed to evaluate the AKUDia application's usability served as the study's instrument. The study's questionnaire adopted the use question set. The questionnaire with 30 statements compensates for usability, ease of use, learning curve, and satisfaction (Setiawan, et al., 2022). To adapt the editor to the particular application being tested, the questions were translated into Indonesian (Lund, 2001). When the Pearson product-moment test was implemented to evaluate the validity of the questionnaire, the results ranged from 0.366 to 0.682. When the Cronbach Alpha coefficient was applied to test for reliability, the results were 0.837. A list of questions categorized based on elements of application usability measurements comprises the questionnaire, as Table 1 illustrates. Filling out the questionnaire involved using a Likert scale with five affirmative questions ranging from strongly disagree to agree strongly. With the Likert scale (1=Strongly Agree to 5=Strongly Disagree), each respondent had an opportunity to complete all of the questionnaire's questions.

Table 1. Use a Questionnaire with a Usability Aspect.

No	Statement
	Usefulness
1.	AKUDia helps me AKUDia helps me be more effective.
2.	AKUDia aids in my increased productivity.
3.	AKUDia is practicalIt's simple to use AKUDia.
4	AKUDia gives me more control over my health.
5.	AKUDia makes it simpler for me to complete the things I want to.
6.	AKUDia is suitable for me.
7.	AKUDia exceeds my expectations in every way.
8.	AKUDia performs all of the functions I would anticipate.
	Ease to Use
9	AKUDia is simple to use.
10	Using AKUDia is easy.
11.	AKUDia is easy to use.
12	My goals for AKUDia can be achieved in the fewest possible steps.
13	AKUDia is able to modify.
14	AKUDia is adaptable and simple to use.
15	I don't need written instructions to use AKUDia
16	To my knowledge, AKUDia is not inconsistent in any manner.
17	AKUDia would be fun for both infrequent and frequent users.
18	When I make mistakes, I can quickly and easily fix AKUDia.
19	Every time I use AKUDia, I am successful.
	Ease of Learning
20	I quickly mastered the use of AKUDia.
21	I recall using AKUDia quickly.
22	Utilizing AKUDia is simple to learn.
23	I mastered AKUDia very quickly.

	Satisfaction
24	I am pleased with AKUDia
25	I would suggest AKUDia to a friend.
26	AKUDia is enjoyable to use
27	AKUDia fulfills my needs in terms of functionality.
28	AKUDia is amazing.
29	I think I have to have AKUDia.
30	AKUDia is a pleasure to use.

The data was collected in November 2022. To ensure that the questionnaire was completed and input into the computer, data screening was done. As a result, all questionnaires had been submitted and no participants pulled out of the study. Under approval number KP-KEPK/0170/2022, the Tasikmalaya Indonesia Ministry of Health Poltekkes Ethics Committee approved the study, which also complies with all applicable ethical standards. This study has implemented the necessary ethical principles, which include providing respondents with adequate free time, maintaining respondents' confidentiality, informing them of the purpose of the study having them sign consent forms, and creating an environment that is as comfortable as possible for data collection.

The AKUDia application's usability was evaluated through descriptive data analysis. The four usability parameters of usability, ease of use, learning, and satisfaction were analyzed by calculating the percentage of respondents who completed the questionnaire. The following formula is used to determine the results of usability measurements: The following formula can be employed to determine the eligibility percentage (%): (score observed) / (score anticipated) = 100. The usability was classified as follows based on how many percentages were interpreted: very bad (<21%), bad (21-40%), enough (41-60%), feasible (61-80%), and very feasible (>80%).

3. RESULTS AND DISCUSSION

The majority of the respondents were female, of legal age, and had completed their high school education, according to Table 2's analysis of their details. The responses provided by participants utilizing the use questionnaire and the AKUDia application are presented in Table 3.

Table 2. Respondent characteristics (n = 30).

Variable	Frequency	Percentage (%)
Gender		
Male	10	33
Female	20	67
Education		
Elementary – Junior High School	8	27
Senior High School	19	63
College/University	3	10
Age		
Adult	23	77
Elderly	7	23

Table 3. The Results of Respondents' Answers.

No	Statement	Likert Scale Assessment					Score
		SDA	DA	UD	A	SA	
1	AKUDia helps me be more effective.	0	0	13	25	12	
2	AKUDia aids in my increased productivity	0	1	15	23	11	
3	AKUDia is practicalIt's simple to use	0	0	11	24	15	
4	AKUDia gives me more control over my health	0	0	0	31	19	
5	AKUDia makes it simpler for me to complete the things I want to	0	0	1	19	30	
6	AKUDia is suitable for me	0	0	7	18	25	
7	AKUDia exceeds my expectations in every way.	0	1	12	32	5	
8	AKUDia performs all of the functions I would anticipate.	0	1	13	25	11	
	Usefulness	0	3	72	197	128	400
9	AKUDia is simple to use.	0	0	0	26	24	
10	Using AKUDia is easy.	0	0	1	23	26	
11	AKUDia is easy to use.	0	0	3	26	21	
12	My goals for AKUDia can be achieved in the fewest possible steps.	0	0	0	21	29	
13	AKUDia is able to modify.	5	10	24	8	3	
14	AKUDia is adaptable and simple to use	0	0	12	24	14	
15	I don't need written instructions to use AKUDia	8	12	18	8	4	
16	To my knowledge, AKUDia is not inconsistent in any manner.	0	0	14	24	12	
17	AKUDia would be fun for both infrequent and frequent users.	0	1	21	23	5	
18	When I make mistakes, I can quickly and easily fix AKUDia.	13	15	18	4	0	
19	Every time I use AKUDia, I am successful.	1	13	18	11	7	
	Ease of Use	27	51	129	198	145	550
20	I quickly mastered the use of AKUDia	0	0	18	17	15	
21	I recall using AKUDia quickly	0	0	15	18	17	
22	Utilizing AKUDia is simple to learn	0	0	1	25	24	
23	I mastered AKUDia very quickly	0	0	12	15	23	
	Ease of Learning	0	0	46	75	79	200
24	I am pleased with AKUDia	0	0	12	14	24	
25	I would suggest AKUDia to a friend	0	0	24	26	0	
26	It is fun to use AKUDia	0	12	16	21	1	
27	AKUDia fulfills my needs in terms of functionality.	0	15	18	16	1	
28	AKUDia is amazing.	0	0	23	21	6	
29	I think I have to have AKUDia.	0	0	25	21	4	

30	AKUDia is a pleasure to use.	0	0	24	20	6	
	Satisfaction	0	27	142	139	42	350
	Total Observation Score	27	81	389	609	394	1500

Using formula 1, the following outcomes were obtained for each aspect to determine a usability presentation value on the usefulness dimension based on data in Table 3:

a. Score for the aspect of Usefulness

$$\text{Usefulness (\%)} = \frac{(0x1)+(3 x 2)+(72 x 3)+(192x4)+(128x5)}{5 x 50 x8} x100\%$$
$$= \frac{1650}{2000} x100\%$$
$$= 83\%$$

The eight questions that encompass the usefulness component had an eligibility rate of 83 percent. Table 3 demonstrates that the AKUDia application has ratings in the feasibility category ranging from 81 to 100, indicating that it is very viable to be applied by individuals with diabetes.

b. Score for the aspect of ease of use

$$\text{Ease of Use (\%)} = \frac{(27x1)+(51 x 2)+(129 x 3)+(198x4)+(145x5)}{5 x 50 x11} x100\%$$
$$= \frac{2033}{2750} x100\%$$
$$= 74\%$$

The section on ease of use consisted of eleven questions. It fulfilled 74% of the requirements for eligibility. Based on the eligibility category within the 61-80 scale and the ease of use experienced by users, diabetics can use the AKUDia application.

c. Score for the aspect of ease of learning

$$\text{Ease of Learning (\%)} = \frac{(0x1)+(0 x 2)+(46 x 3)+(75x4)+(79x5)}{5 x 50 x4} x100\%$$
$$= \frac{833}{1000} x100\%$$
$$= 83\%$$

The Ease of Learning section was comprised of four questions. It fulfilled 83% of the requirements for eligibility. The AKUDia application, which rates between 81 and 100 on a scale, is fairly practical for diabetics to use from the perspective of application simplicity of learning.

d. Score for the aspect of satisfaction

$$\text{Satisfaction (\%)} = \frac{(0x1)+(27 x 2)+(142 x 3)+(139x4)+(42x5)}{5 x 50 x7} x100\%$$
$$= \frac{1246}{1750} x100\%$$
$$= 71\%$$

The satisfaction section consisted of seven questions. It adhered to 71% of the requirements for eligibility. Based on a scale with a score between 61 and 80 for the feasibility category, diabetics can use the AKUDia application with a high degree of satisfaction from users.

Based on the average usability value of the four characteristic aspects (usability, ease of use, ease of learning, and satisfaction), the overall usability of the AKUDia application was estimated to be 78 percent. The results demonstrate that all use queries are quasi-nary. Most

respondents agree that the AKUDia program is useful, easy to use, and understandable; they are also satisfied that it was reasonably priced to purchase. This is in accordance with the earlier research on the Google Classroom application's usability using the use questionnaire, which illustrates that the percentage level of usability using the use questionnaire demonstrates a workable category on the issue of ease of use (Jannah, Sobandi, & Suwatno, 2020).

Results from other studies on cellular mobile applications that validate the utility of health applications (mHealth) using a system usability scale (SUS) and a post-study system usability questionnaire (PSSUQ) have indicated that overall SUS and PSSUQ correlate strongly against m-Health applications, according to statements produced in response to a questionnaire by 128 respondents (Zhou et al., 2019). Further research reveals that the Material Expert was employed as a tool for making decisions in family planning applications. Six midwives were assessed on their ability to assimilate information and suitability for the material using the due diligence questionnaire developed by the material expert. demonstrates that family planning decision tools can be implemented in a way that is considered feasible (Nurcahyani et al., 2022). Hence, even though they implement different methods, they own the same function to examine the usability of an application, which is a crucial factor in the application development stage before being used on a broader scale.

The AKUDia application's exclusive ability to collect data regarding blood sugar levels constitutes a limitation for this study. To see a picture of self-care for people with diabetes to control blood sugar levels, it has not been completely incorporated with the management of DM management, such as monitoring food recall, physical activity, and consumption of blood sugar-lowering drugs. It is recommended that in the future, researchers formulate applications that encompass additional health features, such as food recall monitors, physical activity, and the use of blood sugar-lowering medications, in the process of controlling blood sugar levels in diabetics.

4. CONCLUSION

Using the use questionnaire, the AKUDia application's usability test revealed that it was feasible and appropriate to use as a means of accessing data on blood sugar level readings that are reported in real-time from sensors sent to the AKUDia application. Governments ought to encourage the use and implementation of this innovation in addition to healthcare professionals like doctors and nurses. Information technology systems possess the potential to serve as a tool for preventing diseases, treatment, and rehabilitation in addition to promoting health. Future studies should be enhanced to investigate, through experimental research, how the AKUDia application supports nursing care and health management for individuals with diabetes mellitus and the general population.

REFERENCES

Abidin, M. S., Rajak, A., Salam, R. A., Munir, M. M., & Khairurrijal. (2015). Measurement of glucose in blood using a simple non invasive method. Materials Science Forum, 827, 105–109. https://doi.org/10.4028/www.scientific.net/MSF.827.105

Apple Inc. (2021). *Apple Watch Series 7 - Technische Daten*. Apple Inc.

Badan Penelitian dan Pengembangan Kesehatan Kemenkes Republik Indonesia. (2019). *Laporan Provinsi Jawa Barat, Riskesdas 2018*. Jakarta: Badan Penelitian dan Pengembangan Kesehatan Kemenkes Republik Indonesia

Badriah, S., Bahtiar, Y., & Andang, A. (2022). Near Infrared LEDs-Based Non-Invasive Blood Sugar Testing for Detecting Blood Sugar Levels on Diabetic Care. *Journal of Biomimetics, Biomaterials and Biomedical Engineering*, 55(71), 183–191. https://doi.org/10.4028/p-vthp40

Badriah, S., Sahar, J., Gunawijaya, J., & Prasetyo, S. (2019). Pampering older people with diabetes in Sundanese culture: A qualitative study. *Enfermeria Clinica*, 29 (Insc 2018), 733–738. https://doi.org/10.1016/j.enfcli.2019.04.111

Badriah, S., Sahar, J., Gunawijaya, J., Prasetyo, S., Mariani, D., & Kartilah, T. (2021). Sundanese culture-sensitive family nursing model improves behavior in controlling blood sugar in elderly patients with diabetes. *Enfermeria Clinica*, 31, S361–S365. https://doi.org/10.1016/j.enfcli.2020.09.027

Bruen, D., Delaney, C., Florea, L., & Diamond, D. (2017). Glucose sensing for diabetes monitoring: Recent developments. *Sensors (Switzerland)*, 17(8), 1–21. https://doi.org/10.3390/s17081866

Fitbit. (2019). *Advanced fitness + health tracker | Shop Fitbit Charge 5*. Fitbit

Ariyanto, H., Nurapandi, A., Purwati, A. E., Kusumawaty, J., & Setiawan, H. (2021). Genetic counseling program for patient with hyperglycemic syndrome. *Journal of Holistic Nursing Science*, 8(2), 2–9. https://doi.org/10.31603/nursing.v8i2.4966

Jannah, S. N., Sobandi, A., & Suwatno, S. (2020). The Measurement of Usability Using USE Questionnaire on the Google Classroom Application as E-learning Media (A Case study: SMK Negeri 1 Bandung). *Teknodika*, 18(2), 94. https://doi.org/10.20961/teknodika.v18i2.42486

Kementerian Kesehatan Republik Indonesia. (2017). *Materi evaluasi program Indonesia Sehat.* Jakarta: Kementerian Kesehatan Republik Indonesia.

Lund, A. M. (2001). Measuring usability with the USE questionnaire. *Usability Interface*, 8(2), 3–6.

Mehra, V. M., Costanian, C., McCague, H., Riddell, M. C., & Tamim, H. (2023). The association between diabetes type, age of onset, and age at natural menopause: a retrospective cohort study using the Canadian Longitudinal Study on Aging. *Menopause, 30(1), 37–44.* https://doi.org/10.1097/GME.0000000000002085

Nurcahyani, L., Widiyastuti, D., Hasan, F., Cahyati, Y., & Badriah, S. (2022). Development of Decision-Making Tool for Family Planning Application: Feasibility Test According to Material Experts. *Open Access Macedonian Journal of Medical Sciences*, 10(E), 720–724. https://doi.org/10.3889/oamjms.2022.9315

Pannu, A. K., Saroch, A., Kumar, M., Behera, A., Nayyar, G. S., & Sharma, N. (2022). Quantification of chronic diseases presenting in the Emergency Department and their disposition outcomes: A hospital-based cross-sectional study in north India. *Tropical Doctor*, 52(2), 276–279. https://doi.org/10.1177/00494755211069450

Prawiroredjo, K., & Julian, E. S. (2019). Comparative study of 940 nm and 1450 nm near infrared sensor for glucose concentration monitoring. *Telkomnika (Telecommunication Computing Electronics and Control)*, 17(2), 981–985. https://doi.org/10.12928/TELKOMNIKA.V17I2.10149

Samsung. (2019). *Galaxy Watch4 Bluetooth (40mm) pink-gold.* Samsung.

Setiawan, H., Lutfi, Y. D. S., Andarini, E., Kurniawan, R., Richard, S. D., & Ariyanto, H. (2021). The effect of genetic counseling on depression , anxiety, and knowledge level among diabetes mellitus patients. *Journal of Nursing and Social Sciences Related to Health and Illness*, 23(4), 330–337. https://doi.org/10.32725/kont.2021.035

Setiawan, H., Hidayat, N., Farihatun, A., Indriastuti, M., Kurniawan, R., Firmansyah, A., Andarini, E., & Sandi, Y. D. L. (2023). Usability of Mobile Application for Implementing Genetic Counselling Intervention among Thalassemia Patients and Caregivers: A Case Study of Cyber Gen. Elinvo (Electronics, Informatics, and Vocational Education), 8(1), 130–136. https://doi.org/10.21831/elinvo.v8i1.55688

Zhou, L., Bao, J., Setiawan, I. M. A., Saptono, A., & Parmanto, B. (2019). The mhealth app usability questionnaire (MAUQ): Development and validation study. *JMIR MHealth and UHealth*, 7(4), 1–15. https://doi.org/10.2196/11500

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 681-688
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1388*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Nausea and Vomiting of Pregnancy: Multiple Contributing Factors

Sri Wahyuni[1a*], Noor Pramono[2b], Suharyo Hadisaputro[2c], Annastasia Ediati[3d]

[1] Doctoral Program of Medicine and Health Sciences, Faculty of Medicine, University of Diponegoro, Semarang, Central Java, Indonesia
[2] Faculty of Medicine, University of Diponegoro, Semarang, Central Java, Indonesia
[3] Faculty of Psychology, University of Diponegoro, Semarang, Central Java, Indonesia

[a] Email address: buknunisigit@gmail.com
[b] Email address: noerpramana@gmail.com
[c] Email address: prof_haryo@yahoo.co.id
[d] Email address: ediati.psi@gmail.com

Received: 15 October 2023 Revised: 1 December 2023 Accepted: 8 December 2023

Abstract
Nausea and vomiting are common conditions in earlier pregnancy. Some studies have suggested that nausea and vomiting during pregnancy (NVP) is caused by multiple factors, however, few studies assessed family support and psychological factors. The present study aimed to assess the prevalence of NVP and its contributing factors. A cross-sectional study was conducted in five Primary Health Centers in Semarang during August 2023. A total of 99 eligible pregnant women were included. A logistic regression was used to determine the significant contributing factors of NVP. The prevalence of moderate to severe and mild NVP was 71.7% and 28.3% respectively. Bivariate analysis indicated that gestational age and anxiety level significantly influence NVP (p-value <0.05). Women with greater gestational age (OR= 2.462; 0.954-6.356) and mild anxiety (OR=3.337; 1.240-8.982) were more likely to experience NVP during their pregnancy. Gestational of 12 weeks and mild anxiety are strongly associated with NVP. These findings highlight the crucial of psychological factors despite other health-related conditions.

Keywords: NVP, Risk Factor, First Trimester.

Corresponding Author:

Sri Wahyuni
Doctoral Program of Medicine and Health Sciences, Faculty of Medicine, University of Diponegoro, Semarang, Central Java, Indonesia
Email: buknunisigit@gmail.com

1. INTRODUCTION

Nausea and vomiting during pregnancy (NVP) or emesis gravidarum, are common experiences during pregnancy that range from mild to moderate severity, affecting up to 70 of pregnant women worldwide. However, these symptoms may become more aggravated than is typical – hyperemesis gravidarum, which is reported in 0.3–10.8% of pregnant women. In Indonesia, it was reported rates vary widely, with 1-3% in all pregnancies (Oktavia, 2016), in which 543 cases from 2.203 pregnant women (67.9%), of 60-80% among prim gravida, and 40 – 60% on multigravida (Retni et al., 2020).

NVP, often known as morning sickness, is the second most common indication for pregnancy hospitalization due to severe NVP - hyperemesis gravidarum (HG). Almost 90% of pregnant women experienced nausea, while vomiting may be seen in 28-52% of all pregnancies (Jennings & Mahdy, 2023). Although it is a common symptom during pregnancy, the effects on pregnancy, both short and long-term, have long been debated. Therefore, the mechanism and its contributing factors need to be explored more.

Previous studies have explored multiple factors that cause NVP, from individual characteristics (age, socioeconomic factor, parity), nutrition intake, and hormonal, and psychosocial factors (Retnowati, 2019; Zhang et al., 2020). Furthermore, gestational age has been linked to NVP incidence, yet, different findings have emerged. In some studies, earlier gestational age increased the incidence of NVP, whereas in others, greater gestational age was reported associated with a lower incidence of NVP (Erick et al., 2018; Nurmi et al., 2020; Zhang et al., 2020). However, among those studies, the true potential factors of NVP remain inconsistent.

Additionally, psychosocial, such as perceived social support impact the NVP severity (Bray et al., 2021). The social factor of NVP consists of a lack of family support and friends. Social support is an important factor of life quality in early pregnancy. It was reported that low social support is statistically correlated to a decline in life quality (Junandar et al., 2021). However, this positive relationship between family support and NVP is inconsistent across some studies. A nonsignificant effect of family support, particularly partner support on NVP levels was found in a large study in the UK (Roberts et al., 2023). These differing results may be due to variations in study settings, characteristics, and methods used.

Existing studies have focused on individual factors causing NVP, so some potential risk factors remain unclear. There was a lack of investigation exploring family support as the potential risk factor of NVP. This may allow women to have an essential protective domain from the benefits of the present study. Therefore, this study was aimed at assessing family support along with other risk factors of NVP among pregnant women in their trimester of gestational age. In addition, the prevalence of NVP was determined by a validated tool, based on the PUQE scale.

2. RESEARCH METHOD

A primary health center-based cross-sectional study was conducted in five Primary Health Centers in Semarang, Central Java. A total of 99 eligible subjects who visited those settings during August 2023 were interviewed. The inclusion criteria for this study were the following: pregnant, less than or equal to 12 weeks of gestational age. The criteria for exclusion were pregnant women with more than 12 gestational weeks. Written informed consent was obtained from all the subjects. The Ethical Committee of the Faculty of Medicine, University of Diponegoro approved the proposed study (120/EC/KEPK/FK-UNDIP/IV/2023).

The scale of NVP was measured by using the Pregnancy-Uniques Quantification of Emesin (PUQE). PUQE is a scoring system for nausea and vomiting during pregnancy, which focuses on three symptoms: nausea, vomiting, and retching over the past 24 hours (Hada et al.,

2021). The overall PUQE score is calculated by adding the three question scores, with each question scoring 1 to 5 points. The NVP was divided into mild (4 to 6), moderate (7 to 12), and severe (13 to 15) (Yilmaz et al., 2022).

Demographic information was obtained using a standardized questionnaire. The questionnaire was used to assess age, level of education, occupations, parity, and gestational age. A healthy reproductive stage was those aged 20 to 35, while those under 20 or older than 35 were considered risk reproductive age (Deatsman et al., 2016). Subjects who did not have any formal education or completed their junior high school were classed as low education, completed senior high school were assumed to be middle education levels, and higher education were subjects who graduated from universities.

Investigators confirm the gestational data based on the Maternal and Child Health book. To measure family support, we used the Multidimensional Paternal Perinatal Scale (MPPS), a recently developed tool based on the conceptual framework of paternal perinatal experience (Gemayel et al., 2021). The implementation of the developed questionnaire confirmed the construct validity and internal consistency. An individual anxiety level was assessed by using the Hamilton Anxiety Rating Scale (HARS), a psychological questionnaire used by clinicians to rate the severity of a patient's anxiety (Clark & Donovan, 1994; Hamilton, 1959). The anxiety level was divided into mild (7 to 14), moderate (15 to 27), and severe (more than 27).

Data analysis was conducted using SPSS. The mean and range were presented for continuous variables, while categorical variables were displayed in frequency and percentage. Bivariate and multivariate logistic regression analyses were used to determine the factors influencing NVP. A p-value less than 0.05 was considered statistically significant to increase the risk of NVP.

3. RESULTS AND DISCUSSION

Table 1 shows the NVP, demographic, and health-related characteristics of the study subjects. This study assessed that 67.68% of subjects had moderate NVP, while 4.04% had severe NVP. The mean age was 27.9 with a range between 19 to 40 years old, and most studied subjects were categorized as healthy reproductive age (87.88%). The majority of pregnant women had middle formal education, employee, multigravida, and 12 weeks of gestational age. The mean of family support was 73.27 and higher among those who had good support (52.53%). The mean anxiety level was 14.21 and the majority was classed as mild anxiety (54.555).

Table 1. The Characteristics of Studied Subjects

Variable	Category	Frequency (N= 99)	Percentage
NVP	Severe	4	4.04
	Moderate	67	67.68
	Mild	28	28.28
Age (years)	Mean (Min-Max)	27.9 (19-40)	
	Unhealthy reproductive	12	12.12
	Healthy reproductive	87	87.88
Education	Low	4	4.04
	Middle	75	75.76
	Higher	20	20. 20
Occupation	Unemployed	46	46.46
	Employee	53	53.54
Parity	Prim gravida	36	36.36
	Multigravida	63	63.64
Gestational age	12 weeks	51	51.52
	<12 weeks	48	48.48

Family Support	Mean (Min-Max)	73.27 (20-84)	
	Low	47	47.47
	Good	52	52.53
Anxiety Level	Mean (Min-Max)	14.21 (1-28)	
	Severe	1	1.01
	Moderate	44	44.44
	Mild	54	54.55

Table 2 demonstrates the bivariate analysis of the associations between general variables and NVP. We simplified the NVP into 2 categories due to the small cell number in severe NVP, hence severe was included in the moderate category. These findings indicated that gestational age and anxiety level significantly influence NVP (p-value <0.05).

Table 2. Bivariate Analysis of Risk Factors for Nausea and Vomiting of Pregnancy.

Variables	**Category**	**NVP**		**p-value**
		Mild (N= 28)	**Moderate to Severe (N= 71)**	
Age of Respondent	Healthy reproductive	24 (27.6)	63 (72.4)	0,942
	Unhealthy reproductive	4 (33.3)	8 (66.7)	
Education	Low	3 (75)	1 (25)	0,306
	Middle	17 (22.7)	55 (77.3)	
	Higher	8 (42.1)	11 (57.9)	
Jobs	Employee	15 (28,3)	37 (69,8)	1
	Unemployed	13 (28.3)	33 (71.7)	
Parity	Primigravida	9 (25)	27 (75)	0,752
	Multigravida	19 (30.2)	44 (69.8)	
Gestational Age	12 weeks	19 (37.3)	32 (62.7)	0,041*
	<12 weeks	9 (18.8)	39 (81.2)	
Family Support	Good	16 (30.8)	36 (69.2)	0,723
	Deficient	12 (25.5)	35 (74.5)	
Anxiety Level	Mild	21 (38.9)	23 (61,1)1	0,019*
	Moderate	7 (15.9)	37 (84.1)	
	Severe	0	1 (100)	

** Significant at p-value<0.05*

The variables significantly related to NVP in Table 2 were used in multivariate logistic regression. Table 3 presents the statistically significant variables included in the final model of NVP. We also simplified the category of anxiety level, in which a small subject with severe anxiety merged with a moderate level to get a better analysis result.

Table 3. Final Model of Risk Factors for Nausea and Vomiting of Pregnancy.

Variable	**Category**	**OR**	**CI 95%**	**p-value**
Anxiety Level	Mild	3.337	1.240-8.982	0.017
	Moderate to severe	Ref.	1	
Gestational Age	12 weeks	2.462	0.954-6.356	0.063
	<12 weeks	Ref.	1	

This study investigated the prevalence of NVP and its contributing factors among pregnant women during their first trimester. We recruited women in early pregnancy, which perhaps have better captured early pregnancy conditions since NVP mostly (90%) began within the first trimester, primarily between the second and tenth week of gestation (Chan et al., 2011).

The prevalence of moderate to severe and mild NVP was 71.7% and 28.3% respectively among 99 subjects. The analysis showed that women with greater gestational age and mild anxiety were more likely to experience NVP during their pregnancy (Schetter & Tanner, 2012).

Pregnant women with greater gestational weeks were associated with a higher incidence of NVP in this study, which is inconsistent with previous similar studies. A hospital-based retrospective study in China reported an inverse association where greater gestational age correlated with a lower number of NVP cases (OR= 0.95; 0.93-0.97) (Zhang et al., 2020). Nevertheless, NVP results from multiple metabolic and endocrine factors (Lee & Saha, 2011). The most contributing factor is human chorionic gonadotropin (hCG). This may be associated with the incidence of NVP and the peak of hCG production, which occurs between 12 and 14 weeks of gestation in 90% of women (Royal College of Obstetricians and Gynaecologists, 2016). These sources legitimate the findings of the present study that women with 12 gestational weeks are more likely to increase the risk of NVP by 2.5 times than those with earlier gestational (<12 weeks).

Human chorionic gonadotropin (hCG) is a pregnancy hormone that has been widely recognized as an essential factor in the pathogenesis of NVP (Davis, 2004; Niemeijer et al., 2014). In a prospective study in Malaysia, it was found that hyperemesis gravidarum in first-trimester women resulted in poor short-term outcomes, supported by increased serum hCG levels (Tan et al., 2009). High levels of hCG and beta-hCG increase the severity of NVP (OR= 1.47; 1.11–1.95) (Dekkers et al., 2019). Elevated levels of hCG may cause nausea and vomiting through the hCG receptor located in the posttrauma of the human brain stem. These hormonal changes, particularly the direct effects of hCG, are responsible for the symptoms of NVP (Bustos et al., 2017).

Despite altered reproductive hormones, psychological factors may contribute significantly to the progression of NVP (Liu et al., 2022). Some studies have shown that elevated depressive symptoms in the first trimester and a history of depression were independently associated with the incidence of NVP (Dekkers et al., 2019; Taguchi et al., 2022). Possible adverse psychological factors associated with NVP include depression, anxiety, mood disorders, and stress (Hizli et al., 2012; Uguz et al., 2012). In this study, most of the subjects experienced mild and moderate anxiety levels in the twelve weeks of pregnancy. Those detected with mild anxiety are more likely to develop moderate to severe NVP by three times than moderate to severe anxiety. These results are consistent with a similar cross-sectional study in which those with mild NVP were less stressed than those with moderate to severe NVP (Şahin et al., 2022). This study supports the claim that stress levels may be associated with the severity of NVP and proves the pattern that nausea and vomiting during pregnancy may be the result of a strong effect of anxiety (Tan et al., 2014; Wang et al., 2020). Nonetheless, surprisingly, mild anxiety had a larger effect on NVP than moderate to severe levels of anxiety. This is caused by the fact that NVP is a multifactor incidence, anxiety is not sufficient to cause NVP without interaction with other potential factors.

Although the proposed study may be close evidence of multiple factors for developing NVP by exploring demographic, health-related characteristics, and psychological factors, some limitations should be acknowledged. First, a larger sample size may facilitate more precise findings in a cross-sectional study. Second, the outcome, NVP presented a small number of severe NVP, hence the investigators simplified it into two categories in which severe merged to moderate level of NVP. This decision may present misclassification and may have underestimated the true association.

4. CONCLUSION

The present study shows that gestational age and anxiety level are associated with the incidence of NVP among pregnant women during their first trimester. The findings highlight

the importance of controlling psychological factors despite other health-related conditions during earlier pregnancy. Further studies with an assessment of multiple potential factors to track NVP development are needed to clarify how these findings may change over time.

REFERENCES

Bray, N., Grasby, K. L., Lind, P. A., Painter, J. N., Colodro-Conde, L., & Medland, S. E. (2021). The psychosocial impact of nausea and vomiting during pregnancy as a predictor of postpartum depression. *Journal of Health Psychology*, *26*(7), 1061–1072. https://doi.org/10.1177/1359105319859048

Bustos, M., Venkataramanan, R., & Caritis, S. (2017). Nausea and vomiting of pregnancy-What's new?. *Autonomic Neuroscience*, *202*, 62-72. https://doi.org/10.1016/j.autneu.2016.05.002

Chan, R. L., Olshan, A. F., Savitz, D. A., Herring, A. H., Daniels, J. L., Peterson, H. B., & Martin, S. L. (2011). Maternal influences on nausea and vomiting in early pregnancy. *Maternal and Child Health Journal*, *15*(1), 122–127. https://doi.org/10.1007/s10995-009-0548-0

Clark, D. B., & Donovan, J. E. (1994). Reliability and Validity of the Hamilton Anxiety Rating Scale in an Adolescent Sample. *Journal of the American Academy of Child and Adolescent Psychiatry*, *33*(3), 354–360. https://doi.org/10.1097/00004583-199403000-00009

Davis, M. (2004). Nausea and vomiting of pregnancy: an evidence-based review. *The Journal of perinatal & neonatal nursing*, *18*(4), 312-328.

Deatsman, S., Vasilopoulos, T., & Rhoton-Vlasak, A. (2016). Age and fertility: A study on patient awareness. *Jornal Brasileiro de Reproducao Assistida*, *20*(3), 99–106. https://doi.org/10.5935/1518-0557.20160024

Dekkers, G. W. F., Broeren, M. A. C., Truijens, S. E. M., Kop, W. J., & Pop, V. J. M. (2019). Hormonal and psychological factors in nausea and vomiting during pregnancy. *Psychological Medicine*, *50*(2), 229–236. https://doi.org/10.1017/S0033291718004105

Erick M, Cox JT, & Mogensen KM. (2018). ACOG Practice Bulletin 189: Nausea and Vomiting of Pregnancy. *Obstet Gynecol*, *131*(5), 935. https://doi.org/10.1097/AOG.0000000000002604

Gemayel, D., Wiener, K. K. K., & Saliba, A. (2021). The development and validation of the Multidimensional Paternal Perinatal Scale (MPPS). *Heliyon*, *7*(5). https://doi.org/10.1016/j.heliyon.2021.e06978

Hada, A., Minatani, M., Wakamatsu, M., Koren, G., & Kitamura, T. (2021). The pregnancy-unique quantification of emesis and nausea (Puqe-24): Configural, measurement, and structural invariance between nulliparas and multiparas and across two measurement time points. *Healthcare (Switzerland)*, *9*(11). https://doi.org/10.3390/healthcare9111553

Hamilton, M. (1959). The assessment of anxiety states by rating. *Br J Med Psychol*, *32*, 50–55. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x

Hizli, D., Kamalak, Z., Kosus, A., Kosus, N., & Akkurt, G. (2012). Hyperemesis gravidarum and depression in pregnancy: Is there an association? *Journal of Psychosomatic Obstetrics and Gynecology*, *33*(4), 171–175. https://doi.org/10.3109/0167482X.2012.717129

Jennings, L. K., & Mahdy, H. (2023). *Hyperemesis Gravidarum.* StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK532917/

Junandar, C. Y., Wittiarika, I. D., Utomo, B., & Ernawati, E. (2021). The Relationship of Social Support with The Degree of Nausea and Vomiting in Pregnancy. *Indonesian Midwifery*

and Health Sciences Journal, *4*(1), 26–32. https://doi.org/10.20473/imhsj.v4i1.2020.26-32

Lee, N. M., & Saha, S. (2011). Nausea and vomiting of pregnancy. *Gastroenterology Clinics*, *40*(2), 309-334. https://doi.org/10.1016/j.gtc.2011.03.009

Liu, C., Zhao, G., Qiao, D., Wang, L., He, Y., Zhao, M., ... & Jiang, E. (2022). Emerging progress in nausea and vomiting of pregnancy and hyperemesis gravidarum: challenges and opportunities. *Frontiers in Medicine*, *8*, 809270. https://doi.org/10.3389/fmed.2021.809270

Niemeijer, M. N., Grooten, I. J., Vos, N., Bais, J. M. J., Van Der Post, J. A., Mol, B. W., Roseboom, T. J., Leeflang, M. M. G., & Painter, R. C. (2014). Diagnostic markers for hyperemesis gravidarum: A systematic review and metaanalysis. *American Journal of Obstetrics and Gynecology*, *211*(2), 150.e1-150.e15. https://doi.org/10.1016/j.ajog.2014.02.012

Nurmi, M., Rautava, P., Gissler, M., Vahlberg, T., & Polo-Kantola, P. (2020). Incidence and risk factors of hyperemesis gravidarum: A national register-based study in Finland, 2005-2017. *Acta Obstetricia et Gynecologica Scandinavica*, *99*(8), 1003–1013. https://doi.org/10.1111/aogs.13820

Oktavia, L. (2016). Kejadian Hiperemisis Gravidarum Ditinjau dari Jarak Kehamilan dan Paritas. *Jurnal Ilmu Kesehatan Aisyah*, *1*(2), 42. https://doi.org/10.30604/jika.v1i2.19

Retni, A., Handayani, F., & Mohamad, I. S. W. (2020). Literature Review : Pemberian Aromaterapi Essential Oil Lavender Terhadap Emesis Gravidarum Pada Kehamilan Trimester Pertama. *Journal of Borneo Holistic Health*, *3*(2), 141. https://doi.org/10.35334/borticalth.v3i2.1687

Retnowati, Y. (2019). Faktor - Faktor Yang Memperngaruhi Terjadinya Emesis Gravidarum Pada Kehamilan Trimester I Di Puskesmas Pantai Amal. *Journal of Borneo Holistic Health*, *2*(1), 40–56. https://doi.org/10.35334/borticalth.v2i1.586

Roberts, K., Havlíček, J., Kaňková, Š., Klapilová, K., & Roberts, S. C. (2023). Testing effects of partner support and use of oral contraception during relationship formation on severity of nausea and vomiting in pregnancy. *BMC Pregnancy and Childbirth*, *23*(1), 175. https://doi.org/10.1186/s12884-023-05468-x

Royal College of Obstetricians and Gynaecologists. (2016). *The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum*. Royal College of Obstetricians and Gynaecologists.

Şahin, B., Özçetinkaya Erdoğan, S., Cura Şahin, G., Karlı, P., Kara, O. F., Hatırnaz, Ş., & Tinelli, A. (2022). Nausea and vomiting during pregnancy: a possible correlation with obsessive compulsive disorder and alexithymia. *Journal of Obstetrics and Gynaecology*, *42*(5), 929–934. https://doi.org/10.1080/01443615.2021.1960492

Schetter, C. D., & Tanner, L. (2012). Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. *Current opinion in psychiatry*, *25*(2), 141–148). https://doi.org/10.1097/YCO.0b013e3283503680

Taguchi, K., Shinohara, H., & Kodama, H. (2022). A longitudinal investigation of the influence of psychological factors on nausea and vomiting in early pregnancy. *Archives of Women's Mental Health*, *25*(5), 995–1004. https://doi.org/10.1007/s00737-022-01262-4

Tan, P. C., Tan, N. C., & Omar, S. Z. (2009). Effect of high levels of human chorionic gonadotropin and estradiol on the severity of hyperemesis gravidarum. *Clinical Chemistry and Laboratory Medicine*, *47*(2), 165–171. https://doi.org/10.1515/CCLM.2009.041

Tan, P. C., Zaidi, S. N., Azmi, N., Omar, S. Z., & Khong, S. Y. (2014). Depression, anxiety, stress and hyperemesis Gravidarum: Temporal and case controlled correlates. *PLoS ONE*, *9*(3). https://doi.org/10.1371/journal.pone.0092036

Uguz, F., Gezginc, K., Kayhan, F., Cicek, E., & Kantarci, A. H. (2012). Is hyperemesis gravidarum associated with mood, anxiety and personality disorders: A case-control study. *General Hospital Psychiatry*, *34*(4), 398–402. https://doi.org/10.1016/j.genhosppsych.2012.03.021

Wang, H., Rolls, E. T., Du, X., Du, J., Yang, D., Li, J., Li, F., Cheng, W., & Feng, J. (2020). Severe nausea and vomiting in pregnancy: Psychiatric and cognitive problems and brain structure in children. *BMC Medicine*, *18*(1), 228. https://doi.org/10.1186/s12916-020-01701-y

Yilmaz, T., Dinç Kaya, H., Günaydin, S., Güdücü, N., & Dişsiz, M. (2022). Psychometric properties of the Pregnancy-Unique Quantification of Emesis (PUQE-24) scale. *Journal of Obstetrics and Gynaecology*, *42*(6), 1739–1745. https://doi.org/10.1080/01443615.2022.2036961

Zhang, H., Wu, S., Feng, J., & Liu, Z. (2020). Risk factors of prolonged nausea and vomiting during pregnancy. *Risk Management and Healthcare Policy*, *13*, 2645–2654. https://doi.org/10.2147/RMHP.S273791

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 689-712
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1407*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

Nutrition Counseling, Lipid Profile Improvement and Weight Loss in Obese Patients with Dyslipidemia

Salman[1a], Novian Swasono Hadi[1b], Liean A. Ntau[1c], Nancy Olii[2d], Siti Choirul Dwi Astuti[2e*]

[1] Department of Nutrition, Poltekkes Kemenkes Gorontalo, Gorontalo City, Gorontalo Province, Indonesia
[2] Department of Midwifery, Poltekkes Kemenkes Gorontalo, Gorontalo City, Gorontalo Province, Indonesia

[a] Email address: slmnlukman@gmail.com
[b] Email address: nieno.poenya@gmail.com
[c] Email address: lianntau@gmail.com
[d] Email address: oliinancy7@gmail.com
[e] Email address: sitichoirul13@yahoo.co.id

Received: 26 November 2023 Revised: 29 November 2023 Accepted: 8 December 2023

Abstract

Obesity with dyslipidemia is a serious problem because it risks various degenerative and metabolic diseases. The prevalence of obesity in Indonesia continues to increase every year, currently in the adult population reaching 21.8%. To prevent the onset of degenerative diseases and metabolic disorders, it is important to control obesity with dyslipidemia through weight loss and lipid profile improvement. This study aims to determine the effect of nutritional counseling in losing weight and improving lipid profiles in obese patients with dyslipidemia. This is a pseudo-experimental study with One group Pre and Post Test Design. The initial stage was the identification of obesity and lipid profile. In 100 respondents identified as obese, total cholesterol, LDL and triglycerides were examined. 40 obese respondents with dyslipidemia were determined as samples. The second stage was nutrition counseling intervention. The third stage of evaluation is the re-measurement of body weight and lipid profile. The research result is only 30 respondents participated in the evaluation. Average initial body weight was 75.11 kg and final body weight was 73.14 kg. Average weight loss was 1.97 kg. Average initial cholesterol 233.20 mg/dL and final cholesterol 224.70 mg/dL. Average cholesterol reduction of 8.5 mg/dL. Average initial LDL 152.37 mg/dL and final LDL 139.47 mg/dL. Average decrease in LDL 12.9 mg/dL Average initial triglycerides 161.23 mg/dL and final triglycerides 143.97 mg/dL. The average decrease in triglycerides is 17.26 mg/dL. The statistical test results showed a p-value = 0.000. There is an effect of nutritional counseling on weight loss and improvement of lipid profiles of obese patients with dyslipidemia.

Keywords: Dyslipidemia, Lipid Profile, Nutrition Counseling, Obesity, Weight.

Corresponding Author:

Siti Choirul Dwi Astuti
Department of Midwifery, Poltekkes Kemenkes Gorontalo, Gorontalo City, Gorontalo Province, Indonesia
Email: sitichoirul13@yahoo.co.id

1. INTRODUCTION

Global mortality data, there are more than 7.4 million people died from obesity which is the main cause of death and illness. This condition will continue to grow every year to 9.4 million deaths, and it is estimated that the number will increase to 23.3 million by 2030 (Almigbal et al., 2023). One of the risk factors for obesity is excessive fat intake (Deora & Venkatraman, 2022). The level of lipids in the coronary arteries, the fatty layer, the protrusion of lesions and coronary stenosis and the independent risk factors that modify the complex and chronic vascular inflammatory process eventually manifest as causes i.e. a family history of obesity disease (Navya et al., 2023). If a person lacks physical activity but consumes very excess food, it can increase low density lipoprotein and decrease high density lipoprotein (Dou et al., 2023). The body moves a lot will cause fat not to accumulate in the body so that it can lower cholesterol levels. Physical exercise for 30 minutes a day can lower cholesterol levels (Fernández Granell et al., 2024). Excessive consumption of carbohydrates can trigger heart disease in a person (Islam et al., 2023). Excess carbohydrate intake can increase glucose levels in the blood and result in a higher risk of heart disease (Izoe et al., 2022). High consumption of carbohydrates tends to increase triglyceride levels and lower cholesterol levels (Kamrul-Hasan et al., 2023). Lifestyle such as physical activity that is not good has an impact and affects the quality of individual health, especially at the age of over 30 years. Likewise, an unhealthy diet has a significant effect on lipid levels in the blood such as cholesterol and triglycerides (Karunakar et al., 2023).

Indonesia is currently facing a double nutrition problem. Obesity is a health problem that occurs in many modern times and its incidence every year continues to increase (Katsuyama et al., 2022). Obesity with dyslipidemia can endanger health because it is a risk factor for various degenerative and metabolic diseases such as cardiovascular, diabetes mellitus, cancer, osteoarthritis (Kazemi et al., 2023). Obesity with dyslipidemia occurs due to an imbalance of incoming energy and outgoing energy. High energy intake is caused by the consumption of high energy and fat source foods. Low energy expenditure is due to lack of physical activity (Kim & Park, 2022).

The most important obesity control can be done with dyslipidemia for weight loss and improvement of lipid profiles (total cholesterol and triglycerides) (Kim et al., 2023). Weight loss and improvement of lipid profiles in obese people with dyslipidemia can reduce the risk of hypertension, coronary heart disease and type 2 diabetes mellitus. Conversely, obesity with dyslipidemia if not controlled is at risk of fatty liver which can result in hepatocellular carcinoma (Kirkpatrick et al., 2023).

To control obesity with dyslipidemia can be done with nutritional counseling to facilitate the process of interpersonal communication between counselors and clients in helping to overcome nutritional problems (Li et al., 2023). In conducting nutritional counseling requires counselors whose role is to help clients recognize and overcome nutritional problems (obesity with dyslipidemia) and encourage clients to find and choose ways to solve problems effectively and efficiently (Liang et al., 2023). Nutritional counseling is given to cliiens with obesity and dyslipidemia conditions. The provision of nutritional counseling is expected that obese people with dyslipidemia can improve nutritional behavior, especially in applying the principles of balanced nutrition so that the nutritional status and health of clients become better, namely weight loss and lipid profile improvement in the form of decreased total cholesterol and triglycerides (Lobato Casado et al., 2024). Previous research has found that nutritional counseling with traffic light diet media, food exchange tables and food balance wheels is quite successful, with parents of obese children keeping a family food and drink diary and ensuring that their children live a well-dieted lifestyle (Mansfield et al., 2022). Other studies also found significant differences in average body weight and body mass index with results ($p<0.01$) but

no differences in lipid profile and body composition (p>0.05) before and after the intervention (nutritional counseling). Nutritional counseling when combined with aerobic exercise also has a significant effect on improving cholesterol profiles and weight loss in obese adult women (Mishra et al., 2023).

Increasing socioeconomic levels have resulted in a change in diet from a traditional diet to a western diet such as fast food and high-calorie fats, resulting in a high prevalence of hypercholesterolemia in the community. One effort to reduce lipid profiles is through specific interventions to nutrition education through counseling is very good in improving one's behavior (Misra et al., 2022). Nutrition counseling is a two-way activity process that aims to improve patient behavior so that it can overcome health and nutrition problems, which generally in the implementation of counseling can be combined to be more effective (Muñoz et al., 2024). Therefore, this study aims to determine the effect of nutritional counseling he combination of exercise and nutritional counseling also had a significant effect on weight loss, body mass index, percent body fat (PBF) and visceral fat (p<0.05). Usually, nutritional counseling is only used to determine differences in knowledge and attitudes before and after counseling, but in this study also conducted an objective assessment of the results of changes in knowledge and attitudes after counseling in the form of lipid profiles and weight loss. For this reason, this study aims to determine the effect of nutritional counseling in losing weight and improving lipid profiles in obese patients with dyslipidemia.

2. RESEARCH METHOD

This type of research is a quasi-experimental study with a one group pre and post-test design. Sample of obese adults with dyslipidemia. The number of samples was 30 people. Sample criteria; obese with dyslipidemia, at least elementary school education, age 30-60 years, communication skills, cooperative, willing to be a respondent. Initial stage; purposive and tiered sampling. An obesity survey was conducted to 200 respondents in their homes. The survey was conducted by 5 enumerators, and 106 obese respondents were obtained. Next, dyslipidemia screening (examination of total cholesterol, LDL and triglycerides) by laboratory staff to 100 obese respondents in the meeting room of the Lurah office, obtained 52 obese respondents with dyslipidemia. Furthermore, 40 samples were determined purposively. The second stage; intervention was carried out in the form of providing nutritional counseling to 40 selected respondents. Nutrition counseling for each respondent was given 2 times with an interval of 2 weeks. Nutrition counseling was provided by 4 trained nutrition counselors. Counseling media were leaflets and videos. The third stage was evaluation, which involved measuring and rechecking body weight and lipid profile. Only 30 respondents (75%) participated in the evaluation stage. Data were statistically analyzed using t-student (paired sample test) at 95% confidence level. The measuring instruments used for obesity screening were Krisbow brand digital stepping scales with an accuracy of 0.1 kg and Gea brand microtois with an accuracy of 0.1 cm. For dyslipidemia screening using standard Prodia Laboratory equipment. The instruments used were interview forms and anthropometric measurement forms and dyslipidemia screening results. This research already has a permit by the Research Ethics Commission of the Health Polytechnic of the Ministry of Gorontalo, numbered LB.01.01/KEPK /177/2023.

3. RESULTS AND DISCUSSION

Table 1. Distribution of Lipid Profile of Obese Respondents.

Types of Lipid Profiles	N (83)	%
Total cholesterol		
Normal (< 200 mg/dL)	29	35
High (>200 mg/dL)	54	65
LDL		
Normal (<100 mg/dL)	7	8
High (>100 mg/dL)	76	92
Trigliserida		
Normal (<150 mg/dL)	53	64
High (>150 mg/dL)	30	36

Table show that from 83 obese respondents, lipid profile pictures were obtained; a) Most total cholesterol (65%) is high. b) LDL as large (92%) classified as high and c) triglycerides mostly (64%) classified as normal. The lipid profile assessment indicators are normal if that is less than 200mg/dL and high if more than 200mg/dL. Normal LDL is less than 100 mg/dL. The amount of LDL is said to be high if it is more than 100mg/dL The normal threshold of triglycerides in the body is less than 150mg/dL and if it exceeds that limit triglycerides can be said to be high.

Table 2. Characteristics Responden (n=30).

Characteristic	N (30)	%
Gender		
Man	3	10
Woman	27	90
Education		
Elementary School	4	13,3
Junior High School	7	23,3
High School	18	60,0
College	1	3,3
Occupation		
Housewife	24	80
Labourer	1	3,3
Farmer	1	3,3
Government Employees	1	3,3
Self employed	3	10

Table 2 show that the characteristics of respondents, most of which are female (90.0%), high school education level (60.0%), and unemployed (80.0%).

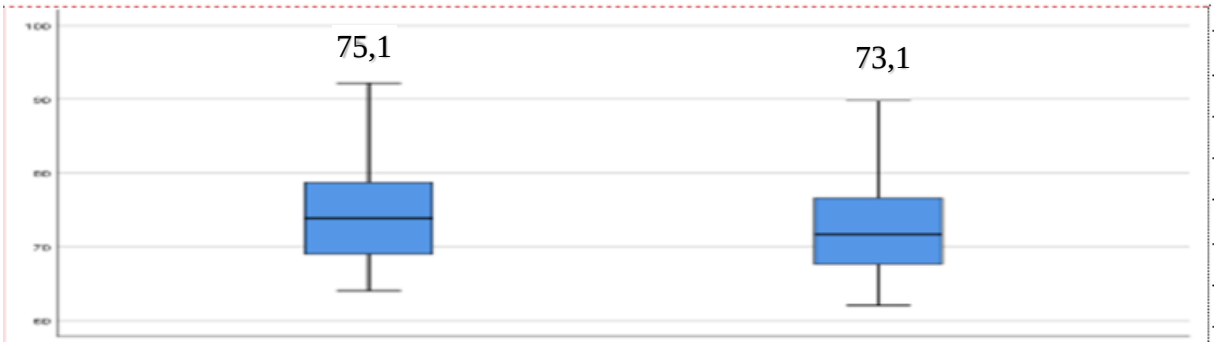


Figure 1. Progress of Weight.

Figure 1 show that the average body weight of respondents before nutrition counseling was 75.1 kg and after nutritional counseling was 73.1 kg. There was an average weight loss of 1.97 kg. Test statistics; p=0.000 (p<0.05). There was a difference in body weight after being given nutritional counseling.

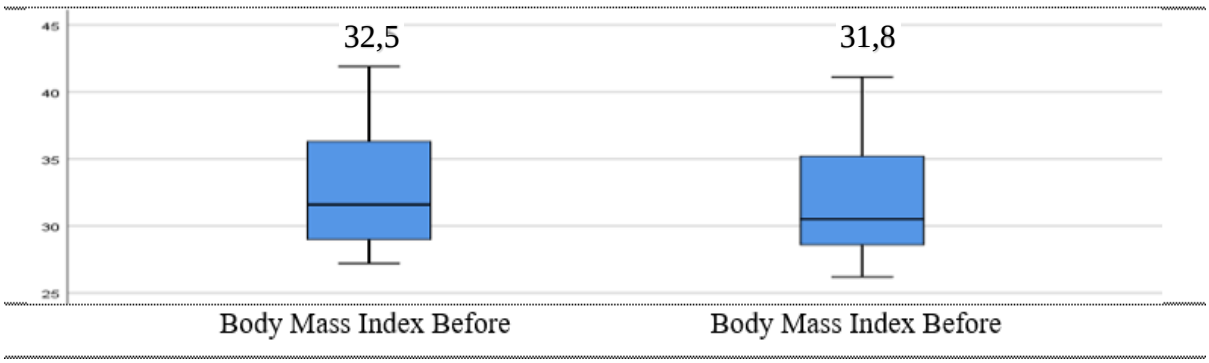


Figure 2. Progress of Body Mass Index

Figure 2 show that the average body mass index of respondents before nutrition counseling was 32.5 and after nutritional counseling 31.8. There was a decrease in the average BMI of 0.7. Test statistics; P=0.000 (p<0.05). There are differences in BMI after nutritional counseling.

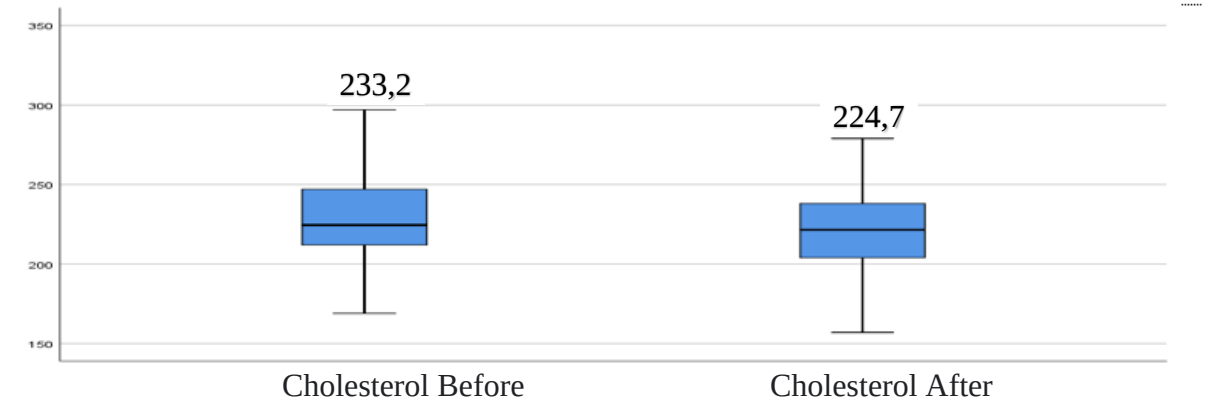


Figure 3. Progress of Lipid Profile Data

Figure 3 show that the average total cholesterol of respondents before nutritional counseling was 233.2 mg/dL and after nutritional counseling was 224.7 mg/dL. There was an average decrease in total cholesterol of 8.5 mg / dL. Test statistics; P=0.036 (p<0.05). There was a difference in total cholesterol after nutritional counseling.

Figure 4. Progress of LDL

Figure 4 show that the average LDL of respondents before nutritional counseling was 152.3 mg / dL and after nutritional counseling 139.4 mg / dL. There was an average decrease in LDL of 12.9 mg/dL. Test statistics; P=0.003 (p<0.05). There is a difference in LDL after nutritional counseling.

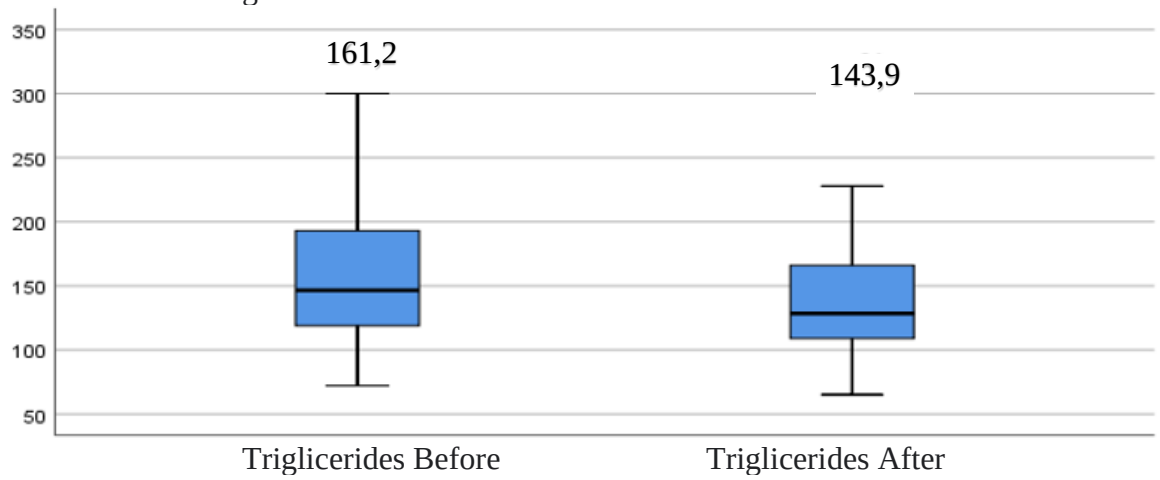


Figure 5. Progress of Triglicerides values

Figure 5 show the average triglyceride of respondents before nutritional counseling was 161.2 mg / dL and after nutritional counseling 143.9 mg / dL. There was an average triglyceride decrease of 17.3 mg / dL. Test statistics; P=0.034 (p<0.05). There are differences in teriglycerides after nutritional counseling.

Table 3. Differences in Body Weight Lipid Profile Before and After Nutritional Counseling.

Parameter	**Mean**	**T**	**p**
Weight			
Early weight	75,1		
Final weight	73,1		
Decrease of Weight	1,97	5,96	0,0001
Body Massa Index			
Early Body Massa Index	32,5		
Final Body Massa Index	31,8		
Decrease of Body Massa Index	0,7	5,11	0,0001
Total Cholesterol			
Early Cholesterol	233,2		
Final Cholesterol	224,7		
Decrease of Cholesterol	8,5	2,20	0,036
LDL			
Early LDL	152,3		
Final LDL	139,4		
Decrease of LDL	12,9	3,20	0,003
Trigliserida			
Early Trigliserida	161,2		
Final Trigliserida	143,9		
Decrease of Trigliserida	17,3	2,22	0,034

The results of the study at the identification stage found that most obese respondents experienced problems with improving lipid profiles, namely high cholesterol. Elevated cholesterol in people with obesity due to obesity can increase the amount of cholesterol made by the liver (Nandasena et al., 2023). This condition can also reduce the clearance of cholesterol levels from the blood. For triglycerides, most of them are normal. The results found an increase in the group of obese patients compared to the non-obese group. A significant correlation between the increase in the blood of obese boys and girls. So the results of this study found the presence of 2 components of the lipid profile that increased in people with obesity, namely total cholesterol (Noh & Lee, 2023). This is not the case with triglycerides. There are differences in the findings of lipid profile components, namely triglyceride levels with may occur due to differences in respondent characteristics (Palikhey et al., 2023).

Effects of Nutritional Counseling on Weight Loss and Lipid Profile Improvement after being given nutritional counseling, respondents lost weight. The occurrence of weight loss is directly related to nutritional intake. Providing nutritional counseling can change respondents' consumption behavior, namely reducing energy intake consistently. This condition certainly affects weight loss (Pan et al., 2023). The results of statistical analysis showed a significant effect of nutritional counseling on weight loss. For the development of body mass index after nutritional counseling there was also a decrease in body mass index. The results of statistical analysis showed a significant effect of nutritional counseling on reducing body mass index. The occurrence of a decrease in body mass index is certainly directly related or as an effect of weight loss (Pinho et al., 2023). Where body weight is one of the parameters of body mass index. The results of this study found the sinific effect of nutritional counseling on weight loss and body mass index of obese respondents (Raja et al., 2023). The effect of module-based nutrition education on adolescent weight change in the intervention group. The occurrence of differences in the results of this study may be due to the characteristics of different samples and nutritional counseling (Skudder-Hill et al., 2023).

For lipid profiles, after nutritional counseling there was a decrease in total cholesterol. The improvement of lipid profiles in respondents, both total cholesterol and triglycerides, is the impact of dietary changes, especially fat consumption patterns, both types and amounts (Thongtang et al., 2022). To lower total cholesterol and terriglycerides, the type of fat that is restricted is saturated fat. Instead increase the consumption of unsaturated fats. The results of statistical analysis showed a significant effect of nutritional counseling on improving lipid profiles (total cholesterol and triglycerides) in dyslipidemia respondents (Williams et al., 2022). The significant decrease in total cholesterol after nutritional and lifestyle counseling has a sinifial influence on the reduction of total cholesterol and terriglycerides (Yan et al., 2022).

Significant effect of nutritional counseling in lowering respondents' cholesterol levels. The characteristics of respondents in this study can have an effect on total cholesterol levels. As we get older, total cholesterol levels are relatively higher at a young age, this is due to reduced receptor activity (Yao et al., 2022). These receptor cells function as hemostasis regulators of cholesterol circulation in the blood and are widely found in the liver, gonadal glands and adrenal glands. The presence of interference with receptor cells will increase cholesterol levels in the blood. The results of the study are more women who suffer from dyslipidemia compared to men (Zhang et al., 2023). Some studies prove that women who have menspose tend to have higher cholesterol levels than adult men due to reduced activity of the hormone estrogen. Estrogen hormones play an important role in controlling cholesterol levels, and also function as antioxidants. The hormone estrogen can prevent the oxidation of LDL cholesterol so that it can reduce plaque in blood vessels (Zhang et al., 2023).

Nutritional counseling is usually used for the purpose of increasing knowledge that provides more specific information. The information conveyed is only in outline so that the

message to be conveyed cannot be too much (Zhao et al., 2023). Increased knowledge score after counseling on knowledge and attitudes found that counseling was very influential on increasing meaningful nutritional knowledge before and after nutrition education interventions 2 times a week (10-15 minutes) for 3 weeks (Zhao et al., 2023). This study shows there is a significant influence between nutritional counseling and knowledge. Improvement in addition to changing one's knowledge and attitudes, counseling is also able to change one's actions (obedience) for the better. This can be because one of the advantages of conveying information briefly so that respondents immediately understand the sentence compared to if it is too much and long (Abdu et al., 2023).

The provision of good nutritional counseling is very influential on reducing cholesterol levels to be able to reduce blood cholesterol levels (Alastalo et al., 2023). Nutritional counseling provides lifestyle changes in cholesterol patients, especially changes in nutritional intake (Chen et al., 2022). Providing nutritional counseling to reduce blood cholesterol levels Personal counseling is one of the roles of health services in creating lifestyle and dietary changes. These educative efforts need to be supported through counseling, clients are expected to have the knowledge and skills to make changes that are the solution to their problems (Garcia et al., 2023). Some other studies that support the results of this study are the effect of counseling there is a decrease in blood cholesterol levels with high total cholesterol while in patients with symptoms of obesity after receiving nutritional counseling. Research on patients with hypercholesterolemia does not use drugs for healing efforts but uses nutritional counseling. Respondents who received nutritional counseling 4 times in 4 months compared to patients who did not receive nutritional counseling (El-kholy et al., 2023). Patients who received counseling experienced a significant decrease in cholesterol while in the control group there was an insignificant decrease in cholesterol levels. The influence of nutritional counseling on reducing cholesterol levels in this study was made possible by three factors, namely patient education factors, counselor factors, and counseling frequency factors given to patients. This study means that counseling conducted during two meetings can generate interest and awareness of respondents. The interest or willingness of respondents and patients' families in the process of empowerment and independence is very necessary for the success of cholesterol sufferers so that the intake consumed is in accordance with the recommendations that have been described (Ermias et al., 2023). However, to achieve maximum results requires counselor knowledge about cholesterol and its management, counselor skills in counseling, and adequate meeting time to create effective counseling (Garling & Wong, 2023).

Effective counseling should take between 20 and 30 minutes per appointment. Counseling is given gradually by means of lectures, discussions, or sharing among high cholesterol sufferers who involve more respondents, and repeated and reviewed before continuing to the next discussion so that respondents more quickly and easily capture or understand the knowledge provided. There is an influence on the success of counseling delivery, so that nutritional counseling does not only take place face-to-face but can be done independently by respondents (Otsuka et al., 2023). In addition, the existence of materials / modules and media is very supportive of changes in knowledge and the success of a counseling activity. This opinion is supported by the success of a training or counseling activity is largely determined by the operations and processes of these activities such as the implementation process, the need for supporting facilities such as media development and the need for evaluation so that participants are more capable and faster in making better decisions, because their technical skills, human skills and managerial skills have increased (Paneque et al., 2023).

Education also contributes to the success of reducing blood cholesterol levels of patients needed to obtain information such as things that support health, so as to improve the quality of life. The higher one's level of education, the easier it is to receive information, so that the more

knowledge one has, while less education will hinder the development of one's attitude towards newly introduced values (Salhia et al., 2023). Education is closely related to the patient's knowledge in receiving information from counseling, which can increase the patient's knowledge. A person who is more educated has better knowledge than a less educated person. It is known that nutritional counseling interventions can lower cholesterol and triglyceride levels. It further proved that statistical test results on all lipid profiles (cholesterol levels, HDL and LDL levels, and triglyceride levels) between before and after nutritional counseling can change significantly (Almigbal et al., 2023). This shows that interventions in the form of nutritional counseling have significant benefits in lowering cholesterol, LDL and triglyceride levels. Intervention in the form of nutritional counseling benefits in lowering cholesterol values. Changes in lifestyle and changes in nutritional value intake in hypercholesterolemic patients are the results of providing nutritional counseling (Deora & Venkatraman, 2022).

Specific interventions with nutritional counseling can improve the understanding and activity patterns of patients who receive health promotion through various counseling for the better (Navya et al., 2023). Individually intervention through nutritional counseling can change lifestyle as well as dietary changes. This is important for health care providers such as hospitals (Dou et al., 2023). Educational efforts are very important which contain material such as diet / nutritional intake and physical activity. Material that is on target and has a good way of delivery, it is very effective in the success of nutrition counseling conducted by counselors. Diet such as carbohydrate and fat intake is very important to consider according to consumption rules such as portions and frequency of meals. Imbalance of lipid profiles in the blood from excessive food and beverages, excessive consumption of carbohydrates and fats is the cause of increasing acetyl-CoA obtained from the phosphorylation decarboxylation process, so that the increase forms cholesterol levels complexly (Fernández Granell et al., 2024). Excessive consumption of carbohydrates will increase blood sugar and increase insulin. The process of insulin action is to move blood sugar into cells and converted into glycogen and energy. Excess blood sugar will then become acetyl-CoA and converted into malonyl-CoA so that it will form free fatty acids that will be stored in the form of triglycerides (Karunakar et al., 2023). Furthermore, high plasma triglyceride concentrations can increase simultaneously will cause cholesterol esters to undergo a process of conversion into triglycerides, the reaction that occurs is mediated by CETP or Cholesterol Ester Transfer Protein (Izoe et al., 2022).

A high-carbohydrate diet in patients has an impact on reducing cholesterol and triglyceride levels through inhibition of the work process of the enzyme type Lecithin Cholesterol Acyltransferase or LCAT and can reduce the main protein component called Apo-lipoprotein A1. Therefore, the higher cholesterol will cause high protection against oxidation. Thus, increasing understanding related to carbohydrate intake and fat intake about consumption imbalances can reduce cholesterol, LDL, triglyceride levels and increase HDL levels (Katsuyama et al., 2022). The next material delivered by counselors in nutrition counseling is related to physical activity. Currently the high mortality rate is a result of diseases due to lifestyle changes and lack of physical activity as well as possible stress factors as risk factors (Kazemi et al., 2023). Therefore, physical activity material is important to be delivered in nutritional counseling related to the effect of physical activity on lipid profiles. In addition to food intake, physical activity factors can affect cholesterol in the blood. Good and regular exercise is very good in lowering blood lipid profiles. The absence of good physical activity or high sedentary factors, are considered risk factors for disease (Kim & Park, 2022). Regular exercise can improve body composition and reduce myocardial oxygen demand and is very beneficial and has an impact on low mortality. Lack of physical activity may be 7.8 times the risk of abnormal lipid profiles in the blood compared to those with good physical activity. Physical activity can lower cholesterol and this can lower risk factors for disease. In addition,

physical activity can lose weight due to excessive fat accumulation (not ideal) and this decrease will simultaneously reduce cholesterol levels. In this counseling, the physical activity recommended by the counselor is adjusted to the patient's condition. In general, forms of physical activity to control weight are directed at moderate activity. Regularity in doing aerobics at least 3 times per week with a duration of approximately 30 minutes, through moderate intensity it can improve the process of fat metabolism in the body (Kim et al., 2023). These exercises such as playing bicycles, running, jogging, walking and or brisk walking and allowing for swimming.

Based on the study's results, a p-value of 0.009 was obtained, which means that there is a relationship between the history of hypertension and the incidence of hypertension in pregnant women (Babys et al., 2021). Results 3,383 means that pregnant women with a history of hypertension are 3.3 times more likely to suffer from hypertension than pregnant women who do not have hypertension (Bijl et al., 2022). Women who develop hypertension in the first pregnancy will increase their hypertension in subsequent pregnancies (Chaemsaithong et al., 2022). The incidence of hypertension would grow in a second pregnancy if there is a pregnancy with too much distance from the child. With a history of hypertension, the probability of primigravida will increase four times (Chen et al., 2022). Most of the respondents who suffer from hypertension have a history of hypertension, namely 64.1% (Maher et al., 2022). Those with no history of hypertension are mostly not suffering from hypertension (Marasing et al., 2021). This shows that the history of hypertension in previous pregnancies plays an essential role in the incidence of hypertension during pregnancy (Miller et al., 2022).

The study's p-value of 0.010 < 0.05 means a relationship between exposure to cigarette smoke and the incidence of hypertension in pregnant women (Sasmaya et al., 2022). Results mean that pregnant women exposed to cigarette smoke are 3.5 times more likely to suffer from hypertension than pregnant women who are not exposed to cigarette smoke (Sibai et al., 2021). Exposure to cigarette smoke during pregnancy determines fetal growth (Wu et al., 2021). The nicotine in cigarette smoke is a vasoconstrictor substance that will cause vasoconstriction of blood vessels and increase heart contractions, increasing blood pressure in pregnant women (Wu et al., 2021).

Most of the respondents who suffered from hypertension were respondents who were exposed to cigarette smoke, which was 57.4%, and respondents who were not exposed to cigarette smoke were mostly not suffering from hypertension (Aryal et al., 2020). This shows that cigarette smoke exposure can affect pregnant women's blood pressure (Bakouei et al., 2020). Researchers assume pregnant women exposed to cigarette smoke will have a greater risk of hypertension (Bhutani et al., 2022). This is because the nicotine in cigarette smoke is a vasoconstrictor substance that can increase the heart's work and blood pressure in pregnant women (Cameron et al., 2020).

Based on the study's results, a p-value of 0.000 < 0.05 means a relationship between obesity and the incidence of hypertension in pregnant women. Results = 5.176 means that obese pregnant women are 5.1 times more likely to suffer from hypertension compared to pregnant women who are not obese (Society for Maternal-Fetal Medicine & Publications Committee, 2022). Obesity is the percentage of fat abnormalities expressed by the body mass index, which compares body weight and height squared in meters (de Haas et al., 2022). Being overweight and having hypertension often go hand in hand because adding kilograms makes the heart work harder (Fakhouri et al., 2020).

Most of the respondents who suffered from hypertension were obese, 65.7%. At the same time, people who are obese and do not suffer from hypertension are only 34.7%. Researchers assume obese people are at risk of suffering from hypertension at the time of pregnancy because, in obese people, there is increased work on the heart to pump blood. Excessive weight

leads to an increase in blood volume and area and expansion of the circulatory system. The greater the body mass, the more blood is needed to supply oxygen and nutrients to the body tissues. This results in the volume of blood circulating through the blood vessels will increase so that the pressure on the arterial walls becomes greater.

This study's results align with the research conducted on the effects of her research and obtained a p-value of 0.001 (Ferrari & Peyvandi, 2020). In line with the analysis, their research received a p-value of 0.001, indicating a relationship between obesity and hypertension (Fletcher et al., 2021). Based on the study's results, a the p-value of 0.125 was obtained, meaning there was no relationship between the physical activity of pregnant women and the incidence of hypertension in pregnant women (García-Romero et al., 2019). Exercise is a type of physical activity defined as an activity that is planned and given a structure in which the movement of a part of the body is repeated to obtain fitness, for example, walking, jogging, swimming and aerobics. Every adult should do at least 30 minutes of moderate-intensity physical activity daily (Goddard et al., 2020). Research results show no relationship between physical activity in pregnant women and the incidence of hypertension in pregnant women (Gonzalez Suarez et al., 2019). The results of this study contradict the research conducted. The effects of their study obtained a p-value of 0.000, meaning there is a relationship between physical activity and hypertension (Guimarães et al., 2019).

Researchers assume that even though there is no relationship between pregnant women and the incidence of hypertension in this study, the physical activity of pregnant women is still a risk factor for pregnancy hypertension (Issue et al., 2022). This is because if pregnant women do enough or do regular physical activity can play an essential role in maintaining a healthy body. Through sports activities, the heart can work more efficiently (Katsafanas & Bushnell, 2022). The frequency of the pulse is reduced, but the power of pumping the heart is getting stronger, the need for heart oxygen at a certain intensity, a reduction in fat and weight and lower blood pressure (Lane-Cordova et al., 2019).

Based on the study's results, a p-value of 0.481 > 0.05 means no relationship exists between salt consumption and hypertension in pregnant women (López-Muñoz et al., 2019). In theory, the World Health Organization (WHO) recommends salt consumption patterns to reduce hypertension risk. The recommended sodium level is no more than 100 mmol (about 2.4 grams or 6 grams of salt) per day or the equivalent of 1 teaspoon daily (Magee, et al., 2022). Excessive sodium consumption causes sodium concentration in the extracellular fluid (Magee, et al., 2022). The intracellular fluid is drawn outwards to normalize, so the extracellular fluid volume rises (Marson et al., 2020). The increased importance of extracellular fluid causes an increase in blood volume, resulting in the onset of hypertension (McNeil et al., 2021).

The results of this study are contrary to the research on the effects of his study obtained a p-value of 0.0001 which means that there is a relationship between salt consumption and the incidence of hypertension (Partash et al., 2022). Research obtained a p-value of 0.001, indicating a relationship between salt consumption and hypertension (Prendes et al., 2020). Researchers assumed that although there was no relationship between salt consumption and the incidence of pregnancy hypertension in this study, excess salt consumption also remained an aggravating risk factor for pregnancy hypertension (Smith et al., 2022). People who consume extra salt every day can lead to hypertensive diseases. This is because excessive salt consumption can increase blood pressure. After all, salt retains water so that blood volume increases and can cause a narrowing of the diameter of arterial blood vessels. This circumstance forces the heart to pump more strongly, increasing blood pressure (Tan et al., 2021).

Based on the study's results, a p-value of 0.000 was obtained, which means that there is a relationship between pregnancy stress and the incidence of hypertension in pregnant women. Results 6.044 means that pregnant women who experience pregnancy stress are 6.0 times more

likely to suffer from hypertension than pregnant women who do not experience pregnancy stress (Tan et al., 2021). Stress can increase blood pressure times (Teirilä et al., 2019). The hormone adrenaline will increase when stressed, and it can cause the heart to pump blood faster so that blood pressure increases. If the stress level decreases, blood pressure will also decrease. According to the study results, most of the respondents who suffered from hypertension were respondents who experienced pregnancy stress, which was 64.5%. This proportion is more significant than the number of non-stressed respondents suffering from hypertension, 23.8% (Tsen & Gelman, 2022).

Researchers assume that stress can increase blood pressure for a while. Blood pressure usually increases when scared, nervous, and chasing time (Vanky & Løvvik, 2020). But in most cases, blood pressure returns to fall again as soon as it begins to relax. Stress can occur when a person is in a state of tension, feeling depressed, sad, frightened and guilty. This condition will stimulate the kidney child to produce the hormone adrenaline, which will spur the heart to pump blood faster and more robust, so blood pressure increases (Alves et al., 2021).

Based on the study's results, a p-value of 0.416 was obtained, meaning there was no relationship between age and hypertension in pregnant women (Cagnacci et al., 2022). The safest age for a woman to become pregnant and give birth is between 20-35 years since they are in a healthy reproductive period. Maternal mortality in expectant and parturient mothers at the age of < 20 years and the age of > 35 years will increase significantly as they are exposed to medical and obstetric complications that can endanger the mother's life (Chikowore et al., 2021). According to researchers, although there is no relationship between age and the incidence of hypertension in pregnant women, age is still a risk factor for hypertension in pregnant women; this is because hypertension is more often obtained in the early and late reproductive years, namely adolescents or over 35 years. Pregnant women < 20 years old easily experience an increase in blood pressure and cause seizures faster, while the age of more than 35 years is also a risk factor for hypertension (Dhawan & Sharma, 2020). So women who are at the beginning or end of reproductive age are more prone to suffer from hypertension during pregnancy (Anisa & Sofwan, 2021).

Based on the study's results, a p-value of 0.047 was obtained, meaning that there was a relationship between parity and hypertension in pregnant women (Aryal et al., 2020). Or result = 2, meaning that pregnant women with primigravida parity are 2.5 times more likely to suffer from hypertension than pregnant women with multigravida parity (Babys et al., 2021). The first pregnancy is mainly in mothers who are > 35 years old (Bakouei et al., 2020). The frequency in primigravida is riskier than in multigravida because immunological theory explains the relationship of parity with the incidence of hypertension (Bhutani et al., 2022). The theory states that blocking antibodies against placental antigens formed in the first pregnancy is the cause of hypertension. This study supported the conclusions of the relationship between parity and the incidence of hypertension in pregnant women and supported other studies that parity is a risk factor for hypertension in pregnant women (Bijl et al., 2022).

People with hypertension were 4.5% aged 20-35 years and 0.7% younger than 20 years old. Women less than 17 years of age or more than 30 years are significantly associated with hypertension (Wu et al., 2021). Women over the age of 35 are a risk factor for developing hypertension. Women under 20 years old have a higher risk of developing hypertension and are at 1.6 times higher risk of death; women over 35 years of age have a 1.2 times higher risk of developing hypertension. For ages, 20-35 years the risk of having risk of developing hypertension is 0.87 (Ahmed et al., 2021).

Inadequate maternal immunological response to inherited fetal antigens has been suggested as one of the mechanisms responsible for the development of hypertension (Albåge et al., 2020). Increased hypertension in primigravida women and reduced incidence in those

with previous abortions or late miscarriages are consistent with immunological causes of hypertension. However, data regarding previous miscarriages are not associated with the risk of hypertension (Arabloo et al., 2022).

Body mass index at the beginning of the second trimester is highly predicted to increase the risk of hypertension, with the highest incidence (12.6%) among women whose body mass index is>34 kg/m^2 (Bektas et al., 2020). These findings are consistent with other studies that report an increased incidence of hypertension in obese women (Bell et al., 2020). Obesity is the main risk factor for cardiovascular and cerebrovascular diseases. Indeed, obese women are at increased risk of hypertension, diabetes mellitus, hyperlipidemia, hyperuricemia, and poor heart function (Bichard et al., 2022).

In addition, obesity harms maternal hemodynamic changes during pregnancy (Chami et al., 2022). It is, therefore, possible that some pathophysiological alterations associated with obesity are also responsible for the incidence of wrinkled hypertension in obese women. The routine balance of pregnant women is an important part of all prenatal visits (Ciriello et al., 2022). The increase in weight gain at each visit is used both to assess status nutrition and to indicate the risk of hypertension. Again at least 2 pounds per week, especially during the third trimester associated with the risk of hypertension (Cui & Song, 2022). However, it should be emphasized that excessive weight gain (oedema) during pregnancy should not be considered diagnostic hypertension but should be noted as a risk factor for the potential development of hypertension (Diffenderfer et al., 2022).

Indeks body mass and systolic and diastolic blood pressure are very close to the risk of hypertension. This information should be useful for counseling mothers and understanding the pathophysiological characteristics of hypertension (Flügge et al., 2018). When using the reported characteristics of patients to predict recurrent hypertension in this group with a high recurrence rate (45.2%), the introduction of women at risk was insufficient. Identification of women at low risk for recurrent diseases, who may benefit from less intensive antenatal surveillance, is not yet possible and individual counselling on risks in subsequent pregnancies remains a challenge (Gooding et al., 2020).

Blood plessure and proteinuria are established as detailed diagnostic criteria for defining hypertension. In addition evaluating the risk factors for hypertension in a group of primigravida showed that systolic and diastolic systolic blood pressure in early pregnancy (before 22 weeks of pregnancy) was very predicted to be the risk of hypertension (Harrison et al., 2021). During pregnancy, normal major physiological changes occur throughout the cardiovascular system, especially the placental. These changes are due to the migratory and endovascular trophoblast action on the walls of the spiral arterioles, which help to transform of the placenta artery bed into low resistance, low pressure, high flow system. It is recommended that things in a bag start in the first trimester dan is usually completed at 20 weeks gestation. This coincides with a physiological decrease in the blood of the mother's systemic pressure during normotensive pregnancy. In contrast, pregnancies are not at risk of hypertension. The inadequate vascular response of the mother to the placenta is usually evident at 20 weeks gestation. Therefore the association of hypertension with an increase in maternal blood pressure reflects this abnormal physiological process (Heyden et al., 2020).

Pressure blood and proteinuria are established as detailed diagnostic criteria for defining hypertension. In addition evaluating the risk factors for hypertension in a group of primigravida showed that systolic and diastolic systolic blood pressure in early pregnancy (before 22 weeks of pregnancy) was highly predicted to be a risk of hypertension (Hossain & Kim, 2022). During pregnancy, normal major physiological changes occur throughout the cardiovascular system, especially sea utero placental culture. These changes are due to the migratory and endovascular trophoblast action on the walls of the spiral arterioles, which help to transform of the placenta

artery bed into low resistance, low pressure, high flow system. It is recommended that things in a bag start in the first-trimester dan is usually completed at 20 weeks gestation. This coincides with a physiological decrease in the blood of the mother's systemic pressure during normotensive pregnancy. Conversely, pregnancies that are not at risk of hypertension, the mother's inadequate vascular response to the placenta is usually proven at 20 weeks gestation (Babys et al., 2021). Therefore the association of hypertension with an increase in maternal blood pressure that we found in our study may reflect this abnormal physiological process.

In women who smoke during the menstruation period, hypertension is found. On the other hand, smoking when not menstruating is not found to risk hypertension. A similar analysis was performed to evaluate the contribution of hidden risk factors to the risk of severe hypertension (Bijl et al., 2022). No smoking during pregnancy in women who smoke during the menstruation period, an increase in hypertension is found. On the other hand, smoking when not menstruating is not found to risk hypertension. A similar analysis was performed to evaluate the hidden contribution of risk factors to the risk of severe hypertension (Bijl et al., 2022). No smoking during pregnancy can be used to protect against hypertension. However, the protective effect of smoking is a contra for women who continue to smoke, especially over 20 weeks of pregnancy. Having a husband who has a habit of smoking can also increase the risk of increased hypertension (Chaemsaithong et al., 2022). Mothers who smoke will increase the risk of hypertension. The prevalence of hypertension is least in women who quit smoking in early pregnancy. An increased risk of hypertension was found in pregnant women who were still smoking during pregnancy for more than 20 weeks. In addition to the time of cigarette consumption, the dose of cigarettes per day also affects hypertension.

Cigarettes of more than three pieces per day can increase hypertension in primigravida mothers. The production of thromboxane A2 through inhibition of thromboxane synthase and placental acetylcholine by the way nicotine acts on nicotinic receptors in the placenta eventually stimulates the release of endothelium-derived relaxing factor and nitric oxide. This beneficial effect of smoking in hypertension can also be mediated by inhibiting cytokine production and the antioxidant activity of nicotine (Chen et al., 2022). Blood lead levels above 4.2 µg/dl may increase the risk of hypertension by 105%. For each increase in blood lead levels, 1 µg/dl. Blood lead levels in pregnancy are a risk factor for hypertension. Blood lead levels in patients with hypertension are higher than in normal pregnant women. Every 1 µg/dl increase in blood lead levels in pregnant women increases the risk of hypertension by 1.6%. The safe range of blood lead levels in pregnant women is 5 µg/dl. With a remarkable reduction in environmental lead sources, blood lead levels have declined over the past few decades. However, lead exposure remains a risk factor for women's health even at low Health. Lower blood lead levels (average = 2.3 µg/dl) were associated with systolic blood pressure. Low blood lead levels in pregnant women have been linked to pregnancy-induced hypertension. Low levels of lead exposure have a dosing effect, and hypertensive relationship at 4.2 µg/dl, The risk of hypertension is almost not significantly increased with an increase in blood lead levels when blood lead levels are lower than 4.2 µg/dl. However, when blood lead levels are higher than 4.2 µg/dl, the risk of hypertension increases by 105% for every 1 µg/dl increase in blood lead levels. Lead exposure can accumulate in pregnant women through the air, skin contact, or the food chain (Maher et al., 2022).

Get is used to protect against hypertension. However, the protective effect of smoking is a contra for women who continue to smoke, especially over 20 weeks of pregnancy. Having a husband who has a habit of smoking can also increase the risk of increased hypertension (Chaemsaithong et al., 2022). Mothers who smoke will increase the risk of hypertension. The prevalence of hypertension is least in women who quit smoking in early pregnancy. An increased risk of hypertension was found in pregnant women who were still smoking during

pregnancy for more than 20 weeks. In addition to the time of cigarette consumption, the dose of cigarettes per day also affects hypertension.

Cigarettes of more than three pieces per day can increase hypertension in primigravida mothers. The production of thromboxane A2 through inhibition of thromboxane synthase and placental acetylcholine by the way nicotine acts on nicotinic receptors in the placenta eventually stimulates the release of endothelium-derived relaxing factor and nitric oxide. This beneficial effect of smoking in hypertension can also be mediated by inhibiting cytokine production and the antioxidant activity of nicotine (Chen et al., 2022). Blood lead levels above 4.2 µg/dl may increase the risk of hypertension by 105%. For each increase in blood lead levels, 1 µg/dl. Blood lead levels in pregnancy are a risk factor for hypertension. Blood lead levels in patients with hypertension are higher than in normal pregnant women. Every 1 µg/dl increase in blood lead levels in pregnant women increases the risk of hypertension by 1.6%. The safe range of blood lead levels in pregnant women is 5 µg/dl. A remarkable reduction in environmental lead sources, blood lead levels have declined over the past few decades. However, even at low blood lead levels, lead exposure remains a risk factor Health. Lower blood lead levels (average = 2.3 µg/dl) were associated with systolic blood pressure. Low blood lead levels in pregnant women have been linked to pregnancy-induced hypertension. Low levels of lead exposure have a dosing effect and hypertensive relationship at 4.2 µg/dl, The risk of hypertension is almost not significantly increased with an increase in blood lead levels when blood lead levels are lower than 4.2 µg/dl. However, when blood lead levels are higher than 4.2 µg/dl, the risk of hypertension increases by 105% for every 1 µg/dl increase in blood lead levels. Lead exposure can accumulate in pregnant women through air, skin contact, or food chains (Maher et al., 2022).

Alcohol consumption may increase the risk of hypertension. A person who consumes alcohol can increase the severity of the disease if they experience hypertension. Blood vessels can become narrower if a person consumes alcohol to trigger damage to organs (Marasing et al., 2021). So far, alcohol consumption can be considered to improve heart health, but it is harmful if consumed within reasonable limits. Consumption of alcohol in small portions can dilate blood vessels, but if consumed in large quantities, it is the opposite (Miller et al., 2022).

Calcium in pregnant women is obtained from food consumed in the amount of 1200 milligrams per day for pregnant women over the age of 30 years, and pregnant women over 20 years old require calcium in the amount of 1300 milligrams per day. In pregnant women, calcium is needed more because it is a substitute for the reserve of tissue formation in the fetus. So that if pregnant women lack calcium can increase the risk of hypertension four times (Sasmaya et al., 2022).

Pregnant women who lack calcium can also trigger the occurrence of hypertension because there is an increase in concentration in the blood and muscle contractions in pregnancy hypertension is very important to pay attention to because calcium deficiency in the diet can trigger hypertension. Calcium maintains concentration in the blood on muscle contraction activity (Sibai et al., 2021).

4. CONCLUSION

In the study, matching was not carried out for the sample and there were no inclusion and inclusion criteria in determining the sample so that the results obtained were only differentiated based on the characteristics of respondents. The study still used heterogeneous samples and the examination was carried out in a fairly close time so that the results obtained did not show too significant differences. Based on the data obtained, it can be concluded that there is a significant

relationship between nutritional counseling, nutrition counseling, lipid profile improvement and weight loss in obese patients with dyslipidemia. The sample size used in subsequent studies is more homogeneous so that each sample must be the same. Checks to see a decrease should be carried out over a long enough period of time so that the results obtained are more valid. The study was conducted using a larger sample. The weakness of this study has not been matched on the sample, so the changes that occur only look at the differences before and after cannot distinguish changes between groups. But this study also has advantages because the assessment is objective so as to minimize the occurrence of bias. Suggestions for further research can be done by differentiating the effect of counseling on obese groups with those who are not obese so that the influence of counseling can be more visible.

REFERENCES

Abdu, H., Ergete, W., Tadele, A., Woldekidan, S., Abebe, A., Meles, M., Shenkut, M., & Seyoum, G. (2023). Effects of Moringa Stenopetala (Baker F.) Cufod Leaf On Reproductive Organs And Serum Biochemical Levels In Male Rats: An In Vivo Reproductive Toxicity Study. *Phytomedicine Plus*, *3*(3), 100473. https://doi.org/10.1016/J.Phyplu.2023.100473

Ahmed, A., Liang, M., Chi, L., Zhou, Y. Q., Sled, J. G., Wilson, M. D., & Delgado-Olguín, P. (2021). Maternal Obesity Persistently Alters Cardiac Progenitor Gene Expression And Programs Adult-Onset Heart Disease Susceptibility. *Molecular Metabolism*, *43*(November 2020), 101116. https://doi.org/10.1016/J.Molmet.2020.101116

Alastalo, N., Siitonen, P., Jyrkkä, J., & Hämeen-Anttila, K. (2023). Exploratory Research in Clinical and Social Pharmacy The Quality Of Non-Prescription Medicine Counselling In Finnish Pharmacies – A Simulated Patient Study. *Exploratory Research In Clinical And Social Pharmacy*, *11*(May), 100304. https://doi.org/10.1016/J.Rcsop.2023.100304

Albåge, A., Alström, U., Forsblad, J., & Welin, S. (2020). Quadruple Bioprosthetic Valve Replacement in A Patient With Severe Carcinoid Heart Disease. *JACC: Case Reports*, *2*(2), 271–276. https://doi.org/10.1016/J.Jaccas.2019.11.030

Almigbal, T. H., Almunif, D. S., Ali Deshisha, E., Altaradi, H., Alrasheed, A. A., Batais, M. A., & Alhabib, K. F. (2023). Physicians' Perceptions And Beliefs On The Current Dyslipidemia Management Practices Within Saudi Arabia. *Saudi Pharmaceutical Journal*, *31*(10), 101759. https://doi.org/10.1016/J.Jsps.2023.101759

Alves, V. P., De Oliveira, R. C., & Gregori, D. (2021). Non-Communicable Chronic Diseases: Mortality of Older Adult Citizens In Brazil And Italy Before The Covid-19 Pandemic. *Health Policy OPEN*, *2*(June), 100041. https://doi.org/10.1016/J.Hpopen.2021.100041

Anisa, N. A., & Indarjo, S. (2021). Perilaku Sehat Pasien Diabetes Mellitus Tipe 2 yang Mengalami Gangren di Puskesmas Halmahera Kota Semarang. *Indonesian Journal of Public Health and Nutrition*, *1*(1), 73-79.

Arabloo, J., Omidi, N., Rezapour, A., Sarabi Asiabar, A., Mojtaba Ghorashi, S., & Azari, S. (2022). The Burden Of Nonrheumatic Valvular Heart Diseases In Iran Between 1990 And 2017: Results From The Global Burden Of Disease Study 2017. *IJC Heart And Vasculature*, *39*(January), 100956. https://doi.org/10.1016/J.Ijcha.2022.100956

Aryal, S. R., Moussa, H., Sinkey, R., Dhungana, R., Tallaj, J. A., Pamboukian, S. V., Patarroyo-Aponte, M., Acharya, D., Bajaj, N. S., Bhattarai, S., Lenneman, A., Joly, J. M., Sibai, B. M., & Rajapreyar, I. N. (2020). Management Of Reproductive Health In Patients With Pulmonary Hypertension. *American Journal Of Obstetrics And Gynecology MFM*, *2*(2), 100087. https://doi.org/10.1016/J.Ajogmf.2020.100087

Babys, D., Idris, I., & Prihantono. (2021). Differences In Serum Magnesium Levels, Folic Acid, And Infant Outcomes In Severe Preeclampsia: A Literature Review. *Medicina Clinica*

Practica, *4*, 100221. https://doi.org/10.1016/J.Mcpsp.2021.100221

Bakouei, F., Delavar, M. A., Mashayekh-Amiri, S., Esmailzadeh, S., & Taheri, Z. (2020). Efficacy of N-3 Fatty Acids Supplementation on The Prevention of Pregnancy Induced-Hypertension Or Preeclampsia: A Systematic Review and Meta-Analysis. *Taiwanese Journal of Obstetrics And Gynecology*, *59*(1), 8–15. https://doi.org/10.1016/J.Tjog.2019.11.002

Bektas, İ., Kır, M., Yıldız, K., Genç, Z., Bektas, M., & Ünal, N. (2020). Symptom Frequency In Children With Congenital Heart Disease And Parental Care Burden In Predicting The Quality Of Life Of Parents In Turkey. *Journal Of Pediatric Nursing*, *53*, E211–E216. https://doi.org/10.1016/J.Pedn.2020.04.012

Bell, J., Alhudairy, M., Kazakova, V., Johnstone, M., & Tsao, L. (2020). Right And Left-Sided Carcinoid Heart Disease In The Setting Of Selective Serotonin Reuptake Inhibitor Use. *JACC: Case Reports*, *2*(12), 1841–1844. https://doi.org/10.1016/J.Jaccas.2020.07.060

Bhutani, N., Jethani, V., Jethani, S., & Ratwani, K. (2022). Coagulation Profile And Platelet Parameters In Pregnancy Induced Hypertension Cases And Normotensive Pregnancies : A Cross-Sectional Study. *Annals Of Medicine And Surgery*, *80*(April), 104124. https://doi.org/10.1016/J.Amsu.2022.104124

Bichard, E., Mckeever, S., Bench, S., & Wray, J. (2022). Experiences Of Siblings Of Children With Congenital Heart Disease During Coronavirus Disease 2019; A Qualitative Interview Study. *Journal Of Pediatric Nursing*, 63, 96–101. https://doi.org/10.1016/J.Pedn.2021.12.019

Bijl, R. C., Cornette, J. M., Brewer, A. N., Zwart, I. F., Franx, A., Tsigas, E. Z., & Koster, M. P. (2022). Patient-reported preconceptional characteristics in the prediction of recurrent preeclampsia. *Pregnancy Hypertension*, *28*, 44-50. https://doi.org/10.1016/J.Preghy.2022.02.003

Cagnacci, A., Londero, A. Pietro, & Xholli, A. (2022). Case Reports In Women ' S Health. *Case Reports In Women's Health*, *34*, E00389. https://doi.org/10.1016/J.Crwh.2022.E00389

Cameron, N. A., Molsberry, R., Pierce, J. B., Perak, A. M., Grobman, W. A., Allen, N. B., Greenland, P., Lloyd-Jones, D. M., & Khan, S. S. (2020). Pre-Pregnancy Hypertension Among Women In Rural And Urban Areas Of The United States. *Journal Of The American College Of Cardiology*, *76*(22), 2611–2619. https://doi.org/10.1016/J.Jacc.2020.09.601

Chaemsaithong, P., Sahota, D. S., & Poon, L. C. (2022). First Trimester Preeclampsia Screening and Prediction. *American Journal Of Obstetrics And Gynecology*, *226*(2), S1071-S1097.E2. https://doi.org/10.1016/J.Ajog.2020.07.020

Chami, J., Nicholson, C., Strange, G., Baker, D., Cordina, R., & Celermajer, D. S. (2022). Hospital Discharge Codes And Substantial Underreporting Of Congenital Heart Disease. *International Journal Of Cardiology Congenital Heart Disease*, *7*(November 2021), 100320. https://doi.org/10.1016/J.Ijcchd.2022.100320

Chen, T. T., Chen, C. Y., Fang, C. P., Cheng, Y. C., & Lin, Y. F. (2022). Causal Influence of Dietary Habits on The Risk of Major Depressive Disorder: A Diet-Wide Mendelian Randomization Analysis. *Journal of Affective Disorders*, *319*(September), 482–489. https://doi.org/10.1016/j.Jad.2022.09.109

Chen, Y., Ou, Q. X., Chen, Y., Zhu, Q. L., Tan, M. H., Zhang, M. M., Wu, S. Z., & Xu, H. Y. (2022). Association Between Trace Elements And Preeclampsia: A Retrospective Cohort Study. *Journal Of Trace Elements In Medicine And Biology*, *72*, 126971. https://doi.org/10.1016/J.Jtemb.2022.126971

Chikowore, T., Kamiza, A. B., Oduaran, O. H., Machipisa, T., & Fatumo, S. (2021). Non-

Communicable Diseases Pandemic and Precision Medicine: Is Africa Ready? *Ebiomedicine*, *65*, 103260. https://doi.org/10.1016/J.Ebiom.2021.103260

Ciriello, G. D., Colonna, D., Romeo, E., & Sarubbi, B. (2022). Cardiac resynchronization therapy-defibrillator implantation guided by electroanatomic mapping in a young adult patient with congenital heart disease. *Indian Pacing and Electrophysiology Journal*, *22*(2), 108-111. https://doi.org/10.1016/J.Ipej.2022.01.003

Cui, J., & Song, L. (2022). Wrist Pulse Diagnosis Of Stable Coronary Heart Disease Based On Acoustics Waveforms. *Computer Methods And Programs In Biomedicine*, *214*, 106550. https://doi.org/10.1016/J.Cmpb.2021.106550

De Haas, S., Mulder, E., Schartmann, N., Mohseni, Z., Abo Hasson, F., Alsadah, F., Van Kuijk, S., Van Drongelen, J., Ghossein-Doha, C., & Spaanderman, M. (2022). Blood Pressure Adjustments Throughout Healthy And Hypertensive Pregnancy: A Systematic Review And Meta-Analysis. *Pregnancy Hypertension*, *27*(April 2021), 51–58. https://doi.org/10.1016/J.Preghy.2021.12.004

Deora, N., & Venkatraman, K. (2022). Aloe Vera In Diabetic Dyslipidemia: Improving Blood Glucose And Lipoprotein Levels In Pre-Clinical And Clinical Studies. *Journal Of Ayurveda And Integrative Medicine*, *13*(4), 100675. https://doi.org/10.1016/J.Jaim.2022.100675

Dhawan, D., & Sharma, S. (2020). Abdominal Obesity, Adipokines And Non-Communicable Diseases. *Journal Of Steroid Biochemistry And Molecular Biology*, *203*(July), 105737. https://doi.org/10.1016/J.Jsbmb.2020.105737

Diffenderfer, M. R., Rajapakse, N., Pham, E., He, L., Dansinger, M. L., Nelson, J. R., & Schaefer, E. J. (2022). Plasma Fatty Acid Profiles: Relationships With Sex, Age, And State-Reported Heart Disease Mortality Rates In The United States. *Journal Of Clinical Lipidology*, 1–13. https://doi.org/10.1016/J.Jacl.2021.12.005

Dou, Y., Chen, B., Yu, X., & Ma, D. (2023). Effectiveness Of Internet-Based Health Management In Patients With Dyslipidemia: A Four-Year Longitudinal Study. *Atherosclerosis*, *376*(April), 34–42. https://doi.org/10.1016/J.Atherosclerosis.2023.04.004

El-Kholy, A. A., Kholy, E. A. El, Abdou, A. H., Ahmed, H., Karar, D., Abdelrhim, M., Abdelaal, K., & Sayed, R. (2023). Prevalence And Associated Factors Of Anemia Among Pregnant Women And The Impact Of Clinical Pharmacist Counseling On Their Awareness Level : A Cross Sectional Study Short Title : Anemia In Pregnancy. *Saudi Pharmaceutical Journal*, 101699. https://doi.org/10.1016/J.Jsps.2023.101699

Ermias, Y., Averbach, S. H., Dey, A. K., Gebrehanna, E., & Holt, K. (2023). The Association Between Quality Of Contraceptive Counseling And Selection Of Contraceptive Method Post-Counseling Among Women In Ethiopia. *Contraception*, *124*, 110060. https://doi.org/10.1016/J.Contraception.2023.110060

Fakhouri, F., Scully, M., Provot, F., Blasco, M., Coppo, P., Noris, M., Paizis, K., Kavanagh, D., Pène, F., Quezada, S., Hertig, A., Kissling, S., O'Brien, P., Delmas, Y., Alberio, L., Winer, N., Veyradier, A., Cataland, S., Frémeaux-Bacchi, V., … Tsatsaris, V. (2020). Management Of Thrombotic Microangiopathy In Pregnancy And Postpartum: Report From An International Working Group. *Blood*, *136*(19), 2103–2117. https://doi.org/10.1182/BLOOD.2020005221

Fernández Granell, I., Fulgencio Delgado, A., López González, J., & Cedeño De Jesús, S. B. (2024). Diffuse Interstitial Lung Disease Caused By Silicosis. *Medicina Clinica Practica*, *7*(1), 100406. https://doi.org/10.1016/J.Mcpsp.2023.100406

Ferrari, B., & Peyvandi, F. (2020). How I Treat Thrombotic Thrombocytopenic Purpura In Pregnancy. *Blood*, *136*(19), 2125–2132. https://doi.org/10.1182/BLOOD.2019000962

Fletcher, B., Chappell, L. C., Lavallee, L., Wilson, H. M., Stevens, R., Mackillop, L., Mcmanus, R. J., & Tucker, K. L. (2021). Changes To Management Of Hypertension In Pregnancy, And Attitudes To Self-Management: An Online Survey Of Obstetricians, Before And Following The First Wave Of The COVID-19 Pandemic. *Pregnancy Hypertension*, *26*(July), 54–61. https://doi.org/10.1016/J.Preghy.2021.08.117

Flügge, A. K., Wasmer, K., Orwat, S., Abdul-Khaliq, H., Helm, P. C., Bauer, U., Baumgartner, H., & Diller, G. P. (2018). Cardiac Resynchronization Therapy In Congenital Heart Disease: Results From The German National Register For Congenital Heart Defects. *International Journal Of Cardiology*, *273*, 108–111. https://doi.org/10.1016/J.Ijcard.2018.10.014

Garcia, A. D., Mullan, B., & Dorina, I. (2023). Predicting discretionary food consumption using temporal self-regulation theory and food reward sensitivity. *Appetite*, *190*, 107010. https://doi.org/10.1016/J.Appet.2023.107010

García-Romero, C. S., Guzman, C., Cervantes, A., & Cerbón, M. (2019). Liver Disease In Pregnancy: Medical Aspects And Their Implications For Mother And Child. *Annals Of Hepatology*, *18*(4), 553–562. https://doi.org/10.1016/J.Aohep.2019.04.009

Garling, K. A., & Wong, B. (2023). An Initial Reliability Analysis Of A Patient Counseling Rubric To Objectively Measure Student Pharmacist Performance. *Heliyon*, *9*(5), E15768. https://doi.org/10.1016/J.Heliyon.2023.E15768

Goddard, J., Wee, M. Y. K., & Vinayakarao, L. (2020). Update On Hypertensive Disorders In Pregnancy. *BJA Education*, *20*(12), 411–416. https://doi.org/10.1016/J.Bjae.2020.07.007

Gonzalez Suarez, M. L., Kattah, A., Grande, J. P., & Garovic, V. (2019). Renal Disorders In Pregnancy: Core Curriculum 2019. *American Journal Of Kidney Diseases*, *73*(1), 119–130. https://doi.org/10.1053/J.Ajkd.2018.06.006

Gooding, H. C., Brown, C. A., Revette, A. C., Vaccarino, V., Liu, J., Patterson, S., Stamoulis, C., & De Ferranti, S. D. (2020). Young Women's Perceptions Of Heart Disease Risk. *Journal Of Adolescent Health*, *67*(5), 708–713. https://doi.org/10.1016/J.Jadohealth.2020.05.010

Guimarães, T., Magalhães, A., Veiga, A., Fiuza, M., Ávila, W., & Pinto, F. J. (2019). Heart Disease And Pregnancy: State Of The Art. *Revista Portuguesa De Cardiologia (English Edition)*, *38*(5), 373–383. https://doi.org/10.1016/J.Repce.2019.06.002

Harrison, D. J., Uzark, K., Yu, S., Lowery, R., Yetman, A. T., Cramer, J., Rudd, N., Cohen, S., Gauvreau, K., & Gurvitz, M. (2021). Transition Readiness In Congenital Heart Disease: Are Teens And Young Adults Getting The Recommended Information? *International Journal Of Cardiology Congenital Heart Disease*, *7*(November 2021), 100311. https://doi.org/10.1016/J.Ijcchd.2021.100311

Heyden, C. M., Moore, J. W., Ryan, J. R., Lederman, R. J., El-Said, H. G., & Ratnayaka, K. (2020). Alternative Access In Congenital Heart Disease. *JACC: Case Reports*, *2*(11), 1734–1735. https://doi.org/10.1016/J.Jaccas.2020.07.040

Hossain, M. A., & Kim, J. H. (2022). Possibility as role of ginseng and ginsenosides on inhibiting the heart disease of COVID-19: A systematic review. *Journal of Ginseng Research*, *46*(3), 321-330. https://doi.org/10.1016/J.Jgr.2022.01.003

Islam, M. T., Samad Talha, M. T. U., Shafiq, S. S., Mazumder, T., Gupta, R. Das, & Siraj, M. S. (2023). Prevalence, Pattern, And Correlates Of Dyslipidemia In Bangladeshi Individuals. *Journal Of Clinical Lipidology*, 1–12. https://doi.org/10.1016/J.Jacl.2023.09.007

Issue, S., Community, T., Lampung, E., Wulandari, L. A., & Retno, S. N. (2022). *Jurnal Aisyah : Jurnal Ilmu Kesehatan Autogenic Relaxation On Anxiety Among Pregnant Women At*. *7*, 1–8. https://doi.org/10.30604/Jika.V7is1.1188

Izoe, Y., Nagao, M., Sato, K., Sakai, A., Ando, K., Kanai, M., Yamamoto, A., Sakai, S., & Chida, K. (2022). Dynamic Coronary CT Angiography-Estimated Coronary Flow In Non-Obstructive, Plaque-Free Coronary Arteries: Association With Dyslipidemia And Diabetes. *IJC Heart And Vasculature*, *42*(August), 101098. https://doi.org/10.1016/J.Ijcha.2022.101098

Kamrul-Hasan, A. B. M., Alam, M. S., Zarin, N., Kabir, M. A., Gaffar, A. J., Hossain, M. F., ... & Selim, S. (2023). Prevalence and patterns of dyslipidemia among lipid-lowering drug-naïve patients with type 2 diabetes mellitus–A countrywide study in Bangladesh. *Endocrine and Metabolic Science*, *13*, 100152. https://doi.org/10.1016/J.Endmts.2023.100152

Karunakar, G., Shreya, G., Shanmukha Priya, G., Vasavi, A., Sriharshini, G., & Mahalakshmi, G. (2023). Unified Time Series Analysis With Bi-Long Short-Term Memory Model For Early Prediction Of Dyslipidemia In Steel Workers. *E-Prime - Advances In Electrical Engineering, Electronics And Energy*, *6*(May), 100302. https://doi.org/10.1016/J.Prime.2023.100302

Katsafanas, C., & Bushnell, C. (2022). Pregnancy And Stroke Risk In Women. *Neurobiology Of Disease*, *169*(September 2021), 105735. https://doi.org/10.1016/J.Nbd.2022.105735

Katsuyama, Y., Kondo, K., Kojima, M., Kamiji, K., Ide, K., Iizuka, G., Muto, G., Uehara, T., Noda, K., & Ikusaka, M. (2022). Mortality Risk In Older Japanese People Based On Self-Reported Dyslipidemia Treatment And Socioeconomic Status: The JAGES Cohort Study. *Preventive Medicine Reports*, *27*(March), 101779. https://doi.org/10.1016/J.Pmedr.2022.101779

Kazemi, T., Mollaei, H., Takhviji, V., Bijari, B., Zarban, A., Rostami, Z., & Hoshyar, R. (2023). The Anti-Dyslipidemia Property Of Saffron Petal Hydroalcoholicextract In Cardiovascular Patients: A Double-Blinded Randomized Clinical Trial. *Clinical Nutrition ESPEN*, *55*, 314–319. https://doi.org/10.1016/J.Clnesp.2023.04.002

Kim, C., & Park, K. (2022). Dietary Niacin Intake And Risk Of Dyslipidemia: A Pooled Analysis Of Three Prospective Cohort Studies. *Clinical Nutrition*, *41*(12), 2749–2758. https://doi.org/10.1016/J.Clnu.2022.10.018

Kim, M. S., Song, M., Kim, B., Shim, I., Kim, D. S., Natarajan, P., Do, R., & Won, H. H. (2023). Prioritization Of Therapeutic Targets For Dyslipidemia Using Integrative Multi-Omics And Multi-Trait Analysis. *Cell Reports Medicine*, *4*(9), 101112. https://doi.org/10.1016/J.Xcrm.2023.101112

Kirkpatrick, C. F., Sikand, G., Petersen, K. S., Anderson, C. A. M., Aspry, K. E., Bolick, J. P., Kris-Etherton, P. M., & Maki, K. C. (2023). Nutrition Interventions For Adults With Dyslipidemia: A Clinical Perspective From The National Lipid Association. *Journal Of Clinical Lipidology*, *17*(4), 428–451. https://doi.org/10.1016/J.Jacl.2023.05.099

Lane-Cordova, A. D., Khan, S. S., Grobman, W. A., Greenland, P., & Shah, S. J. (2019). Long-Term Cardiovascular Risks Associated With Adverse Pregnancy Outcomes: JACC Review Topic Of The Week. *Journal Of The American College Of Cardiology*, *73*(16), 2106–2116. https://doi.org/10.1016/J.Jacc.2018.12.092

Li, Y., Yang, Z., Ren, S., Shen, B., Zhang, Y., Zong, H., & Li, Y. (2023). Association Between GLP-1R Gene Polymorphism And Dyslipidemia In Chinese Patients With Type 2 Diabetes Mellitus: A Case-Control Study. *Gene*, *878*(June), 147589. https://doi.org/10.1016/J.Gene.2023.147589

Liang, Y., Liu, L., & Liang, B. (2023). COVID-19 Susceptibility And Severity For Dyslipidemia: A Mendelian Randomization Investigation. *Heliyon*, *9*(9), E20247. https://doi.org/10.1016/J.Heliyon.2023.E20247

Lobato Casado, P., Ennazeh El Khaili, M., Jamilena López, A., Segundo Rodríguez, J. C.,

Rivero Rodríguez, D., & García Benassi, J. M. (2024). Spontaneous And Sequential Carotid Dissection In A Patient With Antiphospholipid Syndrome. *Medicina Clinica Practica*, *7*(1), 100400. https://doi.org/10.1016/j.Mcpsp.2023.100400

López-Muñoz, E., Mateos-Sánchez, L., Mejía-Terrazas, G. E., & Bedwell-Cordero, S. E. (2019). Hypothyroidism And Isolated Hypothyroxinemia In Pregnancy, From Physiology To The Clinic. *Taiwanese Journal Of Obstetrics And Gynecology*, *58*(6), 757–763. https://doi.org/10.1016/J.Tjog.2019.09.005

Magee, L. A., Brown, M. A., Hall, D. R., Gupte, S., Hennessy, A., Karumanchi, S. A., Kenny, L. C., Mccarthy, F., Myers, J., Poon, L. C., Rana, S., Saito, S., Staff, A. C., Tsigas, E., & Von Dadelszen, P. (2022). The 2021 International Society For The Study Of Hypertension In Pregnancy Classification, Diagnosis & Management Recommendations For International Practice. *Pregnancy Hypertension*, *27*(September 2021), 148–169. https://doi.org/10.1016/J.Preghy.2021.09.008

Magee, L. A., Khalil, A., Kametas, N., & Von Dadelszen, P. (2022). Toward Personalized Management Of Chronic Hypertension In Pregnancy. *American Journal Of Obstetrics And Gynecology*, *226*(2), S1196–S1210. https://doi.org/10.1016/J.Ajog.2020.07.026

Maher, G. M., Khashan, A. S., O'Byrne, L., Flanagan, S., Mortimer, R. M., Kiely, M., O'B. Hourihane, J., Kenny, L. C., Murray, D., & Mccarthy, F. P. (2022). Periconceptual And Prenatal Alcohol Consumption And Neurodevelopment At Age Two And Five Years. *European Journal Of Obstetrics & Gynecology And Reproductive Biology*, *274*(April), 197–203. https://doi.org/10.1016/J.Ejogrb.2022.05.034

Mansfield, B. S., Bhana, S., & Raal, F. J. (2022). Dyslipidemia In South African Patients With Hypothyroidism. *Journal Of Clinical And Translational Endocrinology*, *29*(March), 100302. https://doi.org/10.1016/J.Jcte.2022.100302

Marasing, I. N., Idris, I., Sunarno, I., Arifuddin, S., Sinrang, A. W., & Bahar, B. (2021). Comparison Of Nitric Oxide Levels, Roll Over Test Value, And Body Mass Index In Preeclampsia And Normotension. *Gaceta Sanitaria*, *35*, S306–S309. https://doi.org/10.1016/J.Gaceta.2021.10.041

Marson, E. J., Kamarajah, S. K., Dyson, J. K., & White, S. A. (2020). Pregnancy Outcomes In Women With Liver Transplants: Systematic Review And Meta-Analysis. *Hpb*, *22*(8), 1102–1111. https://doi.org/10.1016/J.Hpb.2020.05.001

Mcneil, A., Chen, J., & Meng, M. L. (2021). Pulmonary Hypertension In Pregnancy-The Anesthesiologist's Perspective. *International Journal Of Cardiology Congenital Heart Disease*, *5*(June), 100234. https://doi.org/10.1016/J.Ijcchd.2021.100234

Miller, E. C., Wilczek, A., Bello, N. A., Tom, S., Wapner, R., & Suh, Y. (2022). Pregnancy, Preeclampsia And Maternal Aging: From Epidemiology To Functional Genomics. *Ageing Research Reviews*, *73*(January), 20–22. https://doi.org/10.1016/J.Arr.2021.101535

Mishra, S., Murry, B., Devi, N. K., Tripathi, S., & Suokhrie, S. (2023). Obesity In Dyslipidemia And Hypertension: A Study Among Young Adults Of Delhi/NCR. *Clinical Epidemiology And Global Health*, *22*(June), 101335. https://doi.org/10.1016/J.Cegh.2023.101335

Misra, S., Lyngdoh, T., & Mulchandani, R. (2022). Guidelines For Dyslipidemia Management In India: A Review Of The Current Scenario And Gaps In Research. *Indian Heart Journal*, *74*(5), 341–350. https://doi.org/10.1016/J.Ihj.2022.07.009

Muñoz, V., Mario, J., Garcés, J., Vanegas, J. M., & Torres, A. (2024). Efectividad De Un Programa Multidisciplinario Para El Manejo De La Obesidad : Cambio En La Calidad De Vida Y En Los Parámetros Clínicos , Fi Siológicos Y Antropométricos. *Medicina Clínica Práctica*, *7*(1), 100404. https://doi.org/10.1016/J.Mcpsp.2023.100404

Navya, P. D., Kaarthikeyan, G., Alamoudi, A., Bahammam, M. A., Khan, S. S., Alzahrani, K. J., ... & Patil, S. (2023). Transcriptional regulatory signatures of systemic diseases in periodontitis with dyslipidemia. *Journal of King Saud University-Science*, *35*(5), 102707. https://doi.org/10.1016/J.Jksus.2023.102707

Nandasena, H. M. R. K. G., Tennakoon, T. M. S. U. B., & Ralapanawa, D. M. P. U. K. (2023). Prevalence And Determinants Of Dyslipidemia Among Adults In The Community: A Cross-Sectional Study In A Selected Province, Sri Lanka. *Clinical Epidemiology And Global Health*, *24*(February), 101442. https://doi.org/10.1016/J.Cegh.2023.101442

Noh, J. W., & Lee, B. C. (2023). LDL Cholesterol-Lowering Effect Of Daeshiho-Tang In Patients With Dyslipidemia: A Pilot Randomized, Double-Blind, Placebo-Controlled Trial. *Heliyon*, *9*(8), E19162. https://doi.org/10.1016/J.Heliyon.2023.E19162

Otsuka, H., Fujiwara, S., & Takano, A. (2023). Changes In Suicide-Related Indices At A Student Counseling Center At A Japanese University Before And After COVID-19. *Asian Journal Of Psychiatry*, *81*(March 2020), 103462. https://doi.org/10.1016/J.Ajp.2023.103462

Palikhey, A., Lodh, A., Shrestha, J., Karki, M., & Shrivastava, A. K. (2023). An Effect Of Statin On Serum Uric Acid In Patients With Dyslipidemia At A Tertiary Care Hospital. *Endocrine And Metabolic Science*, *13*(October), 100146. https://doi.org/10.1016/J.Endmts.2023.100146

Pan, X., Hong, F., Li, S., Wu, J., Xu, H., Yang, S., ... & Zhao, X. (2023). Long-term exposure to ambient PM2. 5 constituents is associated with dyslipidemia in Chinese adults. *Ecotoxicology and Environmental Safety*, *263*, 115384. https://doi.org/10.1016/J.Ecoenv.2023.115384

Paneque, M., Guimarães, L., Bengoa, J., Pasalodos, S., Cordier, C., Esteban, I., ... & Serra, C. (2023). An European overview of genetic counselling supervision provision. *European Journal of Medical Genetics*, 104710. https://doi.org/10.1016/J.Ejmg.2023.104710

Partash, N., Naghipour, B., Rahmani, S. H., Pashaei Asl, Y., Arjmand, A., Ashegvatan, A., & Faridaalaee, G. (2022). The Impact Of Flood On Pregnancy Outcomes: A Review Article. *Taiwanese Journal Of Obstetrics And Gynecology*, *61*(1), 10–14. https://doi.org/10.1016/J.Tjog.2021.11.005

Pinho, J., Carvalho, M., Paiva, M., Teixeira-Tavares, N., Costa-Santos, C., & Sousa, C. (2023). Is dyslipidemia a risk factor for trastuzumab-induced cardiotoxicity in breast cancer patients? A systematic review and meta-analysis. *Revista Portuguesa de Cardiologia*. https://doi.org/10.1016/J.Repc.2022.10.016

Prendes, C. F., Christersson, C., & Mani, K. (2020). Pregnancy And Aortic Dissection. *European Journal Of Vascular And Endovascular Surgery*, *60*(2), 309–311. https://doi.org/10.1016/J.Ejvs.2020.03.052

Raja, V., Aguiar, C., Alsayed, N., Chibber, Y. S., ElBadawi, H., Ezhov, M., ... & Farnier, M. (2023). Non-HDL-cholesterol in dyslipidemia: review of the state-of-the-art literature and outlook. *Atherosclerosis*, 117312. https://doi.org/10.1016/J.Atherosclerosis.2023.117312

Salhia, H., Mutlaq, A., Alshaiban, A., Alsaleh, A., Alzahrani, R., & Alshennawi, M. (2023). Patterns In Counselling Services Provided At Saudi Ministry Of Health Medication Counselling Clinics – Reasons For Referrals And Subjects Discussed: A Cross-Sectional Study. *Saudi Pharmaceutical Journal*, *31*(7), 1157–1166. https://doi.org/10.1016/J.Jsps.2023.05.005

Sasmaya, P. H., Khalid, A. F., Anggraeni, D., Irianti, S., & Akbar, M. R. (2022). Differences In Maternal Soluble ST2 Levels In The Third Trimester Of Normal Pregnancy Versus Preeclampsia. *European Journal Of Obstetrics And Gynecology And Reproductive*

Biology: X, *13*, 1–5. https://doi.org/10.1016/J.Eurox.2021.100140

Sibai, B. M., Ewell, M., Levine, R. J., Klebanoff, M. A., Esterlitz, J., Catalano, P. M., Goldenberg, R. L., & Joffe, G. (1997). Risk Factors Associated With Preeclampsia In Healthy Nulliparous Women. *American Journal Of Obstetrics And Gynecology*, *177*(5), 1003–1010. https://doi.org/10.1016/S0002-9378(97)70004-8

Skudder-Hill, L., Coffey, S., Sequeira-Bisson, I. R., Ko, J., Poppitt, S. D., & Petrov, M. S. (2023). Comprehensive Analysis Of Dyslipidemia States Associated With Fat In The Pancreas. *Diabetes And Metabolic Syndrome: Clinical Research And Reviews*, *17*(11), 102881. https://doi.org/10.1016/J.Dsx.2023.102881

Smith, E. R., Oakley, E., Grandner, G. W., Rukundo, G., Farooq, F., Ferguson, K., ... & Tielsch, J. M. (2023). Clinical risk factors of adverse outcomes among women with COVID-19 in the pregnancy and postpartum period: a sequential, prospective meta-analysis. *American journal of obstetrics and gynecology*, *228*(2), 161-177. https://doi.org/10.1016/J.Ajog.2022.08.038

Society for Maternal-Fetal Medicine & Publications Committee. (2022). Society For Maternal-Fetal Medicine Statement: Antihypertensive Therapy For Mild Chronic Hypertension In Pregnancy–The Chronic Hypertension And Pregnancy Trial. *American Journal Of Obstetrics And Gynecology*, *August*, 24–27. https://doi.org/10.1016/J.Ajog.2022.04.011

Tan, J. S., Liu, N. N., Guo, T. T., Hu, S., & Hua, L. (2021). Genetic Predisposition To COVID-19 May Increase The Risk Of Hypertension Disorders In Pregnancy: A Two-Sample Mendelian Randomization Study. *Pregnancy Hypertension*, *26*(July), 17–23. https://doi.org/10.1016/J.Preghy.2021.08.112

Teirilä, L., Heikkinen-Eloranta, J., Kotimaa, J., Meri, S., & Lokki, A. I. (2019). Regulation Of The Complement System And Immunological Tolerance In Pregnancy. *Seminars In Immunology*, *45*(June), 101337. https://doi.org/10.1016/J.Smim.2019.101337

Thongtang, N., Sukmawan, R., Llanes, E. J. B., & Lee, Z. V. (2022). Dyslipidemia Management For Primary Prevention Of Cardiovascular Events: Best In-Clinic Practices. *Preventive Medicine Reports*, *27*(April), 101819. https://doi.org/10.1016/J.Pmedr.2022.101819

Tsen, L. C., & Gelman, S. (2022). The Venous System During Pregnancy. Part 2: Clinical Implications. *International Journal Of Obstetric Anesthesia*, *50*(February), 103274. https://doi.org/10.1016/J.Ijoa.2022.103274

Vanky, E., & Løvvik, T. S. (2020). Polycystic Ovary Syndrome And Pregnancy – From A Clinical Perspective. *Current Opinion In Endocrine And Metabolic Research*, *12*, 8–13. https://doi.org/10.1016/J.Coemr.2020.01.005

Williams, L., Baker-Smith, C. M., Bolick, J., Carter, J., Kirkpatrick, C., Ley, S. L., Peterson, A. L., Shah, A. S., Sikand, G., Ware, A. L., & Wilson, D. P. (2022). Nutrition Interventions For Youth With Dyslipidemia: A National Lipid Association Clinical Perspective. *Journal Of Clinical Lipidology*, *16*(6), 776–796. https://doi.org/10.1016/J.Jacl.2022.07.011

Wu, S. Z., Xu, H. Y., Chen, Y., Chen, Y., Zhu, Q. L., Tan, M. H., & Zhang, M. M. (2021). Association Of Blood Lead Levels With Preeclampsia: A Cohort Study In China. *Environmental Research*, *195*, 110822. https://doi.org/10.1016/J.Envres.2021.110822

Yan, L., Pang, Y., Wang, Z., Luo, H., Han, Y., Ma, S., Li, L., Yuan, J., Niu, Y., & Zhang, R. (2022). Abnormal Fasting Blood Glucose Enhances The Risk Of Long-Term Exposure To Air Pollution On Dyslipidemia: A Cross-Sectional Study. *Ecotoxicology And Environmental Safety*, *237*(April), 113537. https://doi.org/10.1016/J.Ecoenv.2022.113537

Yao, J., Wang, F., Zhang, Y., Zhang, Z., Bi, J., He, J., Li, P., Han, X., Wei, Y., Zhang, X., Guo,

H., & He, M. (2022). Association Of Serum BPA Levels With Changes In Lipid Levels And Dyslipidemia Risk In Middle-Aged And Elderly Chinese. *Ecotoxicology And Environmental Safety*, *241*(January), 113819. https://doi.org/10.1016/J.Ecoenv.2022.113819

Zhang, K., Shen, F., Lei, W., Han, Y., Ma, X., Lu, Y., Hou, Y., Liu, W., Jiang, M., Zhang, T., & Bai, G. (2023). Ligustilide Covalently Binds To Cys129 Of HMGCS1 To Ameliorate Dyslipidemia. *Biomedicine And Pharmacotherapy*, *166*(June), 115323. https://doi.org/10.1016/J.Biopha.2023.115323

Zhang, M., Peng, K., Zhang, X., Liu, Y. S., Liu, X. Y., Han, G. Y., Shi, Y., Huang, Z. J., Li, C., Zhao, Z. P., Wang, L. M., & Li, Y. C. (2023). Geographic Variations In The Prevalence, Awareness, Treatment, And Control Of Dyslipidemia Among Chinese Adults In 2018–2019: A Cross-Sectional Study. *Biomedical And Environmental Sciences*, *36*(4), 313–323. https://doi.org/10.3967/Bes2023.037

Zhao, F., Chen, L., Jiang, Y., Guo, Y., Lu, L., Lu, C., Xue, X., Liu, X., Jin, X., Liu, J., & Chen, K. (2023). Red Yeast Rice Preparations For Dyslipidemia: An Overview Of Systematic Reviews And Network Meta-Analysis. *Journal Of Functional Foods*, *104*(January), 105508. https://doi.org/10.1016/J.Jff.2023.105508

Zhao, M., Yin, G., Xu, J., Ge, X., Li, A., Mei, Y., Wu, J., Liu, X., Wei, L., & Xu, Q. (2023). Independent, Combine And Interactive Effects Of Heavy Metal Exposure On Dyslipidemia Biomarkers: A Cross-Sectional Study In Northeastern China. *Ecotoxicology And Environmental Safety*, *250*(January), 114494. https://doi.org/10.1016/J.Ecoenv.2022.114494

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 713-720
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1397*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

The Effect of Exposure to Carbon Monoxide (Co) Gas in Pregnant Women on The Incident of Weight Infants Born in Makassar City

Arnita Rapang[1a], Farida Tandi Bara[2b*], Yuni Kusmiyati[3c], Supahar[4d], Nopiyanti[5e]

[1] STIKES Nusantara Lasinrang Pinrang, Pinrang, South Sulawesi, Indonesia
[2] STIKes Bhakti Pertiwi Luwu Raya, Palopo City, South Sulawesi, Indonesia
[3] Poltekkes Kemenkes Yogyakarta, Yogyakarta, Indonesia
[4] Universitas Negeri Yogyakarta, Yogyakarta, Indonesia
[5] Akademi Kebidanan Aisyah Kabupaten Pangkep, South Sulawesi, Indonesia

[a] Email address: lady12arwen@gmail.com
[b] Email address: faridatandibara@gmail.com
[c] Email address: yuni_kusmiyati@yahoo.co.id
[d] Email address: pahar.fis@gmail.com
[e] Email address: nopiyantiandiabbas@gmail.com

Received: 23 October 2023 Revised: 11 December 2023 Accepted: 13 December 2023

Abstract
Exposure to vehicle emissions, particularly carbon monoxide (CO), during pregnancy has been identified as a potential factor contributing to low birth weight in infants. The mechanism of CO's impact on the body involves its binding with hemoglobin (Hb) in red blood cells, leading to placental dysfunction and alterations in oxygen flow efficiency to the uteroplacental. Such disruptions can adversely affect fetal growth. This study focuses on Makassar City, a rapidly developing urban area experiencing substantial growth in infrastructure and transportation. This research aims to assess the impact of carbon monoxide exposure on birth weight in pregnant women residing in Makassar City. The method of this study is a quantitative approach employing a descriptive cross-sectional design was adopted for this study. The research sample consisted of 120 pregnant women categorized based on their CO exposure levels—30 with low exposure, 60 with moderate exposure, and 30 with high exposure. Simple random sampling was utilized for participant selection. CO levels were measured using the Adalog 7000 multi-gas monitor. Data analysis included One Sample ANOVA and Linear Regression. The results show that data analysis indicated that pregnant women with low CO exposure had an average birth weight of 3110.83 grams. In contrast, those with moderate and high CO exposure exhibited average birth weights of 2840.33 grams and 2667.33 grams, respectively. The regression coefficient for CO exposure was -221,750, indicating that a 1 µm increase in carbon monoxide gas correlated with a decrease in birth weight by -221,750. The conclusion is pregnant women who are exposed to high and moderate carbon monoxide gas during pregnancy had an effect on birth weight than mothers who are exposed to low carbon monoxide gas. Future research is needed to measure CO levels in the blood of pregnant women in relation to birth weight.

Keywords: Carbon Monoxide Exposure, Pregnant Woman, Birth Weight.

Corresponding Author:

Farida Tandi Bara
STIKes Bhakti Pertiwi Luwu Raya, Palopo City, South Sulawesi, Indonesia
Email: faridatandibara@gmail.com

1. INTRODUCTION

Large cities are generally characterized by traffic jams that lead to higher pollution concentrations. Pollutants produced by motorized vehicles such as carbon monoxide (CO), nitrogen oxide (NOx), hydrocarbons (HC), sulfur dioxide (SO2), lead (Pb) and carbon dioxide (CO2) have a negative and dangerous impact on the body (Aini et al. al., 2019; Czech, Zabochnicka-Świątek, & Świątek, 2020; Ahmed, et al., 2022; Tang, et al., 2020; Zioła, Błaszczak, & Klejnowski, 2021; Bekesiene, & Meidute-Kavaliauskiene, 2022; Eftekhari, et al., 2023). As much as 70% of air pollution in big cities comes from motorized vehicles (Arsandi et al., 2017). The main source of CO emissions is motorized vehicles (Dey & Dhal, 2019). Research by Zubair, et al on the level of air pollution in the city of Makassar in the polluted air pollution category according to the Quality Status Index (ISM), and the moderate-hazardous category when referring to the Air Pollution Standard Index (ISPU) (Zubair et al., 2013).

Infrastructure and transportation development in the city of Makassar is increasing and there are more and more motorized vehicles on the roads. Carbon monoxide (CO) is a colorless, odorless, and tasteless component that is found in gas form at temperatures above -192 ^{o}C (McAllister, Kunsman, & Levine, 2020; Kumar, et al., 2022; Nami-Ana, et al., 2021; Rawat et al., 2021). In 2014 in Brazil ambient PM 2.5 and carbon monoxide were also found in low birth weight babies, the result of This research states that pregnant women who are exposed to burning biomass or waste (garbage) containing PM 2.5 and CO from the beginning of the trimester to the last trimester have the potential for low birth weight babies, even though the mother is exposed in the second trimester, it still has the same effect on outcomes. birth (Cândido da Silva et al., 2014) . The effect of pollutants on birth weight and IUFD proves that CO has a greater influence than other pollutant variables (Salam et al., 2005).

The reprotoxic effects of pollutants contained in the air can bind directly to hemoglobin, forming carboxyhemoglobin and thereby reducing the oxygen-carrying capacity of the blood, which in turn can result in adverse health effects on the cardiovascular system (Dalefield, 2017) . The ability of hemoglobin to bind oxygen decreases, as does the ability to release oxygen to tissues. Overall oxygen levels in cells decrease. The amount of CO bound to hemoglobin as carboxyhemoglobin (COHb) is a key marker for health effects (Rumchev et al., 2011). Hemoglobin's affinity for CO gas is 200 times greater than its affinity for oxygen. Free Co in plasma can interfere with mitochondrial respiratory function resulting in cell damage (Friedman, 2015).

During pregnancy, the mother's physiological adaptation to her pregnancy occurs. Changes in the cardiovascular and hematological systems during pregnancy are physiological adaptations that play an important role in supplying oxygen to the fetus. This system is sensitive to environmental changes such as the biological environment. During pregnancy CO production increases, due to the enzymatic activity of microbes, increased erythrocytes, and from the fetus (Friedman, 2015). CO gas contained in the air further increases the mother's CO exposure and affects the mother's health which has an impact on the pregnancy and fetus. The impact on the fetus causes placental dysfunction and changes in the efficiency of oxygen flow in the blood to the uteroplacenta which can prevent the fetus from achieving its genetic growth. The incidence of LBW is influenced by environmental factors including air pollution by 45% (Hapsari et al., 2020)

Epidemiological studies on the impact of pollutants contained in the air still receive little attention in Indonesia itself, especially in the city of Makassar. Based on the description above, this research aims to determine the CO exposure of pregnant women to the birth weight of their babies.

2. RESEARCH METHOD

Quantitative descriptive research uses a cross-sectional study design, using the chi square test, One Way ANOVA was used to test the level of exposure to the baby's birth weight. Co exposure data uses retrospective data, the baby's birth weight is obtained from the KIA book. CO measurement using the Adalog 7000 multi gas monitor made by ThermoFisher. Specifications on CO, ranges 0-500ppm and resolution 1 ppm.

The inclusion criteria were mothers who had lived at the research location since pregnancy. The population is mothers who gave birth at term in September-October 2018 in the Rappocini District area. The total sample was 120 people: 30 people in the moderate exposure group, 60 people in the medium exposure group, and 30 people in the high exposure group. Determining the number of samples was based on the Lemeshow formula and a simple random sampling technique.

The research procedure is CO gas sample data collection was carried out in Rappocini District, Makassar at location point 1: T-junction Pelita Raya Street is categorized in the low CO group (24,228.57 µm/mg ^{3}), Point 2: Hertasning Street intersection is categorized in the medium CO group (29,714.29 µm/mg ^{3}), Point 3: Minasa Upa Street intersection is categorized in the high CO group (48,457.14 µm/mg ^{3}), Point 4: Mangasa Street was categorized in the medium CO group (29,485.71 µm/mg ^{3}). After that, a search was carried out for mothers who had given birth within the previous 2 months. Obtained a sample of 120 mothers giving birth who were grouped into each exposure. Sampling of CO exposure was taken by operators from the Environmental Health Laboratory of the Health Polytechnic, Ministry of Health, Makassar. This research has received ethical approval from the Ethics Committee of the Politeknik Kesehatan Kemenkes Yogyakarta with the number LB.01.01/KE-02/VIII/102/2018.

3. RESULTS AND DISCUSSION

Table 1. Characteristics of Respondents

Characteristics	CO Exposure Low	Moderate	High	p-value*
Age				
<20 and >30 year old	11 (26.1)	18 (42.9)	12 (31)	0.09
20-30 year old	19 (24.4)	42 (53.8)	17 (21.8)	
Education				
Low	8 (44.4)	7(38.9)	3 (16.7)	0.9
Middle	13 (23.6)	29 (52.7)	13 (23.6)	
Higher	9 (19.1)	24 (51.1)	14 (29.8)	
Work				
Mother works	12 (22.6)	25 (47.2)	16 (30.2)	0.6
Doesn't work	18 (26.9)	35 (52.2)	14 (20.9)	
Parity				
Primipara	11 (29.7)	15 (40.6)	11 (29.7)	0.52
Multiparous	19 (22.9)	45 (54.2)	19 (22.9)	

Table 1 shows that the p-value is >0.05. Maternal characteristics at each level of CO exposure were not different.

Table 2. Results of normality analysis of baby birth weight data.

Variable	Mean	SD	p-value
Borth weight	2861.58	383.841	0.99

Table 2 show that the asymp sig value for birth weight is 0.99. The p value is> 0.05, so it can be concluded that the data is normally distributed.

Table 3 . Effect of Exposure to Carbon Monoxide Gas on Birth Weight of Babies.

Exposure Group	Birth Weight		
	Mean	SD	p-value
Low	3110.83	322.92	0.000
Moderate	2840.33	353.27	
High	2667.33	303.22	
Total	2864.71	367.56	

From the table above It is known that the higher the level of CO gas exposure, the lower the baby's weight *p-value* = 0.000 < α = 0.05 (*p-value* is smaller than α = 0.05). Birth weight in the carbon monoxide gas exposure group with low exposure was 3110.83 grams, medium exposure 2840.33 grams, and high exposure 2667.33 grams. There is a significant influence between exposure to carbon monoxide gas and the birth weight of the baby.

Table 3. Exposure to CO by pregnant women on birth weight of babies.

Variable				
CO Exposure Group	-221.750	-5.15	0.000	0.428
Contant	3308.208			

Exposure Carbon monoxide gas has a significant effect on birth weight of babies 0.000 (p<0.05). The results of the analysis show that exposure to carbon monoxide gas has a regression coefficient of -221,750, meaning that every 1 µm increase in carbon monoxide gas will have the effect of decreasing the birth weight of the baby by -221,750. This model has an *adjusted R2 value* of 0.428, meaning that exposure to carbon monoxide gas can predict birth weight by 42.8%.

There is an influence of increasing the concentration of carbon monoxide gas on the incidence of birth weight, the value 3308.208 is *the point* where the line can pass through the Y axis (*intercept point* of increasing exposure to carbon monoxide gas on birth weight). The value - 221,750 is the regression coefficient or *slope* of the regression line, to explain the increase in exposure to carbon monoxide gas on birth weight. Based on *linear* regression equation analysis Birth weight = 3308.208 -221.750x $_{1.}$ By looking at the results of the regression equation above it can be interpreted that if the value of exposure to carbon monoxide gas is 0 µm then the birth weight of the baby is 3308.208 grams, and if exposure to carbon monoxide the value increases by 1 µm then the baby's birth weight decreased by 221,750 grams.

During pregnancy, oxygen requirements increase as gestational age increases. Increased need to support fetal and placental growth. Increased respiratory rate and volume do not compensate for changes during pregnancy. Exposure to air pollution will have an impact on reducing oxygen needs and increasing the risk of air pollutants. Exposure to air pollution during pregnancy is associated with fetal developmental problems, premature birth, and pregnancy complications, including pregnancy-induced hypertensive disorders (PIH) (Mozzoni et al., 2022).

Data shows that the higher the exposure to CO gas during pregnancy, the lower the birth weight. The exposure to carbon monoxide gas is significantly related to the birth weight of the

baby. In a meta-analysis study, increasing concentrations of particles with aerodynamic diameters of 10 m (PM_{10}) and 2.5 m ($PM_{2.5}$) across pregnancy were associated with an increased risk of low birth weight (<2,500 g) and reduced birth weight among births. term (37 weeks gestation) (Dadvand et al., 2013) . Reduced exposure to ambient air pollution late in pregnancy is associated with increased birth weight among pregnant women (Septiawati & Listianti, 2019) .

Exposure of pregnant women to $PM_{2.5}$, PM_{10} , SO_2 , and CO during the entire pregnancy and the first and second trimesters significantly reduces birth weight and increases the risk of infant birth weight (Mitku et al., 2023) . Exposure to air pollution is associated with the incidence of pre-eclampsia in pregnancy and prematurity. The possible cause is that exposure to air pollution increases ROS and inflammation during pregnancy (Chiarello et al., 2023).

Hemoglobin (Hb) functions as a carrier of O_2 in the form of oxyhemoglobin (O_2 Hb) from the lungs to body cells, and CO $_2$ in the form of CO_2 Hb from body cells to the lungs (Dey & Dhal, 2019) . COHb is formed when CO binds to hemoglobin with an affinity 200 times greater than oxygen, thereby reducing oxygen transport capacity (Bleecker & Lotti, 2015). Studies on COHb in the fetus were obtained from research on maternal smoking exposure during pregnancy. Pregnant women who are exposed to cigarette smoke are at greater risk of giving birth to LBW babies because increased CO levels in maternal blood cause intrauterine growth disorders (Chelchowska et al., 2013)

Pollutant compounds from the air in the placenta of a healthy pregnancy decrease their presence in the fetal blood, indicating that under normal conditions, the placenta acts as a reservoir reducing transfer from mother to fetus (Dong et al., 2018). CO dissolved in maternal plasma crosses the placenta by passive diffusion and then combines with fetal hemoglobin. The resulting fetal COHb levels are 10–15% higher than maternal levels (Culnan et al., 2018), because fetal hemoglobin has a higher affinity for CO than adult hemoglobin. In addition, CO elimination in the fetus takes longer, because CO dissociates much more slowly from fetal hemoglobin than from adult hemoglobin (Aubard & Magne, 2000). The elimination half-life of the fetus may be 4-5 times longer than that of the mother. Therefore, the severity of fetal poisoning cannot be judged solely on the basis of the mother's condition

The effects of carbon monoxide on fetal development vary depending on the time period. During the embryonic phase, CO can cause various birth defects. During the fetal stage, congenital anomalies are less common, but death or permanent neurological damage may occur (Chiarello et al., 2023).

4. CONCLUSION

The conclusion is pregnant women who are exposed to high and moderate carbon monoxide gas during pregnancy had an effect on birth weight than mothers who are exposed to low carbon monoxide gas. Future research is needed to measure CO levels in the blood of pregnant women in relation to birth weight.

REFERENCES

Ahmed, M. J., Dogo, B., Baba, S. U., Muhammed, A. Y., & Abdulqadir, M. (2022). Assessment of concentration and spatial variation of air pollution in Zaria metropolis, Nigeria. *Science World Journal*, 17(2), 221-226. Retrieved from https://www.ajol.info/index.php/swj/article/view/231317

Aini, N., Ruktiari, R., Pratama, MR, & Buana, AF (2019). Sistem Prediksi Tingkat Pencemaran Polusi Udara dengan Algoritma Naïve Bayes pada Kota Makassar. *Seminar Nasional*

Komunikasi dan Informatika, *3* , 83–90. Retrieved from https://jurnal.kominfo.go.id/index.php/snki/article/view/2567

Arsandi, A. S., Wahyu R, D., Ismiyati, I., & Hermawan, F. (2017). Dampak Pertumbuhan Penduduk Terhadap Infrastruktur Di Kota Semarang. *Jurnal Karya Teknik Sipil*, 6(4), 01-14. Retrieved from https://ejournal3.undip.ac.id/index.php/jkts/article/view/18189

Aubard, Y., & Magne, I. (2000). Carbon monoxide poisoning in pregnancy. *BJOG : An International Journal of Obstetrics and Gynecology*, *107* (7), 833–838. https://doi.org/10.1111/j.1471-0528.2000.tb11078.x

Bekesiene, S., & Meidute-Kavaliauskiene, I. (2022). Artificial Neural Networks for Modelling and Predicting Urban Air Pollutants: Case of Lithuania. *Sustainability*, *14*(4), 2470. https://doi.org/10.3390/su14042470

Bleecker, M. L., & Lotti, M. (2015). Carbon monoxide intoxication. *Handbook of clinical neurology*, *131*, 191-203. Elsevier B.V. https://doi.org/10.1016/B978-0-444-62627-1.00024-X

Cândido da Silva, AM, Moi, GP, Mattos, IE, & Hacon, S. de. (2014). Low birth weight at term and the presence of fine particulate matter and carbon monoxide in the Brazilian Amazon: a population-based retrospective cohort study. *BMC Pregnancy and Childbirth* , *14* (1), 309. https://doi.org/10.1186/1471-2393-14-309

Chelchowska, M., Ambroszkiewicz, J., Jablonka-Salach, K., Gajewska, J., Maciejewski, T.M., Bulska, E., Laskowska-Klita, T., & Leibschang, J. (2013). Tobacco smoke exposure during pregnancy increases maternal blood lead levels affecting neonate birth weight. *Biological Trace Element Research* , *155* (2), 169–175. https://doi.org/10.1007/s12011-013-9775-8

Chiarello, D. I., Ustáriz, J., Marín, R., Carrasco-Wong, I., Farías, M., Giordano, A., ... & Gutiérrez, J. (2023). Cellular mechanisms linking to outdoor and indoor air pollution damage during pregnancy. *Frontiers in Endocrinology*, *14*, 280. https://doi.org/10.3389/fendo.2023.1084986

Culnan, D.M., Craft-Coffman, B., Bitz, G.H., Capek, K.D., Tu, Y., Lineaweaver, W.C., & Kuhlmann-Capek, M.J. (2018). Carbon Monoxide and Cyanide Poisoning in the Burned Pregnant Patient: An Indication for Hyperbaric Oxygen Therapy. *Annals of Plastic Surgery* , *80* (3 Suppl 2), S106–S112. https://doi.org/10.1097/SAP.0000000000001351

Czech, R., Zabochnicka-Świątek, M., & Świątek, M. K. (2020). Air pollution as a result of the development of motorization. *Global NEST Journal*, *22*(2), 220-230.

Dadvand, P., Parker, J., Bell, M.L., Bonzini, M., & Brauer, M. (2013). Research | Children's Health Maternal Exposure to Particulate Air Pollution and Term Birth Weight: A Multi-Country Evaluation of Effect and Heterogeneity. *Environmental Health Perspectives* , *121* (3), 367–373. https://doi.org/10.1289/ehp.1205575

Dalefield, R. (2017). Smoke and other inhaled toxicants. *Veterinary toxicology for Australia and New Zealand, 1st edn. Elsevier*, 361-372. https://doi.org/10.1016/b978-0-12-420227-6.00019-0

Dey, S., & Dhal, G. C. (2019). Materials progress in the control of CO and CO2 emissions at ambient conditions: An overview. *Materials Science for Energy Technologies* , *2* (3), 607–623. https://doi.org/10.1016/j.mset.2019.06.004

Dong, X., Wang, Q., Peng, J., Wu, M., Pan, B., & Xing, B. (2018). Transfer of polycyclic aromatic hydrocarbons from mother to fetus in relation to pregnancy complications. *The Science of the Total Environment*, *636*, 61–68. https://doi.org/10.1016/j.scitotenv.2018.04.274

Eftekhari, A., Won, Y., Morrison, G., & Ng, N. L. (2023). *Chemistry of Indoor Air Pollution*. American Chemical Society.

Friedman, P., Guo, X. M., Stiller, R. J., & Laifer, S. A. (2015). Carbon monoxide exposure during pregnancy. *Obstetrical & Gynecological Survey*, *70*(11), 705-712. https://doi.org/10.1097/01.pec.0000526609.89886.37

Hapsari, D., Nainggolan, O., & Kusuma, D. (2020). Hotspots and Regional Variation in Smoking Prevalence Among 514 Districts in Indonesia: Analysis of Basic Health Research 2018. *Global Journal of Health Science*, *12* (10), 32. https://doi.org/10.5539/gjhs.v12n10p32

Kumar, A., Zhao, Y., Mohammadi, M. M., Liu, J., Thundat, T., & Swihart, M. T. (2022). Palladium Nanosheet-based dual gas sensors for sensitive room-temperature hydrogen and carbon monoxide detection. *ACS sensors*, *7*(1), 225-234. https://doi.org/10.1021/acssensors.1c02015

McAllister, J., Kunsman, G. W., & Levine, B. S. (2020). Carbon monoxide/cyanide. *Principles of Forensic Toxicology*, 545-560. https://doi.org/10.1007/978-3-030-42917-1_30

Mitku, A.A., Zewotir, T., North, D., Jeena, P., Asharam, K., Muttoo, S., Tularam, H., & Naidoo, R.N. (2023). Impact of ambient air pollution exposure during pregnancy on adverse birth outcomes: generalized structural equation modeling approach. *BMC Public Health* , *23* (1), 45. https://doi.org/10.1186/s12889-022-14971-3

Mozzoni, P., Iodice, S., Persico, N., Ferrari, L., Pinelli, S., Corradi, M., Rossi, S., Miragoli, M., Bergamaschi, E., Bollati, V., Alinovi, R., Biggeri, A., Borghi, F., Cantone, L., Catelan, D., Cattaneo, A., Cavallo, D., Dioni, L., Dolo, V., … Vicenzi, M. (2022). Maternal air pollution exposure during the first trimester of pregnancy and markers of inflammation and endothelial dysfunction. *Environmental Research*, *212*, 113216. https://doi.org/10.1016/j.envres.2022.113216

Nami-Ana, S. F., Nasresfahani, S., Tashkhourian, J., Shamsipur, M., Zargarpour, Z., & Sheikhi, M. H. (2021). Nanofibers of polyaniline and Cu (II)–l-aspartic acid for a room-temperature carbon monoxide gas sensor. *ACS Applied Materials & Interfaces*, *13*(33), 39791-39805. https://doi.org/10.1021/acsami.1c07116

Rawat, S., Bamola, P., Dwivedi, C., & Sharma, H. (2021). Two dimensional MoS2 gas sensor to detect carbon monoxide (CO). *Materials Today: Proceedings*, *45*, 4841-4843. https://doi.org/10.1016/j.matpr.2021.01.297

Rumchev, K., Spickett, J., Brown, H., Daube, M., & Bond, L. (2011). Environmental Tobacco Smoke and Health Risk Assessment. In *Encyclopedia of Environmental Health* (pp. 542–550). Elsevier Inc. https://doi.org/10.1016/B978-0-444-52272-6.00451-7

Salam, M.T., Millstein, J., Li, Y.F., Lurmann, F.W., Margolis, H.G., & Gilliland, F.D. (2005). Birth outcomes and prenatal exposure to ozone, carbon monoxide, and particulate matter: Results from the Children's Health Study. *Environmental Health Perspectives* , *113* (11), 1638–1644. https://doi.org/10.1289/ehp.8111

Septiawati, D., & Listianti, A. N. (2019). Exploring Indoor Air Pollution Exposure During Pregnancy and Risk of Low Birth Weight in Seberang Ulu 1, Palembang. *Jurnal Ilmu Kesehatan Masyarakat*, *10*(2), 93-100. https://doi.org/10.26553/jikm.2019.10.2.93-100

Tang, V. T., Oanh, N. T. K., Rene, E. R., & Binh, T. N. (2020). Analysis of roadside air pollutant concentrations and potential health risk of exposure in Hanoi, Vietnam. *Journal of Environmental Science and Health, Part A*, *55*(8), 975-988. https://doi.org/10.1080/10934529.2020.1763091

Zioła, N., Błaszczak, B., & Klejnowski, K. (2021). Long-term eBC measurements with the use of MAAP in the polluted urban atmosphere (Poland). *Atmosphere*, *12*(7), 808. https://doi.org/10.3390/atmos12070808

Zubair, A., Samang, L., Selintung, M., & Usman, H. (2013). Studi Tingkat Pencemaran Udara Di Kota Makassar. *National Seminar III in Civil Engineering, Muhammadiyah University of Surakarta , 2008* , 233–238.

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 721-729
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1129*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

The Impact of Oxytocin Massage and Banana Flower Consumption (*Musa balbisiana colla*) on the Prolactin Level in Breastfeeding Mothers

Nurmiaty[1a*], Sitti Aisa[2b], Aswita[2c], Muliati Dolofu[2d], Nur Rahman[3e], Bringiwatty Batbual[4f]

[1] Department of Midwifery, Poltekkes Kemenkes Palu, Palu, Central Sulawesi, Indonesia
[2] Department of Midwifery, Poltekkes Kemenkes Kendari, Kendari, Southeast Sulawesi, Indonesia
[3] Department of Nutrition, Poltekkes Kemenkes Malang, Malang, East Java, Indonesia
[4] Department of Midwifery, Poltekkes Kemenkes Kupang, Kupang, East Nusa Tenggara, Indonesia

[a] Email address: nurmiaty1908@gmail.com
[b] Email address: sittiaisakeb@gmail.com
[c] Email address: aswita_wita71@yahoo.com
[d] Email address: dolofumuliati@yahoo.com
[e] Email address: rahmancahaya@yahoo.com
[f] Email address: wattybatbual155@gmail.com

Received: 9 March 2023 Revised: 28 December 2023 Accepted: 28 December 2023

Abstract

Since a long time ago, banana flowers have been believed they increase the production of breast milk. Thus, many people consume them as vegetables for breastfeeding mothers. This research aims to examine the impact of oxytocin massage and banana flower consumption on prolactin levels in breastfeeding mothers. The method used a true experiment control group design in which samples were divided into 3 groups; group 1 was treated with oxytocin massage, group 2 was treated with banana flower consumption, and group 3 was given intervention with oxytocin massage and banana flower consumption. The massage was conducted every day with durations of 5-10 minutes. The banana flower vegetable was served as much as 150 grams daily. The first blood sampling was done pre-intervention on the third day of postpartum. The second blood sampling was done after intervention on the tenth day of postpartum. The checkup of prolactin level was through a method of Chemiluminescent Microparticle Immunoassay (CMIA). To analyze the data, this research utilized a T-test exam. The result is the average difference in prolactin levels in pre-and-post intervention in group 1 was -61,75 ng/mL. Although decreasing prolactin levels occurred, yet there was no significant interval between pretest and posttest. The difference in prolactin levels in pre-and-post intervention in group 2 was 103,61 ng/mL. The prolactin level increased but not significantly. In group 3, the difference levels were about 110,22 ng/mL. In this group, a significant prolactin level increase had occurred. The conclusion is the combination treatment of banana flower and oxytocin massage evolved the level of prolactin level in nursing mothers. Research related to strengthening the recommendation of traditional galactagogues consumption to breastfeeding mothers.

Keywords: Prolactin, Banana Flower, Oxytocin Massage.

Corresponding Author:

Nurmiaty
Department of Midwifery, Poltekkes Kemenkes Palu, Palu, Central Sulawesi, Indonesia
Email: nurmiaty1908@gmail.com

1. INTRODUCTION

Breastfeeding has been becoming one of the ways that can be done to ensure infants obtain adequate nutrients in age 0-6 first month. It also could deter stunting. According to that, every mother must breastfeed their infants exclusively in the 0-6 months and it must be continued until the next 2 years. However, breastfeeding in society still shows a low percentage and is far from what is expected. The Indonesian target adequacy of exclusive breastfeeding (0-6) in 2018 is 68,74%. In Southeast Sulawesi, the target adequacy of exclusive breastfeeding is 47,53% (Kementerian Kesehatan Republik Indonesia, 2020). The achievement of target adequacy of exclusive breastfeeding should get more concern.

A low milk supply can cause growth delay that is caused by under-standard body weight and length and vulnerability to infection. Faltering growth can be experienced by all children from 2-6 months old. A result of research in a developing country found that the main factor of nutrient deficiency and retardation in 1-15-month-old babies was the insufficiency of milk supply and poor complementary foods (Shrimpton, et al., 2001). The reasons for the low milk supply are a failure of mothers to breastfeed their infants just after giving birth and the perception of mothers who think that breast milk is insufficient for the fulfillment of their babies nutrient needs "breast milk lack syndrome". As a result, mothers or other family members supply complementary foods before their babies reach 6 months old.

The mother's food indirectly may influence milk production in terms of quality and quantity. Breastfeeding mothers do not have to consume excessive food but enough proportion to maintain their nutrient needs. If breastfeeding mothers cut down on the amount of food they eat or ignore hunger, it will reduce milk production (Aisya, Zakaria & Daud, 2020). Bataknese lactating women in Simalungun District, North Sumatra, Indonesia, have a tradition of consuming Torbangun leaves (*Coleus amboinicus* Lour; CA) after birth. They believe that the consumption of CA for one month after birth increases their breast milk production (Damanik et al., 2001; Damanik et al., 2004). One of plants that are known to be able to improve breast milk production is banana flower. Since a long time ago, banana flowers are believed to increase breast milk production in nursing mothers. Therefore, many people consume it as a vegetable for breastfeeding mothers. Some research reveals that the water of boiled banana flowers is effective to increase breast milk production (Wahyuningsih et al., 2017; Riani, 2017).

To deal with breastfeeding problems, some effort has been done, such as educating mothers about breast milk and breastfeeding through lactation classes (Nurmiaty et al., 2016). The feedback shows that the mothers who join the class were able to maintain exclusive breastfeeding until their babies age 6 months. The impact on the rise of body weight and length was very significant. Nevertheless, the effort of education is thought not enough, thus innovative action is needed to solve those problems such as through massage treatment and giving mothers local foods which are part of their local wisdom. With those local foods, people are not only familiar to process them, but also easy to get them.

A shoulder massage is one of the solutions to cope with abnormalities in breast milk production. The massage along both sides of the spine will stimulate the medulla oblongata to send a message to the hypothalamus in the posterior to release oxytocin hormone and produce breast milk. The benefit of oxytocin massage is to ease swollen breasts (engorgement), reduce blockage of breast milk (plugged/milk duct), and help maintain milk production while mothers and babies are ill. Oxytocin massage is a treatment that aims to induce hormone prolactin and oxytocin during post-pregnancy. Furthermore, the oxytocin hormone can calm mothers, so that breast milk can go out smoothly (Mardiyaningsih, Setyowati, & Sabri, 2011). The production of breast milk is affected by the level of prolactin, the higher level of the prolactin, the higher breast milk production.

Breast milk production is also influenced by food intake. High protein and fat food are also able to increase breast milk production. Besides that, a psychological factor is playing an important role. Mothers who feel psychologically comfortable and happy will produce good breast milk. Banana flowers are known to contain galactagogue that has a potential in stimulating oxytocin hormone and prolactin. A little amount of breast milk is solved by consuming sweat leaves, long beans, chayotes, and banana flowers or well-known banana hearts. The contents of a banana flower such as calories, protein, fat, carbohydrate, vitamin A, vitamin B1, vitamin C, and minerals like phosphor, calcium, and Fe can bolster breast milk production. The nutrient content per 100 grams of fresh banana flower according to the Nutrition Directorate of the Indonesian Health Department contains; fat 31 kkal, protein 1,2 g, fat 0,3 g, carbohydrate 7,1 g, calcium 3,0 mg, phosphor 50 mg, Fe 0,1 mg, vitamin A 170 mg, vitamin B1 0,05 mg, vitamin C 10 mg, water 90,2 g, and BDD 255% (Kementerian Kesehatan Republik Indonesia, 2020).

Banana flowers contain flavonoids, phosphors, protein, minerals, calcium, vitamin B1, vitamin C, high fiber, Fe, and Iodine. Ordinary people especially mothers are familiar with banana flowers to be a vegetable and perceive that its benefit can expedite breast milk. Therefore, we want to know more deeply about what active substances in banana flowers could increase milk production. Based on folk's experience who have utilized banana flowers as part of their diet and some research the water of boiled banana buds can boost the production of breast milk. This research aims to examine the impact of oxytocin massage and banana-flower-contained food consumption on the level of prolactin.

2. RESEARCH METHOD

The research uses a true experiment control group design. The sampling technique was purposive sampling. The samples of this research are 30 people which then were separated into 3 groups and each group consists of 10 people. Group 1 was intervened by oxytocin massage, group 2 was treated with banana flower consumption, and group 3 was approached by a combination treatment of oxytocin massage and banana flower consumption. The banana flowers that were used was the banana flowers of Pisang Batu (*Musa balbisiana colla*) which were processed to be a ready-to-consume vegetable. The vegetable, then, was given to breastfeeding mothers.

The research was done from May to September 2019. The research location was in the working are of Nambo dan Poasia Health Center in Kendari. It comprised two stages. Stage 1 was collecting samples which were pregnant mothers whose ages of pregnancy were 35-40 weeks while filling a form of consent to be samples of this research. After that, in stage 2 all those pregnant mothers were visited regularly just after their delivery process and were given intervention. The breast milk was collected from breastfeeding mothers from the third day to the tenth day postpartum. Blood sampling was done prior to and after the intervention that was undertaken by the staff of Prodia Laboratory and would be sent to Jakarta Prodia Laboratory to determine the biomarker level based on the research variable.

The stages of research comprise: (1) Proposing the Research Ethics Commission to get ethical feasibility; (2) Collecting sampling of banana flowers that were going to be observed. The banana flowers used were from Pisang Kepo Batu of Kendari; (3) Formulating vegetable that uses banana buds as the main ingredient to be given to breastfeeding mothers; (4) Screening pregnant mothers in trimester III who became samples of this research through filling out consent forms; (5) Training husbands/families of mothers in how to practice oxytocin massage; (6) Collecting blood sampling and weighing infants before giving intervention to mothers on the third-day postpartum. Blood sampling was done from 08.00 – 10.00 am; (7) Oxytocin massage was done in the morning in 5-10 minutes duration; (8) Serving the banana flower vegetable to be consumed by mothers in the morning as much as 150 gram; (9) Blood sampling

and breast milk volume of mothers after given intervention in postpartum day 10. Blood sampling was carried out from 08.00 – 10.00 am; (10) Samples were taken by staffs who have been assigned by Kendari Prodia Laboratory and the samples were straightly sent to Jakarta Prodia Laboratory to be observed. The prolactin level measurements utilizes a Chemiluminescent Microparticle Immunoassay (CMIA) method. Data analysis is through univariable analysis namely; mean, median, and deviation standard and bivariable analysis using a T-test exam.

This research has been ethically permitted by the Research Ethic Commission of Health Polytechnic of Kendari, Ministry of Health, No. 1065/KEPK-PTKMKS/X/2019.

3. RESULTS AND DISCUSSION

Table 1. Characteristic of Respondents.

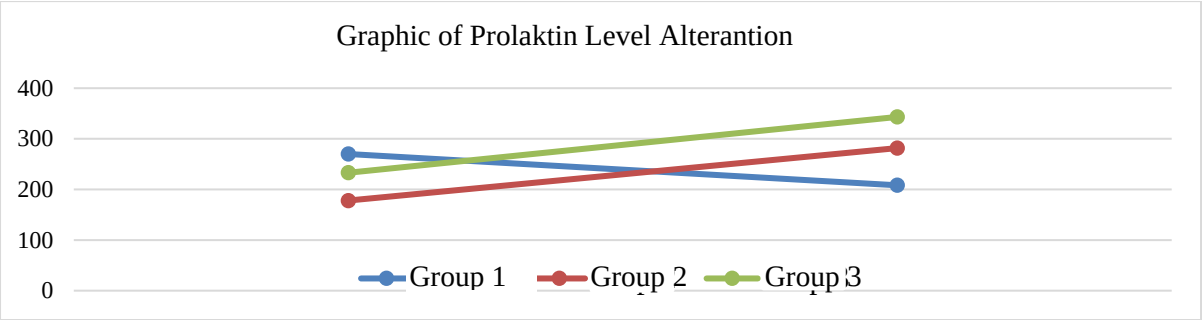
Characteristic	Group 1		Group 2		Group 3		p-value
	n	%	n	%	n	%	
Age of mother							
<20	2	20.0	0	0.0	1	10.0	0.506
20-35	7	70.0	9	90.0	9	90.0	
>35	1	10.0	1	10.0	0	0.0	
Parity							
1	5	50.0	1	10.0	4	40.0	0.483
2	2	20.0	4	40.0	2	20.0	
3	2	20.0	2	20.0	3	30.0	
4	1	10.0	3	30.0	1	10.0	
Mother's education							
Primary - Junior high school	4	40.0	3	30.0	2	20.0	0.621
Senior high school - University	6	60.0	7	70.0	8	80.0	

Table 1 shows that the result exhibits that respondents in each group were average 20-35 years old. For parity, group 1 had 70% parity 1 and 2 and the rest was parity between 3 and 4. In group 2, 50% was parity 1 and 2. In the aspect of education, the majority of respondents had finished senior high school and university.

Table 2. Variable Analysis with Numeric Data.

Variable	Group	$\bar{X}$ ± sd (min-max)
Pretest Prolactin	1	269,96 ± 140,33 (95,15- 459,96)
	2	178,06 ± 66,09 (109,04 - 316,64)
	3	229,77 ± 74,96 (133,01 - 373,38)
Posttest Prolactin	1	208,21 ± 154,67 (42,35 - 443,77)
	2	281,68 ± 180,09 (134,38 - 585,83)
	3	346,42 ± 134,78 (174,63 - 647,53)

Table 2 shows that the result of prolactin level measurement before intervention (pretest) obtained the average highest score in group 1 (269,96 ng/mL) followed by groups 3 and 2 whose scores were (229,77 ng/mL) and (178,06 ng/mL) respectively. The levels of prolactin in the post-intervention showed that the average highest score was in group 3 which was 346,42 ng/mL and the lowest score was in group 1 as much as 208,21 ng/mL.



Graphic 1. Prolaktin Level Alterantion

Graphic 1 show that the result of pre and pro-prolactin levels is shown in the below graphic. At the beginning of prolactin measurement seen in group 1 was the highest of all groups. In the second measurement, it experienced an improvement in prolactin levels in group 3. The groups that experienced improving prolactin levels were groups 3 and 2.

Table 3. Data Normality Test.

Group	Variable	p-value
The Intervention of oxytocin massage	Prolactin Pretest	0.051
	Prolactin Posttest	0.165
The intervention of banana flower vegetable	Prolactin Pretest	0.143
	Prolactin Posttest	0.007
The intervention of banana flower vegetable + oxytocin massage	Prolactin Pretest	0.535
	Prolactin Posttest	0.369

Table 3 shows that the normality data test was done before the multivariable test. The Shapiro Wilk test conducted the normality data test with exam criteria if the score is significant (p-value) > 0,05 so the data was normally distributed.

Table 4. Analysis of Pair T-test among Groups of Approach.

Group	Variable	n	Mean	SD	p-value	Difference	CI 95%
1	Prolactin Posttest	10	208.2	154.66	0.339	-61.75	-200.18-76.68
	Prolactin Pretest	10	269.96	140.33			
2	Prolactin Posttest	10	281.67	180.09	0.132	103.61	-38.12-245.35
	Prolactin Pretest	10	178.06	66.08			
3	Prolactin Posttest	10	343.20	43.01	0.014	110.22	27.50-192.93
	Prolactin Pretest	10	232.98	24.69			

From Table 4, in group 1, the average pretest prolactin level was 269,96 ng/mL and the posttest was 208,2 ng/mL. There was a 61,75 ng/mL difference. The level of prolactin tends to decline. The analysis shows no difference between before and after the intervention of oxytocin massage, which was proved by p-value 0,339. In addition, in group 2, the average pretest prolactin level was 178,06 ng/mL while the post-test was 281,67 ng/mL. There was 103,61 ng/mL in difference which means that the level of prolactin increased. However, the result of the analysis shows that there was no difference in prolactin levels before and after the intervention of banana flower consumption which is seen from a p-value 0,132. A different result was seen in group 3, where the average pretest prolactin level was 232,98 ng/mL and 343,20 ng/mL of the posttest. The difference occurred as much as 110,22 ng/mL or it could be said that the level of prolactin had improved. The result reveals that there was a difference in prolactin levels before and after the intervention of banana flower vegetable consumption and oxytocin massage with p value 0,014. In this measurement, a slight improvement in prolactin level happened from group 2 to group 3. The average difference values were 103,61 ng/ml and 110,22 ng/ml.

This research was conducted from September to November 2019 by involving 30 postpartum mothers. The sample was divided into 3 groups namely: group 1 (intervened by oxytocin massage); group 2 (intervened by banana flower vegetable consumption); and group 3 (intervened by the combination of oxytocin massage and banana flower vegetable consumption). The results showed that in group 1 the results of the second measurement of prolactin levels (day 10) were lower than the first measurement. However, there was no difference in prolactin levels before and after the oxytocin massage intervention which was indicated with a p-value of 0.339. Meanwhile, in group 2 and group 3, after the intervention, prolactin levels showed an increase. In group 2, the analysis results showed no difference in prolactin levels before and after the intervention of banana flower-based food indicated by a p-value of 0.132. In group 3, the results of the analysis showed differences in prolactin levels before and after the intervention of giving banana flower-based food and oxytocin massage marked with a p-value of 0.014

This research found out in this research that oxytocin treatment did not influence the prolactin hormone level. It is different from the result of (Delima, Arni & Rosya, 2016) who saw that oxytocin had an influence on breast milk production. The mothers who received oxytocin massage experienced a significant increase in breast milk production. In group 2 and group 3 there was an increase in prolactin levels which is linear with the study of (Wahyuningsih et al., 2017) who did an approach by giving banana flower-based boiled water. The results obtained that there was a significant impact of the consumption of *Musa balbisiana colla* extract on the volume of breast milk production (p=0.003) and prolactin levels (p=0.001). The effect of banana extract (*Musa balbisiana colla*) is significant in increasing breast milk production and prolactin levels in nursing mothers. The findings of this study can be used as the basis for an alternative menu for postpartum mothers. It is also one of the solutions taken by midwives or health workers to deal with postpartum mothers whose milk production is inadequate and whose prolactin levels are low (Wahyuningsih et al., 2017).

Another study on the effect of banana buds on increasing breast milk production is a study by (Wahyuningsih et al., 2017) that found that mothers who consumed banana flower water experienced an increase in breastfeeding frequency from an average of 5.7 times to 9.75 times. There is also an increase in breast milk production while consuming stone banana flowers. This is certainly related to the increase in the hormone prolactin as an effect of consuming banana flowers.

The results of Musfiroh, et al., (2018) on the effectiveness of banana buds on increasing levels of the hormone prolactin and breast milk production in postpartum mothers showed that there was a significant increase in prolactin hormone levels (79.31 ± 51.46, p-value 0.000). While in the control group, there was a decrease (-12.09±72.42, p-value 0.488). Breast milk production based on the volume of breast milk in the intervention group experienced a significant increase (51.8750±6.36356, p-value 0.000). Banana flower extract is effective against increasing levels of the hormone prolactin. There is a significant effect of banana flower consumption on increasing prolactin levels and milk production.

Many studies have been carried out on the use of herbal plants as galactagogues. Several herbal plants that have proven potential as galactogues are wild asparagus, Torbagun (*Plectranthus amboinicus*), fenugreek, and milk thistle (Mortel & Mehta, 2013). Several other studies have also found plants that can act as galactagogues are (*Musa paradisiacal*) (Mahmood, Omar & Ngah, 2012), Katuk leaves (*Sauropus androgynus)* (Soka, Wiludjaja, & Marcella, 2011) and young papaya (*Carica papaya* L)(Kharisma, Ariyoga & Sastramihardja, 2011). Katuk leaves contain compounds in the form of sterols, alkaloids, flavonoids and tannins that play a role in increasing breast milk production.

Based on the results of bioactive examinations carried out in the laboratory, the content of active substances in banana blossoms that were blended, boiled, or extracted with ethanol is alkaloids, flavonoids, and, terpenoids. These active substances are also found in Rosella flower seeds and young papaya. The research results of Okasha, Abubakar & Bako, (2008) who studied rosella seeds discovered that the suspected bioactive galactagogues in rosella flower seeds are saponins, tannins, alkaloids, flavonoids, and steroids. This is in line with the results obtained in this study. The effect of the galactagogue is to increase serum prolactin and pituitary prolactin. Meanwhile, according to research (Mahmood, Omar & Ngah, 2012), The bioactive substances suspected as galactagogues in banana buds are saponins and tannins.

Galactagogue is a drug or substance that can initiate, maintain, and increase the speed of milk synthesis. The pharmaceutical theory reveals that what causes galactagogues is dopamine antagonists that can increase prolactin secretion and further increase milk secretion. Medicine that had been long known as a galactagogue is domperidone, metoclopramide (Holter, 2012), and sulpiride (Zuppa et al., 2010). Metoclopramide, known as a galactagogue since 1975, is a dopamine antagonist. The mechanism is to block dopamine receptors on the pituitary which causes the amount of prolactin to increase. Domperidone is another dopamine antagonist, that acts by blocking D2 receptors on the pituitary gland (Holter, 2012). Sulpiride as a galactogogum stimulates the hypothalamus to secrete prolactin release factor. The use of galactogogum drugs has side effects on breastfeeding mothers (Holter, 2012). The side effects of metoclopramide are mild headaches and intestine disorders. The side effects of domperidone are dry mouth, peeling skin, itching, headaches, and stomach upset. The side effects of sulpiride are fatigue and headaches (Zuppa et al., 2010). Therefore, the banana flower vegetable can be used as an alternative to change the consumption of galactagogue. The regular consumption of the banana flower vegetable can evoke the production of prolactin hormone and breast milk.

Research on rats showed that aqueous extract and petroleum ether extract of banana flower (*Musa paradisiacal*) could increase milk production in lactating rats by 25% and 18%, respectively. Meanwhile, ethanol extract as a control had no effect. The increase in milk production is thought to be caused by an increase in cell proliferation in the mammary glands due to the consumption of banana flower extract. The components of banana flower compounds that are thought to act as galactagogues are saponins and tannins (Mahmood, Omar & Ngah, 2012).

Previous research on the phytochemical content in the M. Paradisiaca flower showed that this flower contains alkaloids, saponins, glycosides, tannins, flavonoids, and steroids (Mahmood, Ngah, & Omar, 2011). The presence of these compounds such as saponins, tannins, alkaloids, and flavonoids in Hibiscus sabdariffa L. is thought to increase serum prolactin levels, a hormone associated with milk secretion (Okasha, Abubakar & Bako, 2008). Since most of the polar compounds are supposed to be soluble in the polar extraction solvent, it can be concluded that the compounds contained in the aqueous extract are polar compounds. The presence of saponins and tannins in the water extract of the Musa flower (Mahmood, Ngah, & Omar, 2011) shows that at least one of two substances influences the effect of galactagogue in this research.

The results revealed that consumption of several traditional galactagogues was significantly correlated with breast milk volume, including banana flower, lemon basil, Thai basil, bottle gourd, and pumpkin ($p<0.05$). Furthermore, there was a significant relationship between the consumption of several types of protein and the volume of milk, including tofu, eggs, chicken, fish, and seafood ($p<0.05$). Maternal energy and carbohydrate intake were related to breast milk volume ($p<0.05$), but protein intake was not. Certain types of galactagogue and traditional proteins are associated with breast milk volume. However, research relating to the active ingredients in this galactagogue is needed to secure

recommendations on the use of traditional galactagogues among nursing mothers (Buntuchai et al., 2017).

Banana flower is one of the traditional processed foods, known almost throughout the country. Banana flower is also processed into food that can be consumed daily. Banana flower vegetables can be made fresh, stir-fried, or just plain vegetables. The results showed that the galactagogue content in banana buds has the potential to stimulate the hormones oxytocin and prolactin such as alkaloids, polyphenols, steroids, flavonoids, and other substances that are most effective in increasing and facilitating breast milk production (Sriwahyuni, & Marpaung, 2022).

Oxytocin massage can provide a sense of relaxation to mothers because during the massage it will stimulate the production of the hormones oxytocin and prolactin. Meanwhile, food ingredients in the form of the banana flower contain galactagogue which can increase breast milk production. These two things are very well combined because the study results show that the group given the combination intervention of oxytocin massage and banana flower vegetables had higher prolactin levels. There was a significant increase in prolactin levels and there was a significant difference before and after the intervention.

4. CONCLUSION

The difference in average prolactin levels before and after intervention in group 1 was -61,75, group 2 was103,61, and group 3 was 110,22. Group 3 experienced an increase in prolactin levels and there was a significant change in prolactin levels between pretest and posttest. It is important to deliver socialization to increase breast milk production through the combined intervention of oxytocin massage and banana flower vegetable mothers and households. Furthermore, it is necessary to innovate a new extract of banana flowers for an easier way of consumption for nursing mothers. Research related to active substances in galactagogues is also needed to strengthen the recommendation of traditional galactagogues consumption to nursing mothers.

ACKNOWLEDGMENTS

We express our sincere gratitude to the Ministry of Health for generously providing grants that facilitated the completion of this research. Our heartfelt thanks also extend to all mothers and infants who actively participated as respondents in this study.

REFERENCES

Aisya, M. W., Zakaria, F., & Daud, W. (2020). The Effects of Banana Blossom (Musa Acuminate Colla) Consumption on Increased Breast Milk Production in the Work Area of Talaga Jaya. *Journal La Lifesci*, *1*(4), 1-7.

Buntuchai, G., Pavadhgul, P., Kittipichai, W., & Satheannoppakao, W. (2017). Traditional galactagogue foods and their connection to human milk volume in Thai breastfeeding mothers. *Journal of Human Lactation*, *33*(3), 552-559.

Damanik, R., Damanik, N., Daulay, Z., Saragih, S., Premier, R., Wattanapenpaiboon, N., & Wahlqvist, M. L. (2001). Consumption of bangun-bangun leaves (Coleus amboinicus Lour) to increase breast milk production among Bataknese women in North Sumatera Island, Indonesia. *Asia Pacific Journal of Clinical Nutrition*, *10*(4), S67.

Damanik, R., Wahlqvist, M. L., & Wattanapenpaiboon, N. (2004). The use of a putative lactagogue plant on breast milk production in Simalungun, North Sumatra, Indonesia. *Asia Pacific Journal of Clinical Nutrition*, *13*.

Delima, M., Arni, G. Z., & Rosya, E. (2016). Pengaruh pijat oksitosin terhadap peningkatan produksi ASI ibu menyusui di Puskesmas Plus Mandiangin. *Jurnal Ipteks Terapan*, *9*(4), 283–293.

Holter, A. (2012). Galactogogues : Effectiveness and Safety. *Saskatchewan Drug Information Services College of Pharmacy and Nutrition*, 29(2), 29–32.

Kementerian Kesehatan Republik Indonesia. (2020). *Profil Kesehatan Indonesia Tahun 2019*. Kementerian Kesehatan Republik Indonesia.

Kementerian Kesehatan Republik Indonesia, (2020). *Tabel Komposisi Pangan Indonesia*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Kharisma, Y., Ariyoga, A., & Sastramihardja, H. S. (2011). Efek ekstrak air buah pepaya (Carica papaya L.) muda terhadap gambaran histologi kelenjar mamma mencit laktasi. *Majalah Kedokteran Bandung*, *43*(4), 160-165.

Mahmood, A., Ngah, N., & Omar, M. N. (2011). Phytochemicals constituent and antioxidant activities in Musa x Paradisiaca flower. *European journal of scientific research*, *66*(2), 311-318.

Mahmood, A., Omar, M. N., & Ngah, N. (2012). Galactagogue effects of Musa x paradisiaca flower extract on lactating rats. *Asian Pacific Journal of Tropical Medicine*, *5*(11), 882-886.

Mardiyaningsih, E., Setyowati, S., & Sabri, L. (2011). Efektifitas kombinasi teknik marmet dan pijat oksitosin terhadap produksi ASI ibu post seksio di Rumah Sakit Wilayah Jawa Tengah. *Soedirman Journal of Nursing*, *6*, 31-38.

Mortel, M., & Mehta, S. D. (2013). Systematic review of the efficacy of herbal galactogogues. *Journal of Human Lactation*, *29*(2), 154-162.

Musfiroh L., Santoso B., & Runjati. (2018). The effectiveness of Musa balbisiana Colla toward the enhancement of prolactin hormone level and postpartum mother breast milk production. *International Journal of Multidisciplinary Education and Research*, 3(5), 31-34

Nurmiaty, N., Arsin, A. A., Sirajuddin, S., & Syafar, M. (2016). The effect of education lactation on breastfeeding behavior infant 0-6 months in Kendari Indonesia. *Public Health of Indonesia*, *2*(2), 100-111.

Okasha, M. A. M., Abubakar, M. S., & Bako, I. G. (2008). Study of the effect of aqueous Hibiscus sabdariffa Linn seed extract on serum prolactin level of lactating female albino rats. *European Journal of Scientific Research*, *22*(4), 575-583.

Riani, R. (2017). Pengaruh Konsumsi Rebusan Jantung Pisang Terhadap Ekskresi Asi Pada Ibu Menyusui Di Desa Ranah Wilayah Kerja Puskesmas Kampar Tahun 2016. *Jurnal Ners*, *1*(1), 117–124.

Shrimpton, R., Victora, C. G., de Onis, M., Lima, R. C., Blossner, M., & Clugston, G. (2001). Worldwide timing of growth faltering: implications for nutritional interventions. *Pediatrics*, *107*(5), e75-e75.

Soka, S., & Wiludjaja, J., & Marcella (2011). The Expression of Prolactin and Oxytocin Genes in Lactating BALB/C Mice Supplemented with Mature Sauropus androgynus Leaf Extracts. In *International Conference on Food Engineering and Biotechnology (IPCBEE)*, 9, 291–295.

Sriwahyuni, E., & Marpaung, I. S. (2022). Pengaruh Konsumsi Jantung Pisang Terhadap Peningkatan Produksi Asi Ibu Nifas Di Klinik Alisah Treisya Kecamatan Medan Area Tahun 2022. *Jurnal Penelitian Kebidanan & Kespro*, *5*(1), 82-87.

Wahyuningsih, D., Hidayat, S. T., Khafidhoh, N., Suwondo, A., Fatmasari, D., & Susiloretni, K. A. (2017). Effect of Musa balbisiana colla Extract on Breast Milk Production in breastfeeding mothers. *Belitung Nursing Journal*, *3*(3), 174-182.

Zuppa, A. A., Sindico, P., Orchi, C., Carducci, C., Cardiello, V., Catenazzi, P., & Romagnoli, C. (2010). Safety and efficacy of galactogogues: substances that induce, maintain and increase breast milk production. *Journal of Pharmacy & Pharmaceutical Sciences*, *13*(2), 162-174.

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 730-735
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1413*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Effectiveness of Aloe Vera-Based Topical Therapy Products on Breastfeeding Mothers with Milk Scratches in Hamparan Perak Village

Nuriah Arma[1a*], Novy Ramini Harahap[2b], Mayang Wulan[2c], Yuka Okta Firnanda[2d]

[1] Study Program of Midwifery, Helvetia Institute of Health, Medan City, North Sumatra Province, Indonesia
[2] Program Study of Midwife Professional Education, Helvetia Institute of Health, Medan City, North Sumatra Province, Indonesia

[a] Email address: nuriaharma@helvetia.ac.id
[b] Email address: novyramini@helvetia.ac.id
[c] Email address: mayangwulan@helvetia.ac.id
[d] Email address: yukaoktafirnanda@helvetia.ac.id

Received: 10 December 2023 Revised: 27 December 2023 Accepted: 27 December 2023

Abstract

In Indonesia, a study revealed that approximately 86.4% of breastfeeding mothers encounter nipple issues such as blisters, dryness, and pain. The World Health Organization (WHO) emphasizes that chafed nipples contribute to substantial pain, discomfort, and diminished milk production among nursing mothers, thereby posing a hindrance to exclusive breastfeeding initiatives. This study aims to investigate the effectiveness of an aloe vera-based topical therapy product in reducing nipple chafing in breastfeeding mothers in Hamparan Perak District. Conducted as an experimental study with a pre-test and post-test control group design, the research transpired in Hamparan Perak village. The study enlisted breastfeeding mothers experiencing sore nipples, with 20 individuals in the intervention group receiving aloe vera-based topical therapy in gel form, and 20 individuals in the control group receiving a placebo. The assessment of effectiveness centered on measuring blister occurrence and nipple pain scores both before and after the intervention, employing the Mann-Whitney test for data analysis. Bivariate analysis utilizing the Mann-Whitney U-test yielded a significant P-value of 0.001. Consequently, it can be inferred that aloe vera gel demonstrably influences nipple pain, with aloe vera gel proving to be 5,537 times more effective in pain reduction. Future research could incorporate objective measures, such as clinical assessments or laboratory analyses, to validate the reported outcomes.

Keywords: Sore Nipples, Aloe Vera, Topical Gel.

Corresponding Author:

Nuriah Arma
Study Program of Midwifery, Helvetia Institute of Health, Medan City, North Sumatra Province, Indonesia
Email: nuriaharma@helvetia.ac.id

1. INTRODUCTION

Sore nipples represent a common challenge faced by breastfeeding mothers, characterized by dryness, cracks, and pain during nursing sessions, potentially hindering the milk-giving process (Rao, et al., 2017; Lestari, et al., 2021; Maleki, & Youseflu, 2022). A study conducted in Indonesia underscored the prevalence of nipple issues, revealing that approximately 86.4% of breastfeeding mothers grapple with problems such as blisters, dryness, and pain (Santos, et al., 2016; Niazi, et al., 2018). The World Health Organization (WHO) recognizes the impact of chafed nipples, citing substantial pain, discomfort, and reduced milk production as potential consequences (World Health Organization, 2018).

Various factors contribute to sore nipples in nursing mothers, including incorrect breastfeeding techniques such as improper positioning, frequency issues, and flawed insertion or removal techniques, leading to soreness, swelling, and blisters (Amir & Donath, 2007; Frizziero, et al., 2016; Centers for Disease Control and Prevention., 2020). If left untreated, sore nipples can give rise to serious health problems, such as breast infection, increasing the risk of mastitis—a condition that may interfere with milk production (Amir & Academy of Breastfeeding Medicine Protocol Committee, 2014; Niazi, et al., 2021). Difficulties in proper breastfeeding, coupled with pain and discomfort, further exacerbate the impact on milk production (Amir & Donath, 2007; Dennis, et al., 2012; Christensen, et al., 2020).

Addressing chafed nipples involves various strategies, with topical therapy products being one viable option (Nayeri, Kheirkhah, & Janani, 2019). Aloe vera, known for its constituents like aloin, mannan, and polysaccharides, possesses anti-inflammatory, antioxidant, and antibacterial properties (Surjushe, Vasani, & Saple, 2008). These components are believed to mitigate nipple inflammation and expedite the healing of chafed nipple sores (Yustiza, et al., 2023; Itrat, & Zarnigar, 2013)

This study aims to investigate the effectiveness of an aloe vera-based topical therapy product in reducing nipple chafing in breastfeeding mothers in Hamparan Perak District.

2. RESEARCH METHOD

The research employed an experimental design with a pre-test and post-test control group to investigate the effectiveness of aloe vera-based topical therapy products in addressing sore nipples among breastfeeding mothers. The study included a sample of breastfeeding mothers with sore nipples, divided into two groups: an intervention group comprising 20 individuals receiving aloe vera-based topical therapy in gel form (Dewi, Hani, & Anwar, 2020), and a control group comprising 20 individuals receiving a placebo. The assessment of effectiveness involved measuring blister occurrence and nipple pain scores before and after the intervention (Tateoka, 2022). Data analysis was carried out using the Mann-Whitney test.

The pre-test and post-test control group design is a suitable method for evaluating the efficacy of aloe vera-based topical therapy products in addressing sore nipples among nursing mothers. The intervention group received the actual therapeutic product based on aloe vera in gel form, while the control group received a placebo with no therapeutic effect.

Before initiating treatment, both groups underwent a pre-test to assess nipple conditions and the severity of sore nipples. Subsequently, the intervention group received aloe vera-based topical therapy twice daily for one week, while the control group received a placebo using the same schedule.

At the conclusion of the treatment period, both groups underwent a post-test to evaluate the effectiveness of aloe vera-based topical therapy products in addressing sore nipples. Mann-Whitney statistical analysis was employed to ascertain the difference in effectiveness between the two groups. The research adhered to ethical guidelines and received approval from the

Research Ethics Committee of the Faculty of Nursing, University of North Sumatra, with the ethical review number 2920/VIII/SP/2023.

3. RESULTS AND DISCUSSION

Table 1. Frequency Distribution of Control Group Pain Scores.

Pain Scores	f	%
5	4	20
6	4	20
7	6	30
8	3	15
9	3	15
Total	20	100

Table 1 present the results of univariate analysis in the control group showed that respondents experienced more pain on scale 7, namely 6 people (30%) and 15% each on scale 8.9.

Table 2. Frequency Distribution of Post Test Pain Scores in the Intervention Group.

Pain Scores	f	%
0	13	65
1	7	35
Total	20	100

Table 2.present the results of the univariate analysis showed that the majority of respondents experienced scale 0 as much as 65% after the aloe vera gel intervention, while the rest were only on scale 1, namely 35%.

Table 3. Results of Mann Whitney U-Test Analysis for Intervention Group and Control Group.

Control group	N	Mean Rank	Sum of Rank	z	Mann Whitney U-Test
Pre-Test	20	30.50	610.00	-5.537	0,001
Post-Test	20	10.50	210.00		

Table 3 present the results of bivariate analysis using the Mann Whitney U-test showed a p-value of 0.001. So it can be concluded that there is an effect of aloe vera gel on reducing nipple pain, where aloe vera gel is 5,537 times more effective in reducing pain

The presented findings align with several prior studies that highlight the therapeutic potential of aloe vera in alleviating pain across various skin and tissue conditions. For instance, Farzadinia, et al., (2016) observed the anti-inflammatory effects of aloe vera, specifically noting its ability to alleviate pain associated with skin burns. Similarly, Johnson et al. (2020) demonstrated a significant reduction in pain intensity among postoperative patients through the topical application of aloe vera (Farzadinia, et al., 2016; Burusapat, et al., 2018).

Aloe vera's pain-relieving properties can be attributed to its composition of natural anti-inflammatory and moisturizing compounds, including aloin and polysaccharides. These constituents likely contribute to the observed effects on pain and inflammation in the skin. Several mechanisms elucidate the pain-relieving effects associated with aloe vera gel, as follows (Ruauw, Wantania, & Leman, 2016; Abdoli, et al., 2020): 1). Anti-Inflammatory Effects: Aloe vera contains salicylic acid and bradykininase, compounds known for their anti-inflammatory properties (Eshun, & He, 2004). These elements can mitigate the inflammatory response in the skin, consequently reducing pain perception (Alamolhoda, Mirabi, & Mojab,

2020), 2). Natural Moisturizing Effect: The inherent moisturizing components in aloe vera play a role in maintaining skin moisture, lowering the risk of nipple irritation that may lead to soreness (McClellan, et al., 2012; Pezeshki, et al., 2020), 3). Stimulation of Blood Circulation: Aloe vera gel exhibits the capacity to stimulate blood circulation in the applied area, enhancing the supply of nutrients and oxygen to the afflicted skin tissue. 4). Interaction with Pain Receptors: Various compounds present in aloe vera can interact with pain receptors on the skin, diminishing the sensation of pain that reaches the brain (Davis, et al., 1994).

These potential mechanisms collectively form a robust foundation for utilizing aloe vera gel in treating nipple pain (Patiran, Egam, & Kamalah, 2022). The synergistic combination of its anti-inflammatory properties, natural moisturizing effects, and the ability to enhance blood circulation positions aloe vera as a promising agent for reducing pain (Radha, & Laxmipriya, 2015).

These results are consistent with prior research emphasizing the therapeutic properties of aloe vera, particularly in meeting the distinctive needs of this demographic (Shahzad, & Ahmed, 2013). Despite recognizing the limitations inherent in our study, including the necessity for further exploration of long-term effects, the evidence presented herein implies that healthcare practitioners can consider aloe vera as a practical option in their recommendations for alleviating sore nipples. Looking ahead, it is imperative to persist in investigating complementary therapies like aloe vera to enhance the overall well-being of breastfeeding mothers and, consequently, foster successful breastfeeding experiences (Dewi, Hani, & Anwar, 2020).

4. CONCLUSION

The findings of this research underscore the potential of topical aloe vera-based therapy as a valuable and accessible solution for addressing sore nipples in breastfeeding mothers. It can be inferred that aloe vera gel demonstrably influences nipple pain, with aloe vera gel proving to be 5,537 times more effective in pain reduction. Future research endeavors could benefit from the incorporation of objective measures, such as clinical assessments or laboratory analyses, to validate and strengthen the reported outcomes. This approach would further enhance the reliability and robustness of findings in the pursuit of advancing the understanding and implementation of effective interventions for breastfeeding-related concerns.

REFERENCES

Abdoli, S., Jenabi, E., Masoumi, S. Z., Kazemi, F., & Moradkhani, S. (2020). Effect of the Topical form of Achillea millefoliumon on Nipple Fissure in Breastfeeding Women: A Randomized Controlled Clinical Trial. *Iranian Journal of Neonatology*, *11*(2).

Alamolhoda, S. H., Mirabi, P., & Mojab, F. (2020). Effects of both Aloe Vera gel and breast milk on the improvement of nipple soreness in lactating women—A randomized controlled trial. *Journal of Herbal Medicine*, *21*, 100327. https://doi.org/10.1016/j.hermed.2019.100327

Amir, L. H., & Academy of Breastfeeding Medicine Protocol Committee. (2014). ABM clinical protocol #4: Mastitis, revised March 2014. *Breastfeeding medicine : the official journal of the Academy of Breastfeeding Medicine*, *9*(5), 239–243. https://doi.org/10.1089/bfm.2014.9984

Amir, L. H., & Donath, S. (2007). A systematic review of maternal obesity and breastfeeding intention, initiation and duration. *BMC pregnancy and childbirth*, *7*, 9. https://doi.org/10.1186/1471-2393-7-9

Burusapat, C., Supawan, M., Pruksapong, C., Pitiseree, A., & Suwantemee, C. (2018). Topical Aloe vera gel for accelerated wound healing of split-thickness skin graft donor sites: A

double-blind, randomized, controlled trial and systematic review. *Plastic and reconstructive surgery*, *142*(1), 217-226. https://doi.org/10.1097/PRS.0000000000004515

Centers for Disease Control and Prevention. (2020). *Breastfeeding and Special Circumstances.* Centers for Disease Control and Prevention. Retrieved from https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/

Christensen, N., Bruun, S., Søndergaard, J., Christesen, H. T., Fisker, N., Zachariassen, G., ... & Husby, S. (2020). Breastfeeding and infections in early childhood: a cohort study. *Pediatrics*, *146*(5). https://doi.org/10.1542/peds.2019-1892

Davis, R. H., Donato, J. J., Hartman, G. M., & Haas, R. C. (1994). Anti-inflammatory and wound healing activity of a growth substance in Aloe vera. *Journal of the American Podiatric Medical Association*, *84*(2), 77–81. https://doi.org/10.7547/87507315-84-2-77

Dennis, C. L., Schottle, N., Hodnett, E., & McQueen, K. (2012). An all-purpose nipple ointment versus lanolin in treating painful damaged nipples in breastfeeding women: a randomized controlled trial. *Breastfeeding Medicine*, *7*(6), 473-479. https://doi.org/10.1089/bfm.2011.0121

Dewi, P. S., Hani, U., & Anwar, M. (2020). The effectiveness of aloe vera gel in reducing the pain of perineal wound. *Medisains*, *18*(99). http://dx.doi.org/10.30595/medisains.v18i3.8202

Eshun, K., & He, Q. (2004). Aloe vera: a valuable ingredient for the food, pharmaceutical and cosmetic industries—a review. *Critical reviews in food science and nutrition*, *44*(2), 91-96. https://doi.org/10.1080/10408690490424694

Farzadinia, P., Jofreh, N., Khatamsaz, S., Movahed, A., Akbarzadeh, S., Mohammadi, M., & Bargahi, A. (2016). Anti-inflammatory and wound healing activities of Aloe vera, honey and milk ointment on second-degree burns in rats. *The international journal of lower extremity wounds*, *15*(3), 241-247. https://doi.org/10.1177/1534734616645

Frizziero, A., Causero, A., Bernasconi, S., Papalia, R., Longo, M., Sessa, V., Sadile, F., Greco, P., Tarantino, U., Masiero, S., Rovati, S., & Frangione, V. (2016). Efficacy of betamethasone valerate medicated plaster on painful chronic elbow tendinopathy: a double-blind, randomized, placebo-controlled trial. *Muscles, ligaments and tendons journal*, *6*(1), 131–139. https://doi.org/10.11138/mltj/2016.6.1.131

Lestari, M. W., Juwita, C. R., & Silalahi, U. A. (2021). Effect of the Administration of Aloe Vera Gel Extract on the Healing TIME of Nipple Wound in Breastfeeding Mothers. *INTERNATIONAL JOURNAL OF NURSING AND MIDWIFERY SCIENCE (IJNMS)*, *5*(3), 195-201. https://doi.org/10.29082/IJNMS/2021/Vol5/Iss3/347

Itrat, M., & Zarnigar, K. (2013). Aloe vera: a review of its clinical effectiveness. *International Research Journal of Pharmacy*, *4*(8), 75-79.

Maleki, A., & Youseflu, S. (2022). The Effectiveness of Aloe Vera on Relief of Irritation and Nipple Pain in Lactating Women: Systematic Review and Meta-Analysis. *Obstetrics and gynecology international*, *2022*, 7430581. https://doi.org/10.1155/2022/7430581

McClellan, H. L., Hepworth, A. R., Garbin, C. P., Rowan, M. K., Deacon, J., Hartmann, P. E., & Geddes, D. T. (2012). Nipple pain during breastfeeding with or without visible trauma. *Journal of Human Lactation*, *28*(4), 511-521. https://doi.org/10.1177/0890334412444464

Nayeri, S. D., Kheirkhah, M., & Janani, L. (2019). The effect of chamomile ointment on the healing of breastfeeding mothers' nipple sore-a randomized controlled clinical trial. *J Evolution Med Dent Sci*, *8*(17), 1399-404.

Niazi, A., Rahimi, V. B., Askari, N., Rahmanian-Devin, P., & Askari, V. R. (2021). Topical treatment for the prevention and relief of nipple fissure and pain in breastfeeding women:

A systematic review. *Advances in Integrative Medicine*, *8*(4), 312-321. https://doi.org/10.1016/j.aimed.2021.07.001

Pezeshki, B., Pouredalati, M., Zolala, S., Moeindarbary, S., Kazemi, K., Rakhsha, M., ... & Razmjouei, P. (2020). Comparison of the effect of aloe vera extract, breast milk, calendit-E, curcumin, lanolin, olive oil, and Purslane on healing of breast fissure in lactating mothers: a systematic reviwe. *International Journal of Pediatrics*, *8*(2), 10853-10863.

Patiran, M., Egam, A., & Kamalah, R. (2022). Perbedaan efektivitas pemberian kompres lidah buaya dan kompres daun kubis dingin terhadap intensitas nyeri payudara ibu nifas. *Jurnal Kebidanan Sorong*, *2*(1), 24-32. Retrieved from https://poltekkes-sorong.e-journal.id/JKS/article/download/164/104

Radha, M. H., & Laxmipriya, N. P. (2015). Evaluation of biological properties and clinical effectiveness Aloe vera: A systematic review. *Journal of traditional and complementary medicine*, *5*(1), 21-26. https://doi.org/10.1016/j.jtcme.2014.10.006

Rao, S., Hegde, S. K., Baliga-Rao, M. P., Palatty, P. L., George, T., & Baliga, M. S. (2017). An aloe vera-based cosmeceutical cream delays and mitigates ionizing radiation-induced dermatitis in head and neck cancer patients undergoing curative radiotherapy: a clinical study. *Medicines*, *4*(3), 44. https://doi.org/10.3390/medicines4030044

Ruauw, E. F., Wantania, F.E., & Leman, M. A. (2016). Pengaruh lidah buaya (Aloe vera) terhadap waktu penutupan luka sayat pada mukosa rongga mulut tikus wistar. *Pharmacon*, *5*(2), 22-28.

Santos, K. J., Santana, G. S., Vieira, T.deO., Santos, C. A., Giugliani, E. R., & Vieira, G. O. (2016). Prevalence and factors associated with cracked nipples in the first month postpartum. *BMC pregnancy and childbirth*, *16*(1), 209. https://doi.org/10.1186/s12884-016-0999-4

Shahzad, M. N., & Ahmed, N. (2013). Effectiveness of Aloe Vera gel compared with 1% silver sulphadiazine cream as burn wound dressing in second degree burns. *J Pak Med Assoc*, *63*(2), 225-30.

Surjushe, A., Vasani, R., & Saple, D. G. (2008). Aloe vera: a short review. *Indian journal of dermatology*, *53*(4), 163–166. https://doi.org/10.4103/0019-5154.44785

Tateoka Y. (2022). Effectiveness of aloe fomentation for nipple-related complications during the early puerperium period: a randomized, controlled, interventional study. *BMC research notes*, *15*(1), 94. https://doi.org/10.1186/s13104-022-05980-x

World Health Organization. (2018). *Breastfeeding*. World Health Organization. Retrieved from https://www.who.int/news-room/fact-sheets/detail/breastfeeding

Yustiza, N. R., Wijayanti, K., Sunarjo, L., & Widyawati, M. N. (2023). Potency of Aloe Vera Extract Transdermal Patch Treatment in Relief Pain and Breast Engorgement. *Jurnal Aisyah: Jurnal Ilmu Kesehatan*, *8*(3). https://doi.org/10.4081/hls.2023.11788

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 736-748
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1419*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Evaluating the Efficacy of the Zelisken Ball in Shortening the First Stage of Labor: A Quasi-Experimental Study

Zeni Zaenal Mutaqin[1a*], Nurul Lidya[1b], Isroni Astuti[1c] , Niken Meilani[2d]

[1] Department of Midwifery, Poltekkes Kemenkes Jakarta I, Jakarta, Indonesia
[2] Department of Midwifery, Poltekkes Kemenkes Yogyakarta, Yogyakarta, Indonesia

[a] Email address: zeni@poltekkesjakarta1.ac.id
[b] Email address: nurullidya03@gmail.com
[c] Email address: isronieastutie@gmail.com
[d] Email address: niken.meilani@poltekkesjogja.ac.id

Received: 15 December 2023 Revised: 22 December 2023 Accepted: 27 December 2023

Abstract

During labor, mothers frequently report having excruciating contractions that continue for hours or even days. An assistive gadget is required to expedite labor and aid in the baby's head drop. The Zelisken Ball, an invention of the research group, is a bolster-shaped ball used in basic exercises or physical care. The study aimed to determine whether using the Zelisken Ball could shorten the time pregnant mothers spend in the first stage of labor. Pregnant women's level of comfort and satisfaction while using it, along with its effects on each delivery stage, were highlighted. Using a control group, the study used a quantitative methodology and a quasi-experimental post-test-only design. Purposive sampling was employed to identify 50 postpartum patients for the sample. The Zelisken Ball was utilized by the intervention group in this study, while the Peanut Ball was used by the control group. Questionnaires were used to gather data, and SPSS software was implemented to perform an Independent Sample t-test to determine differences between the two groups. The mothers who utilized the Zelisken Ball advanced through the first stage of labor more quickly, according to the data, with a difference of 1.29 hours (77.4 minutes) between them and the control group (8.3 hours) who used the Peanut Ball. The results of the data analysis indicate that mothers who used the Zelisken Ball and those who utilized the Peanut Ball had significantly different first-stage labor durations (p-value of 0.026, <0.05). As a result, the Zelisken Ball shows great promise as a useful tool for accelerating the early stage of labor. The research has been modified to create Zelisken, which is two-thirds the size of a peanut ball and has an indentation of ½ on the ball. The outer material of Zelisken is made of Oscar fabric, and the inside is filled with foam, whereas the peanut ball is made of PVC and has an interior filled with air. Future research, however, needs to increase the sample size to include a wider range of respondents to strengthen the findings' generalizability.

Keywords: Birthing Ball, Labor, Reproductive, Pelvic Rocking.

Corresponding Author:

Zeni Zaenal Mutaqin
Department of Midwifery, Poltekkes Kemenkes Jakarta I, Jakarta, Indonesia
Email: zeni@poltekkesjakarta1.ac.id

1. INTRODUCTION

According to estimates from the World Health Organization (WHO), pregnancy and childbirth-related problems claim the lives of 800 women per day (WHO, UNICEF, UNFPA, World Bank Group & UNDESA/Population Division, 2023). Pregnancy, childbirth, and postpartum problems account for over 80% of mother mortality. The maternal mortality ratio (MMR) for the world is 289,000. The primary causes of maternal deaths are bleeding (25%), infection/sepsis (15%), eclampsia (12%), unsafe abortion (13%), obstructed parts (8%), and other direct causes like embolism, ectopic pregnancy, and issues with anesthesia (8%), other causes (19%), and other causes (19%) (Sulistyorini & Rofingah, 2021). In the world prolonged labor may occur in one in five women (Sørbye et al., 2022). Therefore, enhancing access to quality health services, escalating pregnant women's knowledge and skills about pregnancy, childbirth and infant care, and providing support to family and friends can help pregnant women feel more prepared for labor and reduce stress.

Maternal mortality ratio (MMR) statistics indicated a declining trend, down at an annual rate of 1.80 percent from 390 per 100,000 live births in 1991 to 230 in 2020, according to the Indonesian Health Profile. The MMR drop has not, however, yet reached the 2030 SDGs (Sustainable Development Goals) target, which is fewer than 70 per 100,000 live births, with a target of 102, or the MDGs (Millennium Development Goals) target, which was set in 2015. Likewise, the IMR (infant mortality rate) indicator demonstrated a decrease at a rate of 3.93 percent per year, from 68 in 1991 to 24 in 2017 (Kementerian Kesehatan Republik Indonesia, 2021). This is due to several factors, including low-quality healthcare facilities, pregnant women who lack support from friends and family, and pregnant women who lack knowledge and skills concerning pregnancy, labor, and infant care. If any of these are absent, labor might endure longer than expected.

Long labor, defined as lasting more than 18 hours from the start of labor signs, is a contributing factor to both maternal and fetal mortality. Long labor is associated with a higher risk of mother and fetal death. Maternal death may arise from prolonged labor due to infections, tiredness, dehydration, and postpartum hemorrhage (Ahmady, Ashriady & Mariana, 2020). Extended labor can result in infections, trauma, and hypoxia in the fetus, all of which raise the risk of newborn death. One of the numerous factors that affect the rates of maternal and neonatal mortality is prolonged labor (Rositawati, 2019). Mothers hospitalized in Indonesia due to prolonged labor accounted for 4.3% or 12,176 out of 281,050 deliveries (Batubara, Mahayani, & Agma, 2019).

Prolonged labor is one of several causes of maternal and newborn deaths in Indonesia (Desyanti & Widad, 2023), but not as prevalent as bleeding and hypertension (Dewi et al., 2022). Long labor can result in difficulties and emergencies for both the mother and the baby if it is not addressed or stopped at an early stage. It can cause fetal discomfort, hypoxia, and caput in addition to bleeding, shock, and maternal mortality (Solihah, Nurherliyany, Sandriani, & Putri, 2023). Prior studies show that both before and after therapy, the pain scale decreased. In particular, the pain scale dropped from 7 to 5 during the first 30 minutes and from 5 to 4 during the second 30 minutes. As a result, mothers who received birth ball therapy without the use of medication for an hour received a total of three points for pain reduction (Subagio, 2022). Research has demonstrated that this method is effective in reducing labor pain during the active phase I.

Stage I of labor is a crucial early phase in the birthing process, beginning from the onset of uterine contractions up until the cervix dilates to ten centimeters (Abalos, Chamillard, Díaz, Pasquale, & Souza, 2020). There are serious consequences that can arise from not addressing timing difficulties, such as an increased chance of complications for both the mother and the child (Cohen & Friedman, 2023). Maternal exhaustion, an increased risk of infection, and the need for more intrusive medical operations, such as cesarean sections, might result from labor's

slow progress during the initial stage (Dalbye et al., 2020). Furthermore, an uneven duration of the initial stage of labor may adversely affect a mother's psychological well-being, lead to stress, anxiety, and discomfort that can compromise the overall birthing experience (Salvator et al., 2023).

The phase of cervical opening to 10 centimeters, recognized as the first stage of labor, has a significant impact on the birth process (Kahrs & Eggebø, 2021). At this point, the rate of advancement has significant clinical ramifications for the health of the mother and child and may have an impact on treatment choices (Etty, Damanik, & Gowasa, 2023). To investigate non-pharmacological ways of promoting labor, Zelisken Ball is an alternative therapy whose potential is still unexplored. The Zelisken Ball, in contrast to the Peanut Ball, was created as a physical therapy instrument to aid in the progression of first-stage labor (Solihah et al., 2023). The study team created the Zelisken Ball, a version of the Peanut Ball, to help first-time mothers with the progression of labor. With one leg up and the ball tucked between the thighs, the procedure requires sleeping, and it is anticipated that the force of gravity will accelerate the labor process (Grenvik et al., 2019). Furthermore, the ball's soft cotton fabric and comforting curve, comparable to a customized bolster, stimulate endorphin-releasing receptors in the pelvis (Morales-Alvarado & Paredes-Pérez, 2023). The objective of this study is to investigate how effectively the Zelisken Ball affects the length of the cervical opening during the initial phase of labor.

The scientific understanding of how the Zelisken Ball accelerates the initial stage of labor and its advantages for the health of mothers and newborns is greatly advanced by this study. In addition, the study thoroughly examines the variables affecting the course of first-stage labor to pinpoint the mother groups that stand to gain the most from the Zelisken Ball. The results of this study highlight the possibility of creating non-invasive therapies with higher efficacy for use in midwifery practice. This can result in enhanced outcomes and more widespread implementation.

Other popular methods for quickening the first stage of labor include non-pharmacological methods like massage and acupuncture or the use of medications like oxytocin (Agapoff, Chong, Meek, & van Schalkwyk, 2023). However, the use of medications may pose side effects and risks to both the mother and baby (Tahar, et al., 2021). The mother may have nausea, vomiting, diarrhea, headaches, elevated blood pressure, painful and frequent contractions, infections, and allergic responses as side effects. Infants may experience side effects such as suffocation (respiratory discomfort), hypoxia (lack of oxygen), head injuries, and even death. Using nonpharmacological methods like massage and acupuncture during childbirth is generally safe. However, everyone uniquely reacts to these methods. Therefore, since the Zelisken Ball can accelerate labor and enhance uterine contractions without having a large negative impact, it is a promising approach (Stulz, Dashputre, & Reilly, 2023). Previous studies have demonstrated that employing a birthing ball can shorten the duration of the first stage of labor and reduce the need for medical procedures like cesarean sections and the usage of oxytocin (Wu, Huang, Shan, Li, & Jiang, 2022).

The Zelisken Ball was selected as the main subject of this investigation because it complies with natural childbirth principles and is a non-pharmacological technique (Young, Shipe, & Smith, 2021). Compared to other birthing balls, the Zelisken Ball is expected to perform more effectively by promoting uterine contractions, slowing and regulating the movement of the uterus, potentially accelerating the onset of labor (Outland & Alvarado, 2019). Moreover, this device exhibits promise in enhancing the comfort of expecting mothers, reducing stress and anxiety levels that may affect the progression of labor (Kamath et al., 2022).

The objective of the Zelisken Ball is to enhance the efficiency of uterine contractions in the early stages of labor. According to theory, it is predicated on the idea of peripheral uterine

muscle stimulation using non-pharmacological methods (Jayasudha et al., 2021). According to this notion, the Zelisken Ball's physical stimulation can boost the production of oxytocin, a hormone that is essential for uterine muscle contraction. The effectiveness of the Zelisken Ball at accelerating the first stage of labor has been evaluated in several earlier studies utilizing clinical and observational methods (Ahmadpour, et al., 2021). These studies consistently demonstrate that employing the Zelisken Ball can significantly enhance the frequency and intensity of uterine contractions during the early phases of labor (Ahmed, Mohmed, & Fathalla, 2022).

Although these initial results provide some indication of the Zelisken Ball's efficacy, further comprehensive investigation is required to thoroughly validate and establish its advantages. This ought to involve more meticulously designed randomized clinical studies. Furthermore, previous studies have not yet provided a complete explanation for the physiological processes that underlie the Zelisken Ball's beneficial effects in quickening the first stage of labor. Consequently, the objective of this research is to enhance our understanding of how well the Zelisken Ball functions as a preventative strategy to enhance the management of the first stage of labor and the health of the mother and child.

The Zelisken Ball significantly enhances the benefits of spontaneous uterine muscle contractions by creating movement and pressure (Eprilia, Hidayati, Sari, & Meilati, 2020). The Zelisken Ball can minimize labor time, speed up the first stage of labor, and lower the risk of problems because of this stimulatio (Honaker, 2021). The ergonomic position of the Zelisken Ball during use contributes to improved blood circulation and muscular relaxation during delivery, which is an additional benefit when employing it on mothers. The Zelisken Ball is a helpful instrument in efforts to improve labor efficiency due to these advantages (Sheishaa, El-Mashad, & Khedr, 2019).

This study incorporates the concepts of body mobility during pregnancy and biomechanics to investigate how well the Zelisken Ball accelerates the first stage of labor. The rate of progress in the first stage of labor, which includes cervical dilation, contraction intensity, and baby's head advancement, is the dependent variable. The independent variables under evaluation include the length of time, frequency, and kind of Zelisken Ball motion. The study included control variables such as maternal age, parity, and health status. Data analysis was performed using statistical techniques like regression analysis and t-tests. It is anticipated that this study will significantly advance our understanding of the Zelisken Ball's efficacy concerning labor.

Previous research has explored several non-pharmacological methods to escalate the effectiveness of the first stage of labor (Zuarez-Easton et al., 2023). One method that was investigated involved providing multigravida mothers with a pelvic rocking exercise technique along with a peanut ball combination. Implementing this strategy significantly shortened the first labor stage compared to the control group, according to a quasi-experimental analysis. As an alternative, the research by (Iryani, Pramestigiri, & F, 2022) revealed that employing a birthing ball and endorphin massage therapy during the active period of labor significantly reduced the level of pain. Another investigation corroborated this conclusion (Meliani, Amlah, & Rahmawati, 2022), Research demonstrated that engaging in hypnobirthing, yoga, and pregnancy exercises throughout the third trimester, along with performing breathing techniques while utilizing a birth ball, were all associated with decreased anxiety levels. Furthermore, studies have revealed how effective birth ball exercise is at accelerating the early and second stages of labor. Collectively, these studies indicate that a variety of non-pharmacological techniques can significantly impact both the rate of labor onset and the level of discomfort experienced during labor.

The objective of the study is to promote the development of innovative clinical midwifery practices. A study conducted by the Arso 3 Health Center in Keroom Regency discovered that

birth ball exercise increased the length of kala I and kala II (Suryani & Mufida Dian Hardika, 2022). Additionally, a previous study discovered variances in the duration of the first stage of labor between mothers who used birthing balls and those who did not (Pertasari, 2022). Therefore, to evaluate the Zelisken Ball's effectiveness in accelerating the first stage of labor, this study can adapt or use techniques and findings from earlier studies. Purposive sampling is used in the study to choose pregnant participants based on predetermined inclusion criteria. The control group will receive the Peanut Ball, whereas the treatment group will receive the Zelisken Ball. There will be close observation of the initial stage of labor duration together with meticulous documentation of relevant time parameters. The use of a specific rating scale that adds quantitative dimensions to the labor progress rate and direct monitoring by a trained research team are examples of novel methodologies.

The data will be analyzed using statistical techniques like t-tests and analysis of variance to observe whether there are any significant differences between the treatment and control groups. This study aims to provide significant insight into how effectively the Zelisken Ball manages labor by employing an approach that reduces bias and produces trustworthy, useful scientific results.

This research investigates if early labor is accelerated by the Zelisken Ball. The trial was conducted at the Velia Medika Clinic in South Jakarta for six months commencing in June 2024. Pregnant women at risk of first-stage labor were the focus of the trial. The major intervention was the Zelisken Ball, and this work describes a novel labor-speeding tactic that is non-pharmacological. This study's exclusive Zelisken Ball should increase this group's labor productivity. It is necessary to investigate the benefits of this alternative approach. To expedite the first stage of labor, which involves opening the cervix to 10 cm, the study highlights the significance of examining the Zelisken Ball. The well-being of mothers and babies is impacted by understanding how to enhance comfort and efficiency in this day and age. We therefore started researching how the Zelisken Ball enhances this procedure. The scientific understanding of non-pharmacological labor management should be advanced by this work, particularly in the early stages. By highlighting the potential of the Zelisken Ball, this study may contribute to bettering mother-infant health after birthing. An effective strategy can decrease issues, shorten labor, and enhance the mother's experience. New medications for labor control in contemporary obstetrics may also result from this research. Thus, the advancement of obstetric alternative therapy, mother and baby welfare, and scientific knowledge might benefit from this work.

2. RESEARCH METHOD

This study administered experimental research with a quasi-experimental design to ensure a cause-and-effect relationship encompassing an experimental group and a control group, using a post-test only design with a control group. This design involves measurements taken only at the study's conclusion (Sugiyono, 2019a).

The sample consisted of 50 in partum patients deliberately selected through a strategy that considered particular characteristics. Purposive sampling is a strategy employed by researchers in selecting samples because not all samples meet the requirements specified (Sugiyono, 2019b). Two groups participated in the study: the control group and the intervention group. In the control group were 25 in partum patients treated with Peanut Ball therapy, and the intervention group consisted of 25 patients treated with Zelisken Ball therapy. The inclusion criteria included women who were in labor at the Velia Medika clinic and had a gestational age between 38 and 42 weeks, a single, healthy fetus, a normal head position for the mother during active phase I, no history of using birth balls in the past, no complications associated with labor, and proficient speaking, writing, reading, and hearing. In the first stage, the control group utilized the Peanut Ball and the intervention group received the Zelisken Ball.

Data were gathered through questionnaires administered to all participants. The following sections were included in the study's questionnaire: 1) Respondent identity comprised address, name, age, gestational age, GPA, and gestational age. It additionally requested about past pregnancy history and symptoms of labor, such as contractions, vaginal discharge, and amniotic fluid. 2) Using a Zelisken ball, steps in the birthing process were also highlighted. Using the partograph observation sheet, the research was conducted during the active phase of the first stage and evaluated the progress of labor and the subsequent stage. The pathographic observation sheet documents the number of participants, their age, parity, category, intervention, time of labor onset, duration, and length (in hours and minutes) of phase 1 of active labor.

Ethical approval for the study was granted by the Health Research Ethics Committee of Respati University Indonesia, with document number 441/SK. KEPK/UNR/VII/2023. The study's data collection procedures encompassed the following steps: 1) Completing an agreement with PMB to identify mothers to participate in the study; 2) obtaining research instruments prepared. 3) selecting responders according to preset inclusion standards; 4) acquiring patients' informed consent; 5) providing and explaining the Zelisken ball method SOP sheet and observation sheet; 6) developing a consent form; and 7) maintaining the status of labor. SPSS software was utilized for examining the data in two stages: univariate analysis and bivariate analysis. The frequency distribution of each variable under study was obtained by univariate analysis and presented as a percentage. Frequencies and proportions were employed to represent categorical variables, and mean, standard deviation (SD), and 95% confidence interval (CI) values were applied to represent numerical variables. Furthermore, we performed a bivariate analysis using an independent sample t-test to evaluate the magnitude and significance of differences between variables.

3. RESULTS AND DISCUSSION

Table 1. Distribution Characteristics of Respondents

Variable	Peanut Ball		Zelisken		Total	
	N	%	N	%	N	%
Ages						
<20 Year	0	0.0	1	3.8	1	2.0
20–35 Year	20	80.0	24	92.3	44	86.3
>35 Year	5	20.0	1	3.8	6	11.8
Parity						
Primipara	10	40.0	16	61.5	26	51.0
Multipara	15	60.0	10	38.5	25	49.0
Occupation						
Housewife	14	56.0	11	42.3	25	49.0
Private	10	40.0	11	42.3	21	41.2
Civil Servant	1	4.0	2	7.7	3	5.9
Teacher	0	0	2	7.7	2	3.9
Education						
Elementary School	3	12.0	1	3.8	4	7.8
Junior High School	5	20.0	4	15.4	9	17.6
Senior High School	10	40.0	10	38.5	20	39.2
University	7	28.0	11	42.3	18	35.3

Table 1 above demonstrates that 80% and 92.3%, respectively, of the respondents in the peanut ball and Zelisken groups were between the ages of 20 and 35. The majority of respondents in the peanut ball group had given birth more than once (60%) while the majority in the Zelisken group had given birth for the first time (61.5%).

Of the mothers in the employment variable, 56% and 42.3%, respectively, worked as housewives. According to the degree of education, the majority in the Zelisken group (42.3%) and the peanut ball group (40%) have completed college.

Table 2. Gestational Age and Duration of First Period

Variable	Peanut Ball Group				Zelisken Ball Group			
	Mean	Min	Max	SD	Mean	Min	Max	SD
Pregnancy Age								
UK Weeks	38.0	37	40	0.91	38.0	37	40	0.93
UK Days	3.0	0	6	2.27	4.0	0	6	2.24
Duration of Period I	8.30	5.50	12.41	1.76	7.01	2.50	12.33	2.25

The average gestational age of the peanut ball group, as seen in Table 2 above, is 38 weeks and 3 days. This number is nearly identical to that of the Zelisken group, which has an average gestational age of 38 weeks and 4 days. with a gestational age range of 37 weeks at minimum and 40 weeks at maximum, plus 6 days.

The first stage utilized an average of 8.30 hours in the peanut ball group, with the fastest stage 1 lasting 5.50 hours and the longest being 12.41 hours. In the Zelisken group, the first stage took an average of 7.01 hours, with the fastest stage I ranging from 2.5 hours and the longest being 12.33 hours.

Table 3. Differences in the Length of Period I Using Peanut Ball and Zelisken

Variable	Group	Mean	SD	Min-Max	p-value*
Period I	Peanut Ball	8.30	1.76	5.50-12.41	0.026
	Zelisken	7.01	2.24	2.50-	
	Difference	1.29		12.33	

Table 3 above indicates that the first stage comprised an average of 8.3 hours for the Peanut Ball group and 7.01 hours for the Zelisken group. According to the analysis, mothers who administered Zelisken completed the first stage 1.29 hours sooner than those who received Peanut Ball. With a p-value of 0.026 (<0.05), the results of the study demonstrated a significant difference in the first stage's duration between mothers who used Zelisken and mothers who utilized Peanut Ball.

DISCUSSION

Data analysis results indicate that mothers using the Zelisken Ball pass the first stage of labor more quickly than mothers using the Peanut Ball in the control group. 1.29 hours (77.4 minutes) separated the intervention and control groups. Furthermore, the research revealed a p-value of 0.026 (<0.05) indicating a significant difference in the first stage duration between women using Zelisken and mothers using Peanut Ball. This implies that the Zelisken balls implemented as an intervention in this study had positive effects, particularly in hastening the onset of labor in mothers. Previous research states that the average mother who applies a peanut ball has a duration of labor in Stage I of about 8 hours. This result is in accordance with research conducted by Grenvik, Coleman, and Berghella (2023); Hickey and Savage, (2019); Mercier and Kwan (2018). Therefore, the results of this study evidence the effectiveness of Zelisken ball in accelerating the duration of Stage I labor.

The Zelisken Ball group is a non-pharmacological auxiliary instrument. The results of studies on the use of birthing balls, which lessen labor pain and enhance mother and infant health, support the efficacy of non-pharmacological methods for alleviating laboring mothers' discomfort (Jha, Vyas, Nebhinani, Singh, & T, 2023). The Birthing Ball technique is strongly recommended to be incorporated as an approach to labor management to improve maternal and

fetal well-being (Sundaram, Bhuvaneswari, & Chandrika, 2022). Birth ball exercise has an effect on labor during stage I (Fitria & Wahyuny, 2021; Rukmaini, Oktaviani, & Suciawati, 2023; Telova, 2022). This corroborates the claim presented by Apriani, Herfanda, & Utami, (2020) that using a birth ball during training statistically considerably lowers labor pressure, particularly during the latent and active periods. During the active phase of labor, self-efficacy improved dramatically, despite greater differences in the duration and interval between uterine contractions that were not statistically significant. Another connection between pain during birth and low self-efficacy—roughly 30–40%—has been established (Apriani, Herfanda, & Utami, 2020).

According to Aprilla's, (2014) theory, every mother will experience labor's initial stage differently. The time it takes for a mother to finish opening up decreases with her level of relaxation and movement. The mother should do nothing but lie in bed at the start of the labor process. The labor process will be much aided by shifting postures every half to two hours. She can lean on and wriggle her pelvis while squatting or using a peanut ball or birthing ball. The mother can stand and lean comfortably on the ball while it's on the bed, pressing and swinging the pelvis to facilitate mobilization. The mother may elevate her pelvis and assist the baby in changing to the proper position (head-back position) by kneeling and bending over with her weight resting on the ball while it is on the floor or bed. This allows labor to go more quickly (Aprillia, 2014).

The Zelisken Ball serves as an assistive device to facilitate the labor process by helping the mother maintain an open position in her pelvis, encouraging downward movement of the baby (Aprillia, 2014). The form and size of the pelvis are significantly altered by changes in position throughout labor, which benefits the baby's ability to rotate and transfer its head to the ideal position during the initial stage of labor. Positional adjustments lessen the pressure of the baby's head on the posterior cervix (6 o'clock cervix) compared to mothers who simply lie down throughout stage I. This reduces the possibility of anterior cervical lips, which can impede and exacerbate the labor process (Mathew, Nayak, & K., 2012).

In the first stage of labor, posture and movement play a crucial role in supporting a natural birth (Mirzakhani, Karimi, Vatanchi, Zaidi, & Najmabadi, 2020). Maintaining good posture can increase pelvic room, which can facilitate the baby's easier delivery canal passage (Barrowclough, Kool, & Crowther, 2022). Walking or swaying are gentle motions that make the mother feel more at ease, less in pain, and less anxious (Huang, Zang, Ren, Li, & Lu, 2019). Standing or leaning are examples of vertical postures that use gravity to hasten the baby's descent into the lower pelvis (Kibuka, Price, Onakpoya, Tierney, & Clarke, 2021) This is consistent with Huang's, et al., (2019) research, which revealed that lateral and vertical orientations had a higher potential benefit in enhancing neonatal outcomes and resolving unique obstetric issues. Furthermore, movement eases back pain, opens the cervix, and induces contractions, all of which promote comfort and muscle relaxation during delivery.

Muscle relaxation is a popular tactic employed during the early stages of labor to relieve tension and assist in delivery (Wu, et al., 2022). Through a psychophysical method, where the mother concentrates on deep breathing and conscious relaxation exercises, mother can overcome intense contractions of her uterine and pelvic muscles with muscle relaxation (Koutras et al., 2021). In the opinion of Rosen, & Yogev, (2023) muscle relaxation helps reduce pain and facilitate the process of labor (Rosen & Yogev, 2023). The woman can more successfully open her cervix by using the Zelisken Ball as a tool to assist her in relaxing her pelvic muscles. The Zelisken Ball is a useful tool for providing effective support during the early stage of labor because it stimulates blood flow, relieves muscle tension, and stimulates and massages the Pelvic. The Zelisken Ball stimulates Pelvic rocking motion, which might enhance blood flow and possibly hasten the onset of labor.

The Zelisken Ball can facilitate pelvic rocking, which has an impact on the course of labor. Employing the Zelisken Ball to rock the pelvis helps laboring women accelerate the initial stage of labor. This has been corroborated by Arfah & Tridiyawati, (2022), who states that while pelvic rocking exercises can make expectant mothers feel anxious, they assist decrease the amount of disruption during pregnancy (Arfah & Tridiyawati, 2022). It is implemented to aid in the baby's head's ideal descent into the delivery canal by relaxing the hip region and the force of gravity. The shortest period of the Kala I active phase was observed by respondents who performed pelvic rocking with a Zelisken Ball as opposed to a Peanut Ball. There is a 1.29-hour difference between Zelisken Ball and Peanut Ball. The Zelisken Ball aids in the birth mothers' comfort and calmness during the labor phase. The energy and passion of the laboring women also significantly aided the mother's psychology in processing pain and fostering a favorable environment for the mother's uterus to contract as best it can. Pelvic rocking movements with the Zelisken Ball which is a Birth Ball performed by laboring mothers help mothers adapt to the pain and discomfort they experience (Batubara et al., 2019). In this manner, any woman in labor can have a comfortable labor experience that benefits both her and the unborn child. With the support of the application of best practices of normal labor care that is carried out optimally to prevent the occurrence of various complications so that labor can proceed physiologically, the idea that childbirth is an exhausting and painful experience can be replaced with an amazingly meaningful experience that every laboring mother should feel (Batubara et al., 2019), as a comprehensive service effort (Astuti, et al., 2009).

Future studies on Zelisken Ball's ability to expedite the initial stage of work should include a representative sample of respondents to increase sample coverage. It is essential to take into account confounding variables such as mother's age and socioeconomic status. Furthermore, a more thorough investigation of the psychological aspects affecting mothers has to be conducted. This is because the psychological aspect of maternal comfort was the only one examined by the researchers in this study. There should be a more thorough investigation into the Zelisken Ball's mechanism of action, along with a thorough clinical evaluation of variables including the length of the first stage of labor, the frequency of uterine contractions, and the heart rate of the fetus. To evaluate the long-term safety and efficacy of the Zelisken Ball, it is crucial to track the impact on mother and baby health following delivery. To improve knowledge, longitudinal and qualitative research methodologies are advised. Enhancing multidisciplinary cooperation amongst obstetricians, nurses, and statisticians is vital to guarantee sound research design and precise data analysis. In terms of mother and newborn health, this study should be able to add more to our knowledge of the Zelisken Ball's efficacy.

4. CONCLUSION

The Zelisken Ball significantly shortens the first stage of labor in pregnant women, resulting in a quicker delivery compared to the control group. The intervention group, utilizing the Zelisken Ball, showed a statistically significant reduction in the duration of the first stage of labor ($p = 0.000$, $p < 0.05$) with an average difference of 1.29 hours compared to the peanut ball users. These findings suggest the Zelisken Ball can be an alternative treatment to improve childbirth comfort and efficiency. Additionally, the majority of pregnant women expressed positive satisfaction with the Zelisken Ball, indicating its potential to enhance the birthing experience. However, the study's limited sample size calls for further research with a larger population. Future studies should explore additional variables affecting the Zelisken Ball's efficacy, including psychological factors, to broaden its application in childbirth assistance.

REFERENCES

Abalos, E., Chamillard, M., Díaz, V., Pasquale, J., & Souza, J. P. (2020). Progression of the

first stage of spontaneous labour. *Best Practice and Research: Clinical Obstetrics and Gynaecology*, *67*, 19–32. https://doi.org/10.1016/j.bpobgyn.2020.03.001

Agapoff, J. A., Chong, Z., Meek, M., & van Schalkwyk, G. I. (2023). Pharmacologic and non-pharmacologic interventions for emotional lability: A meta-analysis. *Neuroscience and Biobehavioral Reviews*, *149*(April), 105184. https://doi.org/10.1016/j.neubiorev.2023.105184

Ahmady, A., Ashriady, A., & Mariana, D. (2020). Analysis of prolonged labor and premature rupture of membranes risk factors on the occurrence of asfiksia in a new born babies in Mamuju district, 2017-2018. *Urban Health*, *2*(1).

Ahmadpour, P., Mohammad-Alizadeh-Charandabi, S., Doosti, R., & Mirghafourvand, M. (2021). Use of the peanut ball during labour: A systematic review and meta-analysis. *Nursing open*, *8*(5), 2345-2353. https://doi.org/10.1002/nop2.844

Ahmed, A. H., Mohmed, A. A., & Fathalla, N. F. (2022). Effect of Peanut Birth Ball on The Progress of Labor and Birth Outcome among Primigravidae. *Alexandria Scientific Nursing Journal*, *24*(4), 91-101. https://doi.org/10.21608/asalexu.2022.280357

Apriani, A., Herfanda, E., & Utami, F. S. (2020). *The Effectivity of Birth Ball Exercise on Labor: a Systematic Literature Review*. *24*(Uphec 2019), 189–194. https://doi.org/10.2991/ahsr.k.200311.037

Aprillia, Y. (2014). *Gentle Birth Balance : Persalinan Holistik mind, Body and Soul*. Bandung: Qanita.

Arfah, A., & Tridiyawati, F. (2022). The Effectiveness of Pelvic Rocking Exercises With Birthing Ball on Labor Progress in Maternal in 2022. *International Journal of Medicine and Health (IJMH)*, *1*(3), 22–30.

Astuti, P.A.S., Muliawan, P., Sawitri, A.A.S, & Septarini, N. W. (2009). Status Kesehatan Ibu Di Dusun Muntigunung, Karangasem, Bali, 2009: a Need for Comprehensive Approach. *Jurnal Ilmu Kesehatan Masyarakat*, 1(3), 188–193.

Barrowclough, J., Kool, B., & Crowther, C. A. (2022). Pregnant women's views on the acceptability, enablers, and barriers of participation in a randomized controlled trial of maternal posture for fetal malposition in labor. *European Journal of Midwifery*, *6*(January), 1–9. https://doi.org/10.18332/EJM/144057

Batubara, A., Mahayani, E., & Al Faiq Agma, A. (2019). Pengaruh pelaksanaan pelvic rocking dengan birth ball terhadap kemajuan persalinan pada ibu bersalin di klinik pratama tanjung deli tua tahun 2018. *COLOSTRUM: Jurnal Kebidanan*, *1*(1), 11-18.

Cohen, W. R., & Friedman, E. A. (2023). The second stage of labor. *American Journal of Obstetrics and Gynecology*, 1-11. https://doi.org/10.1016/j.ajog.2022.06.014

Dalbye, R., Blix, E., Frøslie, K. F., Zhang, J., Eggebø, T. M., Olsen, I. C., ... & Bernitz, S. (2020). The Labour Progression Study (LaPS): Duration of labour following Zhang's guideline and the WHO partograph–A cluster randomised trial. *Midwifery*, *81*, 102578. https://doi.org/10.1016/j.midw.2019.102578

Desyanti, H. H., & Widad, S. (2023). The Effect of Birth Ball Use on Labor Progress: A Literature Review. *Jurnal Health Sains*, *4*(2), 25–33. https://doi.org/10.46799/jhs.v4i2.828

Dewi, I. S., Anggraini, H., Dewi, T., Silaban, S., Kader, U., Palembang, B., … Weight, B. (2022). Relationship between Mal Presentation , Contractions and Baby Weight with Prolonged Parturition in the Teluk Lubuk Health Center Working Area in 2020. *Science Midwifery*, *10*(2), 574–579.

Eprila, E., Sari, N. P., Hidayati, N., & Meilati, N. D. (2021, May). Effectiveness of Using Peanut Ball on the Progress of 1st Stage of Chhild Birth in BPM Palembang City. In *Proceeding International Conference On Health, Social Sciences And Technology*, 1(1),4-6.

Etty, C. R., Damanik, E., & Gowasa, I. T. (2023). Midwifery Care for Mrs.S Aged 24 Years

With Prolonged First Stage Parturition. *Tour Health Journal*, *2*(2), 98–109.

Fitria, R., & Wahyuny, R. (2021). Efektivitas Pemberian Metode Birth Ball Terhadap Intensitas Nyeri Persalinan Kala I Fase Aktif Di Bpm Rokan Hulu. *Maternity and Neonatal*, *03*(03), 210–220.

Grenvik, J. M., Coleman, L. A., & Berghella, V. (2023). Birthing balls to decrease labor pain and peanut balls to decrease length of labor: what is the evidence? *American Journal of Obstetrics and Gynecology*, 228(5), s1270-s1273. https://doi.org/10.1016/j.ajog.2023.02.014

Grenvik, J. M., Rosenthal, E., Saccone, G., Corte, L. Della, Quist-Nelson, J., Gerkin, R. D., … Berghella, V. (2019). Peanut ball for decreasing length of labor: A systematic review and meta-analysis of randomized controlled trials. *European Journal of Obstetrics and Gynecology and Reproductive Biology*, 242, 159-165. https://doi.org/10.1016/j.ejogrb.2019.09.018

Hickey, L., & Savage, J. (2019). Effect of Peanut Ball and Position Changes in Women Laboring With an Epidural. *Nursing for Women's Health*, 23(3), 245-252. https://doi.org/10.1016/j.nwh.2019.04.004

Honaker, M. E. (2021). *The use of a peanut ball during labor in nulliparous term singleton vertex pregnancies to decrease the primary cesarean rate: An evidence-based practice ımprovement project*. The University of Tennessee Knoxville.

Huang, J., Zang, Y., Ren, L. H., Li, F. J., & Lu, H. (2019). A review and comparison of common maternal positions during the second-stage of labor. *International Journal of Nursing Sciences*, *6*(4), 460–467. https://doi.org/10.1016/j.ijnss.2019.06.007

Iryani, D., Pramestigiri, I. A. I., & F, H. R. (2022). Pengaruh Terapi Endorphine Massage Kombinasi Birthing Ball Terhadap Intensitas Nyeri Persalinan Kala I Fase Aktif Pada Ibu Bersalin. *Malahayati Nursing Journal*, *4*(7), 1874–1887. https://doi.org/10.33024/mnj.v4i7.6985

Jayasudha, A., Christy, D., Lakshmi, G. S., Priscilla, K., Anitha, P., & Priya, S. K. (2021). *Effectiveness of Peanut Ball On Outcome of First Stage of Labour Among Primi Mothers in Selected Tertiary Care Hospital , Coimbatore*. *4*(3), 73–75.

Jha, S., Vyas, H., Nebhinani, M., Singh, P., & T, D. (2023). The Effect of Birthing Ball Exercises on Labor Pain and Labor Outcome Among Primigraviade Parturient Mothers at a Tertiary Care Hospital. *Cureus*, *15*(3). https://doi.org/10.7759/cureus.36088

Kahrs, B. H., & Eggebø, T. M. (2021). Intrapartum ultrasound in women with prolonged first stage of labor. *American Journal of Obstetrics and Gynecology MFM*, *3*(6), 100427. https://doi.org/10.1016/j.ajogmf.2021.100427

Kamath, P., Pai, M., Shenoy, R., Karkada, S., D'souza, S., & Noronha, J. (2022). Effectiveness of a peanut ball device during labour on maternal and neonatal outcomes: Protocol for a randomised controlled trial. *F1000Research*, *11*, 1–16. https://doi.org/10.12688/f1000research.109537.2

Kementerian Kesehatan Republik Indonesia. (2022). *Profil Kesehatan Indonesia 2021*. Jakarta: Kementerian Kesehatan Republik Indonesia

Kibuka, M., Price, A., Onakpoya, I., Tierney, S., & Clarke, M. (2021). Evaluating the effects of maternal positions in childbirth: An overview of Cochrane Systematic Reviews. *European Journal of Midwifery*, *5*, 1–14. https://doi.org/10.18332/EJM/142781

Koutras, A., Fasoulakis, Z., Syllaios, A., Garmpis, N., Diakosavvas, M., Pagkalos, A., … Kontomanolis, E. N. (2021). Physiology and pathology of contractility of the myometrium. *In Vivo*, *35*(3), 1401–1408. https://doi.org/10.21873/invivo.12392

Mathew, A., Nayak, S., & K., V. (2012). a Comparative Study on Effect of Ambulation and Birthing Ball on Maternal and Newborn Outcome Among Primigravida Mothers in

Selected Hospitals in Mangalore. *Journal of Health and Allied Sciences NU*, *02*(02), 02–05. https://doi.org/10.1055/s-0040-1703561

Meliani, M., Amlah, A., & Rahmawati, E. (2022). Hubungan Antara Hypnobirthing, Yoga Dan Senam Hamil Terhadap Tingkat Kecemasan Ibu Hamil Trimester Iii Di Pmb Oktaris Kec Sumber Marga Telang. *Prepotif: Jurnal Kesehatan Masyarakat*, *6*(1), 607-613. https://doi.org/10.31004/prepotif.v6i1.3007

Mercier, R. J., & Kwan, M. (2018). Impact of peanut ball device on the duration of active labor: A randomized control trial. *American journal of perinatology*, *35*(10), 1006-1011. https://doi.org/10.1055/s-0038-1636531

Mirzakhani, K., Karimi, F. Z., Vatanchi, A. M., Zaidi, F. F., & Najmabadi, K. M. (2020). The Effect of Maternal Position on Maternal, Fetal and Neonatal Outcomes: A Systematic Review. *Journal of Midwifery and Reproductive Health*, *8*(1), 1988–2004. https://doi.org/10.22038/jmrh.2019.38133.1423

Morales-Alvarado, S., & Paredes-Pérez, N. (2023). Birthing balls to decrease labor pain and peanut balls to decrease length of labor: what is the evidence? *American Journal of Obstetrics and Gynecology*, . https://doi.org/10.1016/j.ajog.2023.10.021

Outland, L., & Alvarado, Y. (2019). Preventing cesareans with peanut ball use. *Journal of Nursing Education and Practice*, *10*(1), 107. https://doi.org/10.5430/jnep.v10n1p107

Rosen, H., & Yogev, Y. (2023). Assessment of uterine contractions in labor and delivery. *American Journal of Obstetrics and Gynecology*, *228*(5), S1209–S1221. https://doi.org/10.1016/j.ajog.2022.09.003

Rositawati, R. (2019). Hubungan Antara Paritas dengan Kejadian Partus Lama di RSUD Leuwiliang Kabupaten Bogor Tahun 2017. *Jurnal Ilmiah Kebidanan Indonesia*, *9*(01), 12-17. https://doi.org/10.33221/jiki.v9i01.199

Rukmaini, Oktaviani, F., & Suciawati, A. (2023). Effect of Birthing Balls on the Length of First Stage Labor among Primigravidas at the Barokah Main Clinic Bandung City in 2021. *International Health Sciences Journal*, *1*(1), 10–19. https://doi.org/10.61777/ihsj.v1i1.8

Salvator, M., Girault, A., Sibiude, J., Mandelbrot, L., Goffinet, F., & Cohen, E. (2023). Failed induction of labor in term nulliparous women with an unfavorable cervix: Comparison of cervical ripening by two forms of vaginal prostaglandins (slow-release pessary and vaginal gel). *Journal of Gynecology Obstetrics and Human Reproduction*, *52*(4). https://doi.org/10.1016/j.jogoh.2023.102546

Sheishaa, D. M. R., El-Mashad, H. A. M., & Khedr, N. F. H. (2019). Effect of Birthing Ball Exercises during Pregnancy on the First Stage Progress of Labor. *International Journal of Nursing*, *7*(2), 47–67. https://doi.org/10.15640/ijn.v6n2a6

Solihah, R., Nurherliyany, M., Sandriani, S., & Putri, N. I. (2023). The Effect of Gym Ball on Reducing Low Back Pain, Labor Pain, and Progress in Primigravida Labor. *Nurul Ilmi : Journal of Health Sciences and Midwifery*, *1*(1), 30–36. https://doi.org/10.52221/nuri.v1i1.206

Sørbye, I. K., Gaudernack, L. C., Einarsen, A., Rosseland, L. A., Lukasse, M., Gunnes, N., & Michelsen, T. M. (2022). Study protocol for the BUSCopan in LABor (BUSCLAB) study: A randomized placebocontrolled trial investigating the effect of butylscopolamine bromide to prevent prolonged labor. *PLoS ONE*, *17*(11 November), 1–13. https://doi.org/10.1371/journal.pone.0276613

Stulz, V., Dashputre, A., & Reilly, H. (2023). Midwives' experiences using a peanut ball for women during labour: A qualitative study. *Midwifery*, *125*(February), 103797. https://doi.org/10.1016/j.midw.2023.103797

Subagio, S. U. (2022). Efektivitas Birth Ball Untuk Mengurangi Nyeri Persalinan Pada Ibu Bersalin Ny.Y Kala I Fase Aktif Di Klinik Mahabbah Prima Medika Kota Serang.

Journal of Midwifery, *10*(1), 65–70. https://doi.org/10.37676/jm.v10i1.2321

Sugiyono. (2019a). *Statistik untuk Penelitian*. Bandung: CV. Alfabeta.

Sugiyono. (2019b). *Metode Penelitian Kuantitatif, Kualitatif, dan R&D*. Bandung: CV. Alfabeta.

Sulistyorini, D., & Rofingah, W. (2021). Nyeri dan Lama Persalinan Kala I di Puskesmas Banjarnegara 1 Kabupaten Banjarnegara. *Medsains*, *7*(01), 51–56.

Sundaram, M., Bhuvaneswari, G., & Chandrika, A. (2022). Birthing ball technique and Sacral Massage on Maternal and fetal wellbeing: An Experimental-Pilot report. *Cardiometry*, (23), 173–178. https://doi.org/10.18137/cardiometry.2022.23.173178

Suryani, L., & Mufida Dian Hardika. (2022). Efektifitas Terapi Birthing Ball Terhadap Lama Kala I Dan Intensitas Nyeri Persalinan Pada Ibu Bersalin Primigravida Di Praktik Mandiri Bidan Mufida Dian Hardika Kabupaten Madiun. *Prima Wiyata Health*, *III*(1), 20–29.

Tahar, N., Sakti Parenta, E. D., Febriyanti, A. P., Rusdi, M., & Al Kautsar, A. M. (2021). Evaluasi Tepat Penggunaan Obat Lini Pertama dan Lini Kedua Antihipertensi pada Pasien Preeklampsia: A Literatur Review. *Jurnal Midwifery*, *3*(2), 52–68. https://doi.org/10.24252/jmw.v3i2.24341

Telova, Y. (2022). The Effect Of Counterpressure Birth Ball On The Reduction Of Labor Pain In Bpm Maiharti Kisaran Barat In 2022. *Jurnal Kebidanan Kestra (JKK)*, *5*(1), 161–165. https://doi.org/10.35451/jkk.v5i1.1342

Wu, N., Huang, R., Shan, S., Li, Y., & Jiang, H. (2022). Effect of the labour roadmap on anxiety, labour pain, sense of control, and gestational outcomes in primiparas. *Complementary therapies in clinical practice*, *46*, 101545. https://doi.org/10.1016/j.ctcp.2022.101545

Young, A., Shipe, M., & Smith, M. (2021). Non-Pharmacological Pain Managment in Labor : A Systematic Review. *Williams Honors College, Honors Research Projects*.

Pertasari, R. M. Y. (2022). Efektifitas Birth Ball terhadap Kemajuan Persalinan pada Ibu Bersalin di Klinik Permata Bunda Kota Serang. *Journal of Midwifery*, *10*(1), 77-82. https://doi.org/10.37676/jm.v10i1.2323

Zuarez-Easton, S., Erez, O., Zafran, N., Carmeli, J., Garmi, G., & Salim, R. (2023). Pharmacologic and nonpharmacologic options for pain relief during labor: an expert review. *American Journal of Obstetrics and Gynecology*, *228*(5), S1246–S1259. https://doi.org/10.1016/j.ajog.2023.03.003

WHO, UNICEF, UNFPA, World Bank Group & UNDESA/Population Division. (2023). *Trends in maternal mortality 2000 to 2020*. World Health Organization.

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 749-757
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1382*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Neutrophil-lymphocyte Ratio and Platelet-lymphocyte Ratio as Early Sign Plasma Leakage Process in Dengue Infection

Aisya Nailatul Ashma[1a], Satrio Budi Susilo[2b], Sri Marwanta[3c], Dhani Redhono Harioputro[4d*]

[1] Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Central Java, Indonesia
[2] Department of Internal Medicine, Universitas Sebelas Maret, Moewardi Hospital, Surakarta, Central Java, Indonesia
[3] Division of Hematology and Medical Oncology, Department of Internal Medicine, Universitas Sebelas Maret, Moewardi Hospital, Surakarta, Central Java, Indonesia
[4] Division of Tropical Infection Disease, Department of Internal Medicine, Universitas Sebelas Maret, Moewardi Hospital, Surakarta, Central Java, Indonesia

[a] Email address: aisyaashma08@gmail.com
[b] Email address: robertsatriyo@gmail.com
[c] Email address: drdrmarwantasppdmkes@staff.uns.ac.id
[d] Email address: dhani_redhono@staff.uns.ac.id

Received: 11 October 2023 Revised: 21 December 2023 Accepted: 27 December 2023

Abstract
Dengue hemorrhagic fever remains a global health concern, especially in tropical and subtropical regions, such as Indonesia. Plasma leakage is the main symptom of Dengue infection which be seen through a hemoconcentration. NLR and PLR are cost-effective and easily measurable indexes that help to predict signs of infection. This study aims to analyze the correlation of NLR and PLR as early sign on hemoconcentration in Dengue infection. This study was an analytical observational method with a cross-sectional design. The study was conducted at the inpatient infectious disease wards of Dr. Moewardi General Hospital and Sebelas Maret University Hospital. The data was statistically analyzed using bivariate and multivariate analysis. There were seventy subject which of male was more than female. The result of bivariate analysis showed a statistically significant correlation for NLR (p = 0,008; r = 0,314) and non-significant for PLR (p = 0,150; r = 0,174). Both NLR and PLR were positively correlated with hemoconcentration. The effect of NLR on hemoconcentration was significant. There was a positive correlation significant between NLR and hemoconcentration in Dengue infection.

Keywords: DHF, Plasma Leakage, Hemoconcentration, NLR, PLR.

Corresponding Author:

Dhani Redhono Harioputro
Division of Tropical Infection Disease, Department of Internal Medicine, Universitas Sebelas Maret, Moewardi Hospital, Surakarta, Central Java, Indonesia
Email: dhani_redhono@staff.uns.ac.id

1. INTRODUCTION

Dengue hemorrhagic fever (DHF) is a disease caused by the dengue virus and carried by *Aedes aegypti* mosquitoes to transmit to human (Schaefer et al., 2022). This disease is still a global health problem, especially in tropical and subtropical regions with varying risks influenced by climate, social, and environmental parameters (Wu et al., 2022). Indonesia as one of the dengue-endemic tropical countries has a fluctuating number of cases and the distribution of its territory is expanding annually (Kementerian Kesehatan Republik Indonesia, 2017).

The spectrum of clinical manifestations of dengue infection progresses to undifferentiated fever, DF, DHF, and DSS (WHO, 2022). The main symptom distinguishing DHF from DF is plasma leakage during the critical phase (Kularatne & Dalugama, 2022; Wang et al., 2020). Dengue virus infection develops through three phases of the disease course, namely fever, critical, and recovery (WHO, 2022). The febrile phase occurs for three to seven days after infection with symptoms of high fever, generally accompanied by body aches and headaches (Kularatne & Dalugama, 2022). Patients may also experience hemorrhagic symptoms, such as a positive tourniquet test to spontaneous bleeding (Muller et al., 2017). At the end of the febrile phase, patients tend to develop hypovolemic shock due to plasma leakage (Wang et al., 2020).

Plasma leakage can be seen from a ≥20% increase in hematocrit or the discovery of ascites fluid or pleural effusion on ultrasound examination or thoracic imaging (Halstead, 2019; Pizarro-torres, 2016). Visualization by ultrasound is very sensitive and specific, but not always available especially in hospitals with limited resources (Suwarto et al., 2016). Plasma leakage can be seen from a 20% increase in hematocrit or hemoconcentration obtained from inexpensive examinations, but establishing baseline values is difficult to do in patients who arrive late (Rodrigo et al., 2021). In addition, in clinical practice, doctors often detect pleural effusion and/or ascites in patients with an increased hematocrit value of less than 20% (Suwarto et al., 2016). The use of uniform hematocrit limit values at all ages and genders, without standardization of *cutoff values* can have an adverse impact on DHF management (Anagha *et al.*, 2018). The other assessments are needed to predict plasma leakage so that it can help clinicians in making informed decisions.

The signs of infection can be seen through neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) values as cost-effective and easily measurable biomarkers (Yang et al., 2020). NLR values present the immune response and prognosis of disease progression (Zahorec, 2021). PLR values present inflammatory status, activation of platelets, and aggregation of platelets (Uzun et al., 2017). PLR values have also been shown to be a better parameter than platelets or lymphocytes for predicting the development of systemic inflammation (Gasparyan et al., 2019). In the case of DHF, the NLR value has a significant correlated with the severity seen from the incidence of shock and bleeding manifestations (Koundinya et al., 2021). However, the clinical value of PLR is still rarely considered. Meanwhile, there have been no studies focused on either of them as a prognostic marker for patient's clinical conditions specifically. Based on this background, researchers will analyze the effect of NLR and PLR values on hemoconcentration in Dengue infection.

This study aimed to analized the correlation of NLR and PLR values and hemoconcentration in DHF.

2. RESEARCH METHOD

This study was an observational analytic method with a cross-sectional design approach. The study was conducted in two location of the inpatient infection ward at Dr. Moewardi General Hospital and UNS Hospital with the research subjects, were adult DHF patients from

January 2022 to December 2022. Subjects were selected by simple random sampling based on inclusion criteria, were aged 18-60 years, had positive results on Ig M dengue serology examination, and fulfilled WHO criteria (trombocytopenia <100.000 cells/mm^3; Hct rise ≥20%) and exclusion criteria were suffering from other infectious diseases, such as typhoid fever, pulmonary TB, and pneumonia, having a history of hematological diseases such as ITP and aplastic anemia, and forced discharge before they can be evaluated.

The research subjects were calculated using a single sample formula for the correlation test. The results of these calculations showed that the minimum number of subjects was 51 subjects. Subjects were added by 10% to avoid the possibility of subject dropout (incomplete data). Therefore, the minimum subjects required in this research are 55 subjects.

The independent variables were NLR, PLR. The Confounding variables were age and gender. The dependent variable was hemoconcentration. NLR was the result of dividing the number of neutrophils and lymphocytes (Liu et al., 2019). PLR was the result of dividing the number of platelets and lymphocytes (Kwon et al., 2012). Hemoconcentration was a hematocrit increase of 20% from the baseline hematocrit value (Srikiatkhachorn, 2017). The research data was taken through laboratory examination results in medical records.

The analysis data used SPSS statistic 23 for Windows. The data were analyzed descriptively to obtain the characteristics of the study subjects, followed by bivariate analysis with the Spearman rho test and multivariate with the linear regression with a stepwise method. The ethical review in this study was in accordance with letter number 648/IV/HREC/2023 issued by Dr. Moewardi General Hospital.

3. RESULTS AND DISCUSSION

The population of subjects was adult patients aged 18-60 years with a diagnosis of DHF. The study subjects were taken from populations that had met the inclusion and exclusion criteria and were determined using simple random sampling techniques.

Table 1. Frequency of Characteristic Data.

Variable	Frequency (n)	Percentage (%)
Sex		
Male	36	51,4
Female	34	48,6
Hemoconcentration		
↑ **Hct ≥ 20%**	22	31,4
↑ **Hct < 20%**	48	68,6
Day-fever		
< 3 day	8	11,4
≥ 3-7 day	58	82,9
>7 day	4	5,7
Hematological characteristics		
Leukopenia	47	67,1
Thrombocytopenia	63	90,0
Anemia	7	10,0

The result was obtained from 70 research subjects of DHF patients (Table 1). As many as 51,4% of the subjects were male and 48,6% were female. Among them, as many as 31,4% of subjects were DHF patients who experienced plasma leakage during hospitalization which could be characterized by a ≥20% increase in hematocrit. Based on the onset of fever when coming to the hospital, the highest number was obtained, namely 82,9% of patients who came during fever day 3 to day 7. Based on hematological characteristics, 67,1% of subjects had leukopenia, 90% of subjects had thrombocytopenia, and 10% of subjects had anemia.

Table 2. The Descriptive of Characteristics Data.

Variable	Median (Range)
Age	25,50 (18-58)
Length of Stay	5 (2-9)
NLR	2,43 (0,31-9,52)
PLR	94,89 (13,16-592,06)
Hemoconcentration	13,33 (2,27-48,00)

The characteristics of data descriptively (Table 2) found that the median age of subjects were 25,5 years, length of hospitalization 5 days, NLR 2,43, PLR 94,89, and hemoconcentration 13,33%. The hemoconcentration values of subjects were between a minimum value of 2,27% and a maximum of 48%.

Table 3. The Results of Normality Test.

Variable	df	p-value
NLR	70	0,001
PLR	70	0,000
Hemoconcentration	70	0,009

The normality test is carried out to determine the distribution of each variable whether normal or not and as a determinant of data processing techniques (parametric tests or non-parametric tests). The normality test in this study used the Kolmogorov-Smirnov Normality Test because the sample size obtained exceeded 50. The variable is showed to be normally distributed if p>0,05. Based on the normality test on SPSS 23.0, data variables of this study were not normally distributed.

Table 4. The Results of Bivariate Analysis.

Variable	r	p
NLR and Hemoconcentration	0,314	0,008
PLR and Hemoconcentration	0,174	0,150

Data researchers were not normally distributed, so the analysis bivariate used the Spearman Correlation Test. There was a significant relationship between NLR and hemoconcentration in DHF patients because the p-value was <0,05. PLR value had a p>0,05 value so there was no significant relationship to hemoconcentration. The correlation value of each variable was NLR (r = 0,314), and PLR (r = 0,174). NLR and PLR values were positively correlated to hemoconcentration. This means that the higher of NLR and PLR values, so the higher of hemoconcentration value in dengue infection.

Table 5. The Results of Multivariate Analysis.

Variable	B	P
NLR	1,782	0,001
PLR	-0,133	0,295

The results of linear regression with a stepwise method (Table 5) showed that the independent variable had a significant effect individually on the dependent variable is NLR

with p = 0,001 (p < 0,05). The PLR variable did not have a significant effect on hemoconcentration. The magnitude of the influence can be seen from the R-value of NLR that was 0,385. From this output, a coefficient of determination (R-square) of 0,149 is also obtained which means that the effect of the NLR value on hemoconcentration was 14,9% with a multivariate equation, namely: Y = 9,412 + 1,782X.

DISCUSSION

Plasma leakage is the main clinical sign of DHF which can be seen from an increase in hematocrit level ≥ 20% from the baseline value, also known as hemoconcentration condition (Kularatne & Dalugama, 2022). This study was known that as many as 22 (31,4%) subjects experienced DHF (with increased hematocrit ≥ 20%), while 48 (68,6%) subjects did not experience hemoconcentration during the critical phase. This percentage is not much different from previous studies. It was stated that 37 out of 75 subjects (49%) experienced an increase in hematocrit ≥ 20% at Dr. Soetomo Regional General Hospital. The study was a retrospective study using medical records (Rizaliansyah et al., 2017). Plasma leakage and bleeding are associated with dengue prognosis and mortality. This results from disease pathogenesis through cytokine storms and antibody responses in vascular endothelial cells and hemostatic abnormalities after DENV infection (Talukdar et al., 2021)**.** The hematological parameters of *dengue virus* infection fluctuate during febrile days, particularly on days 3 to 8. It starts with progressive leukopenia followed by thrombocytopenia and hemoconcentration due to plasma leakage (Chaloemwong et al., 2018). The hematological characteristics in this study were 67,1% of subjects had leukopenia, 90% of subjects had thrombocytopenia, and 10% of subjects had anemia.

The Correlation between NLR and hemoconcentration in DHF. The amount of NLR value is influenced by the number of neutrophils and lymphocytes. At the beginning of infection, there is an increase in the percentage of neutrophils so that the NLR value becomes higher. Then, during the acute to critical febrile phase, there will be an increase in lymphocytes due to reactive lymphocytosis and reversal of NLR values. It occurs on fever days 6 to 9 (Chaloemwong et al., 2018). Viral infection induces lymphocyte activation and antibody secretion. The immune defenses against infection depend on T cells than on antibodies. The cytotoxic T cells play an important role in the clearance of virus-infected cells. The cell will secrete several cytokines, such as IFN-γ and TNF. The lymphocytosis causes a decrease in NLR value (Zhu et al., 2013). TNF-α cytokines will induce cell apoptosis, increase vascular permeability, and eventually cause bleeding. Elevated level of TNF-α is associated with increased vascular permeability in dengue infection patients (Jeewandara et al., 2015).

In this study, the median NLR value was 2,43 (0,31-9,52). According to Zahorec (2021), normal NLR values are in the range of 1-2. NLR values of >3 and <0,7 in adults is pathological. NLR values that are in the gray zone between 2,3-3,0 can serve as an early warning of pathological states such as cancer, atherosclerosis, infections, inflammation, psychiatric disorders, and stress (Zahorec, 2021). In COVID-19, high NLR values at hospital admission are associated with the risk of death. NLR values >3 were not survived (Widjaya et al., 2023).

Based on the result of spearman rank test, it was stated that there is correlation significant between NLR (p=0,008) and hemoconcentration in DHF with a positive correlation and a weak correlation level (r = 0,314). In the multivariate analysis, there are significant effect of 14,9%. These results are different from the previous study. The decrease in NLR is significantly related to the severity of DHF, seen from the manifestations of bleeding and shock. This study used hematology data on the 6th fever day and Chi-square Test (Koundinya et al., 2021). A result mismatch occurs due to a difference in NLR data retrieval time. NLR is taken at the beginning of hospital admission with varying fever onset. The onset of fever is most likely to enter the hospital on the 3rd to – 7th day.

The Correlation between PLR and Hemoconcentration in DHF. The decrease of platelet values is due to various mechanisms that occur during viral infections. Generally, the decrease is caused by bone marrow suppression, platelet destruction, and platelet dysfunction (Tasya, Rahmayanti & Fitriangga, 2022). Plasma leakage that marks dengue events is thought to be related to platelet activation, release of inflammatory mediators, and endothelial cells infected with virus (Nascimento et al., 2014; Tasya, Rahmayanti & Fitriangga, 2022). T lymphocytes are the main immune cells active during DHF. $CD8^+$ T cells secrete cytokines that alter endothelial cells and cause plasma leakage resulting in DHF and DSS (Bhatt et al., 2021). An increase in lymphocytes associated with a decrease in platelet count can lead to increased bleeding complications in DHF patients (Clarice et al., 2019). The decrease in platelets occurs from the 3rd to the 10th day (the lowest on the 6th day), while the increase in lymphocytes can be found on the 5th to 9th day (the highest on the 7th day) (Chaloemwong et al., 2018).

In this study, the median PLR value was 94,89 (13,16-592,06). Normal PLR in men is in the range of 36,63-149,13 and women 43,36-172,68 (Wu et al., 2019). DHF patients have low PLR values due to a decrease in platelet count. Platelets infected with dengue virus experience mitochondrial dysfunction that causes cell death. The lowest average PLR score, which was 78,1±44,2 (Rini et al., 2020). This study found no significant relationship between PLR values and hemoconcentration in DHF patients (p=0,150). The previous study have shown that there is no statistically significant relationship between PLR and dengue infection at Syarif Muhamad Alkadrie Hospital. The study used a cross-sectional approach with secondary data in the form of medical records and analyzed with a chi-square test. Hematology data was taken on the third day of fever, where it is still unable to predict the incidence of plasma leakage in dengue cases. (Tasya, Rahmayanti & Fitriangga, 2022). The insignificance in PLR results is thought to be due to data collection time where in this study, the onset of fever in hospital admission varies and is mostly from the third day to the seventh day. On that day, platelets and lymphocytes just begin to change.

There are still a few of study that discuss the relationship between PLR and DHF severity. The PLR value can be utilized for monitoring disease and treatment response which is not only evaluated at one point in time, but can be also utilized by monitoring within a period (Meng et al., 2016). A drastic increase in PLR in COVID-19 can indicate the severity of inflammation. The greater the change in PLR, the more severe the cytokine storm occurs and the worse the patient's prognosis (Qu et al., 2020).

4. CONCLUSION

There was a significant correlation between NLR value and hemoconcentration in DHF patients, with a positive correlation which means that increased value of NLR, so increased level of hemoconcentration. There is no significant correlation between PLR values and hemoconcentration in Dengue infection, with a positive correlation which means that increased value of PLR, so increased level of hemoconcentration. With the research, It is hoped that NLR can be used as an early detection of plasma leakage in dengue infection.

REFERENCES

Anagha A Joshi, Divyashree, B. N., & Gayathri, B. R. (2018). Hematocrit Spectrum in Dengue : A Prospective Study. International Journal of Scientific Study, 5(10), 33–37. https://doi.org/10.17354/ijss/2018/8

Bhatt, P., Sabeena, S. P., Varma, M., & Arunkumar, G. (2021). Current Understanding of the Pathogenesis of Dengue Virus Infection. Current Microbiology, 78(1), 17–32. https://doi.org/10.1007/s00284-020-02284-w

Chaloemwong, J., Tantiworawit, A., Rattanathammethee, T., Hantrakool, S., Chai-Adisaksopha, C., Rattarittamrong, E., & Norasetthada, L. (2018). Useful Clinical Features and Hematological Parameters for the Diagnosis of Dengue Infection in Patients with Acute Febrile Illness: A Retrospective Study. BMC Hematology, 18(1), 1–10. https://doi.org/10.1186/s12878-018-0116-1

Clarice, C. S. H., Abeysuriya, V., de Mel, S., Uvindu Thilakawardana, B., de Mel, P., de Mel, C., Chandrasena, L., Seneviratne, S. L., Yip, C., & Yap, E. S. (2019). Atypical Lymphocyte Count Correlates with the Severity of Dengue Infection. PloS One, 14(5), e0215061. https://doi.org/10.1371/journal.pone.0215061

Gasparyan, A. Y., Ayvazyan, L., Mukanova, U., Yessirkepov, M., & Kitas, G. D. (2019). The Platelet-to-Lymphocyte Ratio as an Inflammatory Marker in Rheumatic Diseases. Annals of Laboratory Medicine, 39(4), 345–357. https://doi.org/10.3343/alm.2019.39.4.345

Halstead, S. (2019). Recent Advances in Understanding Dengue. F1000Research, 8. https://doi.org/10.12688/f1000research.19197.1

Jeewandara, C., Gomes, L., Wickramasinghe, N., Gutowska-Owsiak, D., Waithe, D., Paranavitane, S. A., Shyamali, N. L. A., Ogg, G. S., & Malavige, G. N. (2015). Platelet Activating Factor Contributes to Vascular Leak in Acute Dengue Infection. PLoS Neglected Tropical Diseases, 9(2), e0003459. https://doi.org/10.1371/journal.pntd.0003459

Kementerian Kesehatan Republik Indonesia. (2017). Pedoman Pencegahan Dan Pengendalian Demam Berdarah Dengue Di Indonesia. Jakarta: Kementerian Kesehatan Republik Indonesia.

Koundinya, M. A., Dasari, D., Ashok, S., & Manjula, B. S. V. (2021). Neutrophil To Lymphocyte Ratio As Prognostic And Predictor Factor For Severity Of Dengue Fever - A Retrospective Observational Study In A Tertiary Care Centre. 8(12), 46–52.

Kularatne, S. A., & Dalugama, C. (2022). Dengue Infection: Global Importance, Immunopathology and Management. Clinical Medicine (London, England), 22(1), 9–13. https://doi.org/10.7861/clinmed.2021-0791

Kwon, H.-C., Kim, S. H., Oh, S. Y., Lee, S., Lee, J. H., Choi, H.-J., Park, K.-J., Roh, M. S., Kim, S.-G., Kim, H.-J., & Lee, J. H. (2012). Clinical Significance of Preoperative Neutrophil-Lymphocyte versus Platelet-Lymphocyte Ratio in Patients with Operable Colorectal Cancer. Biomarkers : Biochemical Indicators of Exposure, Response, and Susceptibility to Chemicals, 17(3), 216–222. https://doi.org/10.3109/1354750X.2012.656705

Liu, C.-C., Ko, H.-J., Liu, W.-S., Hung, C.-L., Hu, K.-C., Yu, L.-Y., & Shih, S.-C. (2019). Neutrophil-to-Lymphocyte Ratio as a Predictive Marker of Metabolic Syndrome. Medicine, 98(43), e17537. https://doi.org/10.1097/MD.0000000000017537

Meng, X., Wei, G., Chang, Q., Peng, R., Shi, G., Zheng, P., He, F., Wang, W., & Ming, L. (2016). The Platelet-to-Lymphocyte Ratio, Superior to the Neutrophil-to-Lymphocyte Ratio, Correlates with Hepatitis C Virus Infection. International Journal of Infectious Diseases, 45, 72–77. https://doi.org/10.1016/j.ijid.2016.02.025

Muller, D. A., Depelsenaire, A. C. I., & Young, P. R. (2017). Clinical and Laboratory Diagnosis of Dengue Virus Infection. Journal of Infectious Diseases, 215(Suppl 2), S89–S95. https://doi.org/10.1093/infdis/jiw649

Nascimento, E. J. M., Hottz, E. D., Garcia-Bates, T. M., Bozza, F., Marques, E. T. A. J., & Barratt-Boyes, S. M. (2014). Emerging Concepts in Dengue Pathogenesis: Interplay between Plasmablasts, Platelets, and Complement in Triggering Vasculopathy. Critical Reviews in Immunology, 34(3), 227–240. https://doi.org/10.1615/critrevimmunol.2014010212

Pizarro-torres, D. (2016). Dengue With Severe Plasma Leakage: A New Monitoring Approach. Acta Médica Costarricense, 58(3), 115–121. https://www.scielo.sa.cr/scielo.php?script=sci_arttext&pid=S0001-60022016000300115

Qu, R., Ling, Y., Zhang, Y.-H.-Z., Wei, L.-Y., Chen, X., Li, X.-M., Liu, X.-Y., Liu, H.-M., Guo, Z., Ren, H., & Wang, Q. (2020). Platelet-to-Lymphocyte Ratio Is Associated with Prognosis in Patients with Coronavirus Disease-19. Journal of Medical Virology, 92(9), 1533–1541. https://doi.org/10.1002/jmv.25767

Rini, T. Y., Abadi, S., Katu, S., Bakri, S., Rasyid, H., Kasim, H., Fachruddin, A., Halim, R., & Seweng, A. (2020). Association of Bacterial/Viral Infections Withneutrophil-Lymphocyte Ratio, Monocyte-Lymphocyte Ratio, and Platelet-Lymphocyte Ratio in Patients Presenting with Fever. European Journal of Molecular & Clinical Medicine, 7(3), 1500–1509.

Rizaliansyah, F., Aryati, A., & Rusli, M. (2017). Plasma Leakage Profiles Of Dengue Hemorrhagic Fever Patients in RS Surabaya, East Java, Indonesia January-June 2014. Indonesian Journal of Tropical and Infectious Disease, 6(4), 92. https://doi.org/10.20473/ijtid.v6i4.3456

Rodrigo, C., Sigera, C., Fernando, D., & Rajapakse, S. (2021). Plasma Leakage in Dengue: A Systematic Review of Prospective Observational Studies. BMC Infectious Diseases, 21(1), 1082. https://doi.org/10.1186/s12879-021-06793-2

Schaefer, T. J., Panda, P. K., & Wolford, R. W. (2022). Dengue Fever. Treasure Island (FL): StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK430732/

Srikiatkhachorn, A. (2017). Plasma Leakage in Dengue Hemorrhagic Fever. Physiology & Behavior, 176(5), 139–148. https://doi.org/10.1160/TH09-03-0208

Suwarto, S., Nainggolan, L., Sinto, R., Effendi, B., Ibrahim, E., Suryamin, M., & Sasmono, R. T. (2016). Dengue Score: A Proposed Diagnostic Predictor for Pleural Effusion and/or Ascites in Adults with Dengue Infection. BMC Infectious Diseases, 16, 322. https://doi.org/10.1186/s12879-016-1671-3

Talukdar, S., Thanachartwet, V., Desakorn, V., Chamnanchanunt, S., Sahassananda, D., Vangveeravong, M., Kalayanarooj, S., & Wattanathum, A. (2021). Predictors of Plasma Leakage among Dengue Patients in Thailand: A Plasma-Leak Score Analysis. PloS One, 16(7), e0255358. https://doi.org/10.1371/journal.pone.0255358

Tasya, T, Rahmayanti, S., & Fitriangga, A. (2022). Hubungan Infeksi Dengue Dengan Rasio Trombosit dan Limfosit Pada Pasien Anak Di RSUD Sultan Syarif Mohamad Alkadrie Tahun 2019. *Majalah Kedokteran Andalas*, *45*(1), 1-9.

Uzun, F., Erturk, M., Cakmak, H. A., Kalkan, A. K., Akturk, I. F., Yalcin, A. A., Uygur, B., Bulut, U., & Oz, K. (2017). Usefulness of the Platelet-to-Lymphocyte Ratio in Predicting Long-Term Cardiovascular Mortality in Patients with Peripheral Arterial Occlusive Disease. Postepy w Kardiologii Interwencyjnej, 13(1), 32–38. https://doi.org/10.5114/aic.2017.66184

Wang, H., Urbina, N., Chang, M. R., Assavalapsakul, W., Lu, P. L., Chen, Y. H., & Wang, S. F. (2020). Dengue Hemorrhagic Fever – A Systemic Literature Review of Current Perspectives on Pathogenesis, Prevention and Control. Journal of Microbiology, Immunology and Infection, 53(6), 963–978. https://doi.org/10.1016/j.jmii.2020.03.007

WHO. (2022). Dengue and Severe Dengue. WHO. Retrieved from https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue

Widjaya, K., Harioputro, D. R., Agus Jati Sunggoro, & Arifin. (2023). Albumin Levels, Mean Platelet Volume, and Neutrophil Lymphocyte Ratio as Predictors of COVID-19

Outcomes. GSC Biological and Pharmaceutical Sciences, 23(1), 096–104. https://doi.org/10.30574/gscbps.2023.22.1.0493

Wu, L., Zou, S., Wang, C., Tan, X., & Yu, M. (2019). Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratio in Chinese Han Population from Chaoshan Region in South China. BMC Cardiovascular Disorders, 19(1), 125. https://doi.org/10.1186/s12872-019-1110-7

Wu, T., Wu, Z., & Li, Y.-P. (2022). Dengue Fever and Dengue Virus in the People's Republic of China. Reviews in Medical Virology, 32(1), e2245. https://doi.org/10.1002/rmv.2245

Yang, A.-P., Liu, J.-P., Tao, W.-Q., & Li, H.-M. (2020). The Diagnostic and Predictive Role of NLR, d-NLR and PLR in COVID-19 Patients. International Immunopharmacology, 84, 106504. https://doi.org/10.1016/j.intimp.2020.106504

Zahorec, R. (2021). Neutrophil-to-Lymphocyte Ratio, Past, Present and Future Perspectives. Bratislavske Lekarske Listy, 122(7), 474–488. https://doi.org/10.4149/BLL_2021_078

Zhu, Y., Cao, X., Tao, G., Xie, W., Hu, Z., & Xu, D. (2013). The Lymph Index: A Potential Hematological Parameter for Viral Infection. International Journal of Infectious Diseases : IJID : Official Publication of the International Society for Infectious Diseases, 17(7), e490-3. https://doi.org/10.1016/j.ijid.2012.12.002

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 758-771
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1332*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Comparison of Macronutrient and Micronutrient Adequacy Among Pregnant Women in Urban and Rural Areas

Bestfy Anitasari[1a*], Irmayanti A. Oka[2b]

[1] Department of Nursing, Institut Kesehatan dan Bisnis Kurnia Jaya Persada, Palopo, South Sulawesi, Indonesia
[2] Department of Midwifery, Institut Kesehatan dan Bisnis Kurnia Jaya Persada, Palopo, South Sulawesi, Indonesia

[a] Email address: hbalquis@gmail.com
[b] Email address: irmayantiaoka89@gmail.com

Received: 6 September 2023 Revised: 31 December 2023 Accepted: 31 December 2023

Abstract

Adequate macronutrients and micronutrients during pregnancy can support optimal fetal growth and development in addition to meeting the needs of the mother to ensure a healthy pregnancy. The region of residence is one of the factors that contribute to determining how nutrition is fulfilled in groups of pregnant women. This study aims to compare the adequacy of macronutrients and micronutrients between pregnant women in urban and rural areas. This study involved 50 pregnant women, 25 in urban areas and 25 in rural areas. Nutritional information was obtained using a food recall questionnaire that was assessed for 3 days, namely on 2 working days (not consecutive) and 1 day off and also using a food frequency questioner (FFQ). Data was analyzed using Chi Square and Results showed a difference in carbohydrate (p=0.049) and protein (p=0.045) consumption between urban and rural pregnant women, while energy (p=0.053) and fat (p=0.056) showed no difference in adequacy. For micronutrients, Vitamin A (p=0.043) and B12 (p=0.042) consumption showed differences between urban and rural pregnant women, while for vitamin C (p=0.065), vitamin B1 (p=0.078), vitamin B2 (p=0.084), B3 (p=0.056), B6 (p=0.075), E (p=0.088), Iron (p=0.052), Folic acid (p=0.067), Calcium (p=0.054), Phosphorus (p=0.055), fiber (p=0.079), showed no difference in consumption between urban and rural pregnant women. The consumption of micronutrients and macronutrients of pregnant women in rural and urban areas showed less intake than recommended. Nutrition education needs to be improved not only focusing on pregnant women but also on adolescent groups, pre-conception period so that early on good consumption patterns have been formed which will always be applied throughout life.

Keywords: Macronutrients, Micronutrients, Pregnant Women Rural, Urban.

Corresponding Author:

Bestfy Anitasari
Department of Nursing, Institut Kesehatan dan Bisnis Kurnia Jaya Persada, Palopo, South Sulawesi, Indonesia
Email: hbalquis@gmail.com

1. INTRODUCTION

During pregnancy, physiological changes occur in the mother's body as a process of adaptation to the results of conception. This condition requires adequate nutrient intake to support fetal growth and development and fulfill the metabolic needs of the mother's body (Keats et al., 2019). The macro and micronutrient intake of pregnant women in developing countries is generally still below recommendations. Poor dietary intake or deficiencies in key macronutrients and micronutrients have a major impact on pregnancy outcomes and neonate health (Blumfield et al., 2013). Evidence suggests that the effects of fetal nutrition impact into adulthood and even intergenerationally (Mousa et al., 2019). Some conditions that can occur as a result of malnutrition in pregnant women are disruption of the fetal growth process, miscarriage, abortion, preeclampsia, infection, premature birth, low birth weight and stunting. In addition, malnutrition also increases the risk of maternal and neonatal mortality (Grieger et al., 2014; Sudfeld & Smith, 2019).

Many nutritional problems experienced by pregnant women are Chronic Energy Deficiency (CED) and anemia. The incidence of CED among pregnant women in Indonesia in 2020 was 9.7%. Based on the results of the primary health research (2018), as many as 49.5% of pregnant women consumed protein below 80% of their needs during pregnancy, and 44.8% of pregnant women also received less energy intake in total, which was still below 70% of their needs, while the incidence of anemia reached 48.9% with the consumption pattern of blood supplement tablets given in general not spent up to 90 tablets (Kementerian Kesehatan Republik Indonesia, 2018). Research by Quansah and Boateng (2020), shows that the quality of food consumption that is not diverse is the cause of anemia during pregnancy which has an impact on preterm labor and low birth weight < 2500 grams (Quansah & Boateng, 2020). Nutritional adequacy can be obtained through additional intakes of macro and micronutrients from food and supplements taken. Women who eat less than 3 main meals and 2 snacks daily have been shown to have a 30% higher risk of preterm birth compared to women who eat more frequent meals (Paknahad et al., 2019).

Accurate assessment of the adequacy of food intake is the basis for providing nutrition interventions during pregnancy because inadequate or excessive nutrition can have adverse effects on the mother and fetus (Paknahad et al., 2019). In Indonesia, several methods are used to determine the nutritional status of pregnant women, namely monitoring weight gain, measuring upper arm circumference (LILA), and measuring hemoglobin levels and other micronutrients. However, assessment of food intake and the adequacy of macro and micronutrients is not routinely carried out (Royani et al., 2021). The use of valid dietary assessment tools is essential to compare dietary intake with current nutritional recommendations and to measure the impact of diet on health. Indeed to assess its adequacy, a new approach is used that is simple and non-invasive but can accurately assess nutritional deficiencies or excesses through quantitative and qualitative measurement of individual food consumption, namely by using the *24-hour food recall* method. All methods used to assess daily dietary intake have some limitations in terms of accuracy of portion size estimation. To overcome this, a *food frequency questioneer (FFQ) was* added (Faber et al., 2016; Hardinsyah, & Supariasa, 2016).

Data from the Palopo Health Office, in 2022 the most cases were pregnant women with CED 277 people (7.9%) and anemia as many as 60 people (1.71%) (Asmar, 2022). Currently, the working area of Health center Mungkajang is one of the concerns of the local government because the number of pregnancies in this area is quite high, reaching 279 pregnant women and pregnant women with CED until May 2023 reached 35 people (12.5%). Based on the results of interviews with village midwives, it was stated that the assessment of the nutritional status of pregnant women was only based on the results of weighing their weight and if there was a fixed weight, pregnant women were only advised to increase their food intake or consume foods that

were high in calories such as ice cream and if the weight increased even if it was only 0.2-0.5 kg / month there was no further intervention given. Even though the addition is included in the category of low weight gain for pregnant women, especially in the 2nd and 3rd trimester of pregnancy.

The working area of Mungkajang Community Health Center is also divided into rural areas around the mountains and urban areas around the cross Sulawesi track. This geographical condition determines the food consumption patterns of the people, namely those who live in rural areas consume local foods in addition to other types of food every day and those who live in urban areas have a diversity of foods consumed. So it is necessary to accurately assess the nutritional status of vulnerable populations who live in different areas to assess the adequacy of their intake. This study aims to compare the adequacy of macronutrients and micronutrients between pregnant women in urban and rural areas.

2. RESEARCH METHOD

The research methods used in this study are descriptive, correlation and comparison with a cross sectional design. The initial stages of the study began with the preparation stage, followed by visiting prospective respondents who had agreed to participate in the study for interviews about their food consumption using a 24-hour *food recall* questionnaire. On the day of the interview, the height and weight and upper arm circumference (LILA) of the respondents will be measured. The *food recall* assessment time is carried out for 3 days, namely 2 days on weekdays (Monday-Friday range) and 1 day off. At the time of the interview, respondents will be shown a food table booklet containing food types and portion sizes ranging from large, medium, small portions and household sizes used such as spoons, plates or bowls. After the assessment for 3 days is carried out, followed by giving the FFQ questionnaire to assess the respondent's food intake 1 month earlier, this is done for 1 day. This study will be assisted by research assistants who have previously conducted perceptual similarities on how to conduct 24-hour food recall interviews and FFQ filling. The data obtained from the 3×24 hour *food recall* and FFQ were then analyzed using the Nutrisurvey application. Data analysis using the *chi-square test*.

The population of this study was 279 pregnant women who would be selected by *purposive sampling* method so that the number of samples was 25 mothers in rural areas and 25 mothers in urban areas with inclusion criteria, namely pregnant women in all trimesters, domiciled in the Mungkajang health center working area, able to read and write. The exclusion criteria are pregnant women with health problems, do not want to participate. This study was carried out while adhering to the principles of research ethics and health protocols. This study is an preliminary studies in assessing the nutritional status of pregnant women specifically on the adequacy of macronutrients and micronutrients become the basis in nutrition education for pregnant women

3. RESULTS AND DISCUSSION

The results of this study are described in several tables, namely the table of respondent characteristics, macronutrient intake, adequacy level of macronutrient intake, micronutrient intake, adequacy level of micronutrient intake and frequency of food intake in pregnant women in urban and rural areas. Data on the characteristics of respondents are described in the following table:

Table 1. Distribution of Respondents Based on Characteristics (n=50).

Characteristics	Urban		Rural	
	f	%	f	%
Age				
Reproductively healthy	17	68	16	64
Reproductively unhealthy	8	32	9	36
Education				
High	18	72	14	56
Low	7	28	11	44
Jobs				
Salaried	20	80	4	16
No salary	5	20	21	84
Gravida				
Primigravida	8	32	10	40
Multigravida	17	68	15	60
Economic Status				
income low minimum wage	9	36	15	60
income higher or same minimum wage	16	64	10	40
LILA				
Normal	20	80	18	72
Less	5	20	7	28
Weight gain during pregnancy				
Less	2	8	2	8
Medium	18	72	21	84
High	5	20	2	8
Pregnancy Age				
1st Trimester	5	20	8	32
Trimester 2	19	76	16	64
Trimester 3	1	4	1	4
Hemoglobin levels				
< 11 mg/dl	10	40	13	52
≥ 11 mg/dl	15	60	12	48
Total	25	100	25	100

Table 1 shows that respondents in this study both in rural and urban areas were dominated by pregnant women in healthy reproductive age (age > 20 years) with a high level of education (high school to college), gravida status is multigravida (more than 1 child). There are differences in employment between pregnant women in urban areas, which are dominated by salaried jobs as much as 80%, while pregnant women in rural areas are more unpaid (IRT), namely 84%. There are differences in the economic status of pregnant women, namely in urban areas, family income is more than or equal to the regional minimum wage (UMR) as much as 64%, while in rural areas it is dominated by family economic status with income less than UMR by 60%. The upper arm circumference (LILA) of pregnant women in normal conditions in urban areas is 80% and in rural areas is 72%. The weight gain of pregnant women in both environments showed a moderate increase (0.29-0.44 kg / week), namely in urban areas by 72% and in rural areas by 84%, with gestational age dominated in the second trimester both in urban areas by 76% and in rural areas by 64%.

Table 2. Macronutrient Intake of Pregnant Women in Urban and Rural Areas.

Nutrients	Region		p-value
	Urban	Rural	
	Mean±SD	Mean±SD	
Energy (kcal)	1918.07±431.52	1815.33±402.22	0.053
Carbohydrate (g)	403.62±68.89	400.28±112.45	0.049
Protein (g)	88.25±23.84	86.76±21.67	0.045
Fat (g)	54.27±21.54	52.93±19.65	0.056

The table 2 shows that there is no difference in the intake of macronutrients between pregnant women in urban and rural areas, especially for energy (p=0.053) and fat (p=0.056), although the intake of other substances shows a difference, namely carbohydrates (p=0.049) and protein (p=0.045). The mean intake of macronutrients is still below the recommended amount for pregnant women based on their gestational age.

Table 3. Macronutrient Adequacy Levels of Pregnant Women in Urban and Rural Areas.

Nutrients	Nutrition Adequacy Level						p- value
	More		Normal		Less		
	Urban	Rural	Urban	Rural	Urban	Rural	
	f (%)		f (%)		f (%)		
Energy (kcal)	3 (12)	3 (12)	6 (24)	2 (8)	16 (64)	20 (80)	0.063
Carbohydrate (g)	0 (0)	2 (8)	12 (48)	11 (44)	13 (52)	12 (48)	0.055
Protein (g)	3 (12)	4 (16)	10 (40)	8(32)	12 (48)	13 (52)	0.058
Fat (g)	4 (16)	7 (28)	5 (20)	8 (32)	16 (64)	10 (40)	0.071
Total	10	16	33	29	57	55=200 (n)	

The table 3 shows that there is no difference in nutritional adequacy levels for macronutrients between pregnant women in urban and rural areas with p>α=0.05. Macronutrient adequacy levels were dominated by undernutrition (70-79%) for energy, carbohydrates, protein and fat.

Table 4. Micronutrient Intake Of Pregnant Women In Urban And Rural Areas.

Micronutrients	Region		p-value
	Urban	Rural	
	Mean±SD	Mean±SD	
Vitamin A (mcg)	962.58±601.894	948.34±567.899	0.043
Vitamin C (mg)	67.15±11.55	66.45±10.98	0.065
Vitamin B1 (mg)	1.21±0.58	0.98±0.45	0.078
Vitamin B2 (mg)	0.49±0.03	0.37±0.34	0.084
Vitamin B3 (mg)	12.77±1.34	11.89±0.89	0.056
Vitamin B6 (mg)	0.95±0.13	0.87±0.11	0.075
Vitamin B12 (mg)	4.82±3.49	4.55±3.16	0.042
Vitamin E (mg)	12.44±0.16	12.10±0.08	0.088
Iron (mg)	13.12±13.43	12.13±12.99	0.052
Folic acid (mcg)	476.10±226.11	469.20±201.13	0.067

Calcium (mg)	1130.73±888.19	1056.78±783.34	0.054
Phosphorus (mg)	601.43±342.11	597.55±310.78	0.055
Fiber (gr)	15.77±4.06	14.89±3.98	0.079

The table 4 shows that there is no difference in the amount of micronutrient intake among pregnant women in urban and rural areas with p>α=0.05 for vitamin C, B1, B2, B3, B6, E, iron, folic acid, calcium, phosphorus and fiber, but there is a difference in the amount of consumption for Vitamin A (p=0.043) and Vitamin B12 (0.042). For the level of nutritional adequacy, there was a difference in the adequacy of vitamin A (p=0.024) and vitamin B12 (p=0.048) consumption among pregnant women in urban and rural areas, for other types of micronutrients, there was no difference in the adequacy of consumption with a value of p>α=0.05.

Table 5. Adequacy Level of Micronutrients of Pregnant Women in Urban and Rural Areas.

Nutrients	Nutrition Adequacy Level						p-value
	More		Normal		Less		
	Urban	Rural	Urban	Rural	Urban	Rural	
	f	(%)	f	(%)	f	(%)	
Vitamin A (mcg)	12 (48)	7	12	15	1	3	0.024
Vitamin C (mg)	4 (16)	2	8	9	13	14	0.077
Vitamin B1 (mg)	2 (8)	1	10	11	13	13	0.056
Vitamin B2 (mg)	0 (0)	2	12	9	13	14	0.067
Vitamin B3 (mg)	2 (8)	2	8	10	15	13	0.068
Vitamin B6 (mg)	5 (20)	1	7	13	13	11	0.089
Vitamin B12 (mg)	2 (8)	0	14	15	9	10	0.048
Vitamin E (mg)	3 (12)	1	9	16	13	8	0.058
Iron (mg)	5 (20)	4	8	11	12	10	0.067
Folic acid (mcg)	4 (16)	5	6	8	15	12	0.098
Calcium (mg)	6 (24)	4	7	8	12	13	0.078
Phosphorus (mg)	4 (16)	4	6	8	15	13	0.088
Fiber (gr)	8 (32)	7	7	10	10	13	0.053

Based on the table 5 above, the level of fulfillment of micronutrient intake is dominated by the level of less fulfillment (70-79%) both in urban and rural pregnant women.

Table 6. Frequency Table of Food Substance Intake in Pregnant Women in Urban and Rural Areas.

Products	Frequency of intake	Living location		p-value
		Urban	Rural	
Staple food	1-2 servings a day	12	0	0.063
	> 2 servings a day	88	100	
	Never	0	0	
Fish and its products	1-2 servings a day	8	0	0.072
	> 2 servings a day	92	100	
	Never	0	0	
Meat and its preparations	1-2 servings a day	0	0	0.067
	> 2 servings a day	0	0	
	Never	4	88	
	1 x a month	96	12	
Chicken and its preparations	1-2 servings a day	72	4	0.045

	> 2 servings a day	8	0	
	Never	0	0	
	1 x a month	20	96	
Vegetables	1-2 servings a day	76	21	0.043
	> 2 servings a day	20	79	
	Never	4	0	
Nuts and their preparations	1-2 servings a day	92	76	0.055
	> 2 servings a day	8	0	
	Never	0	20	
	1 x a month	0	4	
Fruits	1-2 servings a day	60	76	0.067
	> 2 servings a day	20	24	
	1 x a month	20	0	
Milk and its preparations	1-2 servings a day	44	72	0.066
	> 2 servings a day	44	28	
	Never	0	0	
	1 x a month	12	0	
Snack Food	1-2 servings a day	8	16	0.055
	> 2 servings a day	88	76	
	Never	0	0	
	1 x a month	4	8	

Based on Table 6 show that the food consumption frequency, there is a difference in the frequency of consumption of vegetables (p=0.043) with pregnant women in rural areas showing the frequency of consumption of vegetables more than women in urban areas, as well as for the type of chicken and its preparations (p=0.045) with women in urban areas showing more frequent consumption when compared to women in rural areas. As for staple foods (p=0.063), fish and its products (p=0.072), meat and its products (p=0.067), nuts (p=0.055), fruits (p=0.067), milk and its products (p=0.066), snacks (p=0.055) showed no difference in consumption frequency.

DISCUSSION

The dietary nutrient intake of the study sample showed that only carbohydrate, protein, vitamin A and vitamin B12 intake met the nutritional adequacy value (RDA) of more than 400 g, 70 g, 900 mg/day and 4.5 mcg. Other nutrients such as energy, fat, calcium, iron, folic acid, vitamins C, B1, B2, B6, E from the diet did not meet the RDA values. The average carbohydrate intake of the study sample exceeded the RDA. Carbohydrates contain 60-70% of the total energy required by the body (Stråvik et al., 2019). This need was met by the research sample by consuming rice, bread, sago, processed flour, cassava and corn equivalent to 5 servings a day in accordance with the recommended intake. The average protein intake was also higher than the RDA value. Fulfillment of protein intake of research samples by consuming more animal protein sources such as fish with its preparations, and less vegetable protein such as nuts with their preparations. In accordance with the recommended protein sources (Retni et al., 2016). Another finding was that vitamin A consumption exceeded the RDA. The high consumption of vitamin A and B12 may be due to the intake of green leafy vegetables and animal foods that are high in vitamin A and B12.

The results showed no difference in the fulfillment of adequate nutritional intake of pregnant women in rural and urban areas for macronutrients, namely energy and fat. The energy intake of pregnant women should increase by about 300 kcal/day during pregnancy from the total age-appropriate needs of 2430 kcal-2550 kcal/day (WHO, 2018). However, in this study, the average intake consumed by the study sample was 1918.07±431.52 for urban areas and 1815.33±402.22 for rural areas. These results indicate that the intake of macronutrients still does not meet the recommended daily needs for women in pregnancy. Although energy needs are generally the same between non-pregnant women and pregnant women in the first trimester, they will increase in the second and third trimesters (Ariyani & Erawati, 2023; Kementerian Kesehatan Republik Indonesia, 2013). In addition, pregnant women require additional protein for the formation of early pregnancy-related tissues and maintaining new tissues (Grenier et al., 2021; Kementerian Kesehatan Republik Indonesia, 2013). In this study, there was no difference in the protein intake of pregnant women in urban and rural areas.

Adequate nutritional intake during pregnancy is very important to support normal fetal growth and development, meet the mother's own nutritional needs without depleting food reserves and damaging maternal tissues and have a positive impact on future fetal life until adulthood (Ariyani & Erawati, 2023; Mousa et al., 2019; Qureshi & Khan, 2015). During pregnancy, a mother must increase the amount and type of food eaten to meet the needs of fetal growth by consuming a variety of foods in a balanced amount and proportion according to what has been determined (Suliga, 2015; Yosephin, 2018). Various research results suggest that many pregnant women still have poor nutritional status, including Chronic Energy Deficiency (CED) and anemia. One of the causes is because her food intake during pregnancy is insufficient for her own needs, let alone for the needs of her baby (Nugrahini et al., 2014; Permatasari et al., 2021). As a result, the fetus does not get the nutrients it needs, thus disrupting its growth and development (Cannon et al., 2020; Suliga, 2015; Yosephin, 2018).

Poor fetal growth results not only from protein and energy deficiencies, but also from inadequate intake of micronutrients that are essential during pregnancy (Mousa et al., 2019; WHO, 2018). The results showed a deficiency in micronutrient intake in the form of iron, vitamins C, E and folic acid which play an important role in the formation and defense of hemoglobin. The iron needs of pregnant women are higher than the average intake of iron that can be absorbed from food so that when the consumption of iron-containing foods decreases, the body will meet the needs of the fetus by taking maternal iron reserves, potentially causing iron deficiency anemia. The prevalence of anemia in developing countries is around 56% (Abay et al., 2017; WHO, 2018). Folic acid plays a role in the metabolism of amino acids needed in the formation of red blood cells (Sendeku et al., 2020). Folic acid is the synthesized form of vitamin B. Food sources rich in folate are oranges, dark green vegetables, beans and liver. The need for folate increases during pregnancy to support the rapid cell division associated with fetal growth. In particular, folic acid supplements (400-800 µg/day) are taken before conception to reduce the occurrence of fetal neural tube defects (Argyridis, 2019). However, none of the respondents in this study consumed folic acid before pregnancy, only consumed folic acid supplements during pregnancy, and even then only by pregnant women in urban areas. This finding is different from Suliga's study, which found that the dominant pregnant women in urban areas had consumed folic acid long before marriage (Suliga, 2015). In fact, to reduce the risk of neural tube defects in the fetus, folic acid consumption is not only recommended through supplements but also from foods that contain folic acid. Based on the results of the respondent's food recall, it shows that folate intake has met the recommended nutritional adequacy rate, which is around 600 mcg (WHO, 2018). Vitamin E helps in the formation of cell membranes which will have an impact on the stability of red blood cell membranes. So if vitamin E deficiency occurs, it can cause the state of red blood cells to be weak and abnormal (Cave et al., 2018; WHO, 2018). This condition causes the hemoglobin levels of pregnant women to

decrease, although some have normal hemoglobin levels. In this study, the dominant sample showed hemoglobin values ≥ 11 gr/dl. This value is considered a normal Hb value. This may be due to the consumption of protein-rich foods that contain high amounts of iron, increased consumption of vitamin B12 which plays a role in the formation of red blood cells and regularity in taking iron supplements given.

Dietary diversity is used as a key indicator in assessing the quality of an individual's or household's diet, indicating adequate nutrient intake through food (Forbes et al., 2018; Sibhatu et al., 2015). The more varied the food, the more complementary nutrients are obtained (Sibhatu et al., 2015; Yeneabat et al., 2019). If the diet of pregnant women lacks variety, it will experience a lack of essential nutrients and as a result the fetus will not get the nutrients needed for healthy growth. The problem of micronutrient deficiencies is a double burden on pregnant women because pregnancy is characterized by increased demand for various types of micronutrients by fetoplacental tissue as well as changes in the metabolism of most low serum micronutrients during pregnancy which become severe as gestational age increases (Forbes et al., 2018; Kazma, 2020). Women's food behavior and intake during pregnancy is greatly influenced by different cultural practices, myths and taboos. Ethnic Indian women usually consume the most locally available, easily accessible and culturally acceptable foods (Kazma, 2020; Sibhatu et al., 2015). Although this study did not find any taboos or myths among pregnant women related to food during pregnancy. However, the provision of foodstuffs in rural women is more from gardening products such as vegetables and those brought by traveling sellers.

Another contributing factor to micronutrient deficiencies is when people do not have access to micronutrient-rich foods such as fruits, vegetables, animal products due to economic conditions, education and/or food shortages (Cannon et al., 2020; Saaka et al., 2021). In this study, the inadequate intake of micronutrients was due to changes in the mother's diet, which before pregnancy liked micronutrient source foods but during pregnancy did not like to consume them or consumption patterns that were monotonous, only liked one or two types of food, did not want to vary it even though they had enough income to buy it. Another factor is that pregnant women from adolescence do not like certain types of food that continue into their pregnancy. These results are in line with research conducted in Pakistan, Kenya and Western Ethiopia (Abay et al., 2017; Kiboi et al., 2017; Qureshi & Khan, 2015).

Varying and increasing the frequency of meals can increase the diversity of a woman's diet. Changing breakfast, lunch and dinner menus can be one way for pregnant women to get adequate nutrition from the diversity of foods consumed (Kiboi et al., 2017). However, in this study, pregnant women both in urban and rural areas have a diet with monotonous types of food and lack of variety in processing which is dominant in cooking clear or fried only for protein sources such as fish, tofu and tempeh, fruits are dominant bananas, vegetables such as spinach, long beans, and kale, while for carbohydrates are dominant white rice. It is known that every meal in one day, pregnant women consume one portion of staple food, generally rice and added with one type of side dish and vegetable, sometimes added fruit if available, even there are pregnant women who only consume staple food and one type of vegetable. To achieve balanced nutrient input is not only fulfilled by one type of food, but must consist of a variety of foodstuffs (Retni et al., 2016). In addition, all women during pregnancy require micronutrient supplements (Haider & Bhutta, 2017). Samples in this study received iron and calcium supplementation, but some samples did not regularly take it because they forgot or because they did not like the taste.

A comparison of the lifestyles of women in urban and rural areas in developing countries shows that the lifestyles of people in rural areas are less healthy, partly due to lack of access to antenatal and adolescent reproductive health services, lower awareness of the importance of

healthy nutrition and poor food quality when compared to urban women (Grenier et al., 2021; Nana & Zema, 2018). It has been shown that rural women have a higher risk of LBW than urban women (Adikari et al., 2016; Ali et al., 2014; Nana & Zema, 2018). However, technological advances, especially in the field of mass media, have penetrated into the lives of rural households and people have begun to imitate urban lifestyles. Rural life is no longer traditional in style, but practices and habits are becoming more similar to urban society. As in this study, consumption patterns, access to maternity services, education level and types of food ingredients and food processing methods were similar between rural and urban women. Although women in rural areas predominantly obtain food items such as vegetables from their farms, sources of protein, fat, carbohydrates are obtained from one source, namely from the central market and fish auction.

Several studies have reported that pregnancy in adolescence is strongly associated with various negative consequences of pregnancy (Čvorović, 2022; Fuada et al., 2020; Samsury et al., 2022). Although the sample was generally in the healthy reproductive age range, about 32% of respondents in urban areas and 36% of respondents in rural areas were less than 20 years old, which is characterized by the condition of reproductive organs that are not yet fully mature and the development of several body parts that require adequate nutritional intake. It is marked that all respondents in the unhealthy reproductive age range experienced chronic energy deficiency characterized by LILA values <23.5 cm and most were primigravida (first pregnancy). These results are in line with several studies that reveal that the pre-marital nutritional status of women who become pregnant before healthy reproductive age greatly affects their food consumption patterns during pregnancy and it was found that most of the deficient nutritional status before pregnancy will continue until pregnancy and even the end of pregnancy (Čvorović, 2022; Nigatu et al., 2018). Some literature shows that undernourished pregnancies (low BMI) and low weight gain during pregnancy can increase the risk of labor complications, maternal tissue depletion and Intra Uterine Growth Retardation (IUGR), stillbirth, and LBW in infants (Grenier et al., 2021; Downs, et al., 2014). In this study, the food consumption habits of pregnant women in both rural and urban areas are more likely to follow consumption patterns during adolescence, namely by choosing certain foods to be consumed, besides that there are those who experience changes in appetite, namely no longer consuming foods that were commonly consumed before pregnancy due to the emergence of dislike for these foods after pregnancy.

Analysis conducted on the frequency of food consumed shows that there is no difference in the consumption of staple foods between urban and rural pregnant women with a frequency of > 1x/day for white rice, sago (kapurung and dange) 4-6x/week, wheat flour (bread), corn and sweet potatoes 1-3x/week,. There is no difference in the consumption of fish, processed products and processing methods, namely boiled and fried in pregnant women in urban and rural areas with a frequency of consumption > 1x/day, eggs that are omelet and boiled 4-6x / week, fried chicken 1-3x / month. Types of legumes and their preparations consumed by pregnant women in urban and rural areas 1-3x / week include types of tofu, tempeh. There is no difference in vegetable consumption among pregnant women in rural and urban areas, in terms of types and processing methods, namely cooked and stir-fried. In general, every meal, pregnant women consume more than one type of vegetable together with a frequency of >1x/day. This finding is in contrast to some research results which show that pregnant women in urban areas consume more staple foods, fish, milk and vegetables, thus indicating that the food intake of pregnant women in rural areas is poor (Suliga, 2015).

4. CONCLUSION

The fulfillment of macronutrient and micronutrient intake of pregnant women in urban and rural areas in this study did not meet the recommended nutritional adequacy standards.

Eating patterns during adolescence that tend to be picky about food and like instant food persist into marriage and pregnancy, preference for only one or two types of food so that they do not want to vary their intake, changes in appetite after pregnancy are factors that cause inadequate intake of some macro and micronutrients of pregnant women in rural and urban areas. Improvements in nutritional status should begin when women are in adolescence. Nutritional patterns that have been well established since adolescence become the foundation in forming optimal nutritional habits in the next life cycle for women. Through proper nutrition education, adolescent girls can improve and increase food consumption patterns in accordance with the recommended recommendations. As for pregnant women, nutrition education during pregnancy can be provided not only using printed media but through accessible nutrition applications that contain the amount of macronutrients and micronutrients needed, food sources and substitutes, practical but still nutritious processing methods, equipped with a 24-hour helpdesk. So that independently, pregnant women can apply it in their daily lives.

REFERENCES

Abay, A., Yalew, H. W., Tariku, A., & Gebeye, E. (2017). Determinants of prenatal anemia in Ethiopia. *Archives of Public Health*, *75*(1), 1–10. https://doi.org/10.1186/s13690-017-0215-7

Adikari, A. M. N. T., Sivakanesan, R., Wijesinghe, D. G. N. G., & Liyanage, C. (2016). Assessment of *nutritional* status of pregnant women in a rural area in Sri Lanka. *Tropical Agricultural Research*, *27*(2), 203. https://doi.org/10.4038/tar.v27i2.8168

Ali, F., Thaver, I., & Khan, S. A. (2014). Original Article Assessment Of *Dietary* Diversity And Nutritional Status Of Pregnant Women In Islamabad , Pakistan Fatima Ali , Inayat Thaver , Shahzad Ali Khan. *J Ayub Med Coll Abbottabad*, *26*(4), 506–509.

Argyridis, S. (2019). Folic acid in pregnancy. *Obstetrics, Gynaecology and Reproductive Medicine*, *29*(4), 118–120. https://doi.org/10.1016/j.ogrm.2019.01.008

Ariyani, N. W., & Erawati, N. L. P. S. (2023). Assessment of nutrient intake and antenatal education method for pregnant women in Gianyar, Bali, Indonesia. *Bali Medical Journal*, *12*(1), 934–939. https://doi.org/10.15562/bmj.v12i1.4194

Asmar. (2022). *Hasil Analisis Data Pengukuran Stunting Tingkat Kota Palopo*. Ritmee. Retrieved from https://ritmee.co.id/hasil-analisis-data-pengukuran-stunting-tingkat-kota-palopo/. 2022

Astika, T., Permatasari, E., Rizqiya, F., Kusumaningati, W., Indraaryani, I., & Hermiwahyoeni, Z. (2021). *Pengaruh pendidikan gizi dan kesehatan reproduksi ibu hamil di Indonesia menggunakan studi eksperimental semu*. 1–15.

Blumfield, M. L., Hure, A. J., MacDonald-Wicks, L., Smith, R., & Collins, C. E. (2013). A systematic review and meta-analysis of micronutrient intakes during pregnancy in developed countries. *Nutrition Reviews*, *71*(2), 118–132. https://doi.org/10.1111/nure.12003

Cannon, S., Lastella, M., Vincze, L., Vandelanotte, C., & Hayman, M. (2020). A review of pregnancy information on nutrition, physical activity and sleep websites. *Women and Birth*, *33*(1), 35–40. https://doi.org/10.1016/j.wombi.2018.12.007

Cave, C., Hanson, C., Schumacher, M., Lyden, E., Furtado, J., Obaro, S., Delair, S., Kocmich, N., Rezac, A., Izevbigie, N. I., Van nOrmer, M., Kamil, A., McGinn, E., Rilett, K., Elliott, E., Johnson, R., Weishaar, K., Olateju, E. K., Akaba, G. A., … Anderson-Berry, A. (2018). A comparison of vitamin E status and associated pregnancy outcomes in maternal–infant dyads between a Nigerian and a United States population. *Nutrients*, *10*(9), 1–14. https://doi.org/10.3390/nu10091300

Čvorović, J. (2022). Maternal age at marriage and child nutritional status and development:

evidence from Serbian Roma communities. *Public Health Nutrition*, *25*(5), 1183–1193. https://doi.org/10.1017/S1368980022000544

Downs, D. S., Savage, J. S., & Rauff, E. L.. (2014). Falling Short of Guidelines? Nutrition and Weight Gain Knowledge in Pregnancy. *Journal of Women's Health Care*, *03*(05). https://doi.org/10.4172/2167-0420.1000184

Faber, M., Kunneke, E., Wentzel-Viljoen, E., & Wenhold, F. (2016). *Dietary Intake Assessment 24-Hour Recall Compiled By: Dietary intake assessment 24-hour recall Dietary intake assessment: 24-hour recall*. http://www.cdc.gov/nchs/nhanes/measuring_guides_dri/measuringguides02.htm

Forbes, L. E., Graham, J. E., Berglund, C., & Bell, R. C. (2018). Dietary change during pregnancy and women's reasons for change. *Nutrients*, *10*(8), 1–10. https://doi.org/10.3390/nu10081032

Fuada, N., Latifah, L., Yunitawat, D., & Ashar, H. (2020). Assessment of nutritional status of children under-five in families of adolescent mothers in Indonesia 2013. *Journal of Nutritional Science and Vitaminology*, *66*(29), S425–S431. https://doi.org/10.3177/jnsv.66.S425

Grenier, L. N., Atkinson, S. A., Mottola, M. F., Wahoush, O., Thabane, L., Xie, F., Vickers-Manzin, J., Moore, C., Hutton, E. K., & Murray-Davis, B. (2021). Be Healthy in Pregnancy: Exploring factors that impact pregnant women's nutrition and exercise behaviours. *Maternal and Child Nutrition*, *17*(1), 1–9. https://doi.org/10.1111/mcn.13068

Grieger, J. A., Grzeskowiak, L. E., & Clifton, V. L. (2014). Preconception dietary patterns in human pregnancies are associated with preterm delivery. *Journal of Nutrition*, *144*(7), 1075–1080. https://doi.org/10.3945/jn.114.190686

Haider, B. A., & Bhutta, Z. A. (2017). Multiple-micronutrient supplementation for women during pregnancy (Review) Summary Of Findings For The Main Comparison. *Cochrane Database of Systematic Reviews*, *4*(4), CD004905. https://doi.org/10.1002/14651858.CD004905.pub5

Kazma, J. M., van den Anker, J., Allegaert, K., Dallmann, A., & Ahmadzia, H. K. (2020). Anatomical and physiological alterations of pregnancy. *Journal of pharmacokinetics and pharmacodynamics*, *47*(4), 271-285. https://doi.org/10.1007/s10928-020-09677-1

Keats, E. C., Haider, B. A., Tam, E., & Bhutta, Z. A. (2019). Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database of Systematic Reviews*, *2019*(3). https://doi.org/10.1002/14651858.CD004905.pub6

Kementerian Kesehatan Republik Indonesia. (2013). *Buku Saku Pelayanan Kesehatan Ibu Di Fasilitas Kesehatan Dasar Dan Rujukan*, Kementerian Kesehatan Republik Indonesia.

Kementerian Kesehatan Republik Indonesia. (2018). *Hasil Riset Kesehatan Dasar Tahun 2018*. Kementerian Kesehatan Republik Indonesia.

Kiboi, W., Kimiywe, J., & Chege, P. (2017). Determinants of dietary diversity among pregnant women in Laikipia County, Kenya: A cross-sectional study. *BMC Nutrition*, *3*(1), 1–8. https://doi.org/10.1186/s40795-017-0126-6

Hardinsyah, M., & Supariasa, I. D. N. (2016). *Ilmu gizi teori dan aplikasi*. Jakarta: Penerbit Buku Kedokteran EGC.

Mousa, A., Naqash, A., & Lim, S. (2019). Macronutrient and micronutrient intake during pregnancy: An overview of recent evidence. *Nutrients*, *11*(2), 1–20. https://doi.org/10.3390/nu11020443

Nana, A., & Zema, T. (2018). Dietary practices and associated factors during pregnancy in northwestern Ethiopia. *BMC Pregnancy and Childbirth*, *18*(1), 1–8. https://doi.org/10.1186/s12884-018-1822-1

Nigatu, M., Gebrehiwot, T. T., & Gemeda, D. H. (2018). Household Food Insecurity, Low

Dietary Diversity, and Early Marriage Were Predictors for Undernutrition among Pregnant Women Residing in Gambella, Ethiopia. *Advances in Public Health*, *2018*, 1–10. https://doi.org/10.1155/2018/1350195

Nugrahini, E. Y., Effendi, J. S., Herawati, D. M. D., Idjradinata, P. S., Sutedja, E., Mose, J. C., & Syukriani, Y. F. (2014). Asupan Energi dan Protein Setelah Program Pemberian Makanan Tambahan Pemulihan Ibu Hamil Kurang Energi Kronik di. *IJEMC (Journal Of Education and Midwifery Care)*, *1*(1), 41–48.

Paknahad, Z., Fallah, A., & Moravejolahkami, A. R. (2019). Maternal Dietary Patterns and Their Association with Pregnancy Outcomes. *Clinical Nutrition Research*, *8*(1), 64. https://doi.org/10.7762/cnr.2019.8.1.64

Permatasari, T. A. E., Rizqiya, F., Kusumaningati, W., Suryaalamsah, I. I., & Hermiwahyoeni, Z. (2021). The effect of nutrition and reproductive health education of pregnant women in Indonesia using quasi experimental study. *BMC Pregnancy and Childbirth*, *21*(1), 1–15. https://doi.org/10.1186/s12884-021-03676-x

Quansah, D. Y., & Boateng, D. (2020). Maternal dietary diversity and pattern during pregnancy is associated with low infant birth weight in the Cape Coast metropolitan hospital, Ghana: A hospital based cross-sectional study. *Heliyon*, *6*(5), e03923. https://doi.org/10.1016/j.heliyon.2020.e03923

Qureshi, Z., & Khan, R. (2015). Diet Intake Trends Among Pregnant Women in Rural Area of Rawalpindi, Pakistan. *Journal of Ayub Medical College, Abbottabad : JAMC*, *27*(3), 684–688.

Retni, R., Margawati, A., & Widjanarko, B. (2016). Pengaruh status gizi & asupan gizi ibu terhadap berat bayi lahir rendah pada kehamilan usia remaja. *Jurnal Gizi Indonesia (The Indonesian Journal of Nutrition)*, *5*(1), 14–19. https://doi.org/10.14710/jgi.5.1.14-19

Royani, I., Mappaware, N. A., Darma, S., Khalid, N., & Utami, D. F. (2021). The Relationship between Nutritional Status of Pregnant Women and Stunted Children. *Green Medical Journal*, *3*(1), 39–46. https://doi.org/10.33096/gmj.v3i1.80

Saaka, M., Mutaru, S., & Osman, S. M. (2021). Determinants of dietary diversity and its relationship with the nutritional status of pregnant women. *Journal of Nutritional Science*, 1–8. https://doi.org/10.1017/jns.2021.6

Samsury, S. F., Ismail, T. A. T., & Hassan, R. (2022). Low birth weight infant among teenage pregnancy in Terengganu, Malaysia: A cross-sectional study. *Malaysian Family Physician*, *17*(1), 44–51. https://doi.org/10.51866/oa.59

Sendeku, F. W., Azeze, G. G., & Fenta, S. L. (2020). Adherence to iron-folic acid supplementation among pregnant women in Ethiopia: A systematic review and meta-analysis. *BMC Pregnancy and Childbirth*, *20*(1), 1–9. https://doi.org/10.1186/s12884-020-2835-0

Sibhatu, K. T., Krishna, V. V., & Qaim, M. (2015). Production diversity and dietary diversity in smallholder farm households. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(34), 10657–10662. https://doi.org/10.1073/pnas.1510982112

Stråvik, M., Jonsson, K., Hartvigsson, O., Sandin, A., Wold, A. E., Sandberg, A. S., & Barman, M. (2019). Food and nutrient intake during pregnancy in relation to maternal characteristics: Results from the nice birth cohort in northern Sweden. *Nutrients*, *11*(7). https://doi.org/10.3390/nu11071680

Sudfeld, C. R., & Smith, E. R. (2019). New evidence should inform WHO guidelines on multiple micronutrient supplementation in pregnancy. *Journal of Nutrition*, *149*(3), 359–361. https://doi.org/10.1093/jn/nxy279

Suliga, E. (2015). Nutritional behaviours of pregnant women in rural and urban environments.

Annals of Agricultural and Environmental Medicine, *22*(3), 513–517. https://doi.org/10.5604/12321966.1167725

WHO. (2018). WHO Recommendation on Antenatal Care for a Positive Pregnancy Experience: Summary. *The Lancet*, *387*(10017), 1–10. https://doi.org/10.1186/1742-4755-10-19.5

Yeneabat, T., Adugna, H., Asmamaw, T., Wubetu, M., Admas, M., Hailu, G., Bedaso, A., & Amare, T. (2019). Maternal dietary diversity and micronutrient adequacy during pregnancy and related factors in East Gojjam Zone, Northwest Ethiopia, 2016. *BMC Pregnancy and Childbirth*, *19*(1), 1–9. https://doi.org/10.1186/s12884-019-2299-2

Yosephin, B. (2018). *Tuntunan Praktis Menghitung Kebutuhan Gizi*. Yogyakarta: Andi. Retrieved from https://pustaka.pekanbaru.go.id/inlislite3/opac/detail-opac?id=28395

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 772-781
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1327*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

SITEPIS Contraception is an Extension Officer in Providing Information on Family Planning in Indonesia

Hariyanti[1a], Husnul Khatimah[1b], Jusuf Kristianto[2c], Intan Gumilang Pratiwi[3d], Baiq Yuni Fitri Hamidiyanti[3e]

[1] Department of Midwifery, Poltekkes Kemenkes Jakarta I, South Jakarta, Jakarta, Indonesia
[2] Department of Dental Health, Poltekkes Kemenkes Jakarta I, South Jakarta, Jakarta, Indonesia
[3] Department of Midwifery, Poltekkes Kemenkes Mataram, Mataram, West Nusa Tenggara, Indonesia

[a] Email address: hariyanti@poltekkesjakarta1.ac.id
[b] Email address: husnulkhatimah916@gmail.com
[c] Email address: jusufkristianto@gmail.com
[d] Email address: intangumil@gmail.com
[e] Email address: baiqdiandanu@gmail.com

Received: 4 September 2023 Revised: 20 December 2023 Accepted: 31 December 2023

Abstract

This study addresses the vital role of information as a reproductive health right and emphasizes the responsibility of family planning officers, including health workers, to disseminate accurate information for ensuring public reproductive health. The research focuses on evaluating the effectiveness of SITEPIS Contraception, an online information service designed to aid family planning officers in conveying contraceptive information. SITEPIS is a web application offering comprehensive information on contraception, medical eligibility criteria, and a live chat service. This study involves 28 family planning officers at sub-district and village levels in Bogor and West Lombok districts. Employing a descriptive research approach, the study includes socialization events introducing Sitepis Contraception, encouraging usage, and collecting officers' evaluations. Results indicate positive feedback from all officers, citing the website's appealing design, user-friendly accessibility, and essential features for effective information delivery. Despite challenges related to internet network support in certain areas, officers express willingness to use the SITEPIS website for their community information duties. Notably, while face-to-face interaction is preferred by most officers, SITEPIS contraception serves as a valuable tool for information dissemination. The study underscores the underutilization of online information as the primary method among family planning officers in Indonesia. Despite this, it recognizes the potential of online platforms, like SITEPIS, in reaching diverse societal levels. The findings emphasize the need for further examination of SITEPIS Contraception from the community's perspective, the primary target audience, to enhance its effectiveness. In conclusion, the study advocates for the integration of online information tools to empower family planning officers in fulfilling their crucial role as information providers.

Keywords: Family Planning, Online Information, SITEPIS Contraception.

Corresponding Author:

Intan Gumilang Pratiwi
Department of Midwifery, Poltekkes Kemenkes Mataram, Mataram, West Nusa Tenggara, Indonesia
Email: intangumil@gmail.com

1. INTRODUCTION

Quality contraceptive information and services help the community to have freedom in determining the number and spacing of births and provide a range of potential benefits that include women's empowerment, economic development, education, and health improvement, including maternal and child health. In 2019, in low- and middle-income countries, there were around 218 million women of childbearing age who still had unmet contraceptive needs, whereas meeting these needs could reduce an estimated 111 million to 35 million unwanted pregnancies annually, 35 to 10 million abortions unsafe conditions, and 299,000 to 113,000 maternal deaths (Ali & Tran, 2022; Guttmacher Institute, 2020)

A comprehensive understanding of effective contraceptive methods is essential for women to protect their health and make informed decisions about sexuality and reproduction (Center for Reproductive Rights, 2011). Health workers are at the forefront of providing contraceptive services to clients, for example providing contraceptive counseling. Health workers are responsible for providing clients with comprehensive and accurate information to help clients make contraceptive decisions (Solo, & Festin, 2019; Soin, et al., 2022).

The quality of contraceptive counseling that women receive from healthcare workers can greatly influence their seeking behavior for further contraceptive services (Sserwanja, et al., 2023). Quality family planning counseling services have been associated with increased client satisfaction and a positive effect on clients' willingness to adopt and continue to use various family planning methods. Adequate counseling further empowers women to obtain information, which is a fundamental right. A comprehensive reproductive health approach demonstrates that quality family planning services must be client-oriented and empower women to make informed choices (Sserwanja, et al., 2023).

Since the start of the pandemic, health technology has been recommended for a variety of contraceptive services, including counseling, checking the appropriateness of contraceptive methods, selecting new methods of contraception, and continuing contraceptive use (Nanda, et al., 2020; Rao et al., 2022). Health technology has proven useful for the continuity of contraceptive services and for expanding access to contraception in remote areas (Sundstrom, et al., 2019; Thompson, Ahrens, & Coplon, 2020; Thompson, et. al., 2020). Online counseling services are an alternative for providing information to clients. Therefore the researchers developed a SITEPIS website to assist health workers in providing contraceptive information.

Various online information platforms have been extensively developed in Indonesia, both unidirectional and interactive in nature (Setiawati, Nurdiana & Yanti, 2020; Samosir, Kiting, & Aninditya, 2020; Wu et al., 2020). Online information channels have been extensively developed in Indonesia, both in unidirectional and interactive forms. However, among the numerous pieces of information or counseling services that have been developed, there is still a lack of online information services that guide the community in independently choosing contraception suitable for their needs. Additionally, there is a dearth of information services that delve into gathering community insights regarding their family planning behaviors. Even though, as we collectively know, the majority of Indonesian society, especially women, are engaged in work, which naturally poses limitations in accessing family planning information directly from officers. Therefore, SITEPIS Contraception serves as an alternative solution to address the information needs related to family planning. SITEPIS Contraception actively and independently provides an understanding of the contraception to be used, supported by a system that directs the community to the nearest health facilities for contraceptive services. SITEPIS Contraception also gathers information on the family planning behaviors, issues faced by clients, and client locations, facilitating easy outreach for officers to provide treatment for clients in need.

2. RESEARCH METHOD

The research design uses a cross-sectional approach. The researcher socialized the contraception SITEPIS website to family planning officers. SITEPIS contraception is a website that contains contraceptive information and medical eligibility criteria modified from the medical eligibility criteria from WHO and the Ministry of Health and is used by officers to screen or screen contraceptive methods according to client needs. The contraception SITEPIS website is also equipped with features to dig up information on client conditions, contraceptive use behavior, respondent's area of residence, and live chat. The following is the appearance of the contraceptive site website:

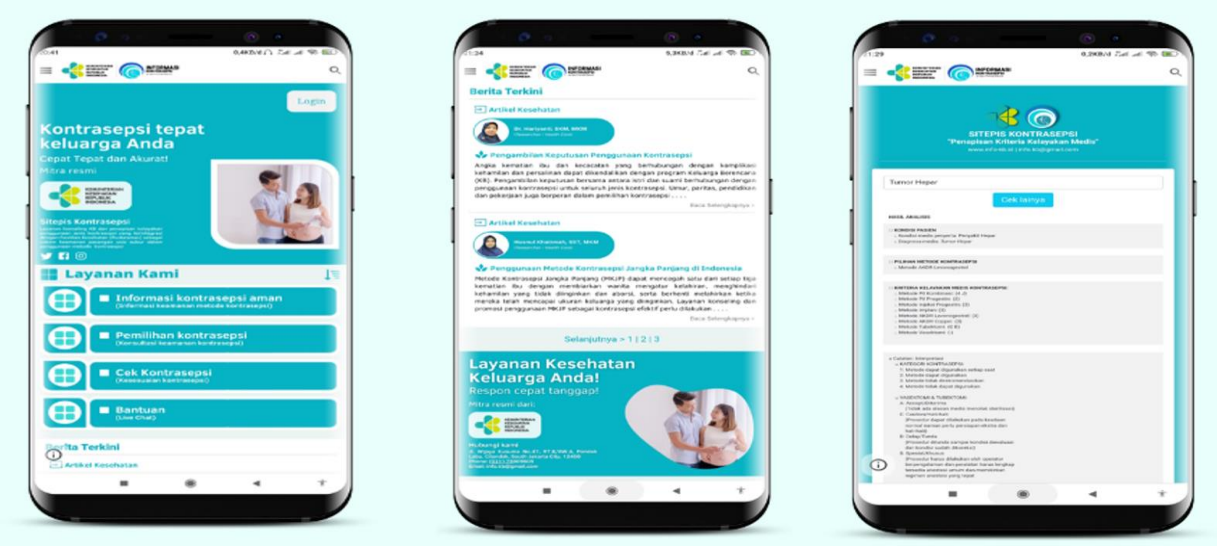


Figure 1. Contraceptive SITEPIS Website.

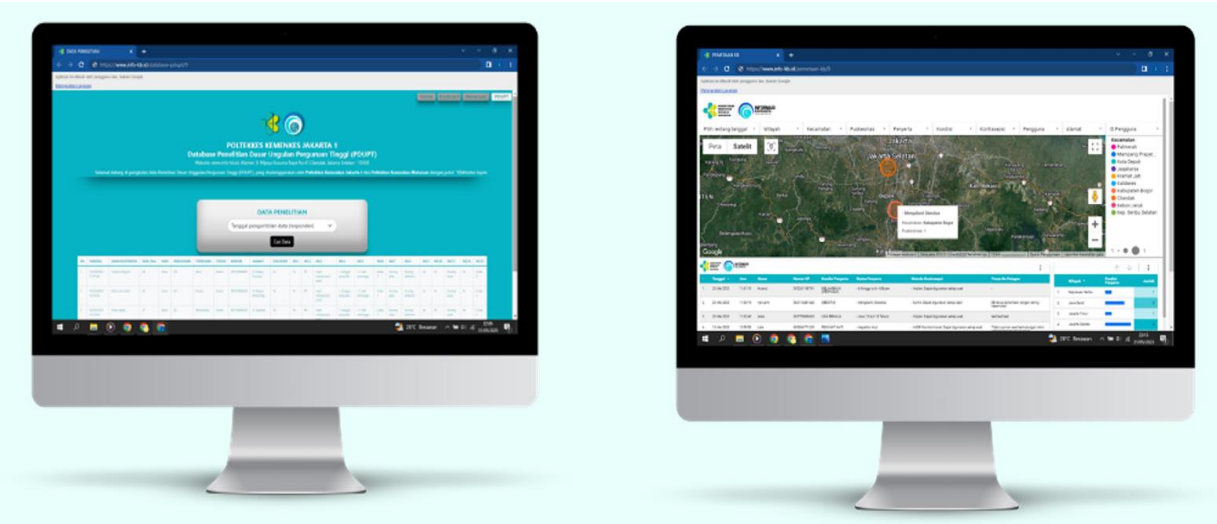


Figure 2. Display of data collection and respondent's residential area on the SITEPIS Contraceptives website.

To assess the functionality and usefulness of the website, the respondents at this stage were family planning officers consisting of midwives, PLKB, and family planning cadres who provide information services to the community at the sub-district and village levels in Bogor Regency and West Lombok Regency, totaling 28 respondents. The selection of respondents was carried out by purposive sampling. The research was conducted in June-July 2023. The data analysis used was descriptive analysis.

In addressing the research objectives, this study employs a descriptive approach by gathering information about SITEPIS Contraception from family planning officers who play a crucial role in providing family planning information. As a research protocol, the researcher obtained permission from the authorized administrators of the research site, in this case, by submitting a request for approval to the Health Department, DP2PKB, Regional Harmony and Political Affairs Office of Bogor Regency, and the Regional Development Planning Agency (Bappeda) of West Lombok Regency. The subsequent legal step involves conducting an ethical fitness test, and it was declared to have passed with the approval number LB.01.03/6/143/2023 issued by the Research Ethics Commission of Health Polytechnic Mataram.

The steps in data collection for this study involve conducting structured and systematic socialization of SITEPIS Contraception to family planning officers. The socialization activities are conducted for one day in each respective region. The socialization event begins with the opening of the research activities by the head of DP3P2KB, in conjunction with the Health Department in the Bogor Regency area, and the head of the community health center in the West Lombok Regency area. Subsequently, the researcher presents a comprehensive overview of SITEPIS Contraception and demonstrates how to utilize this contraceptive method. All respondents directly open and practice the utilization of SITEPIS Contraception. Subsequently, a discussion forum is opened, and at the end of the socialization, respondents are asked to provide assessments of SITEPIS Contraception. The assessment of SITEPIS by respondents is conducted using a questionnaire formulated by the instrument used to evaluate the effectiveness of online information media development. The aspects evaluated include appearance, ease of access, ease of understanding, functionality, and the usefulness of available features, as well as the support of the internet network in the research area.

The research respondents consist of family planning officers, including midwives, family planning counselors (PLKB), and health cadres, totaling 28 respondents. These officers were selected from districts with relatively low family planning achievement rates in the Bogor and West Lombok regencies. Additionally, selected respondents include family planning officers serving both the public and private sectors in their work areas, such as a selected midwife who serves as a coordinator at a community health center while also providing services in Independent Midwife Practice. Furthermore, some midwives also hold positions in professional organizations. Therefore, the information conveyed by these respondents will represent the roles of family planning information providers across various fields. In terms of sampling limitations, the researcher did not proportionally represent each type of family planning officer. However, this is not expected to introduce bias to the information, as midwives are the predominant source of contraceptive services in Indonesia.

3. RESULTS AND DISCUSSION

Table 1. Characteristics of Family Planning Officers in Bogor and West Lombok District in 2023.

Respondent Characteristics	**n**	**%**
Region		
Bogor District	11	39,3
West Lombok District	17	60,7
Position		
Midwife	24	85,7
PLKB	3	10,7
Family planning cadres	1	3,6
Education		
High school	1	3,6
D3 Midwifery	15	53,6

D4/S1 Midwifery	6	21,5
Midwife Profession	4	14,3
Bachelor of Non Health	2	7,1
Total	28	100

Most of the family planning officers in this study came from the West Lombok district and worked as midwives. Based on education level, more than half are D3 Midwifery. Midwives are health workers who mostly provide counseling services. Health care practitioners (midwives) provide information to women and offer them all options of contraceptive methods, as soon as possible within 7 days after delivery (NICE, 2016; Jawad, Jawad, & Alwan, 2019).

Health workers who can provide contraceptive counseling include doctors with various specialties (for example family medicine, pediatrics, obstetrics and gynecology, nurse practitioners, physician assistants, midwives, community health workers, and cadres (Coulter, Jacobson, & Parker, 2000). Personal biases can hinder the ability of health workers to assess clients' needs as a whole and create barriers to choosing contraception. These health workers come from various educational backgrounds, so they have different competence and ability levels in the provision of contraception. Contraceptive counseling practices can also be influenced by their perceptions of the risks of pregnancy, understanding of the adequacy of contraception for certain populations (including eligibility for medical), and training that has been followed (Akers, et al., 2010).

The research results indicate that the majority of respondent characteristics are distributed across several categories. For instance, the most common type of family planning officer in this study is a midwife, and the educational level is predominantly D3 in midwifery. This suggests that the characteristics of the respondents are homogeneous, posing limitations in further analysis. Consequently, the presentation is focused on providing an overview of the respondents' assessments of SITEPIS Contraception without linking these assessments to specific respondent characteristics. Another limitation of this study is the failure to explore information about cultural factors that could potentially influence the research outcomes. Geography is one of the factors influencing internet connectivity. This challenge can be addressed by improving internet access in remote locations through collaboration with the Ministry of Communication and Information.

Table 2. Age and Length of Service Characteristics of Family Planning Officers in Bogor and West Lombok District in 2023.

Variable	**n**	**Average**	**SD**	**Minimum - Maximum**
Age	28	41,6	9	26 - 53
Length of Service	28	17,7	11	0,8 - 33

The age of family planning officers ranged from 26 to 53 years, with an average of 41.6 years. Based on the length of work, it ranges from less than 1 year to 33 years, with an average of 17.7 years.

Table 3. Assessment of Contraceptive Cypriot Websites by Family Planning Officers in Bogor and West Lombok District in 2023.

Website SITEPIS Contraception	**n**	**%**
Display		
Good	23	82,1
Very good	5	17,9
Ease of access		
Good	24	85,7
Very good	4	14,3

Easy to Understand Information		
Good	22	78,6
Very good	6	21,4
Feature		
Good	21	75,0
Very good	7	25,0
Internet Network Support		
Bad	3	10,7
Good	23	82,1
Very good	2	7,1
Total	28	100,0

The family planning officer's assessment of the contraceptive SITEPIS website in terms of appearance, ease of access, easy-to-understand information, and features received good and very good marks. Meanwhile, in the aspect of internet network support, 10.7% of family planning officers gave a bad rating.

Digital health, or the use of digital technologies for health, has become a dominant area of practice in the routine and innovative application of information and communication technologies (Okunlola, 2023; Ugaz, Correa, and E. DeGraw, 2021). Digital technologies provide new opportunities to address health system challenges and offer the potential to improve the scope and quality of healthcare practice. Digital health interventions can be used to facilitate communication with individuals through reminders and health promotion messages to expand access to health information. Digital health interventions can also be targeted at healthcare workers to provide them with quicker access through clinical protocols, decision support mechanisms, or telemedicine consultations with other healthcare workers (Beyond the Phill at UCSF Bixby Center for Global Reproductive Health, 2017; World Health Organization, 2019; Zapata et al., 2015).

The results of the evaluation of the SITEPIS contraceptive website, which is used to assist family planning officers in conveying contraceptive information to the public, is considered to have an attractive appearance, ease of access, easy-to-understand information, and good features. However, currently, the method of providing information that is most preferred or frequently used by health workers is face-to-face counseling.

Healthcare providers trained with supporting processes such as software applications can improve healthcare delivery, strengthen health systems, and support clients. There is increasing evidence that technology can produce time and resource efficiencies and improve the quality of services resulting in better patient outcomes. The World Health Organization (WHO) has issued recommendations for digital interventions to strengthen health systems (World Health Organization, 2019).

Table 4. Methods of Providing Information and Readiness to Use SITEPIS Contraception by Family Planning Officers in Bogor and West Lombok Regencies in 2023.

Methods of Providing Information and Willingness to Use SITEPIS Contraception	**n**	**%**
The method of providing information most preferred or frequently used by officers		
Face to face	27	96,4
On line	1	3,6
Willing to use the SITEPIS contraception website		
Yes	28	100,0
No	0	0,0
Total	28	100,0

The results of a study regarding methods of providing information showed that almost all family planning officers stated that they preferred the face-to-face method compared to online. However, all family planning officers are willing to use the contraceptive site website in carrying out their duties of providing information to the public. This is a very important aspect of family planning services. Quality counseling between clients and providers (medical personnel) is one of the indicators that determine the success of the family planning program (Nirwana, et al., 2023). Assisting also includes the counselor's willingness to listen to the client's life journey, both his past, hopes, unfulfilled desires, failures experienced, trauma, and conflicts that the client is currently facing. Counseling is a face-to-face meeting between two parties, where one party helps the other party to make the right decision for himself and then act according to his decision (Anggraini, Ariestantia, & Yusuf, 2023; Fatima, et al., 2018).

Studies have shown that provider recommendations have a significant and positive impact on patient initiation and choice of contraceptive methods. However, the provision of information highlights the importance of individualized contraceptive counseling through a process of shared decision-making, which is defined as an interactive process in which providers and patients communicate and arrive at mutually agreed decisions. Clients have reported many advantages to the web-based platform, including interactive and the ability to compare contraceptive methods using filters and sorting options. In addition, patients appreciate using decision-making tools before clinical visits to help them narrow their contraceptive options and prepare questions for their providers (Rezel-Potts, et al., 2020; Wu et al., 2020; Wu et al., 2018).

Healthcare providers highlight the benefits of telehealth, including continued access to contraceptive services and accommodating patients who face the challenge of having in-person contraceptive visits. However, many healthcare providers have noted a lack of patient awareness regarding the availability of telehealth services and disparities in access to technology. Service providers feel there is a lack of personal connection in contraceptive counseling if done virtually, are aware of the challenges in maintaining confidentiality, and express concern about the inability to provide all contraceptive methods via telehealth (Akers, et al., 2010; Fataar, Zweigenthal, & Harries, 2022; Lee, et al., 2011; Rao et al., 2022).

4. CONCLUSION

The SITEPIS Contraception website serves as a valuable informational tool for family planning officers, even though the predominant preference remains face-to-face interactions. While the utilization of online platforms presents an effective strategy to disseminate information across all societal levels, family planning officers in Indonesia have not fully embraced online methods as their primary approach. Nevertheless, the continued provision of online information holds the potential to significantly support family planning officers in their pivotal role as information providers. The challenge lies in the shift away from traditional counseling methods, yet this transition offers a promising opportunity to extend services to individuals facing barriers such as work commitments, geographical remoteness, and economic constraints. Government support and policies are integral to encouraging family planning officers to embrace online information services, thereby enhancing public understanding of contraceptive options tailored to individual needs. Additionally, the SITEPIS Contraception website enables the independent reporting of contraceptive conditions by individuals, allowing for the monitoring of community family planning behaviors. Although the current assessment primarily reflects the perspective of family planning officers, future research should expand to incorporate the viewpoint of the community, who are the ultimate beneficiaries of this online information service.

REFERENCES

Akers, A. Y., Gold, M. A., Borrero, S., Santucci, A., & Schwarz, E. B. (2010a). Providers' perspectives on challenges to contraceptive counseling in primary care settings. *Journal of Women's Health (2002)*, *19*(6), 1163–1170. https://doi.org/10.1089/jwh.2009.1735

Ali, M., & Tran, N. T. (2022). Defining counselling in contraceptive information and services: Outcomes from an expert think tank. *BMJ Sexual and Reproductive Health*, Vol. 48, pp. 79–81. https://doi.org/10.1136/bmjsrh-2021-201132

Anggraini, R. D., Ariestantia, D. R., & Yusuf, N. (2023). *Effectiveness of Mobile Website-Based SIPALING KB on The Selection of Contraceptive Methods*. *14*(02), 523–528.

Beyond the Phill at UCSF Bixby Center for Global Reproductive Health. (2017). *Policy Brief : Contraceptive Counseling, Impact Of Contraceptive Counseling On Patient Health Outcomes and Health Costs*. Beyond the Phill at UCSF Bixby Center for Global Reproductive Health.

Center for Reproductive Rights. (2011). *Briefing Paper the Right To Contraceptive Information and Services for Women and Adolescents. Center for Reproductive Rights.*

Coulter, I., Jacobson, P., & Parker, L. E. (2000). Sharing the mantle of primary female care: physicians, nurse practitioners, and physician assistants. *Journal of the American Medical Women's Association (1972)*, *55*(2), 100–103.

Fataar, K., Zweigenthal, V., & Harries, J. (2022). Providers' approaches to contraceptive provision in Cape Town. *Frontiers in Global Women's Health*, *3*, 917881. https://doi.org/10.3389/fgwh.2022.917881

Fatima, P., Antora, A. H., Dewan, F., Nash, S., & Sethi, M. (2018). Impact of contraceptive counselling training among counsellors participating in the FIGO postpartum intrauterine device initiative in Bangladesh. *International Journal of Gynecology and Obstetrics*, *143*, 49–55. https://doi.org/10.1002/ijgo.12605

Guttmacher Institute. (2020). Investing in sexual and reproductive health in low- and middle-income countries. *Guttmacher Institute*. Retrieved from https://www.guttmacher.org/fact-sheet/investing-sexual-and-reproductive-health-low-and-middle-income-countries

Jawad, A., Jawad, I., & Alwan, N. A. (2019). Interventions using social networking sites to promote contraception in women of reproductive age. *Cochrane Database of Systematic Reviews*. https://doi.org/10.1002/14651858.CD012521.pub2

Lee, J. K., Parisi, S. M., Akers, A. Y., Borrerro, S., & Schwarz, E. B. (2011). The Impact of contraceptive counseling in primary care on contraceptive use. *Journal of General Internal Medicine*, *26*(7), 731–736. https://doi.org/10.1007/s11606-011-1647-3

Nanda, K., Lebetkin, E., Steiner, M. J., Yacobson, I., & Dorflinger, L. J. (2020). Contraception in the era of COVID-19. *Global Health: Science and Practice*, *8*(2), 166-168. https://doi.org/10.9745/GHSP-D-20-00119

NICE. (2016). *Contraception*. NICE. Retrieved from https://www.nice.org.uk/guidance/qs129

Nirwana, B. S., Rofiah, K., Awatiszahro, A., Sari, B. F., & Arayan, A. D. (2023). The Effect Of Family Planning With ABPK Counseling On Decision Making Family Planning In Wus (Women Of Reproductive Age). *Journal for Quality in Public Health*, *6*(2), 346-351. https://doi.org/10.30994/jqph.v6i2.452

Okunlola, D. A., Alawode, O. A., Awoleye, A. F., & Ilesanmi, B. B. (2023). Internet use, exposure to digital family planning messages, and sexual agency among partnered women in Northern Nigeria: implications for digital family planning intervention. *Sexual and Reproductive Health Matters*, *31*(4), 2261681. https://doi.org/10.1080/26410397.2023.2261681

Rao, L., Comfort, A. B., Dojiri, S. S., Goodman, S., Yarger, J., Shah, N., … Harper, C. C. (2022). Telehealth for Contraceptive Services During the COVID-19 Pandemic :

Provider Perspectives. *Women's Health Issues*, *32*(5), 477–483. https://doi.org/10.1016/j.whi.2022.05.001

Rezel-Potts, E., Palmer, M. J., Free, C., & Baraitser, P. (2020). A cohort study of the service-users of online contraception. *BMJ Sexual and Reproductive Health*, Vol. 46, pp. 287–293. https://doi.org/10.1136/bmjsrh-2020-200610

Setiawati, R., Nurdiana, A., & Yanti, I. (2020). Rancang Bangun Aplikasi Penapisan Calon Akseptor KB Berbasis Android "Tapis Yuk". *Embrio: Jurnal Kebidanan*, *12*(2), 79-90. https://doi.org/10.36456/embrio.v12i2.2722

Samosir, O. B., Kiting, A. S., & Aninditya, F. (2020). Role of information and communication technology and women's empowerment in contraceptive discontinuation in Indonesia. *Journal of Preventive Medicine and Public Health*, *53*(2), 117–125. https://doi.org/10.3961/jpmph.19.300

Sserwanja, Q., Nuwabaine, L., Kamara, K., & Musaba, M. W. (2023). Determinants of quality contraceptive counselling information among young women in Sierra Leone: insights from the 2019 Sierra Leone demographic health survey. *BMC Women's Health*, *23*, 266. https://doi.org/10.1186/s12905-023-02419-8

Solo, J., & Festin, M. (2019). Provider bias in family planning services: a review of its meaning and manifestations. *Global Health: Science and Practice*, *7*(3), 371-385. https://doi.org/10.9745/GHSP-D-19-00130

Soin, K. S., Yeh, P. T., Gaffield, M. E., Ge, C., & Kennedy, C. E. (2022). Health workers' values and preferences regarding contraceptive methods globally: A systematic review. *Contraception*, *111*, 61–70. https://doi.org/10.1016/j.contraception.2022.04.012

Sundstrom, B., DeMaria, A. L., Ferrara, M., Meier, S., & Billings, D. (2019). "The closer, the better:" the role of telehealth in increasing contraceptive access among women in rural South Carolina. *Maternal and Child Health Journal*, *23*, 1196-1205. https://doi.org/10.1007/s10995-019-02750-3

Thompson, T. A., Ahrens, K. A., & Coplon, L. (2020). Virtually possible: using telehealth to bring reproductive health care to women with opioid use disorder in rural Maine. *mHealth*, *6*, 41. https://doi.org/10.21037/mhealth-19-237

Thompson, T. A., Sonalkar, S., Butler, J. L., & Grossman, D. (2020). Telemedicine for family planning: a scoping review. *Obstetrics and Gynecology Clinics*, *47*(2), 287-316. https://doi.org/10.1016/j.ogc.2020.02.004

Ugaz, J. K. Correa, and E. DeGraw. (2021). *Digital Health Tools to Enhance the Uptake and Use of Contraceptives and Family Planning Services: A Landscape Assessment.* Washington, DC: Palladium, Health Policy Plus.

World Health Organization. (2019). *WHO guideline: recommendations on digital interventions for health system strengthening*. World Health Organization. Retrieved from https://www.who.int/publications/i/item/9789241550505

Wu, A., March, L., Zheng, X., Huang, J., Wang, X., Zhao, J., Blyth, F. M., Smith, E., Buchbinder, R., & Hoy, D. (2020). Global low back pain prevalence and years lived with disability from 1990 to 2017: estimates from the Global Burden of Disease Study 2017. *Annals of translational medicine*, *8*(6), 299. https://doi.org/10.21037/atm.2020.02.175

Wu, J. P., Damschroder, L. J., Fetters, M. D., Zikmund-Fisher, B. J., Crabtree, B. F., Hudson, S. V., ... & Creswell, J. W. (2018). A web-based decision tool to improve contraceptive counseling for women with chronic medical conditions: Protocol for a mixed methods implementation study. *JMIR research protocols*, *7*(4), e9249. https://doi.org/10.2196/resprot.9249

Zapata, L. B., Tregear, S. J., Curtis, K. M., Tiller, M., Pazol, K., Mautone-Smith, N., & Gavin, L. E. (2015). Impact of Contraceptive Counseling in Clinical Settings: A Systematic Review. *American Journal of Preventive Medicine*, *49*(2), S31–S45. https://doi.org/10.1016/j.amepre.2015.03.023

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 782-794
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1336*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Revolution of Bone and Teeth Health: Study of Aloe Barbadensis Instant Powder Formulation

Fahmi Said[1a*], Ida Rahmawati[1b], Neny Setiawaty Ningsih[2c]

[1] Department of Dental Health, Poltekkes Kemenkes Banjarmasin, Banjarmasin, South Kalimantan, Indonesia
[2] Department of Dental Health, Poltekkes Kemenkes Pontianak, Pontianak, West Kalimantan, Indonesia

[a] Email address: fahmialai1959@gmail.com
[b] Email address: idarahmawati102@gmail.com
[c] Email address: nenysetiawaty26@gmail.com

Received: 11 September 2023 Revised: 21 December 2023 Accepted: 31 December 2023

Abstract

Aloe barbadensis is a plant with many applications such as anti-inflammatory, anti-fungal, anti-bacterial, and aiding in cell regeneration. Understanding aloe barbadensis' phytochemical profile and pharmacological action is essential since it is believed to have an impact on the formation of teeth and bones. The stability and bioavailability of Aloe barbadensis can be improved by formulating it as an instant powder. The research's objectives are to ascertain the Aloe barbadensis instant powder's qualitative and quantitative phytochemical profile, dosage formulations, and activity testing on hemoglobin, cholesterol, and red blood cell parameters. Samples of aloe barbadensis were washed, and they were then dried for 72 hours at 50°C. Following a maceration process using a 70% ethanol solvent, the extract was dried. Phytochemical screening, TLC profile, and extract description were employed to test the extract qualitatively. The quantities of total flavonoids, total anthraquinones, and total phenolics were determined to quantitatively test the extract. The formulation of the instant powder was then completed and evaluated on female mice using metrics associated with red blood cells, hemoglobin, and cholesterol levels. Furthermore, observations were made on the mice's liver organs. The study's findings revealed a qualitative profile of Aloe barbadensis extract, which included a tasteless, unique odor, milky white hue, and liquid shape. Aloe barbadensis has been demonstrated to contain flavonoids, phenolics, tannins, saponins, and anthraquinones, according to the results of phytochemical screening. Three spots, identified as Rf 3.2 and Rf 8.5 in the Rf 2.3 area, are visible in the chromatographic pattern. Total anthraquinones were discovered to be 4.59%, total flavonoids to be 0.24%, and total phenolic content to be 1.42%. The third formula of instant Aloe barbadensis pollen has been demonstrated through preclinical examinations to have the capacity to reduce cholesterol, boost hemoglobin, and enhance red blood cell count—all of which are associated with the growth of teeth and bones. An SPSS statistical study demonstrating statistically significant differences with other groups supports this. Mice liver histopathological examinations revealed no liver damage in any of the test groups.

Keywords: Phytochemical Analysis, Oral Health, Clinical Trials.

Corresponding Author:

Fahmi Said
Department of Dental Health, Poltekkes Kemenkes Banjarmasin, Banjarmasin, South Kalimantan, Indonesia
Email: fahmialai1959@gmail.com

1. INTRODUCTION

In contrast to other varieties of aloe, Aloe barbadensis (also known as Aloe barbadensis L.) is a plant from a tribe that is widely used and farmed (Sánchez et al., 2020). People have been using aloe as medicine for hundreds of years, starting in ancient Egypt and continuing through Greece, Rome, China, and India (Sadoyu et al., 2021). The plant Aloe barbadensis possesses several qualities, such as anti-inflammatory, anti-fungal, anti-bacterial, and aids in cell regeneration. Aloe barbadensis has been identified in other studies to have anti-infection properties for skin and burn wounds, as well as laxative properties for its leaves (Guo & Mei, 2016). There is also substantial evidence that aloe barbadensis may affect the growth of human teeth and bones (Kumar et al., 2019). This provides many opportunities for the use of Aloe barbadensis in the field of dentistry.

In Indonesia, aloe barbadensis is prevalent throughout the country, however, studies have indicated that the most optimal locations for discovering it are in West Kalimantan Province (Said et al., 2023). When compared to other plants from South Kalimantan, aloe barbadensis has the highest concentration of active chemicals. The plant's active components are influenced by the environment in which it grows (Adawiyah & Rizki, 2018). The temperature, humidity, rainfall, and environmental factors surrounding the growing region all have an impact on this. To ensure optimal activity, carefully selected plants should originate from growth locations that are optimum for ideal growing conditions.

Standardization is required for natural ingredients intended for use as pharmaceuticals (Sari et al., 2023). Analyzing the plant's unique characteristics can help achieve standardization (Rizki, 2020). Qualitative profiles, chromatographic profiles, phytochemical screening, and quantitative analysis of plant active component levels are examples of specific parameters (Zainab et al., 2022). This is crucial to guarantee the quality of the extract that will be examined for toxicity and pharmacological activity. The effectiveness of a natural element will depend on several factors (Sari et al., 2023). Acquiring the right amount of aloin is crucial because it is the primary ingredient that provides many of the health advantages of aloe barbadensis.

The body's ability to endure and absorb natural compounds is limited (Fitriana et al., 2022). According to Chabib et al. (2015), it is crucial to formulate natural components in dosage form to guarantee their stability and bioavailability. Furthermore, the dosage form will help patients accept the substance. An instant powder formulation is a powdered solid preparation that comprises sugar as one of its ingredients. Instant powder has many benefits, such as ease of formulation, production, and packaging (Deglas & Apriliani, 2022). In addition, users simply need to dissolve instant powder in water because it contains sugar, which provides it a delicious taste (Lubis et al., 2023). Since it can be ingested warm with hot water or cold with ice cubes, its application is more adaptable. It will be simpler for both adults and children to use Aloe barbadensis according to its quick powder format.

It is possible to assess a preparation's pharmacological activity both in vitro and in vivo (Rizki et al., 2021). Because it is conducted directly on live things, in-vivo testing is recommended (Utami et al., 2023). Test animals are available for the test for aloe barbadensis utilizing a variety of techniques and specifications (Utami et al., 2022). As a result of slowing down the body's metabolism, high cholesterol can contribute to a postponement of children's tooth and bone growth. Bone and tooth growth can be impacted by high or low cholesterol levels, as cholesterol performs an essential role in controlling bone and tooth metabolism (Yin et al., 2019). The development of teeth and bones is influenced by hemoglobin and red blood cells. There is a correlation between the prevalence of stomatitis in the teeth and the incidence of iron deficiency, which results in anemia (Mersil, 2021). Bone development is slowed by decreased red blood cell counts (Bernado et al., 2016). Determining the extract's qualitative-quantitative profile, preparation formulation, and activity test on hemoglobin, red blood cell,

and cholesterol parameters from Aloe barbadensis instant powder are the primary objectives of this study.

2. RESEARCH METHOD

This research is experimental research involving instant powder testing on test animals. The following tools were used in this research: a hot plate stirrer (Stuart), a measuring flask (Herma), a UV lamp with a wavelength of 254 and 366 nm, a macerator, a microscope, an object glass, an oven (Vinco), a volume pipette (Iwaki), a propipet (Vitalab), an analytical balance (Pioner), a vortex (Jeio Tech), and a water bath (SMIC).

Aloin fruit peel (Sigma-Aldrich), quercetin (Sigma-Aldrich), distilled water (CV.Viana), Cd(NO2)3 (Merck), ethanol (pa) (Sigma-Aldrich), ethanol (CV.Viana), ethyl acetate (Merck), FeCl3 (Merck), fluoroglucin (Merck), 1% gelatin, potassium hydroxide (Merck), paper Whatman strain, Dragendorff reagent (Merck), Folin-Ciocalteau reagent 5% (Sigma-Aldrich), Mayer reagent, toluene (Merck), alpha mangostin (Sigma-Aldrich), and pregnant female rats were the ingredients in this study. The research will be conducted at the Banjarmasin Pucuk Sirih Herbal Medicine Factory Laboratory which already has a certificate on Good Traditional Medicine Manufacturing Methods (CPOTB) and the Banjarbaru Industrial Research and Standardization Center (Baristan).

The first thing that has to happen when conducting research with live things is research ethics testing. The Muhammadiyah University of Banjarmasin Ethics Committee conducted the ethical evaluation using Statement of Research Ethics Eligibility No. 492/UMB/KE/VI/2023.

Preparation and Manufacture of Extracts. Aloe barbadensis is cleaned and divided into two sections with a knife, and the interior flesh is removed. It is then weighed and allowed to dry for 72 hours at 50°C in a drying cabinet (Rizki et al., 2023). Aloe barbadensis which had been dried was weighed and ground into a powder. After weighing the powder, it was combined with pro-analysis ethanol solvent and heated to 70°C for six hours. The filter paper was used to filter the mixture. Repeated extraction of the filtered residue is required to obtain a clear solution. The filtrate is gathered, dried above a water bath, and then evaporated using a solvent-rotary evaporator (Ikalinus et al., 2015).

Qualitative Phytochemical Profile. The extract's color, taste, smell, and establishment are all highlighted. After the substance under examination had been exposed to air for fifteen minutes, the extract description test was conducted using all five senses. Descriptive explanations are provided for the analysis and display of color, taste, smell, and form data (Marliana et al., 2005). Phytochemical screening incorporates testing using reagents. Tests were conducted for the presence of alkaloids, flavonoids, terpenoids, steroids, saponins, tannins, phenolics and anthraquinones (Panchal & Parvez, 2019; Rizki et al., 2021).

Chromatogram Pattern. A total of 0.1 g of the extract was weighed, and 1 mL of 96% ethanol was applied to dissolve it (Sonam et al., 2017). Spotted on GF TLC plate 254, the solution was eluted with a mobile phase-hexane: ethyl acetate at 4:6 (v/v) and 3:7 (v/v) ratios, respectively. The spots were observed using UV lamps with wavelengths of 254 and 366 nm. For each examined sample, the Rf value was computed and compared (Marliana et al., 2005).

Qualitative Content Up to Phenolic Total. Total phenolic content was ascertained by applying gallic acid standards. Gallic acid standard solution and sample were combined in 0.5 mL with 2.5 mL of 5% Folin Ciocalteau reagent, shaken until smooth, and allowed to sit for 8 minutes. Afterwards, 2 mL of NaOH solution was added, vortexed until smooth, and the mixture was allowed to sit for 30 minutes. A UV-Vis spectrophotometer operating at a wavelength of 742 nm was utilized to measure the absorbance (Rizki et al., 2022).

Determination of total flavonoid levels utilizing quercetin standard. A total of 0.5 mL of solution was added with 1.5 mL of ethanol p.a., 0.1 mL of $AlCl_3$ 10%, 0.1 mL of 5% acetic acid, and 2.8 mL of distilled water in a test tube. Leave it for 20 minutes, absorbance is read employing UV-Vis spectrophotometry at a maximum wavelength of 418 nm (Anwar et al., 2017).

Aloin standards are applied to determine the levels of total anthraquinone. A 5 ml measuring flask was filled with 4 ml of solution, 100 µL KOH 5% was added, and then methanol was added gradually until the mark was reached. The mixture was shaken until it was homogenous, and allowed to stand within the operating time range, and the absorbance was determined using UV-Vis spectrophotometry at the maximum wavelength (Mutiara et al., 2007).

The process of formulation is performed by trial and error. The recipe calls for popular instant powder components, such as lychee flavoring, distilled water, and granulated sugar. For pharmacological testing, a formula that can produce immediate powder will be utilized (Lubis et al., 2023).

Pharmacological Test. White pregnant mice (the rat was born) and twenty Wistar females were utilized as test subjects. The female test subject weighed between 250 and 300 grams. Mice were acclimated (adjusted to their surroundings) for seven days. The test animals were placed in the following treatment groups:

a. Normal Control Group (KN), that is a group of test animals that were given standard food and drink for 14 days.
b. Normal Treatment Control Group (KNP0), that is a group of test animals that were given standard food and drink for 14 days.
c. Treatment Group 1 (KP1), that is a group of test animals that were given standard food and drink, as well as a dose of instant powder 500 Mg/KgBW/Day on days 13-19.
d. Treatment Group 2 (KP2), that is the group of test animals that were given standard food and drink, as well as a dose of instant powder 1000 Mg/KgBW/Day on days 13-19.
e. Treatment Group 3 (KP2), that is the group of test animals that were given standard food and drink, as well as a dose of instant powder 2000 Mg/KgBW/Day on days 13-19 (Wijayatri, 2017).

Before initiating the medication, the mice's blood was extracted and their total blood hematological was examined. To assess the effect of the treatment, a complete blood hematological examination was carried out after it was finished. Next, following the ethical treatment of animals, the mice were put to death. Mice were operated upon, and their liver organs were examined under a microscope to determine the toxicity of the instant powder (Yolanda et al., 2022).

The investigation produced quantitative and qualitative data on extract samples that were descriptively examined as the research's output. Hematology tests were utilized in preclinical testing to compare pre-and post-test findings, and rat organs and fetuses were observed visually.

3. RESULTS AND DISCUSSION

The extract's qualitative characteristics include a tasteless, unique odor, milky white hue, and liquid shape. The Aloe barbadensis meat that has been suspended in distilled water is what provides it its signature milky white hue. The reason the extract has no taste is because Aloe barbadensis does not normally have any taste. The smell that was detected is the characteristic scent of Aloe barbadensis; it is similar to the scent of grass and is unique to Aloe barbadensis alone. The reason for the liquid extract form is that distilled water is added to Aloe barbadensis to increase its dominance, resulting in a liquid extract (Quaye et al., 2023).

Phytochemical Screening Profile. The extract obtained was then identified for the presence of secondary metabolite compounds. This presence was measured utilizing phytochemical screening as presented in the table below.

Table 1. Phytochemical Screening.

No	Phytochemicals	Reactor	Results
1.	Flavonoid	Magnesium and Hydrochloric Acid	+
2.	Phenolic	Iron Chloride	+
3.	Alkaloid	Reagan Meyer	-
4.	Tannin	Gelatin Solution	+
5.	Saponin	Aquades	+
6.	Steroid	Lieberman Burchard	-
7.	Terpenoids	Lieberman Burchard	-
8.	Anthraquinone	KOH 10%	+

Chemicals are employed in tubes for phytochemical screening. As a result, the tube method or reagent method are other names for the phytochemical screening procedure. Aloe barbadensis is believed to contain flavonoids, phenolics, tannins, saponins, and anthraquinones, according to the results of phytochemical screening. Steroids, terpenoids, and alkaloids are absent from aloe barbadensis. These findings are consistent with phytochemical screening results from prior studies (Guo & Mei, 2016), which discovered that Aloe barbadensis includes flavonoids, anthraquinones, saponins, and tannins. Since Aloe barbadensis is known to be high in water, it is unlikely to contain terpenoid or steroid chemicals, which tend to be non-polar or insoluble in water. In Aloe barbadensis, alkaloids are not recognized, despite the reality that they can be identified in some fruit flesh (Ngibad, 2019). Alkaloids are not found in several fruit flesh types. Since every plant is unique, it is possible that a group will not be present in a certain species of plant (Said et al., 2023).

The growth of teeth and bones will be supported with aloe barbadensis. Pathogens can cause problems in the development of teeth and bones. Because bacteria in teeth can harm tooth components, it's critical to employ natural compounds with antibacterial properties, such as aloe barbadensis, which contains flavonoids, phenolics, and tannins. Natural components have also been demonstrated to be safe on a large scale, therefore using them in the mouth is not extremely dangerous. It has also been demonstrated that these secondary metabolites lessen the development of oral illnesses and tooth plaque (Kumar et al., 2021).

Chromatographic Pattern. The objective of chromatography pattern testing is to ascertain the extract's separation pattern on the silica plate. One of the extract's identities—along with a component of extract standardization—will be this pattern of separation. A feature of an extract can be its chromatographic pattern, which can serve as an identifying marker. The table below displays the chromatographic pattern's results.

Table 2. Chromatographic Pattern.

Condition	Chromatography Results	Nilai Rf
Mobile phase n-hexane: ethyl acetate (7:3) Silent phase silica gel 60 F254		Rf_1 = 2,3 Rf_2 = 3,2 Rf_1 = 8,5

The results of the extract's separation or elution on a chromatography plate or silica plate employing a certain mobile phase (solution) generate the chromatographic pattern. Aloe barbadensis extract is chromatographed using a stationary phase comprising a silica plate that fluoresces at a wavelength of 254 and a mobile phase of n-hexane and ethyl acetate at a composition of 7 to 3. Three spots appear on the plate once the extract has been spotted there and the mobile phase has been eluted. The three sets of spots represent the division of active chemicals. These patches show up in the regions of Rf 2.3, Rf 3.2, and Rf 8.5. This is the identification of the Aloe barbadensis extract, which has three spots with spot positions Rf 2.3, Rf 3.2, and Rf 8.5 in the silica gel stationary phase and the mobile phase above. If you ever want to verify the accuracy of the Aloe barbadensis extract, you can utilize this data as identity data (Rizki, 2020).

It is evident from the spot results that certain compound groups are highly patterned (2 bottom spots) and non-polar (1 top spot). According to Marliana et al. (2005), the results demonstrate that Aloe barbadensis still contains some somewhat nonpolar compounds. These compounds are most likely derived from flavonoids, some of which are less polar. On the other hand, the majority of the spots at the bottom are indicative of the presence of groups of compounds that tend to be polar, such as phenolics, saponins, tannins, and anthraquinones.

As part of the quantitative analysis, the amounts of Aloe barbadensis extract are ascertained. One of an extract's quality parameters includes this analysis. Quercetin is employed to determine total flavonoid content, aloin is used to estimate anthraquinone content, and gallic acid standards are utilized to determine total phenolic content. Table III displays the assay's findings.

Table 3. Extract Active Ingredients Rate.

No	Phytochemicals	Standard	Replication	Much	Percent Content
1.	Phenolic	Gallic Acid	1	14,09 µg/mg	1,40 %
			2	14,58 µg/mg	1,45 %
			3	14,19 µg/mg	1,41 %
	Rate			14,29 µg/mg	1,42 %
2.	Flavonoid	Quercetin	1	2,45 µg/mg	0,24 %
			2	2,59 µg/mg	0,25 %
			3	2,33 µg/mg	0,23 %
	Rate			2,46 µg/mg	0,24 %
.	Anthraquinone	I started	1	46,10 µg/mg	4,61 %
			2	45,78 µg/mg	4,57 %
			3	46,10 µg/mg	4,61 %
	Rate			45,99 µg/mg	4,59 %

As per the Indonesian Herbal Pharmacopoeia, level determination is an integral component in standardizing extracts of natural ingredients. The total phenolic content analysis revealed that the extract had an average total phenolic content of 1.42% of its total weight. Typically, the extract's total flavonoid content is less than 0.24% of its total weight. It is known that the anthraquinone content averages 4.59%. These findings demonstrate that anthraquinones predominate in Aloe barbadensis flesh. This is consistent with other studies showing that the anthraquinone group is the dominating group in Aloe barbadensis. Phytochemical screening also revealed the presence and amounts of anthraquinones, which is consistent with the results. The anthraquinone levels found were somewhat higher than the 4.48% anthraquinone levels observed in prior investigations including Aloe barbadensis (Mutiara et al., 2007). This indicates that the findings in this study and those from related studies are not all that different.

Phenolics are identified to be greater than the flavonoid group. This is because the phenolic group of chemicals is present in an extensive range of plants. Flavonoid and tannin chemicals are likewise included in total phenolics, and they similarly build up. Therefore, the phenolic group will often have a higher content than the flavonoid group. Although not all phenolics will be discovered in the flavonoid group, the flavonoid group is a component of the phenolic group. The amount of Aloe barbadensis utilized will be revealed by the data gathered for this study. When materials from different locations are used, one of the quality parameters will be the amount of active chemicals. To preserve the extract's effectiveness, the concentration of each element used—especially when using it in multiple locations—should ideally be ascertained. Low levels will affect the low efficacy that follows (Rizki, 2020).

The pharmacological activity of the sample will be correlated with high levels of total flavonoids and total phenolics. Aloe barbadensis is used in conjunction with phenolics and flavonoids to suppress the formation of bacteria in the mouth and prevent plaque on teeth. Aloe barbadensis can be used to avoid dental issues and promote healthy tooth growth. Elevated phenolic and flavonoid content will boost metabolic functions, speeding up the process of bone formation. The primary chemical in aloe barbadensis that produces the action is anthraquinone. According to Guo and Mei (2016), anthraquinones have anti-inflammatory, antibacterial, and anti-caries effects. Its anti-inflammatory properties will shield teeth wounds from discomfort and hasten their healing. This ability will support aloe barbadensis in its use as a supplement to support tooth and bone growth (Quaye et al., 2023).

Preparation of Formulation. The extracted aloe barbadensis is then combined with other ingredients to create a dosage form. The active components' stability will be preserved and their use will be made easier by the dosage formulation. To facilitate the acceptance or consumption of the chemicals employed, formulation is crucial. The table below displays the dose formula that was derived from the optimization results.

Table 4. Preparation of Formulation

No	Material	Function	Material Weight
1.	Aloe barbadensis flesh	Active Ingredients	100 grams
2.	Granulated sugar	Filling Material	500 grams
3.	Aquades	Solvent	1000 mL
4.	Lychee Flavoring	Seasoning	1 mL

Direct consumption of aloe barbadensis tends to be less acceptable because of its strong odor. It is hard to eat because the fragrance is similar to that of grass. Patients have to discover the dose form to be convenient to use and agreeable. The preparation that was selected is a powder that includes lychee flavoring to mask the off-putting taste and smell of aloe barbadensis, granulated sugar as a filler and sweetener, distilled water as a solvent, and aloe barbadensis as the active ingredient (Deglas & Apriliani, 2022). Through trial and error and compositional tinkering, the formulation that was arrived at was achieved. Following several tests, the mixture indicated in the formula table proved to be the ideal formula.

The powder formulation of aloe barbadensis will make it easier to use. Aloe barbadensis has a disagreeable smell, and when placed in the open it becomes less stable; this formulation will help to keep it fresher and simpler to use. During storage, the powder dose form exhibits greater stability. To use it, simply add water and consume. Aloe barbadensis is easily absorbed by the body because it enters the digestive tract in solution form. Rapid and simple absorption will expedite the intended outcome. Aloe barbadensis powder is a supplement that promotes the growth of teeth and bones. Children who are in the stage of tooth and bone growth will be more receptive to this preparation if it is easy to use. The calcium and magnesium contained in Aloe barbadensis tend to dissolve in water, making it easier to formulate preparations (Fiorentini et al., 2021).

Test animal preparation is the first step in preclinical testing. The test subjects were Wistar strain pregnant female white rats. For seven days, the test animals were acclimated to their cages. Blood hematology, including hemoglobin, cholesterol, and red blood cell counts, are measured prior to testing. It is well-recognized that high cholesterol exacerbates bone disorders. An excessive amount of cholesterol raises the risk of malnutrition (Yin et al., 2019). Anemia is associated with quantities of red blood cells and hemoglobin. The spine produces red blood cells, which are correlated with the spine's health (Quaye et al., 2023). Figure 1 below illustrates the duration of the test animals' treatment and the procedure used for collecting blood from them.

Figure 1. Treatment and Blood Collection

An oral probe was employed to provide therapy to test animals in both the three-dose treatment group and the normal control group. Giving takes place up until the fourteenth day. After the course of treatment, another blood sample was obtained. The mouse orbital sinus in its eye is utilized for blood collection, which has the benefit of allowing for the extraction of 1–2 mL of blood, which facilitates hematological analysis (Sharma et al., 2014). The table below displays the research findings as data from hematological test results.

The study of mouse blood samples using parameters related to cholesterol levels was performed both before and after the treatment. Before the study, the values of cholesterol in all groups were quite similar. The cholesterol levels of each test animal were normal. Furthermore, treatment 1, treatment 2, and treatment 3 groups got Aloe barbadensis at varying doses, whereas the positive control group mice received simvastatin as a cholesterol reducer. Hematological test results collected after the fourteenth day revealed that the normal group's cholesterol levels increased as a result of the mice's constant feeding while they received no medical attention. The delivery of simvastatin, which can lower cholesterol levels, caused the levels of cholesterol in the positive control group to decrease.

Table 5. Rat Cholesterol Test Results

No	Group	Replication	Up to Cholesterol		Up to Hemoglobin		Red Blood Cell Rate (Million/mm3)	
			Before	After	Before	After	Before	After
1	Normal Control Group (KN)	1	45	53	12,3	12,4	8,1	8,2
		2	46	54	13,4	12,8	7,9	7,5
		3	46	56	12,8	13,1	8,3	7,8
		4	45	58	12,9	12,6	7,4	8,1
		Rate	45,5	55,25	12,8	12.7	7,9	7,9

2	Positive Control Group (KKP)	1	44	38	12,4	12,3	8,2	7,4
		2	45	36	12,5	12,5	8,1	8,4
		3	45	38	13,4	13,1	7,6	8,3
		4	48	37	13,1	12,8	8,4	8,1
		Rate	45,5	37,25	12,8	12,6	8,0	8,0
3	Treatment Group 1 (KP1)	1	44	47	13,4	12,4	7,6	8,1
		2	48	47	12,3	13,1	7,9	8,1
		3	46	48	12,5	12,5	8,4	8,3
		4	47	49	13,1	13,2	8,6	7,9
		Rate	46,25	47,75	12,8	12,8	8,4	8,3
4	Treatment Group 2 (KP2)	1	44	43	13,4	13,1	7,9	8,1
		2	46	43	13,1	13,4	7,8	8,2
		3	46	42	12,7	13,4	8,4	8,7
		4	47	41	12,9	13,5	8,1	8,8
		Rate	45,75	42,25	13,0	13,3	8,1	8,4
5	Treatment Group 3 (KP2)	1	47	38	12,4	15,6	8,1	10,2
		2	45	36	13,2	15,1	7,9	9,5
		3	47	38	13,1	15,2	8,1	9,4
		4	47	37	12,6	14,9	7,6	9,8
		Rate	46,5	37,25	12,8	15,2	7,9	9,7

The results of statistical analysis using SPSS demonstrated that there were significant differences between treatment groups 1, 2, and 3 and the normal control group. This demonstrates how administering instant powder affects variations in cholesterol levels. When comparing the positive control group to treatment 3, statistical analysis using SPSS revealed no significant changes. This indicates that treatment 3 can perform on par with the positive control. Children's teeth and bone development are believed to be slowed down in those with high cholesterol. Elevated cholesterol levels cause the body's metabolism to slow down, which hinders the growth of teeth and bones. Low or high cholesterol can have an impact on tooth and bone formation because cholesterol regulates the metabolism of bones and teeth (Yin et al., 2019). Children will have stunted bone and dental growth if they receive inadequate nutrition, particularly in the areas of calcium and magnesium. The eruption status of the mandibular permanent central incisors correlates significantly with poor nutrition (Rahmawati et al., 2014). Previous studies have indicated that aloe barbadensis contains calcium and magnesium, both of which are essential for the development of teeth and bones. Teeth are critical to the body since they are primarily composed of calcium and magnesium (Said et al., 2023).

Hemoglobin level parameters from mice blood analysis were performed both before and after treatment. Before the trial, there were not many differences in the hemoglobin levels among all groups. Before testing, the hemoglobin levels of each test animal were normal. Furthermore, because the same mice were utilized for all treatments, the mice in the positive control group received simvastatin, but the mice in the treatment 1, treatment 2, and treatment 3 groups received varying amounts of aloe barbadensis for each treatment. Hematology test results received after the fourteenth day indicated that the normal group's hemoglobin levels had not significantly changed from the previous day. Simvastatin had no influence on hemoglobin levels, which explains why hemoglobin levels in the positive control group likewise remained unchanged.

In treatment groups 1 and 2 there were no significant differences between before and after treatment. It was discovered that the mice in treatment group 3 had higher hemoglobin levels. These findings suggest that giving mice three doses of Aloe barbadensis for a period of 14 days

can raise their hemoglobin levels. There were noteworthy distinctions between treatment group 3 and the other treatment groups, according to the findings of the statistical analysis conducted with SPSS. This demonstrates how fast powder may raise mice's hemoglobin levels. The incidence of anemia, which is correlated with the growth of teeth and bones, is related to hemoglobin. Patients with low hemoglobin levels have poor bone and tooth growth potential. This is also correlated with the rate of wound healing in patients with low hemoglobin levels following tooth extraction. Hemoglobin also affects bone mineral density. Low hemoglobin levels can cause low bone density. Low hemoglobin levels can also escalate the risk of bone fractures (Yoon et al., 2016).

Red blood cell parameters from mouse blood analysis were measured both before and after therapy. The objective is to ascertain how the medication affects the levels of red blood cells in rats. Before the trial, the red blood cell counts in each group were essentially the same. Prior to testing, the red blood cell counts of all test animals were normal. Furthermore, because the same mice were utilized for all treatments, the mice in the positive control group received simvastatin, but the mice in treatment 1, treatment 2, and treatment 3 groups received varying amounts of aloe barbadensis for each treatment. Hematological test results received after the fourteenth day indicated that the normal group's red blood cell levels had not significantly changed from the initial values. In the positive control group, red blood cell levels also did not change, this is because simvastatin did not have any effect on red blood cell levels. There were no discernible differences between the pre- and post-treatment periods in treatment groups 1 or 2. There was a rise in red blood cell counts in treatment group 3. The statistical analysis conducted using SPSS revealed significant differences between all groups and treatment 3. This demonstrates that treatment 3 can raise the number of red blood cells in mice. These findings suggest that mice's red blood cells were able to proliferate by receiving a third dosage of Aloe barbadensis. Bone development and red blood cells are closely connected processes. Because hematopoiesis and bone homeostasis are interconnected, low red blood cell counts may be a sign of bone health issues.

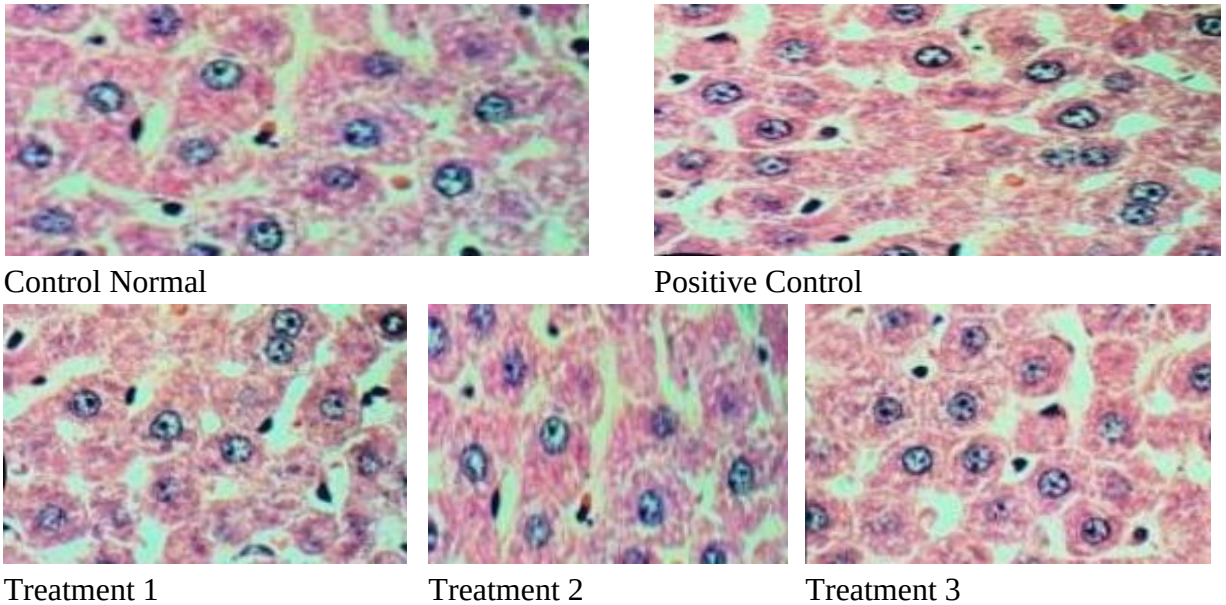


Figure 2. Rat Liver Histopathology Results in the Research Group

The results of histopathology tests conducted on mice are displayed in the figure above. One mouse per research group was employed for histopathological assessment. The study had five groups in total. The phases of euthanizing and necropsying the mice, followed by surgery, liver removal, sectioning the organ, paraffin block creation, hematoxylin-eosin staining, and

40x magnification examination under a microscope are all included in the results of the histological testing. There were no histological changes among the five rat livers observed by the five study groups, according to the findings of their observations. Mice's livers exhibited neither necrosis nor inflammatory development. Additionally unharmed and without granule formation are the livers of rats (Yolanda et al., 2022). These results illustrate that in the five test groups, no toxicity occurred in the rat liver. This confirmed that the Aloe barbadensis administered had no toxic effects at the first, second and third doses. Aloe barbadensis is safe to consume within reasonable limits as needed for 14 days.

4. CONCLUSION

Aloe barbadensis includes flavonoids, phenolics, tannins, saponins, and anthraquinones, according to the results of the qualitative profile analysis. Total anthraquinones were present in amounts of 4.59%, total flavonoids in 0.24%, and total phenolics in 1.42% (quantitative). A combination of 100 g of Aloe barbadensis flesh, 500 g of granulated sugar, 1 mL of lychee flavoring, and 1000 mL of distilled water provides the best results for immediate pollen production. Mice liver histopathological examinations revealed no harm in any of the test groups. The third formula of instant Aloe barbadensis pollen has been demonstrated through preclinical tests to have the capacity to reduce cholesterol, enhance hemoglobin, and improve red blood cell count—all of which are associated with the growth of teeth and bones. Further research can focus on isolating and characterizing specific bioactive compounds from Aloe barbadensis, particularly those identified in the qualitative phytochemical profile. This can provide a more in-depth understanding of the individual components responsible for the observed pharmacological effects.

REFERENCES

Adawiyah, R., & Rizki, M. I. (2018). Aktivitas Antioksidan Ekstrak Etanol Akar Kalakai (Stenochlaena palustris Bedd) Asal Kalimantan Tengah. *Jurnal Pharmascience*, *5*(1), 71-77. https://doi.org/10.20527/jps.v5i1.5788

Anwar, K., Beny, R., Triyasmono, L., Rizki, M. I., Halwany, W., & Lestari, F. (2017). The Influence of Leaf Age on Total Phenolic, Flavonoids, and Free Radical Scavenging Capacity of Aquilaria beccariana. *Research Journal of Pharmaceutical Biological and Chemical Sciences*, *8*(1S), 129–133.

Bernado, P., Rahardjo, R., & Rahajoe, P. S. (2016). Pengaruh Recombinant Human Erythropoietin Terhadap Jumlah Osteoblas, Osteoklas Dan Kadar Hemoglobin Pada Penyembuhan Fraktur Tulang Mandibula. *Jurnal Kedokteran Gigi*, *7*(2), 131–137.

Chabib, L., Indrati, O., & Rizki, M. I. (2015). Formulasi Tablet Effervescent Ekstrak Lidah Buaya (Aloe vera). *Jurnal Pharmascience*, *2*(1), 72–80.

Deglas, W., & Apriliani, F. (2022). Pembuatan Minuman Serbuk Instan Lidah Buaya dengan Penambahan Kacang Hijau. *BIOFOODTECH : Journal of Bioenergy and Food Technology*, *1*(1), 1–8. https://doi.org/10.55180/biofoodtech.v1i1.233

Fiorentini, D., Cappadone, C., Farruggia, G., & Prata, C. (2021). Magnesium: Biochemistry, Nutrition, Detection, and Social Impact of Diseases Linked to Its Deficiency. *Nutrients*, *13*(4), 1136.

Fitriana, M., Halwany, W., Kartika, Y., Anwar, K., Siswadi, S., Rizki, M. I., Rahmanto, B., & Andriani, S. (2022). Formulation and physical stability of syrup containing gaharu (Aquilaria microcarpa Baill.) leaves extract. *Jurnal Riset Industri Hasil Hutan*, *14*(1), 33. https://doi.org/10.24111/jrihh.v14i1.7647

Guo, X., & Mei, N. (2016). Aloe Vera: A Review Of Toxicity And Adverse Clinical Effects. *Journal of Environmental Science and Health, Part C*, *34*(2), 77–96. https://doi.org/10.1080/10590501.2016.1166826

Ikalinus, R., Widyastuti, S. K., & Setiasih, N. L. E. (2015). Skrining Fitokimia Ekstrak Etanol Kulit Batang Kelor (Moringa oleifera). *Indonesia Medicus Veterinus*, *4*(1), 71–79.

Kumar, M., Prakash, S., Radha, Kumari, N., Pundir, A., Punia, S., Saurabh, V., Choudhary, P., Changan, S., Dhumal, S., Pradhan, P. C., Alajil, O., Singh, S., Sharma, N., Ilakiya, T., Singh, S., & Mekhemar, M. (2021). Beneficial Role of Antioxidant Secondary Metabolites from Medicinal Plants in Maintaining Oral Health. *Antioxidants*, *10*(7), 1061. https://doi.org/10.3390/antiox10071061

Kumar, R., Singh, A. K., Gupta, A., Bishayee, A., & Pandey, A. K. (2019). Therapeutic Potential of Aloe vera—A Miracle Gift of Nature. *Phytomedicine*, *60*, 152996. https://doi.org/10.1016/j.phymed.2019.152996

Lubis, R. T., Lubis, M. S., Dalimunthe, G. I., & Yuniarti, R. (2023). Formulasi Sediaan Minuman Serbuk Jeli Lidah Buaya (Aloe vera (L.) Burm.f.). *FARMASAINKES: Jurnal Farmasi, Sains, dan Kesehatan*, *2*(2), 178–188.

Marliana, S. D., Suryanti, V., & Suyono, S. (2005). The Phytochemical Screenings and Thin Layer Chromatography Analysis of Chemical Compounds in Ethanol Extract of Labu Siam Fruit (Sechium edule Jacq. Swartz.). *Biofarmasi Journal of Natural Product Biochemistry*, *3*(1), 26–31.

Mersil, S. (2021). Stomatitis sebagai Manifestasi Oral dari Anemia Defisiensi Zat Besi disertai Trombositosis. *e-GiGi*, *9*(2), 181. https://doi.org/10.35790/eg.v9i2.34481

Mutiara, M., Verdia, E., & Pramono, S. (2007). Pengaruh Komposisi Pelarut Pada Pembuatan Ekstrak Daun Lidah Buaya (Aloe vera L.) Dengan Parameter Kadar Antrakinon Total Dihitung Sebagai Aloin. *Tesis.* Universitas Gadjah Mada.

Ngibad, K. (2019). Phytochemical Screening of Sunflower Leaf (Helianthus annuus) and Anting-Anting (Acalypha indica Linn) Plant Ethanol Extract. *Borneo Journal of Pharmacy*, *2*(1), 24–30.

Panchal, P., & Parvez, N. (2019). Phytochemical Analysis Of Medicinal Herb (Ocimum sanctum). *International Journal of Nanomaterials, Nanotechnology and Nanomedicine*, *5*(2), 008–011.

Quaye, B., Opoku, O., Benante, V., Adjei-Mensah, B., Amankrah, M. A., Ampadu, B., Awenkanab, E., & Atuahene, C. C. (2023). Nfluence Of Aloe Vera (Aloe barbadensis M.) As An Alternative To Antibiotics On The Growth Performance, Carcass Characteristics And Haemato-Biochemical Indices Of Broiler Chickens. *Veterinary Medicine and Science*, *9*(3), 1234–1240. **https://doi.org/10.1002/vms3.1099**

Rahmawati, A. D., Retriasih, H., & Medawati, A. (2014). Hubungan antara Status Gizi dengan Status Erupsi Gigi Insisivus Sentralis Permanen Mandibula. *IDJ*, *3*(1), 16–21.

Rizki, M. I. (2020). *Farmakognosi dan Metabolit Sekunder*. CV. IRDH.

Rizki, M. I., Nurlely, N., Fadlilaturrahmah, F., & Ma'shumah, M. (2021). Skrining Fitokimia Dan Penetapan Kadar Fenol Total Pada Ekstrak Daun Nangka (Artocarpus heterophyllus), Cempedak (Artocarpus integer), dan TARAP (Artocarpus odoratissimus) Asal Desa Pengaron Kabupaten Banjar. *Jurnal Insan Farmasi Indonesia*, *4*(1), 95-102. https://doi.org/10.36387/jifi.v4i1.667

Rizki, M. I., Sari, A. K., Kartika, D., Khairunnisa, A., & Normaidah. (2022). Penetapan Kadar Fenolik Total dan Uji Aktivitas Antioksidan Fraksi dari Ekstrak Etanol Daun Cempedak (Artocarpus integer) dengan Metode DPPH. *MPI (Media Pharmaceutica Indonesiana)*, *4*(2), 168–178. https://doi.org/10.24123/mpi.v4i2.4937

Rizki, M. I., Triyasmono, L., & Rizky, R. A. (2023). Antioxidant Activity And Total Flavonoid Content Kalangkala Leaf Extract (Litsea angulata). *Journal of Current Pharmaceutical Science*, *7*(1), 696–701.

Sadoyu, S., Rungruang, C., Wattanavijitkul, T., Sawangjit, R., Thakkinstian, A., & Chaiyakunapruk, N. (2021). Aloe Vera and Health Outcomes: An Umbrella Review of Systematic Reviews and Meta-Analyses. *Phytotherapy Research*, *35*(2), 555–576. https://doi.org/10.1002/ptr.6833

Said, F., Rahmawati, I., & Ningsih, N. S. (2023). Clinical Study and Toxicity Tests of Disclosing Agent Aloe Vera Gel. *Asian Journal of Pharmaceutical Research and Development*, *11*(2), 15–19.

Sánchez, M., González-Burgos, E., Iglesias, I., & Gómez-Serranillos, M. P. (2020). Pharmacological Update Properties of Aloe Vera and its Major Active Constituents. *Molecules*, *25*(6), 1324. https://doi.org/10.3390/molecules25061324

Sari, A. K., Rizki, M. I., Akbar, N. H., Amaliya, M., Fadlilaturrahmah, & Normaidah. (2023). Determination of Specific and Non-Specific Parameters of Cempedak Leaf Simplisia (Artocarpus Integer) . *International Journal of Pharmaceutical and Bio Medical Science*, *3*(09), 454–459. https://doi.org/10.47191/ijpbms/v3-i9-03

Sharma, A., Fish, B. L., Moulder, J. E., Medhora, M., Baker, J. E., Mader, M., & Cohen, E. P. (2014). Safety and Blood Sample Volume And Quality of A Refined Retro-Orbital Bleeding Technique In Rats Using A Lateral Approach. *Lab Animal*, *43*(2), 63–66. https://doi.org/10.1038/laban.432

Sonam, M., Singh, R. P., & Saklani, P. (2017). Phytochemical Screening and TLC Profiling of Various Extracts of Reinwardtia indica. *International Journal of Pharmacognosy and Phytochemical Research*, *9*(4), 523–527.

Utami, N. K., Amperawati, M., & Rizki, M. I. (2022). Uji In Vivo Terhadap Ekstrak Kayu Secang (Caesalpinia sappan L/Biancaea sappan) Sebagai Disclosing Agent. *An-Nadaa Jurnal Kesehatan Masyarakat*, *9*(2), 203. http://dx.doi.org/10.31602/ann.v9i2.9031

Utami, N. K., Amperawati, M., & Rizki, M. I. (2023). Stability Test And Clinical Trial Of Secang Wood Extract Gel (Biancaea sappan) As Disclosing Agent. *AMJ*, *63*(01), 8609–8618.

Wijayatri, R. (2017). Pengaruh Fraksi Etil Asetat Ekstrak Etanol 96% Akar Pasak Bumi (Eurycoma longifolia Jack) Terhadap Gambaran Histopatologis Hepar Tikus Betina Sprague dawley yang Diberi Karsinogen 7,12-Dimetilbenz(A) Antrasen (DMBA). *Indonesian Pharmacy and Natural Medicine Journal*, *1*(1), 34–47.

Yin, W., Li, Z., & Zhang, W. (2019). Modulation of Bone and Marrow Niche by Cholesterol. *Nutrients*, *11*(6), 1394. https://doi.org/10.3390/nu11061394

Yolanda, S., Masyitha, D., & Sayuti, A. (2022). Gambaran Histopatologi Hati Tikus Putih (Rattus norvegicus) Setelah Pemasangan Implan Wire Material Logam. *Jurnal Ilmiah Mahasiswa Veteriner*, *6*(4), 234–242.

Yoon, J., Kim, D.-J., Sung, H.-H., & Jo, Y.-K. (2016). Analysis of Bone Mineral Density according to Hemoglobin in University Students. *The Korean Journal of Clinical Laboratory Science*, *48*(4), 296–303. https://doi.org/10.15324/kjcls.2016.48.4.296

Zainab, Z., Nurlailah, N., & Rizki, M. I. (2022). Identification of Active Compound and Antibacterial Activity Against Gram-Positive and Gram-Negative Bacteria of Chromolaena odorata Leaf Extract. *Research Journal of Pharmacy and Technology*, *15*(10), 4720–4726. https://doi.org/10.52711/0974-360X.2022.00793

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 795-803
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1339*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

Cytotoxicity of Sodium Bicarbonate Solution to Human Gingival Fibroblast Cells

Erma Mahmiyah[1a*], Jojok Heru Susatyo[1b], Neny Setiawaty Ningsih[1c]

[1] Department of Dental Health, Poltekkes Kemenkes Pontianak, Pontianak, West Kalimantan, Indonesia

[a] Email address: erma.mahmiyah@gmail.com
[b] Email address: drg.jojok@gmail.com
[c] Email address: nenysetiawaty26@gmail.com

Received: 13 September 2023 Revised: 31 December 2023 Accepted: 31 December 2023

Abstract
Immunoglobulin A (IgA) is a crucial antibody originating in mucosal lymphoid tissue, actively distributed across the epithelium. It plays a vital role in binding to and neutralizing microbes that threaten organisms through mucosal organs, thereby contributing to mucosal or secretory immunity. This research aims to determine the Cytotoxicity of Sodium Bicarbonate Solution to Human Gingival Fibroblast Cells. The research method used to investigate the safety and efficacy of various sodium bicarbonate concentrations, we conducted a laboratory experimental study utilizing a post-test-only control group design. Sodium bicarbonate solutions with concentrations of 1%, 2%, 3.5%, 7%, 10%, 15%, and 20% were tested. The results of the study using analysis through ANOVA followed by Tukey HSD revealed that solutions with concentrations of 20%, 15%, and 10% exhibited comparable non-toxicity to fibroblast cells, as they shared the same column. In contrast, concentrations of 7%, 3.5%, 2%, and 1% were found to have toxicity levels that exceeded the IC50 threshold. Further examination using the Tukey HSD test showed that the 2% and 3.5% concentration groups did not show significant differences. In conclusion, the Sodium bicarbonate solutions with concentrations of 7%, 3.5%, 2%, and 1% are not toxic to fibroblast cells and can be used as a basis for further research applications based on sodium bicarbonate materials. It is recommended for future studies to conduct further examinations with different concentrations.

Keywords: Baking Soda (Sodium Bicarbonate), Cytotoxicity, Fibroblasts.

Corresponding Author:

Erma Mahmiyah
Department of Dental Health, Poltekkes Kemenkes Pontianak, Pontianak, West Kalimantan, Indonesia
Email: erma.mahmiyah@gmail.com

1. INTRODUCTION

The oral cavity serves as the primary gateway for microorganisms, making it imperative to employ effective defense mechanisms against pathogenic bacteria (Kitamoto, et al., 2020). Various practices, such as regular teeth brushing, mouth rinsing with antiseptics, interdental cleaning using dental floss, tongue cleaning, and gum chewing, are implemented to mitigate bacterial population in the oral cavity. Caries prevention encompasses multiple strategies, including successful fluoride-based procedures and prolonged restriction of cariogenic sugar consumption, resulting in a substantial reduction in caries (Ahmed, et al., 2022). However, the impracticality of limiting sweets without offering viable alternatives poses challenges. Individual immunity, an intrinsic defense mechanism, also plays a crucial role in preventing bacterial infections.

Sodium bicarbonate, recognized for its antibacterial properties and alkaline nature, can neutralize the oral cavity's pH, inhibiting bacterial metabolic processes that produce acid. The alkaline properties stimulate ion exchange mechanisms, affecting cations like potassium and sodium in extracellular fluids such as saliva. This ion exchange becomes particularly relevant during conditions of increased extracellular hydrogen ions, leading to pH reduction and potassium redistribution. Moreover, sodium bicarbonate's hypertonic nature influences osmotic pressure, causing bacterial cells to lose water, ultimately dehydrating and potentially killing them (Khorolsuren, et al., 2021).

Interventional gargling using sodium bicarbonate introduces a chemical stimulus, derived from its taste, that activates parasympathetic nerves originating from the superior and inferior salivatory nuclei of the brainstem. This stimulation, triggered by tactile and taste stimuli on the tongue, oral cavity, and pharynx, results in an increased salivary flow rate. Sodium bicarbonate, known for stimulating salivary flow and possessing natural alkaline elements, holds promise for xerostomia therapy. Its high buffer capacity maintains pH close to normal limits, enhancing its therapeutic potential (Abbate, et al., 2014).

To advance basic research on the impact of sodium bicarbonate on salivary IgA levels, it is crucial to assess its safety on oral tissues. Preliminary investigations should focus on the substance's toxicity, ensuring biocompatibility and non-inhibitory properties to the surrounding living tissue. A cytotoxicity test, such as the MTT assay, is instrumental in evaluating dental materials' potential impact on fibroblast cell cultures. Fibroblasts, integral to oral mucosa, are pivotal for understanding the substance's effects on cell metabolism and overall safety within the oral environment. This research aims to determine the Cytotoxicity of Sodium Bicarbonate Solution to Human Gingival Fibroblast Cells.

2. RESEARCH METHOD

This study employed an experimental laboratory design with a post-test-only control group. The experiment was conducted at the Pusvetma Surabaya laboratory, utilizing various tools including water baths, digital shakers, rotary evaporators, ELISA readers, 0.2 μm minisart filters, incubators, vortexes, and plastic sample molds with dimensions of 5 mm in diameter and 2 mm in height. Materials involved in the study comprised baking soda, BHK-21 fibroblast cells, Phosphate Buffer Saline (PBS), Minimum Essential Medium Eagle Alpha Modification (Alpha MEM) culture medium, dimethyl sulfoxide (DMSO), MTT powder (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide), and trypsin EDTA.

Sample preparation involved molding on a glass slab with celluloid strips on the mold base. The material weight was determined according to group divisions and stirred on a paper pad for 1 minute until homogeneous. The resulting dough was placed into the molds, allowed to set, removed, and weighed using an analytical balance. Subsequently, samples were ground into fine powder using a mortar and pestle to ensure uniformity across groups. The powdered

samples were then collected, and the specified weight was exposed to human gingival fibroblast culture cells.

Each sample was added to sterile Eppendorf tubes, and 600 µl of Alpha MEM culture medium was introduced to each Eppendorf. After vortexing, the samples were refrigerated for 24 hours, sterilized with 0.2 μ m minisart filters, and placed in Eppendorf tubes according to group assignments.

Human gingival fibroblast cell cultures were seeded in petri dishes and incubated in a CO2 incubator for 24 hours. The cells were observed using an inverted microscope at 100x magnification. The cell culture was then transferred to 96-well microplates at a density of 3-5 x 103 cells per well and further incubated for 24 hours. The microplates were divided into control and treatment groups, with 50 μ l of samples added to designated wells. Incubation continued at 37°C for 24 hours.

Following incubation, 25 µl of MTT solution (5 mg/ml PBS) was added to each well and incubated for an additional 4 hours. The Alpha MEM culture medium was discarded, and 100 μ l of DMSO was added to each well. Formazan absorbance on human gingival fibroblast cells was measured spectrophotometrically using an ELISA reader at 595 nm. The percentage of live cells was calculated using the formula:

$$\% \text{ of live cells} = \frac{\text{OD of treatment - OD of media}}{\text{OD of control cells - OD of media}} \times 100\%$$

Note:
- % of live cells: Percentage of live cells after treatment.
- OD Treatment: Formazan OD (optical density) value of each sample after testing.
- OD Media: Formazan OD (optical density) average for each media control.
- OD Cell: Formazan OD (optical density) average for control cells.

This research has also received ethical approval from the Ethics Commission of the Poltekkes Kemenkes Pontianak with No.176/KEPK-PK.PKP/VII/2022.

3. RESULTS AND DISCUSSION

Table 1. Optical density of the MTT test.

Repetition	Cell Control	1 %	2 %	3,5 %	7 %	10 %	15 %	20 %	Control of Media
1	0,592	0,538	0,569	0,601	0,086	0,067	0,067	0,077	0,054
2	0,552	0,479	0,524	0,545	0,069	0,067	0,065	0,069	0,119
3	0,579	0,645	0,587	0,55	0,076	0,067	0,066	0,071	0,066
4	0,626	0,625	0,602	0,565	0,131	0,07	0,067	0,076	0,081
5	0,651	0,434	0,52	0,484	0,057	0,068	0,067	0,074	0,056
6	0,552	0,538	0,533	0,511	0,111	0,07	0,071	0,076	0,083
7	0,566	0,416	0,454	0,442	0,064	0,069	0,07	0,075	0,054
Mean	0,5883	0,5250	0,5413	0,5283	0,0849	0,0683	0,0676	0,0740	0,0733

Table 1 show that the Optical density of the MTT test with mean cell control 0,5883 and 0.0733 control of media.

Table 2. Percentage of viable cells after exposure to various concentrations of sodium bicarbonate solution.

Repetition	1 %	2 %	3,5 %	7 %	10 %	15 %	20 %
1	105,47	96,40	102,71	90,29	3,02	1,64	1,64
2	102,91	87,53	91,67	78,66	1,92	1,64	1,37
3	111,38	99,95	92,66	78,83	2,86	2,06	1,51
4	107,44	102,91	95,61	69,79	2,89	2,06	1,64

5	115,13	86,74	79,65	74,63	2,61	2,058	1,64
6	103,10	89,31	84,97	78,66	2,89	2,33	2,06
7	90,29	73,69	71,37	66,24	2,75	2,20	2,058
Mean	105,103	90,932	88,377	76,729	2,706	1,998	1,703

Table 2 illustrates the mean percentage of viable cells following exposure to different concentrations of sodium bicarbonate solution. The results indicate that at 1%, the mean viability is 105.103%, at 2% it is 90.932%, at 3.5% it is 88.377%, at 7% it is 76.729%, at 10% it is 2.706%, at 15% it is 1.998%, and at 20% it is 1.703%.

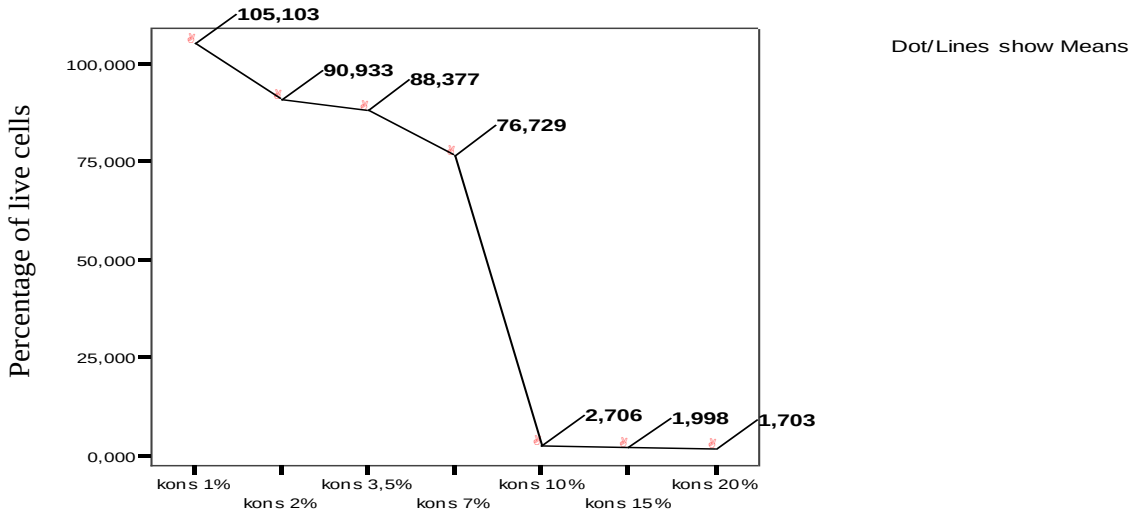


Figure 1. Sodium Bicarbonate.

Table 3. Sample size, mean optical density, percentage of live fibroblasts and standard-deviation.

Group	n	Mean		Standard deviation
		Optical density	Percentage of live	
Sod. bicarbonate 1%	7	0,5250	105,103	0,0885
Sod. bicarbonate 2%	7	0,5413	90,932	0,0499
Sod. bicarbonate 3,5%	7	0,5283	88,377	0,0534
Sod. bicarbonate 7%	7	0,0849	76,729	0,0269
Sod. bicarbonate 10%	7	0,0683	2,706	0,0014
Sod. bicarbonate 15%	7	0,0676	1,998	0,0021
Sod. bicarbonate 20%	7	0,0740	1,703	0,0029
Control cell	7	0,5883	100,000	0,0378
Media controls	7	0,0733	0,000	0,0236

Table 3 illustrates the results of a cytotoxicity test conducted on fibroblast cells, media controls, and cell controls using various concentrations of sodium bicarbonate. The study employed the Inhibitory Concentration 50% (IC50) as the key parameter. IC50 represents the concentration of a substance capable of inhibiting cell proliferation in 50% of the population. Based on the IC50 parameter, it can be inferred that concentrations below 7% are non-cytotoxic to fibroblast cells.

Table 4. Tukey Test (HSD) Percentage of Living Cells

Sodium Bicarbonate	n	Subset (α=0,05)			
Concentration 20%	7	1,70257			
Concentration 15%	7	1,99829			
Concentration 10%	7	2,70571			
Concentration 7%	7		76,72857		
Concentration 3.5%	7			88,37714	
Concentration 2%	7			90,93286	
Concentration 1%	7				105,10286
Sig.		1,000	1,000	0,992	1,000

Table 4 presents the outcomes of the ANOVA test, followed by Tukey's Honestly Significant Difference (HSD) test. The analysis revealed that sodium bicarbonate solutions at concentrations of 20%, 15%, and 10% shared the same column, indicating that these three concentrations did not exhibit a significant difference in the viability of fibroblast cells. This suggests that the cells may experience cytotoxic effects after 24 hours of exposure, as these concentrations fall below the Inhibitory Concentration 50% (IC50).

Conversely, the concentration groups of 7%, 3.5%, 2%, and 1% displayed viability scores above the IC50. The Tukey HSD test further indicated that the viability of fibroblast cells in the 2% and 3.5% concentration groups did not differ significantly. Consequently, concentrations of 7%, 3.5%, and 1% could serve as a foundation for future research applications. Cytotoxicity test is an initial part of the evaluation of a dental material before it is used in humans (Jiang, et al., 2017; Schmalz, & Galler, 2017; Shahi, et al., 2019; Pagano, et al., 2019; Caldas, et al., 2019). The most frequently used method is the Microculture Tetrazolium Technique Assay (MTT Assay) using MTT 3-(4,5-dimethylthiazol-2-yl) 2,5-diphenyl tetrazolium bromide reagent (Khoswanto, Arijani & Soesilawati, 2008; Grela, Kozłowska, & Grabowiecka, 2018; Karakaş, Ari, & Ulukaya, 2017; Stockert, et al., 2018; Kamiloglu, et al., 2020; Oh, & Hong, 2022). The MTT method is based on measuring the mitochondrial activity of living cells. Cells that are still alive and whose metabolism is active, can convert the MTT salt which was originally yellow in color to a purple formazan product through a reduction reaction (Riss, et.al. 2016; Bahuguna, et.al. 2017). The color intensity of the formazan crystals in a 96-well microplate was measured using an Elisa reader. The resulting absorbance is directly proportional to the number of viable cells. A darker color corresponds to a higher absorbance value, indicating a greater number of living cells (Emilda, et al, 2014). The MTT Assay method requires reagent incubation with reduced live cell cultures (Riss, et.al. 2016).

The most commonly employed cell culture for cytotoxicity testing of dental materials is the Baby Hamster Kidney 21 (BHK-21) fibroblast cells, derived from baby hamster kidneys. These cells are extensively utilized due to their resemblance in shape and functionality to human fibroblasts, particularly in the production of growth factors. BHK-21 cells are known for their ease of culture, heightened stability, increased sensitivity, and a reduced likelihood of mutation compared to human fibroblast cells (Dewi, 2007; Emilda, et al, 2014; Holland, 2009: Khoswanto, 2008)

This study conducted a cytotoxicity test on fibroblast cells using sodium bicarbonate. Sodium bicarbonate is soluble in water at typical room temperature (approximately 20˚C) and insoluble in alcohol. To ensure safe use, it is recommended to dilute sodium bicarbonate in water. The compound remains stable in open air and at normal room temperature, allowing for convenient storage in a closed environment without requiring special handling. Sodium bicarbonate, also known as Sodium Hydrogen bicarbonate, baking soda, bread soda, cooking soda, bicarbonate soda, or bicarbonate soda, dissolves in water and presents as thick white crystals. Its abrasive nature contributes to caries control due to the composition of baking soda-

fluoride. Baking soda consists of hydrate silica, whose action aligns with fluoride, effectively reducing stains and calculus on teeth. In addition to its antimicrobial properties, baking soda crystals have the ability to absorb odors. Baking soda, a chemical compound, is widely utilized to remove stains on teeth. Another benefit of baking soda is its capability to reduce bad breath and whiten teeth by inhibiting bacterial growth and minimizing plaque buildup (Paramita, 2015)

Baking soda (sodium bicarbonate) can be used as an alternative to whitening teeth; besides being easy to find in the community. baking soda is also relatively easy to use. The advantages of baking soda compared to chemical solutions are that baking soda is not irritating and abrasive. Baking soda can also be antibacterial (Schuurs, 2013). It has the unique ability to act as a buffer based on its chemical process. Neutralizers function to maintain a balance or neutralize the pH so that it can be used as a mixed substance in toothpaste and mouthwash to maintain the pH of the oral cavity.

As a hypertonic solution. sodium bicarbonate can facilitate the osmotic movement of water from cells. resulting in shrinkage. plasmolysis. and finally. death of cells. including bacteria. (Madeswaran & Jayachandra, 2018). Mechanism of cell death after exposure to sodium bicarbonate with a time of 24 hours and a certain concentration because sodium bicarbonate has the ability to affect the osmotic pressure of water in cells. The hypertonic nature of sodium bicarbonate causes the hypotonic components of the bacterial cells to lose water, so that the cells will become dehydrated resulting in shrinkage, plasmolysis and eventually killing the bacterial cells. (Strassler, 2013; Madeswaran & Jayachandra, 2018). The author analogizes the mechanism of cell death to fibroblast cells.

Sodium bicarbonate also has alkaline properties which can neutralize the pH of the oral cavity so that it can inhibit the metabolic process of bacteria that produce acid. Another factor responsible for baking soda's antibacterial effect is its ability to change osmotic pressure. The hypertonic nature of baking soda causes the hypotonic components of the bacterial cells to lose water, causing dehydration and killing cells. However, it is said that sodium bicarbonate must interact with bacterial cells for at least 30 minutes so that it can effectively kill bacterial cells (Silhacek, 2004; Hewawaduge, Senevirathne, & Lee, 2020; Jaikumpun, et al., 2020; Saleh, et al., 2022; Karim, & Hossain, 2018).

Currently, sodium bicarbonate is often added to toothpaste to clean teeth from plaque, because it has many beneficial properties, including easy to obtain, cheap price, safe, low abrasive level, soluble in water, acid neutralizing properties, compatible with fluorine, and antibacterial ability (Schuurs, 2013). Sodium bicarbonate besides having anti-microbial properties, sodium bicarbonate crystals also have the ability to absorb odors. Sodium bicarbonate is a chemical compound that is effectively used to remove stains on teeth. Another advantage of baking soda is that it reduces bad breath and can whiten teeth because sodium bicarbonate can inhibit bacterial growth and reduce plaque buildup (Paramita, 2015; Ariani et al., 2023; Garcia, Santiago, & Velasco, 2018).

In the field of dentistry, the effect of sodium bicarbonate in the form of chewing gum, gel, or tablets on the pH of the mouth has been widely studied and proves that sodium bicarbonate helps the buffer capacity of saliva (Abbate, 2013). This unique ability is as a buffer based on the chemical process. Neutralizers function to maintain a balance or neutralize pH so that they can be used as antacids for digestive disorders or neutralize acids in the digestive tract, mixed substances in toothpaste and mouthwash to maintain the pH of the oral cavity (Hurlbutt, 2010).

Research conducted by Ghassemi in 2008 showed that sodium bicarbonate was able to damage the bacterial matrix structure and also damage the bond between bacteria and tooth surfaces. The study compared the antibacterial abilities of baking soda toothpaste and triclosan,

the results showed that sodium bicarbonate toothpaste was more effective in inhibiting plaque bacteria (Ghassemi, 2008). Clinical use of 67% sodium bicarbonate toothpaste can improve periodontal tissue health in gingivitis patients (Taschieri, et.al, 2022; Parkinson, Butler, & Ling, 2023).

The statistical analysis of research data revealed a normal distribution with homogeneous variations, allowing for further investigation using the Anova test followed by Tukey's Honestly Significant Difference (HSD) test to assess group differences. Results indicated that as the concentration of sodium bicarbonate increased, the absorbance value decreased. This suggests a reduction in the number of viable cells or an increase in the number of dead fibroblast cells with elevated sodium bicarbonate concentrations.

In summary, the calculation of the percentage of fibroblast cells that perished after exposure to sodium bicarbonate concentrations of 1%, 2%, 3.5%, 7%, 10%, 15%, and 20% respectively was 0%, 9.1%, 11.6%, 23.3%, 97.3%, 98%, and 98.3%. Based on the Inhibitory Concentration 50% (IC50) parameter, sodium bicarbonate concentrations of 10%, 15%, and 20% fall into the toxic category as the percentage of dead cells exceeds 50%, while concentrations of 1%, 2%, 3.5%, and 7% are deemed non-toxic, with the percentage of dead cells being less than 50%. Additionally, the data indicates that a 10% concentration of baking soda exhibits cytotoxic effects, whereas a 7% concentration demonstrates therapeutic properties. The Tukey HSD test revealed a significant difference between the 10% and 7% concentration groups; however, the specific impact of sodium bicarbonate within the range of 10% to 7% concentration on fibroblast cells remains unclear

4. CONCLUSION

In conclusion, the Sodium bicarbonate solutions with concentrations of 7%, 3.5%, 2%, and 1% are not toxic to fibroblast cells and can be used as a basis for further research applications based on sodium bicarbonate materials. It is recommended for future studies to conduct further examinations with different concentrations.

REFERENCES

Abbate, G. M., Levrini, L., & Caria, M. P. (2014). Salivary pH after a glucose rinse: effect of a new mucoadhesive spray (Cariex) based on sodium bicarbonate and xylitol. *The Journal of clinical dentistry*, *25*(4), 71–75.

Ahmed, O., Sibuyi, N. R. S., Fadaka, A. O., Madiehe, M. A., Maboza, E., Meyer, M., & Geerts, G. (2022). Plant extract-synthesized silver nanoparticles for application in dental therapy. *Pharmaceutics*, *14*(2), 380. https://doi.org/10.3390/pharmaceutics14020380

Ariani, D., Herawati, M., Dwiyono, S., & Byungchan, A. (2023). Effects of Sodium Bicarbonate Mouthwash on Saliva pH and Oral Microflora. *Formosa Journal of Applied Sciences*, *2*(9), 2133-2140. https://doi.org/10.55927/fjas.v2i9.6095

Bahuguna, A., Khan, I., Bajpai, V. K., & Kang, S. C. (2017). MTT assay to evaluate the cytotoxic potential of a drug. *Bangladesh Journal of Pharmacology*, *12*(2), 115-118.

Caldas, I. P., Alves, G. G., Barbosa, I. B., Scelza, P., de Noronha, F., & Scelza, M. Z. (2019). In vitro cytotoxicity of dental adhesives: A systematic review. *Dental Materials*, *35*(2), 195-205. https://doi.org/10.1016/j.dental.2018.11.028

Dewi, T. P. (2007). Efek Sitotoksik Tetrahydrozoline HCL Terhadap Viabilitas Sel Fibroblas. *Interdental Jurnal Kedokteran Gigi.* 5(1). 1-7.

Emilda, Y., Budipramana, E., & Kuntari, S. Uji toksisitas ekstrak bawang putih (Allium Sativum) terhadap kultur sel fibroblast. *Dental Journal*, 2014; 47(4): 215-219.

Garcia, M. C. U., Santiago, M. C. S., & Velasco, N. J. (2018). The Effect of Sodium Bicarbonate Abrasives in Toothpaste on Dental Plaque Removal: A Pilot Study. *Philippine Journal of Health Research and Development*, *22*(2), 35-42.

Ghassemi, A., Vorwerk, L. M., Hooper, W. J., Putt, M. S., & Milleman, K. R. (2008). A four-week clinical study to evaluate and compare the effectiveness of a baking soda dentifrice and an antimicrobial dentifrice in reducing plaque. *Journal of Clinical Dentistry*, *19*(4), 120.

Grela, E., Kozłowska, J., & Grabowiecka, A. (2018). Current methodology of MTT assay in bacteria–A review. *Acta histochemica*, *120*(4), 303-311. https://doi.org/10.1016/j.acthis.2018.03.007

Hewawaduge, C., Senevirathne, A., & Lee, J. H. (2020). Enhancement of host infectivity, immunity, and protective efficacy by addition of sodium bicarbonate antacid to oral vaccine formulation of live attenuated Salmonella secreting Brucella antigens. *Microbial pathogenesis*, *138*, 103857. https://doi.org/10.1016/j.micpath.2019.103857

Holland, G. R., & Torabinejad, M. (2015). The dental pulp and periradicular tissues. *Endodontics: principles and practice*, Elsevier.

Hurlbutt, M. (2010). Dental caries: A pH mediated disease. *CDHA J*, *25*(1), 9-15.

Jaikumpun, P., Ruksakiet, K., Stercz, B., Pállinger, É., Steward, M., Lohinai, Z., ... & Zsembery, Á. (2020). Antibacterial effects of bicarbonate in media modified to mimic cystic fibrosis sputum. *International Journal of Molecular Sciences*, *21*(22), 8614. https://doi.org/10.3390/ijms21228614

Jiang, R. D., Lin, H., Zheng, G., Zhang, X. M., Du, Q., & Yang, M. (2017). In vitro dentin barrier cytotoxicity testing of some dental restorative materials. *Journal of dentistry*, *58*, 28-33. https://doi.org/10.1016/j.jdent.2017.01.003

Kamiloglu, S., Sari, G., Ozdal, T., & Capanoglu, E. (2020). Guidelines for cell viability assays. *Food Frontiers*, *1*(3), 332-349. https://doi.org/10.1002/fft2.44

Karakaş, D., Ari, F., & Ulukaya, E. (2017). The MTT viability assay yields strikingly false-positive viabilities although the cells are killed by some plant extracts. *Turkish Journal of Biology*, *41*(6), 919-925. https://doi.org/10.3906/biy-1703-104

Karim, Z., & Hossain, M. S. (2018). Management of bacterial wilt (Ralstonia solanacearum) of potato: focus on natural bioactive compounds. *Journal of Biodiversity Conservation and Bioresource Management*, *4*(1), 73-92. https://doi.org/10.3329/jbcbm.v4i1.37879

Khoswanto, C., Arijani, E., & Soesilawati, P. (2008). Cytotoxicity test of 40, 50 and 60% citric acid as dentin conditioner by using MTT assay on culture cell line. *Dental Journal (Majalah Kedokteran Gigi)*, *41*(3), 103-106.

Khorolsuren, Z., Lang, O., Vag, J., & Kohidai, L. (2021). Effect of dental antiseptic agents on the viability of human periodontal ligament cells. *The Saudi Dental Journal*, *33*(8), 904-911. https://doi.org/10.1016/j.sdentj.2021.09.016

Kitamoto, S., Nagao-Kitamoto, H., Hein, R., Schmidt, T. M., & Kamada, N. (2020). The bacterial connection between the oral cavity and the gut diseases. *Journal of dental research*, *99*(9), 1021-1029. https://doi.org/10.1177/0022034520924633

Madeswaran, S., & Jayachandran, S. (2018). Sodium bicarbonate: A review and its uses in dentistry. *Indian Journal of Dental Research*, *29*(5), 672-677. https://doi.org/10.4103/ijdr.IJDR_30_17

Oh, Y. J., & Hong, J. (2022). Application of the MTT-based colorimetric method for evaluating bacterial growth using different solvent systems. *Lwt*, *153*, 112565. https://doi.org/10.1016/j.lwt.2021.112565

Paramita, D. (2015). Pemanfaatan Bakin Soda untuk Membersihkan Stain pada Gigi Perokok Di Puskesmas Karang Pule. *GaneÇ Swara September*, *2*(9), 108-111.

Pagano, S., Lombardo, G., Balloni, S., Bodo, M., Cianetti, S., Barbati, A., ... & Marinucci, L. (2019). Cytotoxicity of universal dental adhesive systems: Assessment in vitro assays on

human gingival fibroblasts. *Toxicology in vitro*, *60*, 252-260. https://doi.org/10.1016/j.tiv.2019.06.009

Parkinson, C. R., Butler, A., & Ling, M. R. (2023). Antigingivitis efficacy of a sodium bicarbonate toothpaste: Pooled analysis. *International Journal of Dental Hygiene*, *21*(1), 106-115. https://doi.org/10.1111/idh.12626

Riss, T. L., Moravec, R. A., Niles, A. L., Duellman, S., Benink, H. A., Worzella, T. J., & Minor, L. (2016). Cell viability assays. Assay guidance manual. National Center For Biotechnology Information.

Saleh, M. M., Yousef, N., Shafik, S. M., & Abbas, H. A. (2022). Attenuating the virulence of the resistant superbug Staphylococcus aureus bacteria isolated from neonatal sepsis by ascorbic acid, dexamethasone, and sodium bicarbonate. *BMC microbiology*, *22*(1), 1-17. https://doi.org/10.1186/s12866-022-02684-x

Schmalz, G., & Galler, K. M. (2017). Biocompatibility of biomaterials–Lessons learned and considerations for the design of novel materials. *Dental Materials*, *33*(4), 382-393. https://doi.org/10.1016/j.dental.2017.01.011

Schuurs, A. (2013). *Pathology of the hard dental tissues*. John Wiley & Sons.

Shahi, S., Özcan, M., Maleki Dizaj, S., Sharifi, S., Al-Haj Husain, N., Eftekhari, A., & Ahmadian, E. (2019). A review on potential toxicity of dental material and screening their biocompatibility. *Toxicology mechanisms and methods*, *29*(5), 368-377. https://doi.org/10.1080/15376516.2019.1566424

Silhacek, K. J., & Taake, K. R. (2005). Sodium bicarbonate and hydrogen peroxide: the effect on the growth of Streptococcus mutans. *American Dental Hygienists' Association*, *79*(4), 7.

Stockert, J. C., Horobin, R. W., Colombo, L. L., & Blázquez-Castro, A. (2018). Tetrazolium salts and formazan products in Cell Biology: Viability assessment, fluorescence imaging, and labeling perspectives. *Acta histochemica*, *120*(3), 159-167. https://doi.org/10.1016/j.acthis.2018.02.005

Strassler HE. *Toothpaste ingredients make difference: patient-specific recommendations.* Benco Dental supervised study course. Retrieved from http://d3e9u3gw8odyw8.cloudfront.net/toothpaste_ingredients.pdf

Taschieri, S., Tumedei, M., Francetti, L., Corbella, S., & Del Fabbro, M. (2022). Efficacy of 67% sodium bicarbonate toothpaste for plaque and gingivitis control: A systematic review and meta-analysis. *Journal of Evidence-Based Dental Practice*, *22*(2), 101709. https://doi.org/10.1016/j.jebdp.2022.101709

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 804-814
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1340*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Perception and Educational Needs in the Self-Management Type 2 Diabetes Mellitus Patients: A Phenomenological Study Based on Local Wisdom

I Dewa Putu Gede Putra Yasa[1a*], VM Endang SP Rahayu[1b], I Gusti Ayu Ari Rasdini[1c]

[1] Department of Nursing, Poltekkes Kemenkes Denpasar, Denpasar, Bali, Indonesia

[a] Email address: putrayasa718@gmail.com
[b] Email address: endang_madhita@yahoo.co.id
[c] Email address: rasdiniari@gmail.com

Received: 13 September 2023 Revised: 18 December 2023 Accepted: 31 December 2023

Abstract

Lack of knowledge, misperceptions, and the absence of a diabetes management culture pose challenges to providing social support, particularly within families. This is a qualitative phenomenological study aimed at identifying factors contributing to self-management, unearthing the influence of a patrilineal culture, and uncovering the educational needs for local wisdom-based diabetes mellitus self-management in type 2 patients. Data were collected through in-depth interviews and analyzed thematically. The study population consisted of type 2 diabetes mellitus patients living within patrilineal families. The sample size was 10 female individuals aged between 40 and 60 years. The duration of type 2 DM ranged from 6 to 15 years. Four themes emerged from the research: (1) Insufficiency in self-management, (2) Beliefs and perceptions about type 2 diabetes mellitus, (3) The influence of patrilineal families on self-management, and (4) The need for the development of educational programs for self-management type 2 DM management rooted in local culture. According to the results, people with Type 2 Diabetes Mellitus may not be capable of managing their health. Though there are many different opinions and views regarding Type 2 DM, there are frequently gaps in our knowledge. The management of diabetes is greatly impacted by patrilineal family systems. Participants express a significant need for educational programs that are culturally sensitive and improve their ability to control their diabetes.

Keywords: Education, Local Wisdom, Self-Management.

Corresponding Author:

I Dewa Putu Gede Putra Yasa
Department of Nursing, Poltekkes Kemenkes Denpasar, Denpasar, Bali, Indonesia
Email: putrayasa718@gmail.com

1. INTRODUCTION

The height of Diabetes Mellitus (DM) incidents impacts everyone in various aspects of a patient's life. It has profound effects on health, the economy, and mortality. Out of a total of 4.25 million deaths attributable to diabetes mellitus (DM) between 2006 and 2021, there was a notable increase of almost 30% in mortality rates during the pandemic. Specifically, the mortality rate rose from 106.8 per 100,000 individuals in 2019 to 144.1 in 2020 and further to 148.3 in 2021 (Lv et al., 2022). The cost of DM treatment reached 673 trillion in the same year (IDF, 2015). Therefore, effective management of DM is crucial. The primary focus in DM management includes lifestyle changes. Lifestyle management is fundamental in DM treatment and encompasses self-study, support care, physical activity, smoking counseling, and psychosocial care (American Diabetes Association, 2022). It is expected that glycemic control can be improved by changing lifestyle patterns, reducing complications and deaths.

Indicators for glycemic control include fasting blood glucose, blood glucose levels two hours after eating, blood pressure, blood lipid levels, and HbA1C (PERKENI, 2021). However, many DM patients still struggle to achieve optimal glycemic control. According to the National Health and Nutrition Examination Survey (NHANES), only 50% of adult DM patients in America achieved HbA1C levels below 7.0. Previous study with intervention of Diabetes Self-Management Education (DSME) showed 21% of DM achieved HbA1C levels below 7.0 (Emara et al., 2021). The Riskesdas results showed that 10.5% of individuals over 15 years old experienced hyperglycemia (Kementerian Kesehatan Republik Indonesia, 2018). Self-management by Type 2 Diabetes Mellitus (DM) patients is crucial for effective DM management. The success of DM management is significantly influenced by the family's role in supporting self-management. Currently, most educational material focuses only on dietary management for Type 2 DM patients and does not address the role of the family and cultural aspects in maintenance, even though culture plays a vital role in the education and care process for Type 2 DM patients and their families (Sohal et al., 2015).

Lack of knowledge, perceptual errors, and a failure to adapt to cultural aspects in diabetes management are obstacles faced in providing social support, including family support. Improving patient and family knowledge is influenced by several factors, including the family function and educational methods used (Pamungkas et al., 2021a; Sohal et al., 2015). Indonesia adheres to a patrilineal social structure. Culture and religion exert a significant influence on this phenomenon, as traditions are imparted through both formal and informal educational channels (Pamungkas et al., 2021a). The former study found patrilineal system impacts problem-solving skills, ineffective communication and burden, compliance and poor behavior control (Pamungkas et al., 2021a).

Educational models and media significantly impact patients' and families' understanding of DM treatment (Beck et al., 2018). Educating family members about the importance of DM treatment can help them provide better care in the treatment process (Pesantes et al., 2018). Knowledge about the disease, strategies for changing family routines, and optimal ways to address emotional aspects of the disease are essential components of DM self-management that family members need to understand (Bennich et al., 2017). Additionally, the choice of media used for education can influence information acceptance. Audiovisual media in the form of digital video discs (DVDs) is considered more effective than leaflets or booklets for educating DM patients and their families (Estacio et al., 2015; Pamungkas et al., 2017).

Providing education to families and DM patients is an ongoing process and requires repeated efforts. Therefore, a comprehensive educational model that is engaging and incorporates local Balinese patrilineal wisdom is needed. Based on these considerations, the researchers have developed an educational model for fostering self-management based on local wisdom to improve glycemic control and self-efficacy in Type 2 Diabetes Mellitus patients.

2. RESEARCH METHOD

This study utilized hermeneutic phenomenology to explore the experiences of their ability to maintain self-management, the influence of patrilineal culture, and the development of locally based educational models for Type 2 Diabetes Mellitus patients (Spence, 2017; Todres & Wheeler, 2001). Phenomenology seeks to comprehend the human experience through the interpretation of daily encountered phenomena. This study employs Heidegger's philosophical approach, which highlights the influence of an individual's temporal existence on their interpretation of experiences. Heidegger's concept of Dasein, which pertains to human existence, is crucial for contemplating the nature of being (Todres & Wheeler, 2001). Individuals partake in inter-subjectivity, a process wherein they subjectively engage with the objective aspects of the world, in order to contemplate their own existence. This phenomenon aligns with the philosophical notion of Dasein. The philosophical approach employed in this study aligns more closely with individuals' life-world and their everyday interactions (Lamb et al., 2019). This is crucial for comprehending the experiences of patients diagnosed with Type 2 Diabetes Mellitus.

The respondents were selected from one area at Mengwi 1 Public Health Center. The sample was recruited with purposive sampling with criteria: receiving regular treatment, effective communication skills, at least a high school education, and aged between 40 and 60 years (1 May 2021– 31 August 2022). Throughout the course of the study, a total of five participants declined to disclose information for a variety of reasons, including personal unease with the subject matter, apprehension regarding potential consequences, and a sense of insecurity. Ultimately, a total of ten participants were incorporated into the study. The determination of the sample size was made based on the point of data saturation, which occurs when no new codes are identified. The researchers conducted data analysis following each interview.

The interviews were administered in accordance with the patient's temporal and spatial context. The interviews, analysis, and interpretation in this study were conducted using the Bahasa Indonesia language. The primary author conducted individual interviews with each participant, lasting approximately one hour, predominantly within the confines of the patient's residence. A semi-structured interview guide was developed, with the initial query being, "Kindly provide an account of your self-management practices in order to uphold your condition." The interviews conducted exhibited a dialogical nature, wherein particular attention was given to the topics of self-management, patrilineal culture, and locally based educational models for individuals diagnosed with Type 2 Diabetes Mellitus. The interviewer utilized the responses to the main question as a basis for posing additional exploratory inquiries regarding the patient's self-management practices, drawing upon local knowledge. This was achieved by requesting further elaboration with the prompt, "Could you provide additional details?" Could you kindly provide an illustrative example, please?

The research team consisted of three individuals, namely the lead investigator and two researchers. The study's progress and conclusions were monitored by the research team members through the utilization of online meetings. Each member possesses a background in nursing research. This study did not involve conducting multiple interviews with the participants, and it is important to acknowledge that there were no pre-existing relationships between the researchers and participants that could have potentially influenced the responses.

To better grasp the significance of the individuals' lived experiences, the researchers employed Van Manen's approach (van Manen, 2016), which provides four levels of analysis. In order to extract thematic descriptions, one must first identify thematic aspects (Ritruechai et al., 2018), then extract thematic statements (Ritruechai et al., 2018), and finally create linguistic transformations (Ritruechai et al., 2018). Multiple readings of the interview transcripts were

done to ensure a thorough understanding of the material. Codes were placed on all of the pivotal components. The first and second authors performed the initial Bahasa Indonesia coding, and then they organized the collected data into overarching themes and their respective subthemes. The findings were originally written in Bahasa and translated into English by the first two authors, who were then checked for accuracy by the third pair. The team finally reached consensus on the underlying concepts and overarching themes.

The researchers employed rigorous criteria and specific rules to ensure the methodological soundness and trustworthiness of the study. The utilization of established phenomenological research method ensured rigor (van Manen, 2016). The study employed evaluation methods which involved maintaining long-term contact with participants, being transparent about the study's focus, conducting thorough data analysis, discussing emerging themes with participants, and adjusting themes based on participant input (Polit & Beck, 2017). The processes were recorded in Excel files to ensure the reliability and validity of the study. The final report included participant descriptions to demonstrate the relevance of the study's findings. Participants were provided with a process summary and diagram to enhance the study's credibility, and member checks were performed. Qualitative research and diabetes mellitus experts were consulted to enhance the accuracy of the study. Transferability was ensured by comprehensively explaining the study's context, background, and stage in the introduction and selecting participants with a wide range of characteristics.

This study has received ethical approval from the Health Polytechnic Ministry of Health Denpasar's Ethics Study Commission, registered as LB.02.03/EA/KEPK/0440/2023, dated May 8, 2023. Participants received both written and verbal information about the study's purpose and methods prior to their participation. Participants had the option to withdraw from the study at any time prior to the completion of data collection, after signing the consent form and arranging the interview details. To maintain confidentiality and safeguard the privacy of participants, each interview was assigned a code instead of using personal names or institutional affiliations. Consequently, their identities and information were maintained in strict confidentiality.

3. RESULTS AND DISCUSSION

The study involved ten female participants aged between 40 and 60 years, with diabetes mellitus (DM) duration ranging from 6 to 15 years. Four themes emerged from the data analysis:

Table 1. Themes overview

Quotes	Subthemes	Themes
"I am not able to check my blood sugar by myself... I don't understand the procedure, and I'm afraid of making mistakes." (P2) "I don't know how much my blood sugar should be... I don't understand whether it's normal or not." (P3) “I don't know the right glucose….I suddenly knew my glucose was high.”(P5)	Inactive self-glucose check	Insufficiency in self-management

“I can’t check it [blood glocuse] by myself…it is difficult to do.” (P9)		
“I find it difficult to manage my diet... it's complicated." (P5) “I think it is difficult to manage diet, moreover choosing the right food.” (P6) “I can eat, but I can’t manage it…I is messy, I can’t eat this one, that one.” (P10)	Poor diet management	
"I can't take care of my foot……I don't know how to do it."(P1) "I don't know if my foot needs special care." (P3) "I don't understand that even foot have to be cared for properly." (P5) "I don't understand how to take care of my foot, sir. All I do is take a shower and wash my foot, sir." (P6) "I also don't know if my feet need to be treated." (P7)	Unknown foot treatment	
"I think exercise is good for my health, but I'm not sure if it can lower my blood sugar." (P1) Walking would make me healthier, but they say it can lower blood sugar, sir. Is that true? (P7) Does walking affect my sugar? (P9)	Doubt about exercise	
"I just know that diabetes is caused by many things like excessive eating." (P3) "I don't understand about the cause... some say obesity, some say it's because of eating too much." (P8) My knowledge of the cause is very limited, but I do know that genetics, obesity, and inactivity are contributing factors (P10)	Negative perception	Beliefs and Perceptions About Type 2 Diabetes Mellitus
"My husband decides where I should get treatment." (P4)	Authoritarian man	

"If my husband doesn't agree, then I have to cancel it... I wait for his decision." (P7) "It's up to my husband to determine that. I'll just go along with it." (P9) "When my husband and I have different opinions, my husband's decision prevails." (P5) “Sometimes we argue first... in the end, yes, follow my husband” (P10)		The Influence of Patrilineal Family Structures on Self-Management
"My spouse is attentive to me as well, but it can be challenging at times to be left behind." (P6) "Yes, sir, my husband will definitely pay attention." (P9) "When I need something to treat my pain, call my husband" (P10)	Spouse caring	
"I want to study carefully about how to manage my diabetes independently." (P3) "I need comprehensive guidance to be able to manage it myself." (P5) "I want to start from the beginning with good guidance." (P9)	Independent learning	Hope for the Development of Educational Programs
"I want the explanations to use Balinese language." (P2) "Teach us using methods that are adapted to our daily lives." (P5) "The language and approach should be easy to understand." (P9)	Local wisdom	

Theme 1. Insufficiency in self-management

Participants expressed their inability to manage diabetes mellitus independently. They lacked the skills and knowledge required for self-care management. This theme encompassed categories such as the inability to self-monitor blood glucose, set glycemic control targets, manage dietary choices, and provide adequate foot care and regular exercise. The statements revealed a lack of understanding and capability in critical aspects of diabetes self-care management.

Theme 2. Beliefs and Perceptions About Type 2 Diabetes Mellitus

Participants held diverse and often limited beliefs and perceptions about Type 2 DM, including its causes, treatments, and complications. They mentioned causes like excessive eating, obesity, and heredity. Their perceptions of dietary management were also unclear, and they expressed uncertainty about the benefits of physical activity. The statements in Table 1 highlighted a need for better education on the causes and management of diabetes.

Theme 3. The Influence of Patrilineal Family Structures on Self-Management

Participants revealed the influential role of patrilineal family structures in diabetes management. Husbands, as heads of the family, played a dominant role in decision-making and care for diabetes patients. Categories within this theme included decision-making, family support during complaints, and conflict resolution. The statements highlighted the dominant role husbands played in diabetes management decisions. This reflected the cultural context of patrilineal family structures in Bali.

Theme 4. Hope for the Development of Educational Programs

Participants expressed a strong desire for structured and culturally sensitive educational programs to enhance their ability to manage diabetes independently. They hoped for programs that incorporated local Balinese culture, including language and terminology. The statements underscored the need for culturally tailored educational programs to improve diabetes self-care management.

DISCUSSION

This study has identified four significant themes related to self-management based on local wisdom in Type 2 Diabetes Mellitus patients, which will be discussed below:

Insufficiency in self-management. Participants in this study exhibited inactive self-glucose checks, poor diet management, unknown foot treatment, and doubt about exercise in managing diabetes mellitus. They expressed their inability to fully engage in self-care management for diabetes. This overarching theme emerged from various participant statements that can be categorized into several sub-themes.

The research findings align with previous studies on self-care management, indicating that participants struggle to perform all self-management activities according to guidelines. While some can manage their diet and avoid excessive carbohydrate intake, they still face challenges in adhering to health recommendations fully. Other aspects of self-care tend to rely more heavily on medication for blood glucose control (Bhandari & Kim, 2016).

The sub-themes within this theme encompass diet management, physical activity, foot care, and glucose monitoring, all performed independently to some degree. However, participants admitted that they were not yet fully proficient in these areas (Mikhael et al., 2019). Other research suggests that only a small fraction of participants can perform some aspects of self-care, and even fewer can do so independently. Some individuals rely on recommendations from healthcare professionals, such as doctors or nurses, rather than being fully autonomous in self-care management (Murphy et al., 2015).

It's essential to recognize that self-care management is an ongoing developmental process for individuals with diabetes mellitus. This process involves mastering seven crucial activities: monitoring blood glucose levels, dietary management, taking medication as prescribed, problem-solving, coping, engaging in physical activity, and behavior modification (Shrivastava et al., 2013). Successful self-care management necessitates adequate knowledge and skills to perform these activities effectively and independently. This theme also underscores the prevalence of skill deficits, problem-solving difficulties, and challenges in behavior management among participants (Pamungkas et al., 2021b).

Beliefs and Perceptions Regarding Type 2 Diabetes Mellitus. Participants held diverse beliefs and perceptions about type 2 diabetes mellitus. However, these beliefs were often incomplete and marked by limited knowledge. Their perceptions encompassed various aspects,

including the causes, management, and consequences of diabetes mellitus. This theme emerged from participant statements related to their beliefs and perceptions.

It is important to note that self-care management depends on having positive beliefs and perceptions regarding diabetes. These beliefs significantly influence patients' self-care skills. Confidence serves as a motivating factor for effective self-care management, including accepting the illness and having the desire to improve one's health (Shakibazadeh et al., 2011).

Perceptions concerning physical activity, particularly sports, were generally unfavorable and highlighted a lack of understanding of its importance in managing diabetes. Participants attributed this lack of engagement in physical activity to a dislike of exercise and a shortage of time (Tewahido & Berhane, 2017). Additionally, perceptions related to diabetes mellitus were often underdeveloped, with some participants not considering diabetes a serious disease and having difficulty recognizing the importance of self-care management (Tan et al., 2018).

Influence of Patrilineal Family Structures on Self-Management. The influence of patrilineal family structures on the independence of diabetes mellitus patients was a prominent theme. Participants revealed that their husbands, as heads of the family, played a dominant role in decision-making and the management of their diabetes. This theme is based on several categories, including decision-making, family support during health complaints, and conflict resolution.

Balinese culture is deeply rooted in Hinduism (Juanamasta et al., 2020), emphasizing patriarchy and the central role of men in family dynamics (Sudarta, 2017). The patrilineal system places men in a more important position than women, as evident in Balinese wedding ceremonies that adhere to the "purusa" concept, signifying the male head of the family (Rahmawati, 2016).

Within this patriarchy, men are viewed as the leaders and organizers of the household and primary breadwinners, while women take on dual roles as mothers and contributors to the family's Consequently, husbands actively influence decisions and rule-making within the family, including healthcare decisions (Omodara et al., 2022).

Hope for the Development of Culturally Tailored Educational Programs. Participants expressed a strong desire for structured and culturally sensitive educational programs to enhance their ability to manage diabetes independently. They sought programs that incorporated local Balinese culture, including language and terminology. This theme emerged from participant statements related to their educational needs and preferences.

Participants emphasized the need for culturally adapted educational programs that provide comprehensive guidance. They expressed a desire to start from the basics and receive clear instructions to enable them to manage diabetes independently (Pamungkas et al., 2021a).

Cultural adaptation is crucial to improving participants' understanding of diabetes mellitus and its management. This adaptation encompasses language, terminology, environmental context, and the availability of locally relevant dietary options (Alaofè et al., 2021). Culturally sensitive educational programs can positively impact participants' comprehension and empower them to take charge of their self-care (Stone, 2006).

Sensitivity to local culture in diabetes educational programs also opens up alternative approaches, methods, and educational materials that can alleviate learning constraints (Omodara et al., 2022). The focus on cultural adaptation extends to the entire education team, emphasizing the importance of understanding local culture, selecting appropriate teaching materials, and delivering education in a manner that resonates with the local context (Juanamasta et al., 2021; Lamptey et al., 2022; Suardana et al., 2023).

Studying has several limitations. First, related to the sample size, the findings may not be easily generalizable to populations outside of the specific cultural and geographical context of the study. Second, participants' responses can be subject to bias. They might provide socially desirable responses or unintentionally misrepresent their experiences. Last but not least, the

study is based on the experiences of individuals with diabetes mellitus in a specific cultural context (Balinese culture), the findings may not fully apply to individuals from different cultural backgrounds. It's crucial to acknowledge this cultural bias.

4. CONCLUSION

In conclusion, the study involved participants aged 40-60 years, all of whom were women. The findings suggest that there is a lack of ability in self-management among Type 2 Diabetes Mellitus patients. Beliefs and perceptions about Type 2 DM are diverse but often limited by knowledge gaps. The influence of patrilineal family structures is significant in diabetes management. Participants strongly desire culturally adapted educational programs to enhance their diabetes management skills.

Based on these findings, it is recommended that diabetes education teams consider cultural adaptation in their programs to enhance acceptance, understanding, and implementation by patients. Future research should explore local culture more deeply to develop materials, media, and educational content for independent diabetes management programs. This will help bridge the gap between cultural context and effective diabetes care.

REFERENCES

American Diabetes Association. (2017). 4. Lifestyle Management. *Diabetes Care*, *40*(Supplement_1), S33–S43. https://doi.org/10.2337/dc17-S007

American Diabetes Association. (2022). 6 . Glycemic Targets : Standards of Medical Care in Diabetes—2022. *Diabetes Care*, *45*(Supplement_1), S83–S96. https://doi.org/10.2337/dc22-S006

Alaofè, H., Yeo, S., Okechukwu, A., Magrath, P., Amoussa Hounkpatin, W., Ehiri, J., & Rosales, C. (2021). Cultural Considerations for the Adaptation of a Diabetes Self-Management Education Program in Cotonou, Benin: Lessons Learned from a Qualitative Study. *International Journal of Environmental Research and Public Health*, *18*(16), 8376. https://doi.org/10.3390/ijerph18168376

Beck, J., Greenwood, D. A., Blanton, L., Bollinger, S. T., Butcher, M. K., Condon, J. E., Cypress, M., Faulkner, P., Fischl, A. H., Francis, T., Kolb, L. E., Lavin-Tompkins, J. M., MacLeod, J., Maryniuk, M., Mensing, C., Orzeck, E. A., Pope, D. D., Pulizzi, J. L., Reed, A. A., … Wang, J. (2018). 2017 National Standards for Diabetes Self-Management Education and Support. *Diabetes Educator*, *44*(1), 35–50. https://doi.org/10.1177/0145721718754797

Bennich, B. B., Røder, M. E., Overgaard, D., Egerod, I., Munch, L., Knop, F. K., Vilsbøll, T., & Konradsen, H. (2017). Supportive and non-supportive interactions in families with a type 2 diabetes patient: An integrative review. *Diabetology and Metabolic Syndrome*, *9*(1), 1–9. https://doi.org/10.1186/s13098-017-0256-7

Bhandari, P., & Kim, M. (2016). Self-Care Behaviors of Nepalese Adults with Type 2 Diabetes: A Mixed Methods Analysis. *Nursing Research*, *65*(3), 202–214. https://doi.org/10.1097/NNR.0000000000000153

Emara, R. A., Hamed, M., Awad, M., & Zeid, W. (2021). Effect of diabetes self-management education program on glycemic control in diabetic patients attending the family medicine outpatient clinic, Suez Canal University Hospital, Ismailia, Egypt. *The Egyptian Journal of Internal Medicine*, *33*(1), 1-6. https://doi.org/10.1186/s43162-021-00058-9

Estacio, E. V., McKinley, R. K., Saidy-Khan, S., Karic, T., Clark, L., & Kurth, J. (2015). Health literacy: why it matters to South Asian men with diabetes. *Primary Health Care Research & Development*, *16*(2), 214–218. https://doi.org/10.1017/S1463423614000152

IDF. (2015). International Diabetes Federation. IDF Diabetes Atlas, 7th edn. Brussels, Belgium: International Diabetes Federation. *International Diabetes Federation*. https://doi.org/10.1289/image.ehp.v119.i03

Juanamasta, I. G., Aungsuroch, Y., Gunawan, J., Suniyadewi, N. W., & Nopita Wati, N. M. (2021). Holistic Care Management of Diabetes Mellitus: An Integrative Review. *International Journal of Preventive Medicine*, *12*, 69. https://doi.org/10.4103/ijpvm.IJPVM_402_20

Juanamasta, I. G., Wati, N. M. N., & Widana, A. A. G. O. (2020). Covid-19: A Balinese Viewpoint. *Belitung Nursing Journal*, *6*(4), 143-144. https://doi.org/10.33546/BNJ.1133

Kementerian Kesehatan Republik Indonesia. (2018). *Hasil utama RISKESDAS 2018*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Lamb, C., Babenko-Mould, Y., Evans, M., Wong, C. A., & Kirkwood, K. W. (2019). Conscientious objection and nurses: Results of an interpretive phenomenological study. *Nursing Ethics*, *26*(5), 1337–1349. https://doi.org/10.1177/0969733018763996

Lamptey, R., Davies, M. J., Khunti, K., Schreder, S., Stribling, B., & Hadjiconstantinou, M. (2022). Cultural adaptation of a diabetes self-management education and support (DSMES) programme for two low resource urban settings in Ghana, during the COVID-19 era. *BMC Health Services Research*, *22*(1), 996. https://doi.org/10.1186/s12913-022-08390-8

Lv, F., Gao, X., Huang, A. H., Zu, J., He, X., Sun, X., Liu, J., Gao, N., Jiao, Y., Keane, M. G., Zhang, L., Yeo, Y. H., Wang, Y., & Ji, F. (2022). Excess diabetes mellitus-related deaths during the COVID-19 pandemic in the United States. *EClinicalMedicine*, *54*, 101671. https://doi.org/10.1016/j.eclinm.2022.101671

Mikhael, E. M., Hassali, M. A., Hussain, S. A., & Shawky, N. (2019). Self-management knowledge and practice of type 2 diabetes mellitus patients in Baghdad, Iraq: A qualitative study. *Diabetes, Metabolic Syndrome and Obesity*, *12*, 1–17. https://doi.org/10.2147/DMSO.S183776

Murphy, K., Chuma, T., Mathews, C., Steyn, K., & Levitt, N. (2015). A qualitative study of the experiences of care and motivation for effective self-management among diabetic and hypertensive patients attending public sector primary health care services in South Africa. *BMC health services research*, *15*, 1-9. https://doi.org/10.1186/s12913-015-0969-y

Omodara, D. A., Gibson, L., & Bowpitt, G. (2022). Exploring the impact of cultural beliefs in the self-management of type 2 diabetes among Black sub-Saharan Africans in the UK–a qualitative study informed by the PEN-3 cultural model. *Ethnicity and Health*, *27*(6), 1358–1376. https://doi.org/10.1080/13557858.2021.1881764

Pamungkas, R. A., Chamroonsawasdi, K., & Usman, A. M. (2021a). Unmet basic needs and family functions gaps in diabetes management practice among Indonesian communities with uncontrolled type 2 diabetes: A qualitative study. *Malaysian Family Physician*, *16*(3), 23–35. https://doi.org/10.51866/oa1123

Pamungkas, R. A., Chamroonsawasdi, K., & Usman, A. M. (2021b). Unmet basic needs and family functions gaps in diabetes management practice among Indonesian communities with uncontrolled type 2 diabetes: A qualitative study. *Malaysian Family Physician*, *16*(3), 23–35. https://doi.org/10.51866/oa1123

Pamungkas, R. A., Chamroonsawasdi, K., & Vatanasomboon, P. (2017). A systematic review: family support integrated with diabetes self-management among uncontrolled type II diabetes mellitus patients. *Behavioral Sciences*, *7*(3), 62. https://doi.org/10.3390/bs7030062

PERKENI. (2021). *Pedoman Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 di Indonesia 2021*. PB PERKENI.

Pesantes, M. A., Del Valle, A., Diez-Canseco, F., Bernabé-Ortiz, A., Portocarrero, J., Trujillo, A., Cornejo, P., Manrique, K., & Miranda, J. J. (2018). Family Support and Diabetes: Patient's Experiences From a Public Hospital in Peru. *Qualitative Health Research*, *28*(12), 1871–1882. https://doi.org/10.1177/1049732318784906

Polit, D. F., & Beck, C. T. (2017). *Nursing research: Generating and assessing evidence for nursing practice*. Lippincott Williams & Wilkins.

Rahmawati, N. (2016). Perempuan Bali dalam Pergulatan Gender. *Jurnal Studi Kultural*, *1*(1), 58–64. http://journals.an1mage.net/index.php/ajsk

Ritruechai, S., Khumwong, W., Rossiter, R., & Hazelton, M. (2018). Thematic analysis guided by Max van Manen: Hermeneutic (interpretive) phenomenological approach. *Journal of Health Science Research*, *12*(2), 39–48. https://he01.tci-thaijo.org/index.php/JHR/article/view/164236/119020

Shakibazadeh, E., Larijani, B., Shojaeezadeh, D., Rashidian, A., Forouzanfar, M. H., & Bartholomew, L. K. (2011). Patients' perspectives on factors that influence diabetes self-care. *Iranian journal of public health*, *40*(4), 146.

Shrivastava, S. R., Shrivastava, P. S., & Ramasamy, J. (2013). Role of self-care in management of diabetes mellitus. *Journal of diabetes & Metabolic disorders*, *12*(1), 1-5. https://doi.org/10.1186/2251-6581-12-14

Sohal, T., Sohal, P., King-Shier, K. M., & Khan, N. A. (2015). Barriers and facilitators for type-2 diabetes management in south asians: A systematic review. *PLoS ONE*, *10*(9), 1–15. https://doi.org/10.1371/journal.pone.0136202

Spence, D. G. (2017). Supervising for Robust Hermeneutic Phenomenology: Reflexive Engagement Within Horizons of Understanding. *Qualitative Health Research*, *27*(6), 836–842. https://doi.org/10.1177/1049732316637824

Suardana, I. W., Yusuf, A., Hargono, R., & Juanamasta, I. G. (2023). Spiritual Coping "Tri Hita Karana" among Older Adults during Pandemic COVID-19: A Perspective of Balinese Culture. *Universal Journal of Public Health*, *11*(3), 297–304. https://doi.org/10.13189/ujph.2023.110303

Sudarta, W. (2017). Pengambilan keputusan gender rumah tangga petani pada budidaya tanaman padi sawah sistem subak di perkotaan. *Jurnal Manajemen Agribisnis*, *5*(2), 59-65.

Stone, M. A., & Drake, L. (2006). Cultural awareness in diabetes education. *Practice Nursing*, *17*(6), 1-5.

Tan, C. C. L., Cheng, K. K. F., Sum, C. F., Shew, J. S. H., Holydard, E., & Wenru, W. A. N. G. (2018). Perceptions of diabetes self-care management among older Singaporeans with type 2 diabetes: A qualitative study. *Journal of Nursing Research*, *26*(4), 242-249. https://doi.org/10.1097/jnr.0000000000000226

Tewahido, D., & Berhane, Y. (2017). Self-care practices among diabetes patients in Addis Ababa: a qualitative study. *PloS one*, *12*(1), e0169062. https://doi.org/10.1371/journal.pone.0169062

Todres, L., & Wheeler, S. (2001). The complementarity of phenomenology, hermeneutics and existentialism as a philosophical perspective for nursing research. *International Journal of Nursing Studies*, *38*(1), 1–8. https://doi.org/10.1016/S0020-7489(00)00047-X

van Manen, M. (2016). *Researching Lived Experience, Second Edition*. New York: Routledge. https://doi.org/10.4324/9781315421056

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 815-822
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1355*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Is Infection Prevention and Control Training Can Increase Knowledge and Compliance of Nurses?

Ni Made Nopita Wati[1a*], Elmy Subyaktien[2b], Tri Rahyuning Lestari[3c], Diah Pusparini Pendet[4d], Nunung Rachmawati[5e], I Gede Juanamasta[1f], Yupin Aungsuroch[6g]

[1] Department of Nursing, STIKES Wira Medika Bali, Denpasar, Bali, Indonesia
[2] RSUP Prof. dr.I.G.N.G Ngoerah, Denpasar, Bali, Indonesia
[3] Department of Nursing, STIKES Widya Dharma Husada, Tangerang, Banten, Indonesia
[4] Department of Nursing, STIKES Kesdam IV/Udayana, Denpasar, Bali, Indonesia
[5] Department of Nursing, Akper YKY Yogyakarta, Yogyakarta, Indonesia
[6] Faculty of Nursing, Chulalongkorn University, Bangkok, Thailand

[a] Email address: ners.pita@gmail.com
[b] Email address: trilestari100@gmail.com
[c] Email address: diahpusparinipendet@gmail.com
[d] Email address: rachmawa84@gmail.com
[e] Email address: juana.masta.90@gmail.com
[f] Email address: elmysubyartien@yahoo.com
[g] Email address: yupin.a@chula.ac.th

Received: 18 September 2023 Revised: 27 November 2023 Accepted: 31 December 2023

Abstract
One of the indicators of service quality at the hospital is Healthcare-Associated Infections (HAIs) that can be prevented by hand hygiene, which is a procedure for cleaning hands with soap water, or alcohol-based liquids. This study aimed to identify the effect of Infection Prevention and Control (IPC) training on the level of knowledge and compliance of five moments for hand hygiene in nurses at the Dharma Yadnya Hospital in Denpasar. This study used a pre-experimental one-group pre-post test without a control group design. The number of samples was 42 nurses with purposive sampling techniques that met the inclusion and exclusion criteria. The results showed that before training 26 nurses (61.9%) had a good level of knowledge, and after training, 41 nurses (97.6%) had good knowledge. With regard to compliance with five moments for hand hygiene, before training 22 nurses (52.4%) were not compliant, and after training 29 nurses (69%) imperfectly adhered to the procedure. Mandatory training in IPC influences the level of knowledge and adherence to the five moments for hand hygiene among nurses. Suggestions for hospitals to provide continuity of education related to IPC, monitor nurses' compliance behaviors of the five moments for hand hygiene, either by direct observation or electronically, and provide rewards and punishments for behavioral evaluations.

Keywords: Compliance, Hand Hygiene, Hospitals, Knowledge, Nurse.

Corresponding Author:

Ni Made Nopita Wati
Department of Nursing, STIKES Wira Medika Bali, Denpasar, Bali, Indonesia
Email: ners.pita@gmail.com

1. INTRODUCTION

HAIs are infections that occur in patients during treatment in hospitals and other health care facilities where there was no infection, not incubated, in the beginning of the patient treatment, including infections in the hospital but appear after the patient returns home, also infections due to work, hospital staff and health workers related to the process of health services in health care facilities (Kementerian Kesehatan Republik Indonesia, 2017). The most common types of HAIs in health services, especially hospitals, are Ventilator Associated Pneumonia (VAP), Bloodstream Infection (BSI), Urinary Tract Infection due to catheterization (UTI), Surgical Site Infection (SSI) (Centers for Disease Control and Prevention, 2014; Kementerian Kesehatan Republik Indonesia, 2017). The high prevalence of HAIs is a threat to hospital services.

According to the data from the CDC contained in the national and state HAI progress report SIR acute care hospitals data (Centers for Disease Control and Prevention, 2016), it is mentioned that from a total of 53 states in the USA (United Stated America) there was an increase in the number of HAIs within a year in several states, such as the IAD (Blood Flow Infection) rate in Puerto Rico increased 45%, the incidence of UTI (Urinary Tract Infections) in Vermont increased by 60%, the incidence of VAP (Ventilator Associated Pneumonia) in Nevada increased by 30%, the IDO number (Regional Infection Operations) Colon surgery in Alaska increased 335%, the number of MRSA (Multidrug Resistant Staphylococcus Aureus) in Texas 9%. The incidence of HAIs occurs in 15% of all hospitalized patients. HAIs account for around 4-56% of neonatal deaths, with an incidence rate of around 75% in Southeast Asia and Sub-Saharan Africa. The incidence of HAIs in Indonesia is taken from 10 education hospitals that conduct active surveillance obtained a figure of 6-16% with an average of 9.8% (Kementerian Kesehatan Republik Indonesia, 2017). The incidence of HAIs in health workers was found to be more than 8 million exposed to blood or other body fluids. The most frequent contamination pathway is through contact wound types with contaminated sharp instruments such as needle punctures and scalpels (82%), contact with mucous membranes of the eyes, nose and mouth (14%), exposed to peeling or damaged skin (3%) (Centers for Disease Control and Prevention, 2016).

An increase in the incidence of HAIs in a hospital will have an impact on lengthening day care, patient death, the increase of care costs, as well as resulting in poor service quality and hospital image (Stewart et al., 2021). Other impacts are increasing functional helplessness, emotional distress, disability, and decreasing quality of life, even death (Ernawati et al., 2014). As a result of the spread of infection globally will also increase the incidence of MRSA in health facilities and the unavailability of new generation antimicrobials will be a serious problem. Safety for health workers is also a concern to reduce the number of injuries caused by exposure to HAIs, which can affect the quality of health services provided.

HAIs can be prevented if health services are able to implement the IPC program consistently. IPC is an effort to ensure that everyone is protected from the possibility of contracting infection from public sources, and while receiving health services in various health facilities, by breaking the cycle of transmission of the disease including infectious agents, reservoirs, portal of exit, transmission methods, portal of entry, and host vulnerable so that infection can be prevented or stopped (Komite PPI RSUP Sanglah Denpasar, 2019). IPC activity is a standard of service quality and is important for patients, health workers, and visitors from the incidence of infection by taking into account the cost effectiveness (Kementerian Kesehatan Republik Indonesia, 2017).

The implementation of IPC in health service facilities aims to protect patients, health workers, visitors who receive health services and the community in their environment through standard precautions and transmission-based (Kementerian Kesehatan Republik Indonesia,

2017). Hand hygiene is the first point in 11 standard precautionary programs that must be routinely implemented by health workers. WHO sparked a global patient safety challenge, clean care is safe care, that is, formulating innovative strategies for implementing hand hygiene for health workers with five moments for hand hygiene. Hand hygiene is an effort to clean the hands from microorganisms with soap and water wash (hand wash) and hand rubs alcohol-based liquid antiseptic, by way of six steps and carried out in accordance with five moments for hand hygiene, namely, before contact with the patient, before the aseptic action, after contact with the patient, after contact with the patient's body fluids, and after contact with the patient's environment (World Health Organization, 2009).

Nurses as health workers with a longer intensity accompanying patients in providing nursing care, are required to have good knowledge, skills and attitudes while caring for patients. Nurse compliance in doing hand hygiene is one of the keys to success in preventing HAIs. The results of the nurses' compliance study conducted hand hygiene at Graha Husada Hospital in Bandar Lampung from 47 respondents, 38.3% were compliant with six steps of five moments for hand hygiene and 61.7% were not compliant (Hermawan et al., 2018). Other research conducted at the Dr. Soepraoen Malang of 51 nurses to obtain data of five moments for hand hygiene. For the moment 1 before contact with patients, mostly the nurses did not do hand hygiene for 362 times (82.27%), for moment 2 before the aseptic action, the nurses did not do hand hygiene for 379 times (86.14%), for moment 3 after contact with the patient's body fluids, most of them did hand hygiene for 276 times (72.33%), while for moments 4 and 5 all had hand hygiene for 440 times (100%) (Nurmayunita & Hastuti, 2017). This study aims to identify the effect of the IPC mandatory training on the level of knowledge and compliance of five moments for hand hygiene in nurses.

2. RESEARCH METHOD

This study uses a quantitative approach with a pre-experimental one group pre-post test design without control group design. The study was conducted at the Private Hospital held on September 14-October 31, 2019. This study uses two variables, namely independent variables namely compulsory training on IPC, the dependent variable is the level of knowledge and compliance of five moments for hand hygiene to nurses.

The population used in this study were all nurses of RSU Dharma Yadnya, as many as 68 people, with purposive sampling techniques that met the inclusion and exclusion criteria set by the researchers. Inclusion criteria were practical nurses in the Ayodya Room, Bharata Room, ICU (Intensive Care Unit), Hemodialysis Room, and Emergency Room Installation (IGD), and willing to act as respondents by signing informed consent. Exclusion criteria were nurses on leave or illness during the research process, nurses on assignments studying or attending education/training leaving hospital assignments, nurses on structural duty in hospitals, IPCN (Infection Prevention Control Nurse), and IPCLN (Infection Prevention Control Link Nurse). The number of samples that met the inclusion and exclusion criteria was 42 people.

The data collection instrument used was a questionnaire consisting of nurses' characteristics and nurses' knowledge about IPC material adopted from Imallah (2015) in the form of pre and post-test and observation sheets of compliance of five moments for hand hygiene for nurses.

The Principal Investigator (PI) developed Nurses IPC Knowledge Questionnaire in Bahasa. The questionnaire consisted of 20 questions covering the definition and purpose of hand hygiene, techniques and time to clean hands, the reasons why nurses need to wash their hands, and five moments of washing hands. The questionnaire was developed in the form of multiple choice questions with four answer choices. Respondents' answers are adjusted to the answer key, the correct answer will get a value of 1 while the wrong answer is given a value of 0. Total scores on each question will be added up and given a good grade (16-20), enough (12-

15), less (≤ 11). This research has passed the test of validity and reliability. The results of the validity test show the value of r 0.396-0.814 (r table = 0.361) this shows a valid questionnaire shown by r arithmetic> r table. The reliability test results showed Alpha Cronbach value of 0.886.

The observation sheet used to see nurses' compliance in performing the five moments for hand hygiene and the six steps consists of three scores in each moment that will be observed in each nurse for the pre and post IPC training on one occasion. The value of the observation sheet consists of 1) a score of 2 for respondents compliant to do hand hygiene with a technique of 6 perfect steps at each moment, 2) a score of 1 for respondents doing hand hygiene with a technique of 6 steps less than perfect at each moment, 3) A score of 0 for respondents who did not do hand hygiene at each moment. Then each score at each moment will be added up and given a score of perfect obedience (score 10), less than perfect obedience (score 5-9), non-compliance (score 0-4). This research has passed the test of validity and reliability. The results of the validity test show the value of r 0.532-0.943 (r table = 0.361) this shows a valid questionnaire shown by r arithmetic> r table. The reliability test results showed Alpha Cronbach value of 0.968.

The researcher likened the perceptions of the 2 enumerators who helped to observe five moments for hand hygiene in the respondents determined by the researcher, by explaining the observation sheet and how to assess the respondent's compliance according to the researcher's objectives. Then, the researcher takes an informal approach by explaining the purpose and objectives of the study, research procedures, rights and obligations when becoming a respondent, and signing an informed consent, if the respondent is willing. Respondents who have signed an informed consent were observed on September 14-19, 2019 by enumerators and researchers to assess nurses' compliance in carrying out five moments for hand hygiene, six steps at a time.

Respondents were invited back on 20 September 2019 at 12.00 pm (GMT+7) for a pre-test which was divided into two sessions of the total sample. The researcher was assisted by the Hospital IPC team (IPCN) in providing interventions in the form of IPC compulsory training which was divided into two meeting sessions, where each material delivery session was conducted for two hours, and provided training modules to all respondents.

Researchers invited respondents back on October 21, 2019 at 12.00 pm to conduct a post test that was divided into two sessions of total respondents. Respondents were re-observed by enumerators and researchers to assess compliance in carrying out five moments for hand hygiene six steps in one chance on 23 to 31 October 2019.

Researchers re-examined the completeness of the questionnaire filled out by respondents and conducted data processing on the collected questionnaires and checked return the observation sheet data that has been collected. The study includes a univariate analysis of age, sex, education, work experience, knowledge, and compliance. The bivariate analysis employed the non-parametric McNemar test to assess the disparity between the pre- and post-intervention groups.

3. RESULTS AND DISCUSSION

The research was conducted from September to October 2019 with 42 nurses as a sample. The characteristics of nurses are displayed in Table 1, while the research results of the intervention are in Table 2 below.

Table 1. Distribution of respondents.

Variables	**F (n=42)**	**%**
Age		
Late adolescence (17-25 years)	6	14,3

Variables	F (n=42)	%
Early adulthood (26-35 years)	27	64,3
Late adulthood (36-45 years)	7	16,7
Early elderly (46-55 years)	2	4,8
Sex		
Male	13	31,0
Female	29	69,0
Education		
Vocational	33	78,6
Bachelor	9	21,4
Work experience		
1-10 years	32	76,2
11-20 years	5	11,9
21-30 years	5	11,9

Table 1 showed characteristics of respondents based on the age of majority in early adulthood (26-35 years) with 27 respondents (64.3%), the majority were female respondents with 29 respondents (69.0%), the majority were graduates of DIII Nursing with 33 respondents (78.6%), and the majority had worked in the Dharma Yadnya Hospital in Denpasar for 1-10 years, totaling 32 respondents (76.2%).

Table 2. Pre-post intervention analysis (n=42).

Variables	Before		After		p-value
	F	%	F	%	
Level of knowledge					
Low of knowledge	1	2,4	0	0	
Moderate of knowledge	15	35,7	1	2,4	0.000
High of knowledge	26	61,9	41	97,6	
Compliance					
Not compliant	22	52,4	0	0	
Less than compliant	19	45,2	29	69	0.000
Perfectly compliant	1	2,4	13	31	

Table 2 shows the level of knowledge of nurses before being given compulsory training on IPC, namely, those having good knowledge with 26 respondents (61.9%), sufficient knowledge with 15 respondents (35.7%), and 1 respondent (2.4%) with less knowledge. The results of the questionnaire answers were that 32 respondents (76.2%) answered incorrectly on item number 13 regarding the theory of HAIs, and only 10 respondents (23.8%) answered correctly. After receiving 2 hours of required IPC training from the IPC Hospital team, the level of knowledge among nurses increased. There were 41 respondents (97.6%) have good knowledge, and only 1 respondent (2.4%) has sufficient knowledge, meaning that of the 42 respondents who participated in the training, 41 respondents (97.6%) understood well the material provided and were able to answer well 20 questionnaire questions that were distributed 1 month after the training was given.

Each respondent in this study was observed on one occasion an activity that has an indication to perform the six steps hand hygiene based on five moments. The results showed nurses' adherence to five moments for hand hygiene before being given compulsory training on IPC, 22 respondents (52.4%) were not compliant, 19 people (45.2%) were less than compliant, and only 1 respondent (2.4%) were perfectly obedient. Most did not do hand hygiene at the first moment, namely before contact with patients, 24 respondents (57.1%) and only 1 respondent (2.4%) were perfectly obedient.

Nurse compliance with five moments for hand hygiene after IPC compulsory training is 0% not compliant, 29 respondents (69%) are less than compliant, and 13 respondents (31%) are perfectly obedient, there is an increase in nurse compliance compared to before training. All nurses have done five moments for hand hygiene both by hand wash or hand rub techniques, although they are still less than perfect six steps. This is because respondents begin to understand the benefits of preventing germ transmission infections when they are obedient in carrying out five moments for hand hygiene with a perfect 6-step technique.

Analysis on the effect of mandatory IPC training on the level of nurse knowledge and compliance ($p<.05$). There is the influence of mandatory IPC training on the level of nurses' knowledge and compliance in Dharma Yadnya public hospitals Denpasar. Based on the results of the output rank of a total of 42 respondents obtained the mean value of knowledge, 35 respondents showed an increase in knowledge, 7 respondents with no change of knowledge, and no respondent showed a decrease. Meanwhile, 33 people showed an increase in compliance, 3 people did not change, and 6 people showed a decrease.

The distribution of module as a source of reading for nurses is useful for repeating IPC material that has been given so that it is more effective to remember without going through the face-to-face process with IPCN trainers repeatedly. Modules can be duplicated not only for nurses but other health workers so that exposure to IPC material is more effective and efficient. The more information a person receives, the more the knowledge of that person increases, giving rise to the awareness of that person behaving in accordance with the knowledge he/she has. This is in line with Nicen (2018), there were significant differences in knowledge, attitudes, and skills after a bundle care management training using questionnaire instruments, observation sheets, and modules on hospital IPC, with 80 respondents which were divided into 40 respondents in the treatment group and 40 respondents in the control group with a p value<0.005.

According Dewi, (2018) assessed the effectiveness of IPC training on the knowledge of employees of the National Brain Center Hospital (RSP PON) through evaluating the pre and post test results of 30 respondents which obtained 100% of respondents experienced an increase in test results. Person's knowledge is mostly acquired or captured through the five senses, the more senses are used to receive information, the more knowledge obtained will be more and more clear (Best & Cameron, 1986). Human knowledge can be obtained through the eyes and ears, through the process of seeing or listening, and also through the process of experience and learning process, such as training from the hospital as a means of providing information, not only delivered verbally but also by performing a demonstration of the movement to truly understand what is the right flow and movement to carry out the 6 steps of hand hygiene as a basis for applying the five moments for hand hygiene. Knowledge become an important determinants of the nurse hand hygiene (Labrague et al., 2018; Setyorini et al., 2022; White et al., 2015). Nurses' hand hygiene intentions will increase whereby knowledge of these factors increased, included subjective norm and knowledge, group norm, perceived behavioral factor, and risk susceptibility (White et al., 2015).

According Mustariningrum & Koeswo, (2015), there was a significant relationship between the provision of training programs organized by the IPC committee and IPCLN management with the increase in the knowledge, attitudes, and skills of officers in Dr. Iskak Tulungagung Hospital. The training program succeeded in increasing the knowledge of officers. Moreover another study showed structured training program and multimodal intervention could improve hand hygiene compliance (Alp et al., 2011; Laskar et al., 2018; Oh et al., 2012). Training will improve knowledge, perceived hand hygiene practice, good adherence, and easy to perform (Laskar et al., 2018; Oh et al., 2012).

4. CONCLUSION

IPC training on respondents' give positive impact, they increased the level of knowledge and compliance. Increasing the knowledge and compliance of nurse in conducting five moments for hand hygiene in more detail to prevent the transmission of germs from patients to officers and vice versa. There shall be continuous education related to IPC in the form of training, in-house training, and through audio-visual media. Therefore, IPC Committee, namely IPCN and IPCLN, is better monitor the nurse's compliance behavior in five moments for hand hygiene both by direct observation and electronically, give rewards and punishment for behavioral evaluation.

REFERENCES

Alp, E., Ozturk, A., Guven, M., Celik, I., Doganay, M., & Voss, A. (2011). Importance of structured training programs and good role models in hand hygiene in developing countries. *Journal of Infection and Public Health*, *4*(2), 80–90. https://doi.org/10.1016/j.jiph.2011.03.001

Best, J. A., & Cameron, R. (1986). Health Behavior and Health Promotion. *American Journal of Health Promotion*, *1*(2), 48–57. https://doi.org/10.4278/0890-1171-1.2.48

Centers for Disease Control and prevention. (2014). *Types of Healthcare-associated Infections*. Centers for Disease Control and prevention. https://www.cdc.gov/hai/infectiontypes.html#print

Centers for Disease Control and prevention. (2016). *National and State Healthcare Associatied Infection.* Centers for Disease Control and prevention.

Dewi, N. F., & Hikmah, Y. (2018). Efektivitas Program Pelatihan Program Pengendalian Infeksi (Ppi) Melalui Evaluasi Pre Test Dan Pos Test Di Bagian Diklat Rumah Sakit Pusat Otak Nasional (RSP PON). *Jurnal Administrasi Bisnis Terapan (JABT)*, *1*(1),51-57. https://doi.org/10.7454/jabt.v1i1.23

Ernawati, E., Rachmi, A. T., & Wiyanto, S. (2014). Penerapan hand hygiene perawat di ruang rawat inap rumah sakit. *Jurnal Kedokteran Brawijaya*, *28*(1), 89–94. https://doi.org/10.21776/ub.jkb.2014.028.01.30

Hermawan, D., Junika, E., & Nadeak, J. (2018). Hubungan Kepatuhan Perawat Melaksanakan Standar Prosedur Operasional (SPO) Cuci Tangan Terhadap Kejadian Phlebitis Di Rumah Sakit Graha Husada Bandar Lampung Tahun 2018. *Holistik Jurnal Kesehatan*, *12*(3), 196–204.

Imallah, R. N. (2015). *Pengaruh Feedback Intervention Trial (FIT) Terhadap Kepatuhan Perawat Melakukan Kebersihan Tangan di Rumah Sakit Pusat Angkatan Darat (RSPAD) Gatot Subroto.* Universitas Indonesia.

Kementrian Kesehatan Republik Indonesia. (2017). *Pedoman Pencegahan dan Pengendalian Infeksi di Fasilitas Pelayanan Kesehatan*. Kementerian Kesehatan Republik Indonesia.

Komite PPI RSUP Sanglah Denpasar. (2019). *Pencegahan dan Pengendalian Infeksi di Rumah Sakit Sanglah Denpasar*. RSUP Sanglah.

Labrague, L. J., McEnroe-Petitte, D. M., van de Mortel, T., & Nasirudeen, A. M. A. (2018). A systematic review on hand hygiene knowledge and compliance in student nurses. *International Nursing Review*, *65*(3), 336–348. https://doi.org/10.1111/inr.12410

Laskar, A. M., R, D., Bhat, P., Pottakkat, B., Narayan, S., Sastry, A. S., & Sneha, R. (2018). A multimodal intervention to improve hand hygiene compliance in a tertiary care center. *American Journal of Infection Control*, *46*(7), 775–780. https://doi.org/10.1016/j.ajic.2017.12.017

Mustariningrum, D. L. T., & Koeswo, M. (2015). Kinerja IPCLN dalam pencegahan dan pengendalian infeksi di Rumah Sakit: peran pelatihan, motivasi kerja dan supervisi. *Jurnal Aplikasi Manajemen*, *13*(4), 643–652.

Nicen, S. (2018). *Efektivitas Manajemen Bundle Care Terhadap Kompetensi Profesional Perawat dalam Mengelola Healthcare Associated Infections*. Universitas Andalas.

Nurmayunita, H., & Hastuti, A. P. (2017). Pengaruh Penerapan Pencegahan Medication Error Terhadap Perilaku Perawat Tentang Tujuh Benar Pemberian Obat Di RSUI Kabupaten Malang. *Jurnal Kesehtan Hesti Wira Sakti*, *5*(1), 16–23.

Oh, E., Mohd Hamzah, H. B., Chain Yan, C., & Ang, E. (2012). Enhancing hand hygiene in a polyclinic in Singapore. *International Journal of Evidence-Based Healthcare*, *10*(3), 204–210. https://doi.org/10.1111/j.1744-1609.2012.00277.x

Setyorini, Y., Ardesa, Y. H., & Darmawan, R. E. (2022). Indonesians' readiness in facing long-term COVID-19 pandemic. *Jurnal Ners*, *17*(1), 14–18. https://doi.org/10.20473/jn.v17i1.28707

Stewart, S., Robertson, C., Pan, J., Kennedy, S., Haahr, L., Manoukian, S., Mason, H., Kavanagh, K., Graves, N., Dancer, S. J., Cook, B., & Reilly, J. (2021). Impact of healthcare-associated infection on length of stay. *Journal of Hospital Infection*, *114*, 23–31. https://doi.org/10.1016/j.jhin.2021.02.026

White, K. M., Starfelt, L. C., Jimmieson, N. L., Campbell, M., Graves, N., Barnett, A. G., Cockshaw, W., Gee, P., Page, K., Martin, E., Brain, D., & Paterson, D. (2015). Understanding the determinants of Australian hospital nurses' hand hygiene decisions following the implementation of a national hand hygiene initiative. *Health Education Research*, *30*(6), 959–970. https://doi.org/10.1093/her/cyv057

World Health Organization. (2009). *Guidelines on Hand Hygiene in Health Care: a Summary*. *Geneva: WHO*.

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 823-830
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1066*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Persistence of Antibody Response Against SARS-CoV-2 After Vaccination

Heri Setiyo Bekti[1a*], Nur Habibah[1b], I Gusti Agung Ayu Dharmawati[1c], Fusvita Merdekawati[1d], Ganjar Noviar[1e]

[1] Department of Medical Laboratory Technology, Poltekkes Kemenkes Denpasar, Denpasar, Bali, Indonesia

[a] Email address: herisetiyob7@gmail.com
[b] Email address: nurhabibah.polkesden@gmail.com
[c] Email address: ayu_dharmawati@yahoo.com
[d] Email address: fusvitamerdekawati@gmail.com
[e] Email address: ganjar.noviar@gmail.com

Received: 10 February 2023 Revised: 22 December 2023 Accepted: 31 December 2023

Abstract
SARS-CoV-2 is the causative agent of the disease known as COVID-19. COVID-19 is spreading very fast around the world. One of the immune responses that play a role in against SARS-CoV-2 infection is the production of antibodies, which is 3 weeks after infection. Where within 3 weeks after infection, antibodies will be produced against RBD and the S1 and S2 domains in glycoprotein S and nucleocapsid protein N. The ability of an antibody to inhibit viral infection is determined by its level or titer. This study aims to determine the description of antibody levels against SARS-CoV-2 after vaccination. This type of research is descriptive research. Measurement of antibody levels for SRBD SARS-CoV-2 was carried out using the CLIA method using the MAGLUMI tool. Of the 30 respondents, 23 people had received the third vaccine. The results of this study showed that the average level of SRBD antibodies against SARS-CoV-2 in respondents with 2 doses of vaccine (1.063,786 BAU/mL) was higher than in respondents with 3 doses of vaccine (535.651 BAU/mL). Vaccine intervals of more than 6 months (908.338 BAU/mL) have higher antibody levels than respondents with vaccine intervals of 1-6 months (228.006 BAU/mL). The conclusion of this study is the highest antibody titers are produced >6 months after vaccination, antibody titers are still detectable after 12 months of vaccination, and for further research, it can be measured antibody levels against SARS-CoV-2 from people who have got vaccination for a duration of 2 years or more.

Keywords: COVID-19, Immune Response, SARS-CoV-2, SRBD SARS-CoV-2, Vaccines.

Corresponding Author:

Heri Setiyo Bekti
Department of Medical Laboratory Technology, Poltekkes Kemenkes Denpasar, Denpasar, Bali, Indonesia
Email: herisetiyob7@gmail.com

1. INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic is caused by severe acute respiratory-syndrome-coronavirus-2 (SARS-CoV-2) (Hou et al., 2020). The first case of SARS-CoV-2 infection in humans was reported from the Chinese city of Wuhan in December 2019 (Alsagaby et al., 2021; Rauf et al., 2020). Within three months of the first case report, global human COVID-19 infection spread rapidly (Ejemel et al., 2020), and was declared a global health problem by WHO on 11 March 2020 (Gao et al., 2020). Data as of October 18, 2022, the number of COVID-19 cases worldwide reach 622 million cases of COVID-19 with 6 million deaths reported to WHO (WHO, 2022a). While in Indonesia there is a total of 6 million more confirmed cases with a death toll of 158,345 cases (WHO, 2022b).

COVID-19 is transmitted through droplets that come out when coughing and sneezing so that the transmission of SARS-CoV-2 can occur very quickly (Han & Yang, 2020). When SARS-CoV-2 enters human cells for infection, it will bind to the angiotensin-converting enzyme 2 (ACE-2) receptor molecule on target cells, where the part of the virus that attaches is spike protein (S). This attachment occurs in the receptor binding domain (RBD) in the S1 domain. After that, it is followed by the formation of the S2 domain pathway of the virus which aims to release nucleic acid (RNA) in the target cell for replication. At this stage the body's immune system will begin to actively work to fight the virus that causes infection, which consist of a cellular immune response and an immune response humoral (Li, 2020). The immune system is the best defense because it provides the body's natural ability to fight virus and infections that occur (Chowdhury, Hossain, Kashem, Shahid, & Alam, 2020).

One of the immune responses that play a role against SARS-CoV-2 infection is the production of antibodies. Three weeks after infection the body will produce antibodies against RBD, S1 and S2 domain of the spike glycoprotein (S) and nucleocapsid protein (N) (L'Huillier et al., 2021). Characteristics of a persistent humoral response over a long period of time play a role in defense against SARS-CoV-2 infection. The humoral immune response, main role by antibody production, where are the antibodies play inhibits the adhesion of SARS-CoV-2 to target cells and helps in neutralizing the virus (Syahniar et al, 2020).

Several studies have shown the role of antibodies against SARS-CoV-2 infection, namely: antibodies to protein S persisted for 75 days post-infection in >59% of patients (Iyer et al., 2020); antibody titers did not decrease after 4 months of infection. Intervention in prevention and treatment are important in overcoming current problem (Gudbjartsson et al., 2020) and humoral response persisted during the early 6 months of the pandemic by showing mild clinical symptoms of COVID-19 (L'Huillier et al., 2021). The fact that in COVID-19, sufferers who are symptomatic and have mild can transmit the virus. This is in contrast to SARS-CoV-1 and MERS-CoV, which are transmitted from patients who show clinical symptoms. Several things can be done to prevent this pandemic are implementing hygiene and sanitation as well as maintaining distance, monitoring the virus, and increasing population immunity (Speiser & Bachmann, 2020).

Diagnosis of SARS-CoV-2 infection divided into 2 types, namely: tests for detection infection and tests to detection immunity. Diagnosis infection done by detects genetic material of the virus and detects viral protein (s) from a nasopharynx or saliva swab, or detection of viral antigen proteins. In individuals the results will show positive in a relatively short time after the onset of clinical symptoms, an average of 14 days. However, further positive results of detection of genetic material or viral protein, it cannot be concluded that the infected person has immunity (WHO, 2022a). Diagnosis immunity to Detects antibodies against the virus from prior infection or vaccination. Uses serum/plasma or whole blood specimens to detect antibodies generated by prior SARS-CoV-2 infection or vaccination. SARS-CoV-2 antibodies are usually detectable 1-2 weeks after infection or vaccination. Therefore, serology-based tests

that can detect various antibodies in the blood and are persistent for months or even years are needed (Speiser & Bachmann, 2020; WHO 2023).

The vaccination program against SARS-CoV-2 in Indonesia officially started on January 13, 2021 and by October 9, 2021, 438,885,586 had received the vaccine (WHO, 2022b). The vaccines used in Indonesia are vaccines derived from whole virus, vector viruses, recombinant protein vaccines, and RNA vaccines (Kementerian Kesehatan Republik Indonesia, 2021).

Antibody production in the human body will from on the 7th day after exposure to antigen and it takes about 18 days of the formation of long-lived plasma cells. Research on SARS-CoV-1 in 2003 showed that antibody titers survivors above average over a 2 year period (Jacofsky, Jacofsky, & Jacofsky, 2020).

The ability of antibodies to inhibit viral infection is also determined by the titer. Therefore, a quantitative examination is needed that can measure how much antibody is in the body (Speiser & Bachmann, 2020). One method for examining antibody titers is the Chemiluminescence immunoassay (CLIA) which is a technique for detecting the bonding reaction between antigen and antibody. This examination method has high sensitivity and good specificity (Jacofsky, Jacofsky, & Jacofsky, 2020; Wang, Wu, Zong, Xu, & Ju, 2012). The implementation of the COVID-19 vaccination in Indonesia has not yet measured antibody levels both before and after vaccination. Form the explanation above, the authors are interested to measured of antibody levels against SARS-CoV-2 after vaccination, to provide information on how long and antibody levels after vaccination.

2. RESEARCH METHOD

This type of research is a descriptive study, where this study was conducted to determine the description of antibody levels against SARS-CoV-2 after vaccination. The sample size in this study was determined based on a simple random sampling technique, which is based on the number of residents who have received the SARS-CoV-2 vaccine in the city of Denpasar, Bali, and Cimahi Regency, West Java.

This research was conducted by involving research respondents with the following stages: (1) filling out informed consent, here participants receive information regarding the purpose of the research, potential risks, and their rights; (2) filling out questionnaires, here participants fill out a form containing questions, including: name, age, gender, address and history of Covid-19 vaccination.; (3) health examination, here, health examination are carried out, including: checking blood pressure and body temperature. This is done to ensure that participants are healthy and that samples can be taken properly when taken; (4) sampling (in the form of venous blood) then put into a blood tube with clot activator; and (5) After collection of the whole blood, allow the blood to clot by leaving it undisturbed at room temperature. This usually takes 15–30 minutes. Remove the clot by centrifuging at 1,000–2,000 x g at 2-8^{0}C for 10 minutes in a refrigerated centrifuge (Thermo Fisher Scientific, 2023).

This study were examined 30 samples. The examination method used to determine the antibody titer of respondents who have been vaccinated is using the CLIA method using the MAGLUMI tool. Chemiluminescent immunoassay (CLIA) is an immunoassay technique where the label, i.e. the true ‘‘indicator’’ of the analytic reaction, is a luminescent molecule. In general, luminescence is the emission of visible or near-visible (k = 300–800 nm) radiation which is generated when an electron transitions from an excited state to ground state. The resultant potential energy in the atom gets released in the form of light (Cinquanta, 2017). The CLIA antibody reagents against SARS-CoV-2 is removed from the box, then the barcode on the reagent is entered into the CLIA tool system, until the lot number of the reagent is detected by the device. The microbead was resuspended and completely homogenized. Then click the calibrate button to run the calibration. Patient serum is placed in the “sample area” and click

the button to run the test. This study has received ethical approval No: LB.02.03/EA/KEPK/ 0138/2022 from Health Research Ethics Committee Poltekkes Kemenkes Denpasar.

3. RESULTS AND DISCUSSION

From the research results obtained 30 respondents with a total of 5 male respondents and 25 female respondents. The characteristics of the respondent's data can be seen in Table 1.

Table 1. The Characteristics of Respondents Data

The Characteristics of Respondents	Total	Percentage (%)
Gender		
Male	5	16,67
Female	25	83,33
Vaccine Dose		
1st Dose	30	100
2nd Dose	30	100
3rd Dose	23	76,67
Long After the Vaccine		
1-6 months	11	36,67
> 6 months	19	63,33
Vaccine Type		
1st Vaccine		
Sinovac/Coronavac	17	56,67
Astra Zeneca	12	40,00
Moderna	1	3,33
2nd Vaccine		
Sinovac/Coronavac	17	56,67
Astra Zeneca	12	40,00
Moderna	1	3,33
3rd Vaccine		
Sinovac/Coronavac	1	3,33
Astra Zeneca	10	33,33
Moderna	6	20,00
Pfizer	6	20,00

Table 1 present that out of 30 respondents, 23 people had received the third dose of vaccine and 7 people had just received the second dose of vaccine. The types of vaccines received by respondents were Sinovac/Coronavac, Astra Zeneca, Moderna, and Pfizer.

Table 2. SARS-CoV-2 SRBD Antibody Levels.

Antibody Levels	BAU/mL
Lowest	25.779
Highest	3536.086
Average	658.883

Table 2 show that the highest antibody levels was 3536.086 BAU/mL and the lowest was 25.779 BAU/mL with an average of 658.883 BAU/mL.

Of the 30 respondents, 23 people had received the third vaccine dose. The average respondent antibody levels based on the number of vaccines and the duration of the vaccine can be seen in Table 3.

Table 3. The Average of SARS-CoV-2 SRBD Antibody Levels.

	Total Respondents	SARS-CoV-2 SRBD Antibody Levels (BAU/mL)
Number of Vaccines		
Twice	7	1,063.786
Three times	23	535.651
Vaccine Time		
1 – 6 months	11	228.006
> 6 months	19	908.338

Table 3 shows that 7 people received 2 doses of the vaccine with a SARS-CoV-2 SRBD antibody level of 1,063.786 BAU/mL, and antibody levels in respondents with 3 doses of vaccine were 535.651 BAU/mL. Antibody levels in respondents who received 2 doses of vaccine were higher than those who received 3 doses of vaccine, possibly due to the distance between vaccines in respondents with 2 vaccines does of more than 6 months, namely between 8 – 15 months. In respondents with a vaccine duration of more than 6 months, the average antibody level was 908.338 BAU/mL. The results of antibody levels were higher than respondents with vaccine interval between 1 – 6 months.

Until now, SARS-CoV-2 infection is a serious global health threat because of its severity and rapid spread throughout the world. The development of a vaccine to control the spread of SARS-CoV-2 is very rapid. The basis for assessing vaccine efficacy is immune surveillance by measuring antigen-specific antibodies. Although SARS-CoV-2 infection can induce the production of antibodies that recognize different viral antigens, antibodies directed against RBD are the most relevant because of their neutralizing activity. Therefore, most of the SARS-CoV-2 vaccines were developed to induce the production of antibodies against the SARS-CoV-2 spike protein. Thus, measurement of circulating levels of anti-S-RBD can provide valuable information about acquired immunity against SARS-CoV-2 (Lo Sasso et al., 2021).

Different vaccines can cause different levels of antibody response (Alsagaby et al., 2021) The CDC, (2020) compared two mRNA vaccines, namely mRNA-1273 with BNT162b2, where two doses of mRNA-1273 induced higher antibody titers with a Geometric Mean Titer (GMT) of 3.836U/mL. Whereas two doses of BNT162b2 (GMT 1.444 U/mL) (CDC, 2020) Faico-Filho et al., (2020) suggested the possibility that there was a difference in the antibody response produced by BNT162b2 and AZ1222 where both elicited IgM and IgG response (Faíco-Filho, Passarelli, & Bellei, 2020). Alharbi et al., (2022) conducted a study to determine the antibody response induced by the COVID-19 vaccine, namely BNT162b2 and AZD1222 against 432 individuals. Anti-SARS-CoV-2 IgG spikes in most of the subjects after the first vaccine and remains high after 6 months. At 1 year post-vaccination, antibody levels were low then increased again after receiving the third dose. The third dose is given an average of 250 days after the second dose (Alharbi et al., 2022).

Based on the results of the study, the antibody level of the second dose of vaccine was higher than the third dose, possibly due to the duration of the vaccine in the second dose between 8 – 15 months. Recent studies have shown that the humoral response continues to develop long after vaccination, with memory B cells after vaccination showing an increase in both quality and number compared to the start of vaccination (Bates et al., 2021; Turner et al., 2021; Wang et al., 2021)

The reported effectiveness of the Sinovac vaccine against COVID-19 infection was 49.4% at ≥14 days after vaccination (Hitchings et al., 2021). The efficacy of the Astra Zeneca vaccine against infection ranged from 33.5% at ≥14 days after vaccination, 25% to 63.9% at 22 – 90 days after vaccination (Madhi et al., 2021). Vaccine efficacy after 14 days after the second dose was 66.7%. Voysey et al., (2021) noted that differences in the efficacy of the first and second doses of vaccine could be attributed to several factors, such as the intensity of the

COVID-19 pandemic in different countries and the length of the prime-boost interval between the first and second doses. Longer prime-boost intervals (≥12 weeks) indicate higher vaccine efficacy (Voysey et al., 2021)

The efficacy of the first dose of Moderna vaccine against infection was 95.2% at ≥14 days after vaccination (Baden et al., 2021). Studies show that the effectiveness of the Pfizer vaccine increases gradually, starting 14 days after the first dose, and finally reaching a peak of 91% effectiveness on day 21 (Hunter & Brainard, 2021). Mohammed et al., (2022) concluded that a single dose of vaccination with the Pfizer vaccine significantly reduced symptoms of SARS-CoV-2 infection and provided protection against severe infection. This protection is maintained for > 6 weeks (Mohammed et al., 2022).

Different factors influencing antibody response to SARS-CoV-2 vaccination such as age, vaccination regimen, days since vaccination, and previous infection. The number of samples in this study is still small which can cause differences in results with other studies that use different sample sizes.

4. CONCLUSION

From the results of this study it can be concluded, among others: (1) The conclusion of this study is the highest antibody titers are produced >6 months after vaccination, antibody titers are still detectable after 12 months of vaccination; and (3) for further research, it can be measured antibody levels against SARS-CoV-2 from people who have got vaccination for a duration of 2 years or more.

REFERENCES

Alharbi, N. K., Al-Tawfiq, J. A., Alwehaibe, A., Alenazi, M. W., Almasoud, A., Algaisi, A., … Alsagaby, S. A. (2022). Persistence of Anti-SARS-CoV-2 Spike IgG Antibodies Following COVID-19 Vaccines. *Infection and Drug Resistance*, *15*(July), 4127–4136. https://doi.org/10.2147/IDR.S362848

Alsagaby, S. A., Aljouie, A., Alshammari, T. H., Mir, S. A., Alhumaydhi, F. A., Abdulmonem, W. Al, … Alharbi, N. K. (2021). Haematological and radiological-based prognostic markers of COVID-19. *Journal of Infection and Public Health*, *14*(11), 1650–1657. https://doi.org/10.1016/j.jiph.2021.09.021

Baden, L. R., El Sahly, H. M., Essink, B., Kotloff, K., Frey, S., Novak, R., … Zaks, T. (2021). Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *New England Journal of Medicine*, *384*(5), 403–416. https://doi.org/10.1056/nejmoa2035389

Bates, T. A., Leier, H. C., Lyski, Z. L., Goodman, J. R., Curlin, M. E., Messer, W. B., & Tafesse, F. G. (2021). Age-Dependent Neutralization of SARS-CoV-2 and P.1 Variant by Vaccine Immune Serum Samples. *JAMA*, *328*, 868–869. https://doi.org/10.1056/nejmoa2034577

CDC. (2020). *Real-Time RT-PCR diagnostic panel*. CDC. Retrieved from https://www.fda.gov/media/134922/download

Chowdhury, M. A., Hossain, N., Kashem, M. A., Shahid, M. A., & Alam, A. (2020). Immune response in COVID-19: A review. *Journal of Infection and Public Health*, *13*(11), 1619–1629. https://doi.org/10.1016/j.jiph.2020.07.001

Cinquanta, L., Fontana, D. E., & Bizzaro, N. (2017). Chemiluminescent immunoassay technology: what does it change in autoantibody detection?. *Autoimmunity highlights*, *8*, 1-8. https://doi.org/10.1007/s13317-017-0097-2

Ejemel, M., Li, Q., Hou, S., Schiller, Z. A., Tree, J. A., Wallace, A., … Wang, Y. (2020). A cross-reactive human IgA monoclonal antibody blocks SARS-CoV-2 spike-ACE2 interaction. *Nature Communications*, *11*(1), 1–9. https://doi.org/10.1038/s41467-020-

18058-8
Faíco-Filho, K. S., Passarelli, V. C., & Bellei, N. (2020). Is higher viral load in SARS-CoV-2 associated with death? *American Journal of Tropical Medicine and Hygiene*, *103*(5), 2019–2021. https://doi.org/10.4269/ajtmh.20-0954
Gao, Q., Bao, L., Mao, H., Wang, L., Xu, K., Yang, M., ... & Qin, C. (2020). Development of an inactivated vaccine candidate for SARS-CoV-2. *Science*, *369*(6499), 77-81.
Gudbjartsson, D. F., Norddahl, G. L., Melsted, P., Gunnarsdottir, K., Holm, H., Eythorsson, E., … Stefansson, K. (2020). Humoral Immune Response to SARS-CoV-2 in Iceland. *New England Journal of Medicine*, *383*(18), 1724–1734. https://doi.org/10.1056/nejmoa2026116
Han, Y., & Yang, H. (2020). The transmission and diagnosis of 2019 novel coronavirus infection disease (COVID-19): A Chinese perspective. *Journal of Medical Virology*, *92*(6), 639–644. https://doi.org/10.1002/jmv.25749
Hitchings, M. D. T., Ranzani, O. T., Torres, M. S. S., Oliveira, S. B. de, Almiron, M., Said, R., … Croda, J. (2021). Effectiveness of CoronaVac among healthcare workers in the setting of high SARS-CoV-2 Gamma variant transmission in Manaus, Brazil: a test-negative case-control study. *The Lancet Regional Health - Americas*, *9*(28). https://doi.org/10.1101/ 2021.04.07.21255081.
Hou, H., Wang, T., Zhang, B., Luo, Y., Mao, L., Wang, F., … Sun, Z. (2020). Detection of IgM and IgG antibodies in patients with coronavirus disease 2019. *Clinical and Translational Immunology*, *9*(5), 1–8. https://doi.org/10.1002/cti2.1136
Hunter, P. R., & Brainard, J. (2021). Estimating the effectiveness of the Pfizer COVID-19 BNT162b2 vaccine after a single dose. A reanalysis of a study of 'real-world'vaccination outcomes from Israel. *Medrxiv*, 2021-02. https://doi.org/10.1101/2021.02.01.21250957
Iyer, A. S., Jones, F. K., Nodoushani, A., Kelly, M., Becker, M., Slater, D., … Charles, R. C. (2020). Persistence and decay of human antibody responses to the receptor binding domain of SARS-CoV-2 spike protein in COVID-19 patients. *Science Immunology*, *5*(52), 1–13. https://doi.org/10.1126/sciimmunol.abe0367
Jacofsky, D., Jacofsky, E. M., & Jacofsky, M. (2020). Understanding Antibody Testing for COVID-19. *Journal of Arthroplasty*, *35*(7), S74–S81. https://doi.org/10.1016/j.arth.2020.04.055
Kementerian Kesehatan Republik Indonesia. (2021). Question (Faq) Pelaksanaan Vaksinasi Covid-19. Jakarta: Kementerian Kesehatan Republik Indonesia.
L'Huillier, A. G., Meyer, B., Andrey, D. O., Arm-Vernez, I., Baggio, S., Didierlaurent, A., … Kaiser, L. (2021). Antibody persistence in the first 6 months following SARS-CoV-2 infection among hospital workers: a prospective longitudinal study. *Clinical Microbiology and Infection*, *27*(5), 784.e1-784.e8. https://doi.org/10.1016/j.cmi.2021.01.005
Li, L. (2020). Neutralizing Antibodies to SARS-CoV-2: An Important Mechanism of Immunity. *Scientific Review*, *3*, 1–4. Retrieved from https://doi.org/10.1016/j.autrev.2020.102554
Lo Sasso, B., Giglio, R. V., Vidali, M., Scazzone, C., Bivona, G., Gambino, C. M., … Ciaccio, M. (2021). Evaluation of anti-sars-cov-2 s-rbd igg antibodies after covid-19 mrna bnt162b2 vaccine. *Diagnostics*, *11*(7), 1–9. https://doi.org/10.3390/diagnostics11071135
Madhi, S. A., Baillie, V., Cutland, C. L., Voysey, M., Koen, A. L., Fairlie, L., … Izu, A. (2021). Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant. *New England Journal of Medicine*, *384*(20), 1885–1898. https://doi.org/10.1056/nejmoa2102214
Mohammed, I., Nauman, A., Paul, P., Ganesan, S., Chen, H., Muhammad, S., … Zakaria, D. (2022). The efficacy and effectiveness of the COVID-19 vaccines in reducing infection ,

severity , hospitalization , and mortality : a systematic review. *Human Vaccines & Immunotherapeutics*, *18*(1). https://doi.org/10.1080/21645515.2022.2027160

Rauf, A., Abu-Izneid, T., Olatunde, A., Khalil, A. A., Alhumaydhi, F. A., Tufail, T., … Rengasamy, K. R. R. (2020). COVID-19 pandemic: Epidemiology, etiology, conventional and non-conventional therapies. *International Journal of Environmental Research and Public Health*, *17*(21), 1–32. https://doi.org/10.3390/ijerph17218155

Syahniar, R., Purba, M. B., Bekti, H. S., & Mardhia, M. (2020). Vaccines against Coronavirus Disease: Target Proteins, Immune Responses, and Status of Ongoing Clinical Trials. *Journal of Pure & Applied Microbiology*, *14*(4), 2253-63. https://doi.org/10.22207/JPAM.14.4.03

Speiser, D. E., & Bachmann, M. F. (2020). Covid-19: Mechanisms of vaccination and immunity. *Vaccines*, *8*(3), 1–22. https://doi.org/10.3390/vaccines8030404

Thermo Fisher Scientific. (2023). *Plasma and Serum Preparation*. Thermo Fisher Scientific. Retrivied from https://www.thermofisher.com/id/en/home/references/protocols/cell-and-tissue-analysis/elisa-protocol/elisa-sample-preparation-protocols/plasma-and-serum-preparation.html#:~:text=Serum%20is%20the%20liquid%20fraction,removed%20using%20a%20Pasteur%20pipette.

Turner, J. S., O'Halloran, J. A., Kalaidina, E., Kim, W., Schmitz, A. J., Zhou, J. Q., … Ellebedy, A. H. (2021). SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses. *Nature*, *596*(7870), 109–113. https://doi.org/10.1038/s41586-021-03738-2

Voysey, M., Costa Clemens, S. A., Madhi, S. A., Weckx, L. Y., Folegatti, P. M., Aley, P. K., … Zuidewind, P. (2021). Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *The Lancet*, *397*(10277), 881–891. https://doi.org/10.1016/S0140-6736(21)00432-3

Wang, C., Wu, J., Zong, C., Xu, J., & Ju, H. X. (2012). Chemiluminescent immunoassay and its applications. *Chinese Journal of Analytical Chemistry*, *40*(1), 3–10. https://doi.org/10.1016/S1872-2040(11)60518-5

Wang, Z., Muecksch, F., Schaefer-Babajew, D., Finkin, S., Viant, C., Gaebler, C., … Nussenzweig, M. C. (2021). Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection. *Nature*, *595*(7867), 426–431. https://doi.org/10.1038/s41586-021-03696-9

WHO. (2023). Diagnostic testing for SARS-CoV-2 infection. WHO. Retrivied from https://www.who.int/multi-media/details/diagnostic-testing-for-sars-cov-2-infection

WHO. (2022a). WHO Coronavirus (COVID-19) Dashboard | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. Retrieved from https://covid19.who.int/

WHO. (2022b). WHO Coronavirus Disease (COVID-19) Dashboard: Indonesia Situation. WHO. Retrieved from https://covid19.who.int/region/searo/country/id

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 831-843
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1401*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

What Makes Woman Afraid of Their Childbirth?: A Qualitative Study

Siti Nurhidayati [1a*], Revi Gama Hatta Novika[1b], Nurul Jannatul Wahidah[1c], Atriany Nilam Sari[1d], Luluk Fajria Maulida[1e], Rufidah Maulina[1f], Chusna Habiba[1g], Ramadhani Anggi[1h]

[1] Department of Midwifery, Faculty of Medical, Universitas Sebelas Maret, Surakarta, West Java, Indonesia

[a] Email address: sitinurhidayati@staff.uns.ac.id
[b] Email address: revi.gama@staff.uns.ac.id
[c] Email address: njwahidah@staff.uns.ac.id
[d] Email address: atriany.ns@staff.uns.ac.id
[e] Email address: lulukfajria@staff.uns.ac.id
[f] Email address: maulinarufidah@staff.uns.ac.id
[g] Email address: chusnahabiba14@student.uns.ac.id
[h] Email address: anggiiwn7@student.uns.ac.id

Received: 30 October 2023 Revised: 19 December 2023 Accepted: 31 December 2023

Abstract
Fear generally fills the minds of pregnant women as they enter the third trimester of gestation. The older the gestational age, the more attention and thoughts of pregnant women are drawn to the approaching climax of childbirth, intensifying their anxiety and fear. This study aimed to assess the knowledge of birth preparedness and fear of childbirth. A qualitative facility-based descriptive study design and client exit interview questionnaire were utilized, conducted in Primary Health Care Mondokan, Sragen, from April until June 2023 with 33 pregnant women. Study participants were selected through purposive sampling. Three categories highlighted the preparedness for childbirth, including finding primary sources of information, the importance of birth companions, and reminding about the natural process of childbirth. The fear of childbirth was associated with fear of the childbirth process, fear of the tools used during childbirth, and the condition of the unborn baby. The findings suggest that pregnant women should prepare for childbirth and increase their knowledge of delivery by participating in antenatal classes to reduce fear about the childbirth process. Therefore, family healthcare providers, health facilities, other partners, program-level managers, and policymakers must take responsibility for improving health education and increasing preparedness and complication readiness through easily accessible health education strategies.

Keywords: Birth Preparedness, Fear of Childbirth, Knowledge, Health Facilities.

Corresponding Author:

Siti Nurhidayati
Department of Midwifery, Faculty of Medical, Universitas Sebelas Maret, Surakarta, West Java, Indonesia
Email: sitinurhidayati@staff.uns.ac.id

1. INTRODUCTION

The process of pregnancy induces various changes in a woman, encompassing both physiological and psychological transformations. This process is characterized by the natural occurrence of fertilization, resulting in the development of a fetus within the mother's womb, commencing from conception, and persisting until childbirth (Kementerian Kesehatan Republik Indonesia, 2019). Each woman envisions the childbirth and motherhood journey, and this perception significantly shapes her response to pregnancy. In the period leading up to delivery, numerous concerns occupy the mother's thoughts, such as the fear of surgical procedures, bleeding, potential complications, congenital disabilities, pain during childbirth, and the fear of post-childbirth challenges like intense straining or vaginal tearing, possibly requiring suturing. There may even be a fear of mortality, leading to apprehension about adequately caring for and raising the child (Munkhondya et al., 2020).

Typically, fear becomes more prominent in the minds of pregnant women as they enter the third trimester (28-40 weeks). As gestational age increases, attention and thoughts are increasingly drawn to the impending climax, intensifying anxiety and fear as childbirth approaches (Hidayat & Sumarni, 2016). From a psychological standpoint, fear can result in heightened pain, decreased uterine contractions, and prolonged labor (Dwiarini et al., 2022). This fear triggers muscle tension, particularly in the birth canal, making the labor process less smooth (Syada & Ramaida, 2017)

One significant factor contributing to the high incidence of Maternal Mortality Rate is the unpreparedness of mothers for childbirth. Lack of understanding about necessary preparations leads to obstetric complications, preventing timely and appropriate services and resulting in delays in referral (Kementerian Kesehatan Republik Indonesia, 2019). Essential preparations for pregnant women include developing delivery plans, making emergency decisions, understanding transportation systems, adopting saving patterns, and ensuring readiness with the necessary equipment (Naha & Handayani, 2020); moreover, engaging in positive affirmations, seeking expert consultation, and garnering support from loved ones play pivotal roles in easing the impending challenges of childbirth.

Analyzing the fear of childbirth stands as an early prevention measure, guiding the topics covered during prenatal education. Fear before childbirth correlates with emotional well-being, stress symptoms, depression risks, reduced confidence during childbirth, diminished ability to care for the child, and decreased maternal involvement in meeting fetal development requirements (Wigert et al., 2020). Emotional and psychological well-being are intertwined with perceptions and experiences of prenatal and childbirth, influencing decisions about the childbirth method. For instance, traumatic previous childbirth experiences can lead women to opt for a cesarean section, a global concern due to its potential impact on physical and psychological morbidity, uterus scarring, and associated costs (Fenwick et al., 2015).

However, a previous study investigating decision-making and respectful maternity care in Indonesia found that pregnant women received a moderate level of autonomy in decision-making and low levels of respectful maternal health care (Maulina et al., 2023). This finding highlights the importance of improved quality prenatal care and education, which can enhance midwives' awareness about related risks that are caused by low respect and decision-making, such as fear of childbirth. A previous study in Indonesia also found that fear of childbirth was a predicting factor of longer duration during the first stage and second stages of childbirth (Dwiarini et al., 2022).

Factors such as satisfaction with husband support, education level, number of ultrasound examinations, and participation in prenatal yoga classes can reduce fear of childbirth (Astuti & Kao, 2019; Marcelina et al., 2019). Exploring what mothers afraid of during childbirth and how they already prepare for childbirth can deepen and broaden our understanding of women’s feeling during pregnancy and childbirth. However, Indonesian mothers' fear of childbirth is

essential to understand since cultural and social contexts may influence mothers' experience of fear of childbirth. Therefore, Indonesian-based and exploratory studies need to be conducted to enhance our understanding and determine the topic in prenatal education that would be taught to overcome their fear.

2. RESEARCH METHOD

A qualitative descriptive approach was used to explore how women have prepared for childbirth comprehensively and their perspective on their fear during childbirth. Qualitative methodology and a descriptive study design were used to obtain participant group interviews. This design was appropriate for the study because it allowed the researchers to explore the experience and expectations of the participants about preparation and childbirth fear.

Midwives contacted potential participants over the phone to provide information about the focus group discussions (FGDs) and invite them to participate. Thirty-eight pregnant women agreed to participate in the FGDs, and 33 attended.

The study was conducted at an antenatal class in a village in Sragen. The FGDs were conducted in a single session, with the principal researcher as the moderator. Research assistants carried out recording and documentation. The leading researcher guided the FGD until the end of the session. The FGDs occurred in a private room, specifically in the local community meeting room.

The participants consisted of 33 pregnant women who were purposely selected. To be recruited in the study, a pregnant woman had to meet the following criteria: i) their pregnancy from 28 to 40 weeks in the gestation period, ii) a singleton pregnancy without obstetric complication, iii) to be fluent in the Indonesian language. The sample was carried out by purposive sampling by inviting specific mothers for this study. The size of the sample was determined by saturation theoretical.

To gather the data, focus group discussions (FGD) for birth preparation and semi-structured interviews for childbirth fear. The researcher guided the FGD by paying attention to the flow of the discussion according to the interview guide, while a research assistant assisted with note-taking. The selected research assistants were midwives and final-year student midwives who had been given a briefing before the FGD was conducted. The data were collected during pregnancy class.

The FGD concluded when data collected from the informants reached data saturation. Data saturation occurs when researchers continue to collect data until nothing new is added to their arguments or conclusions based on the interview guide. The audio recordings were stored and lasted approximately 1 hour and 18 minutes in the local language. There was no prior relationship between the participants and the researcher.

The results of the FGDs were transcribed and translated into English. Following the steps outlined by Braun and Clarke in 2006, an inductive thematic analysis was employed to identify patterned meanings across the FGDs (Braun & Clarke, 2006). The objective of the FGDs was to gain insights into mothers' perspectives regarding preparedness and fear of childbirth about societal opinions, either directly or indirectly.

To conduct the thematic analysis, the researchers followed the steps proposed by Braun and Clarke, which included familiarizing themselves with the data by reading and re-reading the transcripts and noting down initial thoughts.

The script contained six questions, which were used flexibly depending on how the dialogue developed. The questions were divided into two themes: three questions about preparations for birth and three about childbirth fear. The questions are shown below;

Table 1. Questions guideline for Focus Group Discussion (FGD).

Theme	**Subtheme**	**Questions**
Preparedness	Information source acquired	Where did you obtain the information related to childbirth preparation
	Accompanied person during childbirth	What is the mother's opinion regarding the presence of a birthing companion?
	Mother preparation	What is the most dominant preparation that a mother undertakes to face the childbirth process?
Fear of Childbirth	Fear before childbirth	What fears does the mother experience before the childbirth process
	Fear during the childbirth process	What fears does the mother experience during the childbirth process
	Fear of baby's condition	What other fears does the mother experience related to the mother and baby?

The data was processed involving four phases: transcription, reduction, codification, and categorization, and the theme was to be a final data analysis. This study's rigor was triangulation data with FGD and provider interviews; three researchers did the coding. To ensure the participants' answers, researchers repeated the questions for consistency. The research team discussed the differences in time to reach the final code to ensure the dependability and consistency of the findings. This study was approved by the Health Research Ethics Committee of Dr Moewardi General Hospital in Surakarta (No. 409/III/ HREC/2023) on April 10, 2023. All methods were performed following the relevant guidelines and regulations.

3. RESULTS AND DISCUSSION

The researchers assessed 33 women during the third trimester of pregnancy to explore their preparedness and fear of childbirth regarding this pregnancy. The semi-structured questionnaire used in this study was about childbirth preparedness and fear of childbirth made by the researchers.

Table 1. Maternal socio-demographic variables, theory knowledge on birth preparedness, and fear of delivery.

Variables	**Frequency (n)**	**Percentage (%)**
Age		
<17	8	25
17-35	19	57,6
>35	6	17,4
Educational status		
Primary	10	30,3
Secondary and above	23	69,7
Occupation		
Housewife	8	24,2
Gov employed	13	39,4
Private employed	9	27,3
Private Business	3	9,1
Husband Educational Status		
Primary	4	12,1
Secondary and above	28	84,8
Not having husband	1	3,1

Family Size		
1-2	14	42,4
3-4	11	33,3
>4	8	24,3
Total	33	100

Table 1 shows that most respondents were during their 17-35th years old, 57,6% (n=33). The highest level of education was secondary and above 69,7 %, and the number of government employees was 39,4 %. Besides, their husband's level of education was mainly secondary and above 84,8 %, and 42,4 % of women had 1-2 family members.

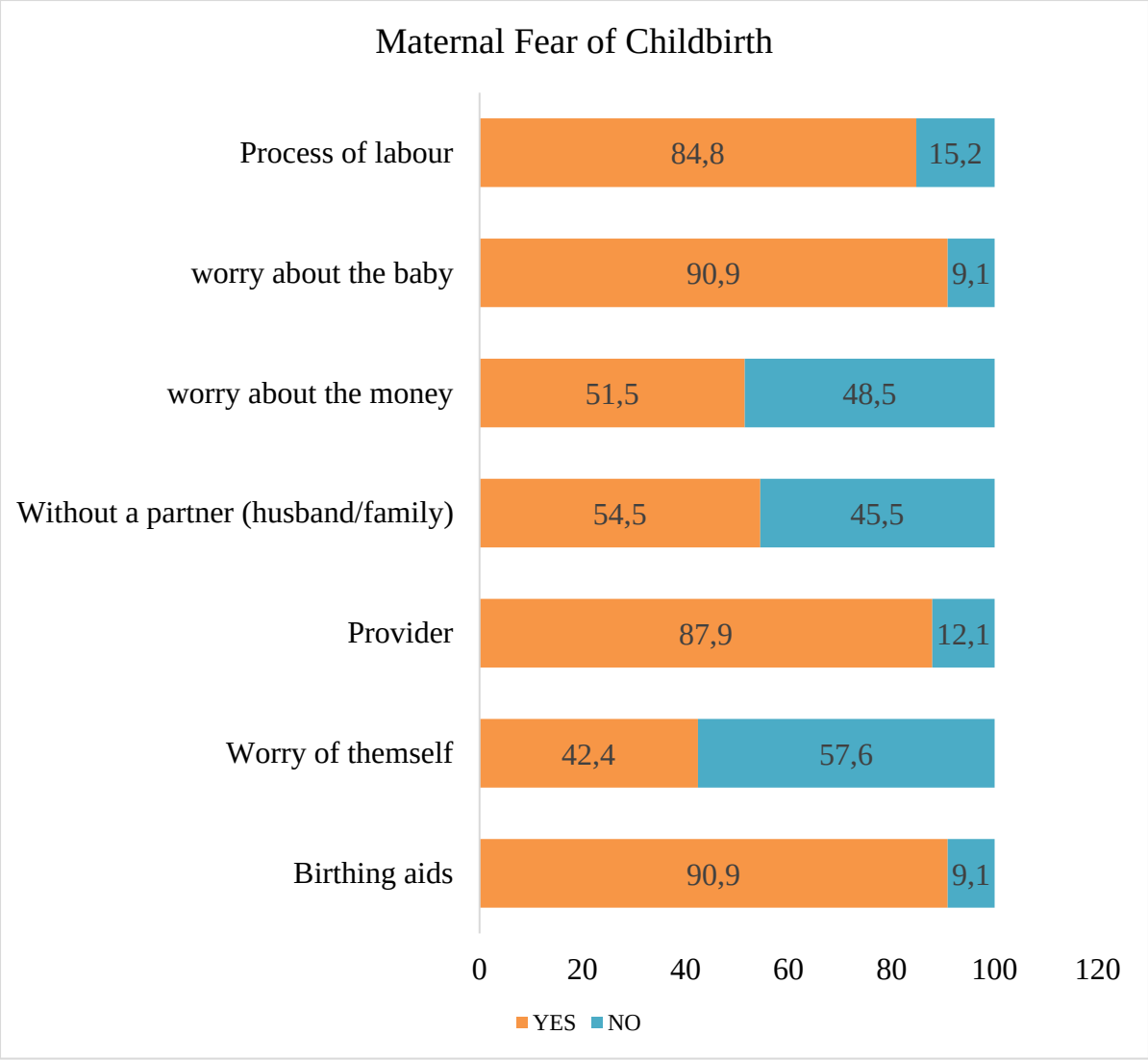


Chart 1. Maternal Fear of Childbirth

Chart 1 shows that regarding fear of childbirth, the majority express fear of the labor process (n=28, 84.8%), worry about the baby (n=30, 90.9%), concern about money (n=17, 51.5%), fear of childbirth process accompanied by their husband or family (n=18, 54.5%), worry about the provider (n=29, 87.9%), and fear of birthing aids (n=30, 90.9%).

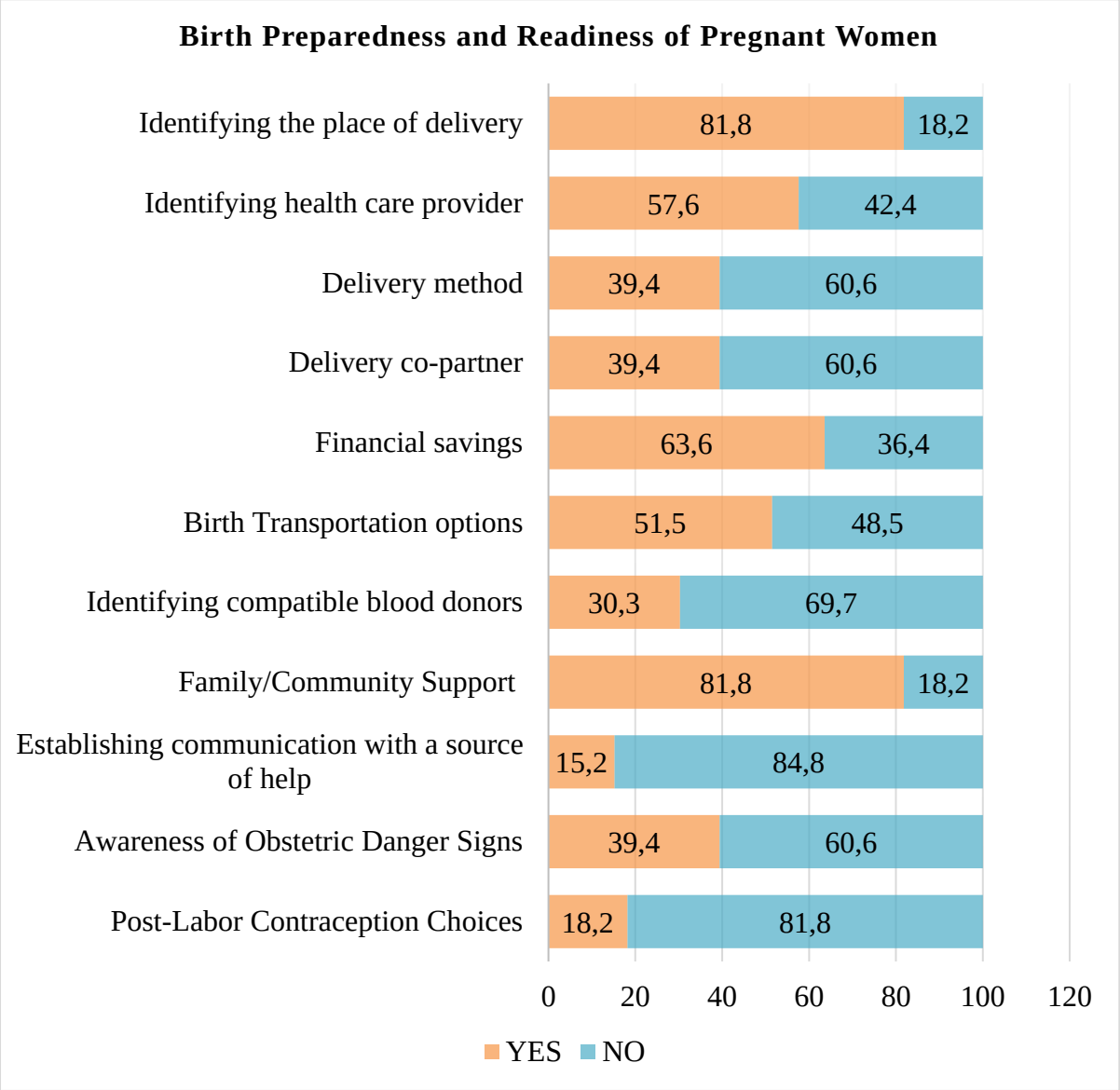


Chart 2. Birth Preparedness and Readiness among Pregnant Women.

Chart 2 shows that most respondents had already identified the place of delivery (81.8%, n=27) and the healthcare provider (57.6%, n=19). The pregnant women were also aware of having a co-partner during delivery (75.7%, n=25), saving money to prepare for childbirth (63.6%, n=21), identifying transportation options for childbirth (51.5%, n=17), having support from family (81.8%, n=27). However, they did not know the method of delivery (60.6%, n=20), did not identify compatible blood donors (69.7%), did not arrange a way to communicate with a source of help (84.8%, n=28), did not understand awareness of danger signs of obstetrics (60.6%, n=20), and did not know contraception to use after labor (81.8%, n=27).

A focus group discussion involving 33 pregnant women and two healthcare workers was performed with the results as follows;

1. Childbirth fear

1.1 Worried about Process

The labor process is a source of worry and fear for the mother before facing labor, such as worrying about not being able to push, the pain that arises, prolonged labor, running out of energy, and the baby not being born. Some informants said as follows:

"If you hear from some stories, it seems like straining is very difficult, especially when I imagine a 3kg baby coming out of our vagina. How can I do that?"
"Some brothers told me that when they are sick and want to give birth, it is like their backbones are broken, the pain in the stomach is unbearable, even if I am underweight, even though I am only underweight, I am already in pain, I am afraid if the pain occurs later, what should I do."
"I know that childbirth will be painful; I am just worried that the process will take a long time and I will run out of energy, then I will be weak, and my child will not be able to be born, worried that my baby will not be safe and I will be stigmatized as a bad mother."

1.2 Afraid of the Medical Tools Used.

Another fear that mothers feel is the tools used during childbirth. Fear of having an episiotomy, being sutured, fear of the tools available, and fear of the operation. Some informant statements are as follows:

"I am terrified that if my baby grows up, I will have to cut it, I imagine it is going to be very painful."
"what if the tear later has to be sewn up? Imagining being sewn up scares me. The thing I fear the most is being sewn up."
"If I am born later, I imagine the tools, scissors, needles, all the things used, ma'am. I am afraid; I imagine the tools there will be used for all of me."

1.3 Condition of the born baby.

The fear that arises in the mother can also come from a sense of worry about the baby being born. Worried about his imperfect shape and body parts that are unlike others. The informant's statement is as follows;

"I am afraid that my child will have missing parts of his body; I am worried about how he will be after birth."
"If the shape does not suit other children, I am afraid of being seen and ridiculed by my relatives and neighbors that I have a bad history of women."

2. Preparedness

2.1 Social media as their primary source to get their information

Information regarding birth preparedness for mother and baby was obtained by internet searching, especially from mothers who experienced a birth process. One participant said:

"Preparation for my baby and me, I am searching from social media about the birth story from the mother's experience, then I make a list for my preparation."
"I am searching through my phone, from my friends upload and browsing result in social media then I added (the list)"

2.2 Birth companion is important.

Some mothers feel comfortable and safe when they are accompanied during the childbirth process. Participants acknowledge the presence of birth companions such as their husband, mother, mother-in-law, and whoever they already knew.

"I feel that I need my husband to accompany me during my childbirth, whether I will do it normally (pervaginam) or Cesarean Section. I hope my husband still accompanies me so he knows the process."
"Whoever will accompany me be, the importance is presence, whether it will be my husband, mother, or mother-in-law."
"Yes, when being asked, (I prefer) husband and mother, but whoever they are, (they need to be) present because I do not know anybody in Primary Health Care."

2.3 Childbirth is a natural process.

Most participants believe that childbirth preparedness is to control worry about childbirth. They believe that childbirth can pass and many women can pass, too. Participants stated that:

"The fear is always there, but I am sure I can get through it. Many mothers have succeeded safely, and I definitely can."

"I am actually scared, but I am more impatient to meet my son, so I am sure I can."

"Very scared, but I was always reminded by my mother that it is natural for women to be given the same strength as above (God) "

This study explored childbirth preparation, birth plans, and childbirth fear from the perspectives of pregnant women, birth companions, and healthcare providers in a rural setting in Sragen. According to the results, women received their first information during the second trimester, with the majority being primigravida. Childbirth fear experienced by first-time mothers extends beyond the birthing process. It includes concerns about the process of labor, health providers, birthing tools, the baby's condition, financial issues, and lack of companionship. Interestingly, mothers mainly were not worried about themselves when they faced childbirth.

The intense process of labor and birthing equipment, cesarean section, and episiotomy were reported to be the source of fear of childbirth (Johnson et al., 2019). They were being affected by care providers such as care providers' disagreement with medical professionals regarding the intervention, disrespect, neglect, and lack of communication and support, leading to not feeling safe during their safe (Viirman et al., 2023).

A study from Finland revealed that disrespectful care and obstetric violence lead to negative childbirth experiences and be a ground for childbirth fear (Larsson et al., 2023). Furthermore, negative childbirth experience has been linked to problems in breastfeeding, post-traumatic stress disorder, and postpartum depression that may delay further pregnancy (Dencker et al., 2019; Viirman et al., 2023). In Indonesia, women experienced a low level of respect for maternity services during the COVID-19 pandemic, which may be caused by high workloads and adaptation to new protocols (Maulina et al., 2023). This study identifies women afraid of the labor process, health care providers, and birthing aids. To reduce this fear, women should suggest participating in antenatal education classes focused on childbirth preparedness, including handling themselves during childbirth labor, such as relaxation techniques, birthing position, and mental health support during labour. Studies showed that antenatal education reduces fear of childbirth and increases maternal self-efficacy(Pinar et al., 2018; Kızılırmak & Başer, 2016). On the other hand, midwives should also be encouraged to work with more respect toward women and give them more autonomy regarding their decisions (Maulina et al., 2023).

Regarding worry about the unborn baby, mothers can be facilitated to have an ultrasound examination during the first and third trimesters (Wiraswati, 2022). In the latest ANC guideline, it was issued that mothers should have at least six times antenatal care, including two times to do ultrasound checks. Prenatal identification of congenital anomalies during a prenatal ultrasound can reduce women's anxiety about the fetal condition; hence, prenatal consultation can lower it (Simó et al., 2019; Yang et al., 2023).

In Indonesia, national health insurance, or *Jaminan Kesehatan Nasional*, covers maternal healthcare services, including pregnancy, childbirth, and postpartum. However, problems arise when women still need to pay for extra payments such as drugs, medication, or baby and mother essentials that need to be covered by JKN (Nugraheni et al., 2020). Another issue, only 15% of mothers who are in low economic status use JKN optimally (Nugraheni et al., 2020), putting them at a higher risk of failing into poverty because of a lack of maternal health care utilization services (Nugraheni et al., 2020). Women who experienced financial strains would lead to stunting and their children and adverse mental health outcomes (Marcil et al., 2020; Sari et al., 2020). These issues will be tackled if midwives and other healthcare providers could identify families experiencing financial problems and join advocacy to address women with financial issues (Marcil et al., 2020), at least during prenatal education.

A meta-synthesis of a qualitative study revealed that mothers mostly face childbirth as 'being at a point' with no return, a lack of control over themselves, and a lack of support in understanding their fear (Wigert et al., 2020). This study highlighted that societal ideas can exacerbate the fear of childbirth. Societal notions, such as infidelity by the husband, contribute significantly to childbirth fear. Fear of not being accompanied by a spouse or family member is a prevalent reason for mothers fearing childbirth. Educating husbands or spouses during childbirth or prenatal education increased their skill in childbirth support and maternal-neonatal outcomes (Sulistianingsih et al., 2023). Culturally specific treatments should be developed to support vulnerable pregnant women facing these issues, including inviting their husbands to prenatal education.

The study revealed that primigravid mothers get information from social media. Some mothers made preparations based on internet sources and midwives. In fact, according to Sanders et al. (2018), birth information significantly influences a pregnant woman's response to the birthing process (Sanders & Crozier, 2018). A previous study investigated that prenatal education delivered by social media did not differ significantly from those who receive an education from in-person education intervention (Mousavi et al., 2022). Even social media-based prenatal education can also lead women to give birth vaginally (Mousavi et al., 2022). This can be a new approach for healthcare providers to develop prenatal education programs that can reach women in many areas.

Birth preparedness and readiness of pregnant women relate to all the preparations made by mothers and infants during childbirth. Elements directly related to maternal preparations, which mothers can independently undertake and seek through social media sources (identifying the place of delivery, healthcare providers, financial savings, birth transportation options, and family and community support), have values trending above 50%. However, some aspects related to information that healthcare professionals should provide, particularly in obstetrics, require clarification (delivery method, delivery co-partner, identifying compatible blood donors, establishing communication with a source of help, awareness of obstetric danger signs, and post-labor contraception choices) and are less than 50% among pregnant women who have undertaken birth preparedness and readiness. This result also has been found in previous study that blood donors and complication readiness were less understood and prepared by mothers (Orwa et al., 2020)

Not all information related to these preparations can be determined by seeking information on social media only, which is needed from professionals with the capability. Based on the findings of the study by Kovala et al., (2016), some pregnant women and families consider expanding their knowledge through prenatal education to access reliable health information that can support decision-making during the childbirth process (Kovala et al., 2016). Consequently, some pregnant women who have not yet determined the components of preparedness and readiness for childbirth may not have been exposed to comprehensive health information about themselves and their infants

Childbirth preparedness is crucial, and it must be ensured that mothers are comprehensively prepared. However, some aspects of childbirth preparation, such as donor availability, awareness of danger signs, and post-labor contraception, needed to be given adequate attention by mothers in this study. Despite midwives conveying this information during ANC and pregnancy classes, some mothers still lacked understanding. One reason behind this may be associated with inadequate counseling during ANC and no actual birth plan-making during ANC. A previous study found that lack of childbirth preparedness and complication readiness was associated with lack of counseling during ANC (Orwa et al., 2020)

Therefore, more preparation is essential to mothers and neonatal well-being(JHPIEGO, 2009). Understanding warning signals of obstetric difficulties during pregnancy, labor, the postoperative period, and the neonatal period is a crucial aspect of birth preparation, contributing to appropriate and early referrals (Kaso & Addisse, 2014). A smooth delivery

necessitates pregnant women's knowledge and preparation for welcoming their child, and adequate preparations reduce confusion and fear during delivery, increasing the likelihood of receiving appropriate and timely care (Pantiawati, 2016). While attending regular childbirth education classes is crucial, providing flexibility in the format, such as offering two or eight short sessions and incorporating technology-based instruction, may better cater to women's needs, especially those relying on public health services (Meedya et al., 2021). In addition, more comprehensive counseling during ANC and making an actual birth plan that respects the mother's choice and decision is recommended as long as it still follows the guidelines of ANC. Moreover, in this setting, midwives can create an educational program based on the internet or social media, which also can promote respectful maternity care to make women less fearful about midwives and birthing aids.

This study, the first to explore childbirth fear during late pregnancy in a low-resource community, included perspectives from birth companions and healthcare providers to ensure robust findings. However, limitations include the study's relatively small geographical area, limiting generalizability, and potential bias due to the recruitment of pregnant women within the community. Future studies should verify why women need more understanding of complication readiness and how midwives perform during ANC sessions. Also, midwives need to make innovative interventions to minimize childbirth fear in a sociocultural context, utilizing antenatal classes to increase knowledge and awareness and investigating the effectiveness of practicing the delivery process. Screening for childbirth fear during pregnancy is also recommended, providing appropriate information from health workers tailored to individual needs. This approach can create positive first experiences of giving birth, reducing childbirth fear in subsequent pregnancies and increasing satisfaction with maternal healthcare services.

4. CONCLUSION

This study has revealed findings about preparedness for childbirth and childbirth fear. Fear of childbirth which were fear about baby's condition, labour process, without companion during childbirth, afraid of healthcare providers and birthing tools. Moreover, women already identify place of delivery, healthcare providers, financial saving, transportation modes, and companionship during labour. The findings suggest that pregnant women should prepare for childbirth and enhance their knowledge of delivery by participating in antenatal classes to reduce the fear of childbirth. Recommending the creation of a birth plan can provide pregnant women with a broader overview of what they should prepare for and enhance their understanding of complications readiness.

ACKNOWLEDGEMENT

Researchers express our sincere gratitude to LPPM Universitas Sebelas Maret for their invaluable support in facilitating this study. Special thanks to all participants whose active involvement significantly enriched our findings.

REFERENCES

Astuti, Y., Chou, H., Liu, C., & Kao, C. (2021). The Effect of Prenatal Gentle Yoga on Maternal-Fetal Attachment among First-time Expectant Mothers in Indonesia. Journal of Midwifery and Reproductive Health, 9(3), 2873-2882. https://doi.org/10.22038/jmrh.2021.54803.1670.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2), 77–101. https://doi.org/10.1191/1478088706qp063oa

Dencker, A., Nilsson, C., Begley, C., Jangsten, E., Mollberg, M., Patel, H., Wigert, H., Hessman, E., Sjöblom, H., & Sparud-Lundin, C. (2019). Causes and outcomes in studies

of fear of childbirth: A systematic review. *Women and Birth*, *32*(2), 99–111. https://doi.org/10.1016/j.wombi.2018.07.004

Dwiarini, M., Chou, H.-F., Gau, M.-L., & Liu, C.-Y. (2022). Relationship between fear of childbirth, self-efficacy, and length of labor among nulliparous women in Indonesia. *Midwifery*, *105*, 103203. https://doi.org/10.1016/j.midw.2021.103203

Fenwick, J., Toohill, J., Gamble, J., Creedy, D. K., Buist, A., Turkstra, E., Sneddon, A., Scuffham, P. A., & Ryding, E. L. (2015). Effects of a midwife psycho-education intervention to reduce childbirth fear on women's birth outcomes and postpartum psychological wellbeing. *BMC Pregnancy and Childbirth*, *15*(1), 284. https://doi.org/10.1186/s12884-015-0721-y

Hidayat, S., & Sumarni, S. (2016). Kecemasan ibu hamil dalam menghadapi proses persalinan. *Jurnal Wiraraja Medika*, 67–72.

JHPIEGO. (2009). *Monitoring birth preparedness and complication readiness tool and indicator for maternal and newborn care*. Matern Neonatal Health Program.

Johnson, A. R., Kumar G, M., Jacob, R., Jessie, M. A., Mary, F., Agrawal, T., & Raman, V. (2019). Fear of Childbirth among Pregnant Women Availing Antenatal Services in a Maternity Hospital in Rural Karnataka. *Indian Journal of Psychological Medicine*, *41*(4), 318–322. https://doi.org/10.4103/IJPSYM.IJPSYM_292_18

Kaso, M., & Addisse, M. (2014). Birth preparedness and complication readiness in Robe Woreda, Arsi Zone, Oromia Region, Central Ethiopia: a cross-sectional study. *Reproductive Health*, *11*(1), 55. https://doi.org/10.1186/1742-4755-11-55

Kementerian Kesehatan Republik Indonesia. (2019). *Profil Kesehatan Indonesia Tahun 2019*. Kementerian Kesehatan Republik Indonesia.

Kızılırmak, A., & Başer, M. (2016). The effect of education given to primigravida women on fear of childbirth. *Applied Nursing Research*, *29*, 19–24. https://doi.org/10.1016/j.apnr.2015.04.002

Kovala, S., Cramp, A. G., & Xia, L. (2016). Prenatal Education: Program Content and Preferred Delivery Method From the Perspective of the Expectant Parents. *The Journal of Perinatal Education*, *25*(4), 232–241. https://doi.org/10.1891/1058-1243.25.4.232

Larsson, B., Rubertsson, C., & Hildingsson, I. (2023). Previous negative experiences of healthcare reported by Swedish pregnant women with fear of birth - A mixed method study. *Sexual & Reproductive Healthcare*, *36*, 100859. https://doi.org/10.1016/j.srhc.2023.100859

Marcelina, L. A., Rachmawati, I. N., & Ungsianik, T. (2019). Dissatisfaction with the husband support increases childbirth fear among Indonesian primigravida. *Enfermería Clínica*, *29*, 379–383. https://doi.org/10.1016/j.enfcli.2019.04.047

Marcil, L. E., Campbell, J. I., Silva, K. E., Hughes, D., Salim, S., Nguyen, H.-A. T., Kissler, K., Hole, M. K., Michelson, C. D., & Kistin, C. J. (2020). Women's Experiences of the Effect of Financial Strain on Parenting and Mental Health. *Journal of Obstetric, Gynecologic & Neonatal Nursing*, *49*(6), 581–592. https://doi.org/10.1016/j.jogn.2020.07.002

Maulina, R., Jannah, S. L., Gita Kostania, Revi Gama Hatta Novika, Argaheni, N. B., & Prabasari, S. N. (2023). Women's Autonomy And Respectful Care In The Maternity Care During Covid-19 Pandemic. *Indonesian Midwifery and Health Sciences Journal*, *7*(2), 153–163. https://doi.org/10.20473/imhsj.v7i2.2023.153-163

Meedya, S., Win, K., Yeatman, H., Fahy, K., Walton, K., Burgess, L., McGregor, D., Shojaei, P., Wheatley, E., & Halcomb, E. (2021). Developing and testing a mobile application for breastfeeding support: The Milky Way application. *Women and Birth*, *34*(2), e196–e203. https://doi.org/10.1016/j.wombi.2020.02.006

Mousavi, S. R., Amiri-Farahani, L., Haghani, S., & Pezaro, S. (2022). Comparing the effect of childbirth preparation courses delivered both in-person and via social media on

pregnancy experience, fear of childbirth, birth preference and mode of birth in pregnant Iranian women: A quasi-experimental study. *PLOS ONE*, *17*(8), e0272613. https://doi.org/10.1371/journal.pone.0272613

Munkhondya, B. M. J., Munkhondya, T. E., Msiska, G., Kabuluzi, E., Yao, J., & Wang, H. (2020). A qualitative study of childbirth fear and preparation among primigravid women: The blind spot of antenatal care in Lilongwe, Malawi. *International Journal of Nursing Sciences*, *7*(3), 303–312. https://doi.org/10.1016/j.ijnss.2020.05.003

Naha, M., & Handayani, S. (2020). Hubungan Pengetahuan Ibu Hamil tentang Persalinan dengan Kesiapan Menghadapi Persalinan pada Trimester III di Puskesmas Umbulharjo I Yogyakarta. *Jurnal Kesehatan Samodra Ilmu*, *9*(2), 158–168. Retrieved from https://stikes-yogyakarta.e-journal.id/JKSI/article/view/101

Nugraheni, W. P., Mubasyiroh, R., & Hartono, R. K. (2020). The influence of Jaminan Kesehatan Nasional (JKN) on the cost of delivery services in Indonesia. *PLOS ONE*, *15*(7), e0235176. https://doi.org/10.1371/journal.pone.0235176

Orwa, J., Gatimu, S. M., Mantel, M., Luchters, S., Mugerwa, M. A., Brownie, S., Subi, L., Mrema, S., Nyaga, L., Edwards, G., Mwasha, L., Isangula, K., Selestine, E., Jadavji, S., Pell, R., Mbekenga, C., & Temmerman, M. (2020). Birth preparedness and complication readiness among women of reproductive age in Kenya and Tanzania: a community-based cross-sectional survey. *BMC Pregnancy and Childbirth*, *20*(1), 636. https://doi.org/10.1186/s12884-020-03329-5

Pantiawati, I. (2016). *Asuhan Kebidanan I (Kehamilan)*. Yogyakarta: Nuha Medika.

Pinar, G., Avsar, F., & Aslantekin, F. (2018). Evaluation of the Impact of Childbirth Education Classes in Turkey on Adaptation to Pregnancy Process, Concerns About Birth, Rate of Vaginal Birth, and Adaptation to Maternity: A Case-Control Study. *Clinical Nursing Research*, *27*(3), 315–342. https://doi.org/10.1177/1054773816682331

Sanders, R. A., & Crozier, K. (2018). How do informal information sources influence women's decision-making for birth? A meta-synthesis of qualitative studies. *BMC Pregnancy and Childbirth*, *18*(1), 21. https://doi.org/10.1186/s12884-017-1648-2

Sari, D. D. P., Sukanto, S., Marwa, T., & Bashir, A. (2020). The Causality between Economic Growth, Poverty, and Stunting: Empirical evidence from Indonesia. *Jurnal Perspektif Pembiayaan Dan Pembangunan Daerah*, *8*(1), 13–30. https://doi.org/10.22437/ppd.v8i1.8834

Simó, S., Zúñiga, L., Izquierdo, M. T., & Rodrigo, M. F. (2019). Effects of ultrasound on anxiety and psychosocial adaptation to pregnancy. *Archives of Women's Mental Health*, *22*(4), 511–518. https://doi.org/10.1007/s00737-018-0918-y

Sulistianingsih, A., Fitria, F., Septiasari, Y., Madiyanti, D. A., Anggraeni, S., & Sasih, I. C. (2023). Effect of husband education in childbirth support on women's self efficacy and labor outcomes: a quasi-experimental study. *Nursing and Midwifery Studies*, *12*(4), 197–205. https://doi.org/10.48307/nms.2023.414828.1259

Syada, S., & Ramaida, R. (2017). Pengaruh Hypnobirthing terhadap Kala I pada Ibu Bersalin di Klinik Pratama Mulia Medica Desa Sungai Buluh Kecamatan Singingi Hilir Kabupaten Singingi Tahun 2015. *Jurnal Endurance*, *2*(2), 151–157. http://doi.org/10.22216/jen.v2i2.1304

Viirman, F., Hess Engström, A., Sjömark, J., Hesselman, S., Sundström Poromaa, I., Ljungman, L., Skoog Svanberg, A., & Wikman, A. (2023). Negative childbirth experience in relation to mode of birth and events during labour: A mixed methods study. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *282*, 146–154. https://doi.org/10.1016/j.ejogrb.2023.01.031

Wigert, H., Nilsson, C., Dencker, A., Begley, C., Jangsten, E., Sparud-Lundin, C., Mollberg, M., & Patel, H. (2020). Women's experiences of fear of childbirth: a metasynthesis of

qualitative studies. *International Journal of Qualitative Studies on Health and Well-Being*, *15*(1), 1704484. https://doi.org/10.1080/17482631.2019.1704484

Wiraswati, A. (2022). *Pelayanan Antenatal Care (ANC) pada Masa Pandem Covid-19*. Direktorat Jenderal Pelayanan Kesehatan, Kementerian Kesehatan Republik Indonesia. Retrieved from https://yankes.kemkes.go.id/view_artikel/1098/pelayanan-antenatal-care-anc-pada-masa-pandem-covid-19

Yang, J., Baker, Z., Dillon, H., Hannallah, A., Klecha, I., SooHoo, M., Ko, J., De Filippo, R., & Vasquez, E. (2023). Reduction in maternal anxiety following prenatal pediatric urology consultation. *Frontiers in Urology*, *2*. https://doi.org/10.3389/fruro.2022.1089135

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 844-853
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1412*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Improving Students' Knowledge of Breakfast Energy and Protein Consumption through E-Booklet Media

Bastianus Doddy Riyadi[1a]*, Pony Puspa Ayu[1b], Juin Hadisuyitno[1c]

[1] Bachelor of Applied Nutrition and Dietetics Study Program, Poltekkes Kemenkes Malang, Malang, East Java, Indonesia

[a] Email address: b.doddyriyadi@gmail.com
[b] Email address: puspaareyou22@gmail.com
[c] Email address: juinhadi@gmail.com

Received: 9 December 2023 Revised: 31 December 2023 Accepted: 31 December 2023

Abstract
Malnutrition remains an important health issue in Indonesia, especially among undernourished children. The current nutrition intervention program, Family Nutrition Awareness, emphasizes the importance of breakfast in combating malnutrition. The purpose of this study was to determine the differences in maternal knowledge, energy, and protein consumption of students before and after counseling on breakfast using e-booklet media. This study used a pre-experimental type with a one-group pretest-posttest design. Maternal knowledge was assessed through a questionnaire, and energy and protein consumption was measured using a food recall form. The statistical analysis used was the paired T-test for normally distributed data and the Wilcoxon test for non-normally distributed data. The results showed significant differences in maternal knowledge and children's energy and protein intake before and after the e-booklet-based educational intervention (p=0.002 and p=0.000). This shows the effectiveness of e-booklets as a nutrition education media, which has the potential to positively influence maternal knowledge and improve children's breakfast habits. In conclusion, there is a difference in nutritional knowledge, energy, and protein consumption before and after counseling on breakfast using e-booklets. This study emphasizes the importance of innovative and accessible educational tools in combating malnutrition in Indonesia.

Keywords: Nutrition Counseling, E-Booklet Media, Maternal Knowledge, Energy, Protein Consumption of Students, Breakfast.

Corresponding Author:

Bastianus Doddy Riyadi
Bachelor of Applied Nutrition and Dietetics Study Program, Poltekkes Kemenkes Malang, Malang, East Java, Indonesia
Email: b.doddyriyadi@gmail.com

1. INTRODUCTION

The multiple nutrition problems experienced by developing countries, including Indonesia, are undernutrition and overnutrition. The impact of malnutrition on children is not optimal growth, causing a lack of energy for activities, reduced immunity and antibodies in the body so that children are susceptible to disease, malnutrition can affect brain growth because brain cells cannot develop, and children who experience malnutrition can have behavior that is not calm (Aprilidia et al., 2021; Simbolon et al., 2023). In addition, other impacts caused by malnutrition according to Gizella et al, impaired brain development and intelligence, impaired physical growth and body metabolism, as well as decreased cognitive abilities and learning achievement (Gizella et al., 2016).

In school-age children (6-12 years) breakfast is very important to carry out activities. Breakfast is useful for providing energy, if school children do not eat breakfast, they will experience a decrease in blood sugar levels which is a source of energy to help the brain work, then the body will break down glycogen stores to maintain normal sugar levels (Anggoro et al., 2021). According to Verdiana and Muniroh, children who eat breakfast every day have more energy than children who do not eat breakfast. Children who do not eat breakfast usually show weakness, dizziness or even fainting (Verdiana & Muniroh, 2018). Breakfast or morning meal must also fulfill balanced nutrition. Based on research conducted by Dewi et al, the results showed that the better the breakfast pattern, the better the concentration in students (Dewi et al., 2020). Children's breakfast habits are influenced by several factors, namely environmental factors, family background, diversity of choices and access to locations to get food(Ludin dan Lim, 2016). Based on research conducted by Gemily et al, the factors that influence breakfast habits are gender, mother's education, mother's occupation, breakfast habits in the family, and family encouragement(Gemily et al., 2017).

Maternal knowledge of food and nutrition can affect the nutritional status of children, and the level of maternal knowledge about nutrition also plays a role in the magnitude of nutritional problems. Maternal knowledge can be improved by providing nutrition education through counseling. In order to implement the nutrition counseling process to achieve maximum results, tools or media are needed that can support the delivery of information. The right media and delivery methods will support the process of implementing nutrition counseling (Bertalina, 2013). One of these media is e-booklet media. E-booklets are classified as electronic learning media that can be used anywhere and are easy to carry anywhere(Utami et al., 2019).

Children and adolescents are a vulnerable group to health problems such as overweight, obesity, eating disorders and social media addiction. Therefore, promotional media can be used to increase their knowledge about the importance of a healthy diet and lifestyle, as well as the negative impact of excessive social media. One important health topic to promote is the importance of breakfast for children and adolescents. Breakfast is the first meal consumed after fasting overnight, and can provide energy, nutrition, and cognitive benefits to those who consume it. However, many children and adolescents skip breakfast for various reasons, such as lack of time, appetite, or access to healthy food. This can have a negative impact on their physical and mental health, as well as their academic and social performance(Hoyland et al., 2009; Nicklas et al., 2004).

To address this issue, promotional media can be used to increase children's and adolescents' awareness and knowledge of the benefits of breakfast, as well as provide suggestions and examples of healthy and easy-to-prepare breakfast foods. Some of the promotional media used are Posters, brochures, or pamphlets that feature attractive and easy-to-understand images and messages about breakfast, such as "Breakfast is important", "Breakfast is fun", or "Breakfast is healthy". These print media can be distributed in schools, homes, or other public places frequented by children and adolescents. Videos, podcasts or animations featuring stories, testimonials or scientific facts about breakfast, such as "Breakfast makes you smarter", "Breakfast makes you happier" or "Breakfast makes you healthier"(Keski-

Rahkonen et al., 2003; Sincovich et al., 2022). These electronic media can be shown on television, radio, internet, or social media that are popular among children and teenagers..

Effective promotional media should take into account the characteristics, needs, and preferences of the target audience, and use language, style, and design that are appropriate to them. In addition, promotional media should be supported by credible and reliable sources, and include citations and references that are in line with academic standards. E-booklet media is a media to convey material in a concise manner and given attractive images, and specially designed so as to be able to produce interesting learning media. E-booklet is a combination of print and computer media, so that it is able to present information in a structured and interesting way and has a high interactive level.(Rahmiyati et al., 2019). According to research conducted by Rahmiyati et al, it shows that knowledge in the mother's group before and after being given treatment in the form of e-booklet media has increased with an average score before 84.82, increasing to 97.94.(Rahmiyati et al., 2019). Further research is needed to complement existing research, especially regarding "Differences in Maternal Knowledge, Energy and Protein Consumption of Breakfast Students Before and After Counseling About Breakfast with E-Booklet Media.

2. RESEARCH METHOD

This study employs a quantitative research approach with a pre-experimental design, specifically utilizing the One Group Pretest Posttest design. The research is conducted at Public Elementary School III Tegalharjo, Glenmore Subdistrict, Banyuwangi Regency. The study is carried out online through a dedicated WhatsApp Group. The population under investigation comprises mothers of students at Public Elementary School III Tegalharjo, Glenmore Subdistrict, Banyuwangi Regency, totaling 160 individuals. The sample consists of 24 respondents selected based on inclusion criteria.

The sampling method employed is Non-Probability Random Sampling, using purposive sampling techniques. In this approach, the sample includes mothers with children actively enrolled in Public Elementary School III Tegalharjo who willingly agree to participate and complete the provided questionnaire.

Data analysis is performed to discern the differences in knowledge and nutritional consumption among elementary school students in the treatment group. Significance is determined at a p-value < 0.05. Data normality is assessed using the Kolmogorov-Smirnov test, where results exceeding a 5% alpha level ($p > 0.05$) indicate normal distribution. For normally distributed data, the parametric paired t-test is applied, while non-normally distributed data are subjected to the non-parametric Wilcoxon signed-rank test.

3. RESULTS AND DISCUSSION

From Table 1, it can be seen that the majority of respondents were between 26-35 years old, as many as 13 people (54.16%), while the rest were 36-45 years old as many as 11 people (45.83%). In terms of the mother's education level, most of the respondents have elementary school education background, as many as 13 people (54.16%), followed by high school education background as many as 6 people (25.00%), and junior high school education as many as 5 people (20.83%). The majority of respondents' mothers worked as self-employed, namely 14 people (58.33%), and the majority of respondents' parents' income was more than ≥2,000,000.00, namely 14 people (58.33%). In addition, there was a striking difference in the age of the students, where 13 students (54.16%) were 9 years old, while 11 students (45.83%) were 8 years old.

Table 1. Characteristics of respondent

Distribution of respondents	Total of Respondents	
	Total (n)	Percentage (%)
Age		
26-35	13	54.16
36-45	11	45.83
Total	24	100.0
Mathers of Education level		
Elementary School	13	54.16
Junior High School	5	20.83
Senior High School	6	25.00
Total	24	100.0
Mathers of Occupation		
Farmer	2	8.33
Self-employed	14	58.33
Private Employee	1	4.16
Laborer	1	4.16
Not Working	6	25.00
Total	24	100.0
Parent's income		
≥2,000,000.00	14	58.33
<2,000,000.00	10	41.66
Total	24	100.0
Age of Student		
8 years old	11	45.83
9 years old	13	54.16
Total	24	100.0
Gender		
Male	14	46.66
Female	16	53.33
Gender	30	100.0
Grade Level		
II	11	45.83
III	13	54.16
Total	24	100.0

Table 2. Average Mother's Knowledge Score based on Questionnaire Materials.

Number of Instrument Material		Number of Correct Answers				% Improvement
		Pre-test		Post-test		
		N	%	N	%	
1	Definition of Breakfast	17	70.8	22	91.6	20.8
2	Protein source foods for breakfast	13	54.1	16	66.6	12.5
3	Examples of breakfast menus that comply with balanced nutrition guidelines	11	45.8	17	70.8	25.0
4	Meal portions in one day	17	70.8	20	83.3	12.5
5	Vegetable protein food sources	14	58.3	19	79.1	20.8

6	Food ingredients that are a source of energy	21	87.5	23	95.8	8.3
7	Good breakfast time	19	79.1	22	91.6	12.5
8	Benefits of breakfast	17	70.8	20	83.3	12.5
9	One serving of fish for children	11	45.8	13	54.1	8.3
10	Characteristics of a healthy breakfast according to balanced nutrition guidelines	19	63.3	22	73.3	10.0
11	One of the points of balanced nutrition message	13	54.1	15	62.5	8.4
12	Food sources of animal protein	18	75.0	21	87.5	12.5
13	Protein needs of children aged 7-9 years	9	37.5	11	45.8	8.3
14	Energy needs of children aged 7-9 years	10	41.6	15	62.5	20.9
15	Programs that have been implemented to overcome nutrition problems	16	66.6	21	87.5	20.9
16	Impact of not having breakfast	13	54.1	18	75.0	20.9
17	Breakfast proportion of daily needs	7	29.1	14	58.3	29.2
18	Vegetables that contain high fiber	18	75.0	23	95.8	20.8
19	Balanced nutrition message for children aged 6-9 years	14	58.3	18	75.0	16.7
20	Use of oil in 1 serving	15	62.5	16	66.6	4.1

According to Table 2, the average knowledge score of mothers based on the questionnaire material before the intervention showed that the respondents answered most of the questions about the need for breakfast proportion of daily needs. Before counseling using e-booklets, out of 24 mothers, only 7 mothers answered correctly (29.1%). However, there was a decrease in the number of respondents who answered incorrectly after the intervention so that there were 10 mothers who answered incorrectly (41.6%) and 14 mothers who answered correctly (58.3%). The increase in knowledge scores before and after the intervention was not only due to the counseling media in the form of e-booklets that were easy to understand, but also because of the counseling methods used, namely lectures and questions and answers.

The highest value of knowledge before the intervention lies in the material of understanding breakfast, food ingredients that become a source of energy, good breakfast time, food sources of animal protein, the impact caused by not having breakfast, the characteristics of a healthy breakfast in accordance with balanced nutrition guidelines, and vegetables that contain high fiber. After the e-booklet-based educational intervention, there was an increase in the number of correct answers starting from questions number 1 to 20. This shows that respondents have understood the breakfast material, balanced nutrition guidelines, and balanced nutrition messages for children aged 6-9 years. However, the lowest score for knowledge was during the pre-test on the proportion of breakfast to daily needs. Out of 24 respondents, only 7 mothers answered correctly. However, based on the final post-test score, there was an increase in the number of respondents who answered correctly to 14 out of 24 respondents. This shows that e-booklet-based educational interventions are effective in increasing mothers' nutritional knowledge and improving children's breakfast habits.In this study, there were several respondents who answered correctly during the pre-test, but answered incorrectly during the post-test. For example, respondents with a high school education background and working as self-employed in question numbers 2,3,7,11,14,15,18,19 answered correctly during the pre-test, but answered incorrectly during the post-test. Meanwhile, respondents with a high school education and not working/housewife at question numbers 9,17,19,20 answered incorrectly during the pre-test, but answered correctly during the post-test

after being given counseling. Respondents with a junior high school education and not working/housewife at question numbers 4, 8, 9, 14, 15, 17, 19 answered incorrectly during the pre-test and still answered incorrectly during the post-test.

At the time of the post-test, most respondents experienced an increase in nutritional knowledge, which was indicated by several questions that were answered correctly by respondents. The questions that were answered most correctly by respondents were numbers 1, 3, 7, 8, 16, and 18, which related to the definition of breakfast, examples of breakfast menus in accordance with balanced nutrition guidelines, good breakfast time, the benefits of breakfast, the impact of not having breakfast, and examples of foods that contain fiber. Meanwhile, the questions that could not be answered correctly by some respondents were numbers 10, 11, 13, 14, 17, and 9, which related to the characteristics of breakfast in accordance with balanced nutrition guidelines, one of the messages of balanced nutrition, nutrient needs based on the 2019 RDA, and the proportion of breakfast.

This study showed that an e-booklet-based educational intervention was effective in increasing mothers' nutrition knowledge and improving children's breakfast habits. However, it should be noted that the results of this study are pre-experimental with a one-group pretest-posttest design, so the results need to be interpreted with caution.

Table 3. Distribution of Average Knowledge Score of Mothers Before and After Counseling with E-booklet Media.

Knowledge Variable	N	Mean	Std. Deviation	Average difference	*p-value**
Before counseling	24	58.33	13.324	13.75	0.002
After counseling	24	72.08	16.999		

**Paired T-test. Significant > 0.05*

Table 3 shows an increase in the average score of knowledge about breakfast before and after counseling using e-booklet media. The increase in the average knowledge score was due to the fact that most respondents had never received counseling about breakfast, so when filling out the questionnaire before the intervention, the respondents answered less precisely. However, after being given counseling, respondents could answer the questionnaire more precisely. The results of the analysis using the Paired T-test showed that the average knowledge of respondents before being given counseling with e-booklet media was 58.33, while after being given counseling with e-booklet media, the average knowledge of respondents increased to 72.08. The statistical test results showed a value of p=0.002 <0.05, which means that at 5% alpha, there is a significant difference in the average score of knowledge about breakfast before and after nutrition counseling with e-booklet media on student mothers.

Table 4. Average Distribution of Children's Breakfast Energy Consumption Values Before and After Counseling.

Variable energy	N	Mean	Std. Deviation	Average difference	*p-value*
Before counseling	24	147.70	38.699	50.9	0.000
After counseling	24	198.60	42.718		

Based on Table 4, it is known that as many as 8 children (33.3%) have consumed breakfast energy in accordance with the proportion of breakfast, namely 15-30% of daily needs before the intervention in the form of counseling with e-booklet media. Meanwhile, after the intervention, there was a change in energy intake in accordance with the proportion of breakfast of 15-30% in 18 children (75%). The average breakfast consumption score before the intervention was 147.70, while after the intervention, the average breakfast consumption

increased to 198.60. Obtaining the value of energy consumption in children was carried out using a food recall questionnaire given during the first week before the intervention (pre-test) and given again in the third week after the intervention (post-test). Based on the results of the analysis using analytical tests, the highest average student energy consumption before being given counseling with e-booklet media was 205.7 kcal, while after being given counseling with e-booklet media, the average student energy consumption increased to 298.3 kcal. Statistical test results showed a value of p=0.000 <0.05, which means that at 5% alpha, there is a significant difference in the average score of children's breakfast consumption before and after nutrition counseling with e-booklet media.

Table 5. Average Distribution of Children's Breakfast Protein Consumption Value Before and After Counseling.

Variable energy	N	Mean	Std. Deviation	Average difference	*p-value*
Before counseling	24	5.28	2.021	2.33	0.000
After counseling	24	7.61	2.539		

Table 5, it is known that children's protein consumption showed that the highest protein consumption before counseling was 10.4 grams, while the protein consumption with the lowest value was 2.36 grams. The average score of breakfast protein consumption before the intervention was 5.28, while after the intervention, the average breakfast protein consumption increased to 7.61. In fulfilling protein consumption at breakfast, only a proportion of about 15-30% of daily needs is needed. In this study, 11 children (45.97%) were in accordance with protein adequacy before the intervention in the form of counseling, while after the intervention, 19 children (79.16%) were in accordance with protein adequacy.

From the results of the analysis using analytical tests, it was obtained that the average breakfast protein consumption of students before being given counseling with e-booklet media was 5.38 grams, while after being given counseling with e-booklet media, the average breakfast protein consumption of students increased to 7.73 grams. Statistical test results showed a value of p=0.000 <0.05, which means that at 5% alpha, there is a significant difference in the average score of children's breakfast protein consumption before and after nutrition counseling with e-booklet media.

According to a study conducted by Fachruddin Perdana and Hardinsyah, the ten types of food most consumed during breakfast are rice, kale, chicken eggs, fish, tempeh, instant noodles, tofu, bread, chicken meat, and biscuits; the five types of drinks most consumed during breakfast are water, tea, milk, coffee, and syrup. Foods consumed with an average of more than 5 g/day during breakfast were rice, kale, chicken eggs, fish, tempeh, and instant noodles. Beverages consumed with an average of more than 15 mL/day during breakfast were water, tea, and milk. Only 10.6% of children's breakfasts met an energy intake of >30% of the RDA(Perdana & Hardinsyah, 2013).

Breakfast can provide energy, nutrition and cognitive benefits for those who consume it regularly. However, many children and adolescents skip breakfast for various reasons, such as lack of time, appetite or awareness. Promotional media can help increase breakfast intake among children and adolescents by providing information on the physical and mental health benefits of breakfast, such as improving metabolism, concentration, memory and mood. Presenting examples of healthy, balanced and attractive breakfasts, such as ready-to-eat cereals and milk, fruits, whole grain bread, eggs or yogurt. Using idol figures, celebrities, or athletes admired by children and adolescents as models or endorsers for breakfast. Creating campaigns or programs that involve schools, families, or communities to encourage and facilitate

breakfast, such as providing free or subsidized breakfast, creating breakfast clubs, or holding breakfast contests.(Mhurchu et al., 2012; Ni Mhurchu et al., 2010; Zhou, 2020).

According to a study involving 234 adolescents aged 11-13 years, a breakfast of ready-to-eat cereal and milk compared with no breakfast had acute positive effects on cognitive function and subjective state(Adolphus et al., 2021). Promotional media can increase breakfast intake among children and adolescents. For example, a UK study found that children who watched advertisements for ready-to-eat cereals and milk were more likely to eat breakfast than those who did not (Adolphus et al., 2021). Another study in the United States found that children exposed to breakfast campaigns featuring cartoon characters were more likely to eat breakfast and choose a healthier breakfast than those who were not exposed (Laska et al., 2015). Several studies have shown that promotional media can reduce problematic social media use among children and adolescents. For example, a study in Ghana found that adolescents who were exposed to messages about the negative impacts of social media were more likely to reduce their social media use than those who were not exposed(Oduro et al., 2023). Another study in South Korea found that adolescents who were exposed to campaigns featuring famous athletes as models to reduce social media use were more likely to reduce social media use than those who were not exposed (Faris et al., 2023).

4. CONCLUSION

The intervention using e-booklet media significantly improved mothers' knowledge on nutrition, with the mean score increasing from 58.33 to 72.08. In addition, there was a significant increase in the mean scores of breakfast energy consumption (from 147.70 to 198.60) and protein intake (from 5.28 to 7.61) after counseling guided by the e-booklet. Statistical analysis using paired t-test showed significant differences in both maternal knowledge and students' energy and protein consumption before and after the e-booklet intervention, as evidenced by p values of 0.002, 0.000, and 0.000, respectively ($p<0.05$). This demonstrates the effectiveness of the e-booklet intervention in positively influencing mothers' knowledge and improving students' nutritional habits.As recommendations for future research, exploring long-term effects, investigating diverse demographic groups, and assessing the sustainability of post-intervention behavior change will provide valuable insights into the broader impact of such educational strategies.

REFERENCES

Adolphus, K., Hoyland, A., Walton, J., Quadt, F., Lawton, C. L., & Dye, L. (2021). Ready-to-eat cereal and milk for breakfast compared with no breakfast has a positive acute effect on cognitive function and subjective state in 11–13-year-olds: a school-based, randomised, controlled, parallel groups trial. *European Journal of Nutrition*, *60*, 3325–3342. https://doi.org/10.1007/s00394-021-02506-2

Anggoro, S., Isnaningsih, T., & Khamid, A. (2021). Edukasi Pentingnya Sarapan untuk Meningkatkan Konsentrasi Belajar. *Jurnal Peduli Masyarakat*, *3*(3), 323–330. https://doi.org/10.37287/jpm.v3i3.707

Aprilidia, N., Husada, D., & Juniastuti, J. (2021). The Impact of Malnutrition on Gross Motoric Growth of The Children Whose Age Between 3 Months And 2 Years Old. *Indonesian Midwifery and Health Sciences Journal*, *4*(1), 8–17. https://doi.org/10.20473/imhsj.v4i1.2020.8-17

Bertalina, B. (2013). Faktor–Faktor Yang Berhubungan Dengan Status Gizi Anak Usia Sekolah (6-12 Tahun). *Jurnal Ilmiah Keperawatan Sai Betik*, *9*(1), 5–12.

Dewi, N. P. S. R., Citrawathi, D. M., & serfi Giada, G. (2020). Hubungan Pola Sarapan dengan Konsentrasi Belajar Belajar Siswa SMP Negeri 2 Banjar. *Wahana Matematika Dan Sains: Jurnal Matematika, Sains, Dan Pembelajarannya*, *14*(1), 168–180.

Faris, M. E., Al Gharaibeh, F., Islam, M. R., Abdelrahim, D., Saif, E. R., Turki, E. A., Al-Kitbi,

M. K., Abu-Qiyas, S., Zeb, F., & Hasan, H. (2023). Caffeinated energy drink consumption among Emirati adolescents is associated with a cluster of poor physical and mental health, and unhealthy dietary and lifestyle behaviors: a cross-sectional study. *Frontiers in Public Health*, 11, 1259109. https://doi.org/10.3389/fpubh.2023.1259109

Gemily, S. C., Aruben, R., & Suyatno, S. (2017). Faktor-Faktor Yang Berhubungan Dengan Kebiasaan Dan Kualitas Sarapan Siswa Kelas V Di Sdn Sendangmulyo 04 Kecamatan Tembalang, Semarang Tahun 2015. *Jurnal Kesehatan Masyarakat*, *3*(3), 246–256.

Gizella, G., Hilmanto, D., & Rachmadi, D. (2016). Role of Hearth Program with Undernutrition Incidence among Toddlers in Tangerang City. *Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*, *11*(1), 14–19.

Hoyland, A., Dye, L., & Lawton, C. L. (2009). A systematic review of the effect of breakfast on the cognitive performance of children and adolescents. *Nutrition Research Reviews*, *22*(2), 220–243. https://doi.org/10.1017/S0954422409990175

Keski-Rahkonen, A., Kaprio, J., Rissanen, A., Virkkunen, M., & Rose, R. J. (2003). Breakfast skipping and health-compromising behaviors in adolescents and adults. *European Journal of Clinical Nutrition*, *57*(7), 842–853. https://doi.org/10.1038/sj.ejcn.1601618

Laska, M. N., Hearst, M. O., Lust, K., Lytle, L. A., & Story, M. (2015). How we eat what we eat: identifying meal routines and practices most strongly associated with healthy and unhealthy dietary factors among young adults. *Public Health Nutrition*, *18*(12), 2135–2145. https://doi.org/10.1017/S1368980014002717

Mhurchu, C. N., Gorton, D., Turley, M., Jiang, Y., Michie, J., Maddison, R., & Hattie, J. (2012). Effects of a free school breakfast programme on children's attendance, academic achievement and short-term hunger: results from a stepped-wedge, cluster randomised controlled trial. *J Epidemiol Community Health*, *1-8*.

Ni Mhurchu, C., Turley, M., Gorton, D., Jiang, Y., Michie, J., Maddison, R., & Hattie, J. (2010). Effects of a free school breakfast programme on school attendance, achievement, psychosocial function, and nutrition: a stepped wedge cluster randomised trial. *BMC Public Health*, *10*(1), 1–6. https://doi.org/10.1186/1471-2458-10-738

Nicklas, T. A., O'Neil, C., & Myers, L. (2004). The importance of breakfast consumption to nutrition of children, adolescents, and young adults. *Nutrition Today*, *39*(1), 30–39.

Oduro, M. S., Katey, D., Morgan, A. K., & Peprah, P. (2023). Problematic social media use and overweight/obesity: explanatory pathway analysis of 124 667 in-school adolescents in 39 high-income countries. *Pediatric Obesity*, *18*(11), e13073. https://doi.org/10.1111/ijpo.13073

Perdana, F., & Hardinsyah, H. (2013). Analisis jenis, jumlah, dan mutu gizi konsumsi sarapan anak Indonesia. *Jurnal Gizi Dan Pangan*, *8*(1), 39–46. https://doi.org/10.25182/jgp.2013.8.1.39-46

Rahmiyati, R., Widyasih, H., & Santi, M. Y. (2019). *Pengaruh E-booklet Tentang ASI Eksklusif Terhadap Peningkatan Pengetahuan Ibu Hamil Trimester III*. Poltekkes Kemenkes Yogyakarta.

Simbolon, D., Oktavia, R., & Krisnasary, A. (2023). Relationship of Nutrition Knowledge and Macronutrient Intake with Nutrition Status Athletes. *MEDIKORA: Jurnal Ilmiah Kesehatan Olahraga*, *22*(2), 67–78.

Sincovich, A., Moller, H., Smithers, L., Brushe, M., Lassi, Z. S., Brinkman, S. A., & Gregory, T. (2022). Prevalence of breakfast skipping among children and adolescents: A cross-sectional population level study. *BMC Pediatrics*, *22*(1), 1–10. https://doi.org/10.1186/s12887-022-03284-4

Utami, R. B., Sari, U. S. C., Yulianti, E., & Wardoyo, S. (2019). Education for working mothers uses leaflet and electronic media to increase exclusive breastfeeding. *Journal of Education and Health Promotion*, *8*, *229*. https://doi.org/10.4103/jehp.jehp_187_19

Verdiana, L., & Muniroh, L. (2017). Kebiasaan Sarapan Berhubungan Dengan Konsentrasi Belajar Pada Siswa SDN Sukoharjo I Malang. *Media Gizi Indonesia*, *12*(1), 14-20. https://doi.org/10.20473/mgi.v12i1.14-20

Zhou, M. (2020). *An Examination of Celebrity Endorsement Used to Promote Branded Food and Beverage Products to American Children, Adolescents and Young Adults to Inform Policies to Promote Healthy Food Environments*. Virginia Tech.

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 854-863
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1292*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Risk Factors Related to Stunting

Tri Anugrah Oktaviani[1a], Linda Suwarni[1b*], Selviana[1c]

[1] Department of Public Health, Faculty of Health Science, Universitas Muhammadiyah Pontianak, West Kalimantan, Indonesia

[a] Email address: 211510074@unmuhpnk.ac.id
[b] Email address: linda.suwarni@unmuhpnk.ac.id
[c] Email address: selviana@unmuhpnk.ac.id

Received: 26 July 2023 Revised: 12 December 2023 Accepted: 31 December 2023

Abstract
Childhood stunting, or low height for age, continues to be a concern for world health since it raises the possibility of both mortality and growth and development disorders. West Kalimantan province ranks seventh with the highest prevalence of 29.8% by 2021. But little is known about Pontianak's children's stunting risk factors, especially in the UPT Puskesmas Pal Lima (one of the community health centers with a high prevalence of stunting). The study aimed to determine risk factors associated with stunting in the UPT Puskesmas Pal Lima, such as high-risk pregnant women, pregnant women with chronic energy deficiency, communication of educational information about stunting, occupancy density, and age of pregnant women in the UPT Puskesmas Pal Lima. Cross-sectional study design was used. The research was conducted in February-March 2023. The population in this study were all stunted toddlers in the UPT work area of the Pal Lima Health Center. Sampling used quota sampling with all 75 stunted toddlers. Data analysis used univariate and bivariate analysis (chi square test with 95% CI). This research found that 61,3% with high risk pregnant women, 21,3% with chronic energy deficiency, 52% not exposed to information communication and education about stunting, 32% occupancy density were not qualified, 48% risk at age of pregnant mothers, 32% severe stunting and 68% stunting. There was a significant relationship between high-risk pregnant women (p-value = 0,015), pregnant women with chronic energy deficiency (p-value = 0,001), the information communication and education about stunting (p-value = 0,046), occupancy density (p-value = 0,043), and the age of pregnant women (p-value = 0,049), and the incidence of stunting in toddlers in the working area of UPT Puskesmas Pal Lima, West Pontianak District. Based on the results of this study can be used as a basis for the primary prevention of stunting in pregnant women.

Keywords: High Risk Pregnant Women, Chronic Energy Deficiency, Information Communication Education about Stunting, Occupancy Density, Age of Pregnant Women Stunting.

Corresponding Author:

Linda Suwarni
Department of Public Health, Faculty of Health Science, Universitas Muhammadiyah Pontianak, West Kalimantan, Indonesia
Email: linda.suwarni@unmuhpnk.ac.id

1. INTRODUCTION

Malnutrition that occurs at an early age can increase infant and child mortality, cause intelligence to decrease, and even result in long-term economic losses for a nation (Govender et al., 2021). Stunting is a condition where a child's height is too low compared to other children (Palino, Majid, & Ainurafiq, 2017). Stunting and severe stunted based on age namely height that is below minus two standard deviations (<-2SD) from the WHO child growth standard nutritional status table. Stunting has the impact of poor nutritional intake of both quality and quantity as well as high rates of pain. This condition is often found in states with poor economic conditions (Boucot & Poinar, 2018).

In 2020, there were approximately 149.2 million (22.0%) stunted children under the age of five worldwide, despite the fact that the frequency of stunting has consistently decreased over the past 20 years. In 2019, Asia accounted for over half of all stunted children under five, while Africa accounted for two out of every five. In Southeast Asia, stunting affects 25.8% of children under five (UNICEF, 2021). The problem that is still the focus of the government in Indonesia today is the problem of nutrition, which is characterized by high rates of stunting in children. Indonesia is ranked as the third country with the highest prevalence in the Southeast Asia/South-East Asia Regional (SEAR) region according to the prevalence of stunting news data collected by the World Health Organization (WHO). The average incidence of stopping news in Indonesia was 36.8% in 2010 or 35.6% and in 2013 the incidence increased to 37.2% consisting of 18% of severe stunting and 19.2% of stunting (Selvia & Wahyuni, 2022). Based on the stunting rate obtained from JME and the UNICEF World Bank in 2020, the stunting rate in Indonesia reached the 115th position out of 151 countries (Tobing et al., 2021). *Riskesdas* data (2018) show that 30,8% or around 7 million children under the age of 5, are stunted, which shows a fundamental difference from the WHO limit for reducing stunting cases which is a maximum of 20% (Kementerian Kesehatan Republik Indonesia, 2018). Therefore, Indonesia is included in the list of countries with high stunting problems.

The Province of West Borneo is ranked as the seven province with the highest prevalence of stunting after the Provinces of NTT, West Sulawesi, Aceh, NTB, North Sulawesi, and South Borneo, with a rate of 29,8% in 2021 (Indonesian The Ministry of Health, 2021). According to the 2022 Indonesian Nutritional Status Survey (SSGI), the prevalence of stunting in under-fives (height for age) in West Borneo Province reached 27,8% with the highest stunting prevalence occurring in the Melawi Regency area, reaching 44,1%, while in Pontianak City the stunting rate was 19,7% (Munira, 2023). The prevalence of nutritional status of children under five based on indicators of height and age in districts and cities in West Borneo Province in 2018 for the very short category was 11,4% and the short category was 21,9% (Kementerian Kesehatan Republik Indonesia, 2018).

Many factors influence the incidence of stunting in toddlers, so it is necessary to study the determinant factors that can affect the incidence of stunting to become a reference in tackling existing stunting problems. Several factors from parents that cause stunting can be seen in the condition of the mother during pregnancy as measured by the upper arm circumference (LILA), which describes chronic energy deficiency, or what is known as CED (Ruaida & Soumokil, 2018). Many other factors also affect children born short, and one that must be considered is the age of the mother during pregnancy. Mothers aged 21 years or >35 years have a high risk of health threats and death to the mother or the fetus during pregnancy or the puerperium (Sani et al., 2019). In addition, mothers who have high risks, such as having a history of hypertension in pregnancy, also affect the health of the fetus they contain (Pongrekun, Sunarsieh & Fatmawati, 2020). In previous studies, it was found that there was a relationship between maternal risk factors that could affect the growth and development of

children under five and cause stunting, such as pregnant women with Chronic Energy Deficiency (CED), low knowledge of the Information, Communication and Education model (ICE) about stunting, and the age of pregnant women who were too young or too old for the stunting incident (Wardani, 2022; Istiningsih & Riyanti, 2022).

Globally, a number of research have examined the connection between risk factors and stunting in children. Stunting is frequently associated with issues relating to the mother, child, household, and accessibility of services. Most people are aware that teenage mothers who become pregnant typically have underweight children, minimal maternal weight gain, and a significant risk of anemia (le Roux et al., 2019; Nabugoomu et al., 2018). Stunting in the toddlers can be caused by several factors, one of which is pregnancy (Najah & Darmawi, 2022). UPT Puskesmas Pal Lima is one of the public health centers in Pontianak City with a high prevalence of stunting, reaching 5,91%. The working area of the Pal Lima Health Center UPT is characterized by a densely populated community, most of whom live on the banks of the river, and a relatively low level of community education. However, little is known about how maternal characteristics and background contribute to child stunting in UPT Puskesmas Pal Lima, Pontianak City.

Emergency research stunting in UPT Puskesmas Pal Lima is supported by gap research in some previous research on risk factors related to stunting, but in some research only explain the risk factors of stunting from the condition of nutrition in the toddlers. Meanwhile, it is important to know that there are several other risk factors that can cause stunting. The purpose of this study was to determine the relationship between risk factors for stunting such as high-risk pregnant women, pregnant women with CED or ICE about stunting, occupancy density, and the age of pregnant women on stunting in toddlers. The benefit of this research is to provide information and add insight about the relationship between maternal risk factors and the incidence of stunting in toddlers.

2. RESEARCH METHOD

The research design used in this study is an analytic observational design using the cross-sectional method. This research was conducted to determine the relationship between maternal risk factors and the incidence of stunting in UPT Puskesmas Pal Lima. The population in this study were all stunted toddlers in the UPT work area of the Pal Lima Health Center. Sampling used quota sampling with all 75 stunted toddlers.

The dependent variable in this study is the incidence of stunting. Stunting is divided into two categories, namely severe stunting and stunting (using secondary data from the Pal Lima Community Health Center UPT). The independent variables in this study include high risk pregnant women (have a history of hypertension and other diseases or not), CED pregnant women (Upper Arm Circumference less or more than 23.5 cm), communication of information and education about stunting (exposed or not), occupancy density (qualified >8m^2/person or unqualified <8m^2/person), and age of pregnant women (less or more than 21 years old).

The type of data collected is primary data collected through interviews using a questionnaire measuring instrument that is distributed to mothers who have stunting toddlers and secondary data obtained through the Health Profile of the UPT Puskesmas Pal Lima. This research was conducted in the work area of UPT Puskesmas Pal Lima, West Pontianak District, in March-April 2023. Data analysis used univariate and bivariate analysis (chi square test with 95% CI). This research has also received research ethics permit from Public Health with No: 002/KEPK-FIKES/UMPONTIANAK/2023.

3. RESULTS AND DISCUSSION

Tabel 1. Show univariat analysis of stunting risk factors in UPT Puskesmas Pal Lima.

Variable	n	%
High Risk pregnant Women		
Risk of stunting	46	61,3
No risk of stunting	29	38,7
Nutritional Status of Pregnant Women		
With chronic energy deficiency	16	21,3
No chronic energy deficiency	59	78,7
Information Communication and Education about stunting		
Exposed	39	52,0
Not exposed	36	48,0
Occupancy Density		
Qualify	24	32,0
Not qualified	51	68,0
Age of Pregnant Women		
Less than 21th	36	48,0
More than 21th	39	52,0
Total	75	100,0

Source: Primer Data, 2023

The table showed based on univariate analysis it is concluded that the majority of high-risk pregnant mothers suffered stunting with a total of 46 people (61.3%), pregnant women with an arm circumference of less than 23.5 cm with a chronic energy deficiency category were 16 (21.3%); pregnant non-exposed mothers communicated educational information about stopping with 36 (48%). The majority of the population did not qualify for the population density of 51 people (68%) and the age of pregnant mothers less than 21 years old of 36 people (48%).

Table 2. Cross-tabulation of Risk Factors Associated with Stunting.

Variable	Stunting				p-value	PR (95% CI)
	Severe Stunting		Stunting			
	f	%	f	%		
High Risk Pregnant Women						
Yes	20	43.5	26	56.5	0.015	3.152
No	4	13.8	25	86.2		(1.198 – 8.296)
Nutritional Status of Pregnant Women						
Upper Arm Circumference less than 23.5 cm	11	68.8	5	31.3	0.001	3.120
Upper Arm Circumference more than >23.5 cm	13	22.0	46	78.0		(1.742 – 5.588)
Information Communication and Education about stunting						

No	17	43.6	22	56.4	0.046	2.242
Yes	7	19.4	29	80.6		(1.054 – 4.768)
Occupancy Density						
Qualified	12	50.0	12	50.0	0.043	2.125
Not Qualified	12	23.6	39	76.5		(1.125 – 4.015)
Age of Pregnant Women						
Less than 21th	16	44.4	20	55.6	0.049	2.167
More than 21th	8	20.5	31	79.5		(1.057 – 4.441)

Source: Primer Data, 2023

The table 2 showed that high-risk pregnant women had a significant association with the incidence of stunting in toddlers. Based, on Prevalence Ratio, it could be concluded that pregnant women are at risk of potentially experiencing stunting 3,152 more times in the very short category (severe stunting) compared to pregnant women who are not at risk. Maternal nutritional status during pregnancy was also significantly related to the incidence of stunting in children under five. Based in the Prevalence Ratio, it can be concluded that mothers who experience CED have the potential to experience stunting in the very short category (severe stunting) 3.120 more times than the mothers who do not experience CED. Mothers' knowledge had a significant relationship with the incidence of stunting in toddlers. Mothers who don't have good knowledge about stunting have a 2.242 times higher chance of having very short children (severe stunting) compared to mothers who have knowledge about stunting. Occupancy density is significantly related to the incidence of stunting in toddlers. The respondent which occupancy density not qualified had the potential to experience stunting in the very short category (severe stunting) 2.125 more times higher than the occupancy density qualified. Maternal age during pregnancy is significantly related to the incidence of stunting in infants. Pregnant women less than 21 years old have a 2.167 times greater chance of experiencing stunting in the very short category (severe stunting) compared to pregnant women more than 21 years old.

Relationship Between High-Risk Pregnant Women and Stunting. According to this study pregnant women who were at high-risk of severe stunting had a gestational age that was 13,8% higher than that of pregnant women who were not at risk for stunting, and statistical test results showed a significant relationship. Pregnancy hypertension is one of the elements that supports high-risk pregnant women, specifically, situations that put the mother at risk for difficulties during pregnancy or childbirth. Mothers who have a history of high blood pressure during pregnancy run the danger, such as kidney, liver, or heart failure due to cerebral bleeding (Cunningham & LaMarca, 2018). This can potentially result in a significant delay in the onset of consciousness for a considerable amount of time (Widyaningsih & Dewi, 2021).

A decrease in uteroplacental circulation could be brought on by high blood pressure during pregnancy because it can make the lining of the arteries stiff and prevent distention and vasodilation from happening (Hu & Zhang, 2021). Decreased uteroplacental circulation can also result in blood flow and nutrient flow to the placenta not being optimal, which can inhibit fetal growth and cause complications in the fetus such as low birth weight and premature birth (Safitri & Djaiman, 2021). Low Birth Weight (LBW) is a sign that the fetus was malnourished while it was growing inside the mother, and stunting is a symptom of chronic or long-term malnutrition. Compared to women who don't suffer hypertension during pregnancy, mothers who do have it throughout pregnancy run a 4.086 times higher chance of giving birth to toddlers who are stunted (Wardani, 2022). Stunting is 4.967 times more likely to occur in infants whose

mothers had a history of hypertension during pregnancy than it is in mothers without such a history (Nengsih & Wirastuti, 2020).

The findings of this research can be used as a reference in early prevention programs for stunting in pregnant women, especially in pregnant women with high blood pressure. Appropriate intervention and assistance is needed so that it can reduce existing risks (Fitriani et al., 2020).

Relationship Between Nutritional Status of Pregnant Women and Stunting. The rate of Chronic Energy Deficiency (CED) among pregnant women in the very short group was 68,8% greater than the rate among pregnant women who didn't have CED, which was lower by 22,0% and the prevalence of stunting in toddlers and mothers' nutritional status during pregnancy are related. The upper arm on the region of the hand not used for daily activities can be used to observe or measure pregnant women who are classified as having Chronic Energy Deficiency (CED) with an arm circumference of less than 23,5 cm (Khairunisa et al., 2022). The upper arm's circumference can provide information about the health of the underlying fat and muscle tissue. Finding out whether pregnant women fall into the CED category or the normal category is the goal of the upper arm's circumference measurement. It's crucial to do this activity in order to understand the potential risk of stunting (Rohmawati et al., 2020).

The mother's nutritional status both before and throughout pregnancy has a significant impact on how the fetus develops inside the mother. However, if the mother's nutritional health before and during pregnancy is adequate, it is likely that she will give birth to a healthy, full-term baby who weighs a normal amount. Therefore, it can be said that the quality of the fetus is greatly influenced by the mother's nutritional health status before and during pregnancy (Ibrahim et al., 2019). Therefore, Low Birth Weight (LBW) and Short Birth Length (SBL) in the newborn are likely if the baby's development is less than ideal in pregnant women with CED. Pregnant women with chronic energy deficiency may not have enough nutritional reserves to meet the physiological demands of pregnancy, such as hormonal changes, and may increase blood volume for fetal growth, which reduces the fetus's access to nutriens and stunts its growth and development during pregnancy. Stunted in the womb, low body weight, short or even very short height, or growth retardation (Eka et al., 2021). The findings of this study are in line with previous studies (Ruaida & Soumokil, 2018; Alfarisi et al., 2019).

Relationship Between Information, Communication and Education About Stunting and Stunting. Women who had never received information, communication and education about stunting scored 43,6% higher in the extremely short group than mothers who had (19,4%). We can draw the conclusion that the occurance of stunting in toddlers was correlated with women who don't obtain communication of education information. Stunting is caused by a poor socio-economic background and a lack of education (Murti et al., 2020). The prevention of stunting and raising toddlers parents' knowledge and awareness of the value of child growth and development in overcoming stunting are essential goals of communication, information and education.

One of the factors contributing to moms' lack of knowledge, particularly in the area of education, a mother's knowledge may be impacted by her poor level of schooling. The nutritional status of children can be improved thanks to mothers' awareness. Knowing that it is inadequate will change a mother's perspective and conduct when it comes to feeding the toddlers healthy food (Saragih et al., 2020). Furthermore, having a toddler with a proper nutritional status doesn't always result from a mother who is knowledgeable. Mothers who are well-informed are expected to be able to use their knowledge in real life. Additionally, because a mother controls a toddler's entire food intake, the mother's parenting style also affect the likelihood of stunting in toddlers. As a result, it's important to educate moms of toddlers about

stunting so that they can improve their awareness of the condition and their parenting abilities and keep their children's growth and development on track for health (Amalia et al., 2021; Olsa et al., 2018; Samiati et al., 2022).

Relationship Between Occupancy Density and Stunting. The occupancy density in the very short category that complied with the regulations was 50.0% greater than the density that didn't, which was 23,5% and the prevalence of stunting in toddlers and occupancy density are related. The state of the environment today is something that still requires attention because it has the potential to impact the community's level of health. One of them is occupancy density, which includes access to clean water, trash removal, waste management, and private latrine ownership. Occupational density is defined as the ratio of the number of occupants to the square footage (m^2) of the room occupied by the patient, with a minimum need of 8 m^2/patient. The occupancy density standards were not met by 51 of the 75 respondent.

Based on the fact that 76,5% of toddlers in the short category and 23,6% of those who are very short are stunted, the average toddler who is stunted comes from a home with a poor environment. Research findings in the West Pontianak Subdistrict, where UPT Puskesmas Pal Lima is located, reveal that environmental conditions are still very poor, particularly in terms of residential density and its effects on latrine ventilation, waste processing, and the prevalence of for consumption in daily life can have an impact in health and nutritional status, particularly malnutrition, while simultaneously preventing the development of disease. The presence of various diseases is made possible by the density of residents who don't fulfill minimum health standards. Toddlers' nutritional status is significantly impacted by the state of the home. Stunting in toddlers can be reduced or even avoided with good environmental sanitation. According to studies done in the Samarinda seberang district, there is a direct correlation between environmental factors and the prevalence of stunting in young children (Cleopatra et al., 2018; Zahrawani et al., 2022).

Relationship Between the Age of Pregnant Women and Stunting. The age of pregnant women under 21 years old with a very short category was found to be 44,4% lower than that of pregnant women over 21 years, at 20,5% and the likelihood of stunting in toddlers is correlated with the age of pregnant women. The mother's age has a strong correlation with birth weight; when the mother is still young or under 21 years old, the development of the reproductive organs and physiological processes is still not optimal. Additionally, psychologically speaking, it is not development enough for the mother to handle pregnancy completely, and issues frequently arise. The frequency of preeclampsia and inadequate fetal growth are directly connected to the risk of pregnancy in women who gives birth at ages between 21 and 35 years old (Sari & Sartika, 2021).

The mother is too young to be pregnant, which raises the possibility of an early delivery, uterine growth impairment, and possibly mortality for both the mother and the fetus. When compared to the ideal pregnancy age (21-53 years), young moms typically have low nutritional conditions (Dewey, 2016). Premature newborns, chromosal abnormalities and uterine growth retardation are all high-risk pregnancy outcomes for pregnant women who are too old (Fall et al., 2015). Malnutrition and other growth deficits that may result in stunting are likely to be caused by this, which will have an impact on children's growth and development (Pusmaika et al., 2022; Wanimbo & Wartiningsih, 2020; Nurhidayati, Rosiana & Rozikhan, 2015).

4. CONCLUSION

There is a relationship between risk factors such as high-risk pregnant women, pregnancies with chronic energy deficiency (CED), communication of educational information about stunting, labor intensity and the age of pregnant mothers with stunting. It is recommended

for UPT Puskesmas Pal Lima to improve information communication and education to the community related to stunting, while for parents is expected to the pregnant mother at high risk to check herself routinely, to know the condition of LILA to prevent the occurance of Chronic Energy Deficiency (CED), meet the standard conditions of housing density, and determine the age of pregnancy matured is >21 years and increase care for the growth of toddlers by meeting the nutritional needs of toddlers.

REFERENCES

Alfarisi, R., Nurmalasari, Y., & Nabilla, S. (2019). Status Gizi Ibu Hamil Dapat Menyebabkan Kejadian Stunting Pada Balita. *JKM (Jurnal Kebidanan Malahayati)*, *5*(3), 271-278. https://doi.org/10.33024/jkm.v5i3.1404

Amalia, I. D., Lubis, D. P. U., & Khoeriyah, S. M. (2021). Hubungan Pengetahuan Ibu tentang Gizi Dengan Kejadian Stunting Pada Balita: Relationship Between Mother's Knowledge on Nutrition and The Prevalence of Stunting on Toddler. *Jurnal Kesehatan Samodra Ilmu*, *12*(2), 146–154. https://doi.org/10.55426/jksi.v12i2.153

Boucot, A., & Poinar Jr., G. (2018). Stunting. *Fossil Behavior Compendium*, *5*, 243–243. https://doi.org/10.1201/9781439810590-c34

Cleopatra, A. B., Fitriangga, A., & Fahdi, F. K. (2018). Faktor – Faktor Yang Berhubungan Dengan Penggunaan Rokok Elektrik Di Wilayah Kecamatan Pontianak Barat. *ProNers*, 4(1), 1–10.

Cunningham, M. W., & LaMarca, B. (2018). Risk of cardiovascular disease, end-stage renal disease, and stroke in postpartum women and their fetuses after a hypertensive pregnancy. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *315*(3), R521–R528. https://doi.org/10.1152/ajpregu.00218.2017

Dewey, K. G. (2016). Reducing stunting by improving maternal, infant and young child nutrition in regions such as South Asia: Evidence, challenges and opportunities. *Maternal and Child Nutrition*, *12*, 27–38. https://doi.org/10.1111/mcn.12282

Eka, M. B., Krisnana, I., & Husada, D. (2021). Risk Factors of Stunting Events in Toddlers Aged 24-59 Months. *Indonesian Midwifery and Health Sciences Journal*, *4*(4), 374–385. https://doi.org/10.20473/imhsj.v4i4.2020.374-385

Fall, C. H. D., Sachdev, H. S., Osmond, C., Restrepo-Mendez, M. C., Victora, C., Martorell, R., Stein, A. D., Sinha, S., Tandon, N., Adair, L., Bas, I., Norris, S., Richter, L. M., Barros, F. C., Gigante, D., Hallal, P. C., Horta, B. L., Ramirez-Zea, M., Bhargava, S. K., … Stein, A. (2015). Association between maternal age at childbirth and child and adult outcomes in the offspring: A prospective study in five low-income and middle-income countries (COHORTS collaboration). *The Lancet Global Health*, *3*(7), e366–e377. https://doi.org/10.1016/S2214-109X(15)00038-8

Fitriani, H., R, A. S., & Nurdiana, P. (2020). Risk Factors of Maternal Nutrition Status During Pregnancy to Stunting in Toddlers Aged 12-59 Months. *Jurnal Keperawatan Padjadjaran*, *8*(2), 175–183. https://doi.org/10.24198/jkp.v8i2.1305

Govender, I., Rangiah, S., Kaswa, R., & Nzaumvila, D. (2021). Malnutrition in children under the age of 5 years in a primary health care setting. *South African Family Practice*, *63*(1), a5337. https://doi.org/10.4102/safp.v63i1.5337

Hu, X., & Zhang, L. (2021). Uteroplacental Circulation in Normal Pregnancy and Preeclampsia: Functional Adaptation and Maladaptation. *International Journal of Molecular Sciences*, *22*(16), 8622. https://doi.org/10.3390/ijms22168622

Ibrahim, I. A., Bujawati, E., Syahrir, S., Adha, A. S., & Mujahida, M. (2019). Analisis determinan kejadian Growth failure (Stunting) pada anak balita usia 12-36 bulan di

wilayah pegunungan desa Bontongan Kecamatan Baraka Kabupaten Enrekang. *Al-Sihah: The Public Health Science Journal*, *11*(1), 50–64.

Indonesian The Ministry of Health. (2021). *Results of the Indonesian Gizi Status Study (SSGI) National level, Province, District/City in 2021*. Indonesian The Ministry of Health

Istiningsih, T., & Riyanti, R. (2022). Maternal Risk Factors Against Stunting Balita Aged 12 – 24 Months In Puskesmas Mantangai District of Kapuas Province of Kalimantan. *Malahayati Nursing Journal*, *4*(7), 1828–1838. https://doi.org/10.33024/mnj.v4i7.6673

Khairunisa, R., Mitra, M., Purba, C. V. G., Alamsyah, A., & Abidin, A. R. (2022). Faktor Risiko Ibu pada Saat Hamil dengan Kejadian Stunting pada Anak Balita di Kota Pekanbaru. *Jurnal Kesehatan Global*, *5*(3), 150-160.

le Roux, K., Christodoulou, J., Stansert-Katzen, L., Dippenaar, E., Laurenzi, C., le Roux, I. M., Tomlinson, M., & Rotheram-Borus, M. J. (2019). A longitudinal cohort study of rural adolescent vs adult South African mothers and their children from birth to 24 months. *BMC Pregnancy and Childbirth*, *19*(1), 24. https://doi.org/10.1186/s12884-018-2164-8

Munira, S. L. (2023). *Hasil Survei Status Gizi Indonesia (SSGI) 2022*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Murti, L. M., Budiani, N. N., & Darmapatni, M. W. G. (2020). Hubungan pengetahuan ibu tentang gizi balita dengan kejadian stunting anak umur 36-59 bulan di Desa Singakerta Kabupaten Gianyar. *Jurnal Ilmiah Kebidanan (The Journal Of Midwifery)*, *8*(2), 62-69.

Nabugoomu, J., Seruwagi, G., Corbett, K., Kanyesigye, E., Horton, S., & Hanning, R. (2018). Needs and Barriers of Teen Mothers in Rural Eastern Uganda: Stakeholders' Perceptions Regarding Maternal/Child Nutrition and Health. *International Journal of Environmental Research and Public Health*, *15*(12), 2776. https://doi.org/10.3390/ijerph15122776

Najah, S., & Darmawi, D. (2022). Hubungan Faktor Ibu Dengan Kejadian Stunting Di Desa Arongan Kecamatan Kuala Pesisir Kabupaten Nagan Raya. *Jurnal Biology Education*, *10*(1), 45-55. https://doi.org/10.32672/jbe.v10i1.4234

Nengsih, Y., & Warastuti, D. (2020). Faktor Risiko Kejadian Stunting Pada Bayi Dan Balita Di Desa Ciambar Kecamatan Ciambar Kabupaten Sukabumi Tahun 2019. *Jurnal Kesehatan Dan Kebidanan (Journal of Health and Midwifery)*, *9*(1), 1-11.

Nurhidayati, T., Rosiana, H., & Rozikhan, R. (2020). Usia Ibu Saat Hamil Dan Kejadian Stunting Pada Anak Usia 1-3 Tahun. *Midwifery Care Journal*, *1*(5), 122-126.

Olsa, E. D., Sulastri, D., & Anas, E. (2018). Hubungan sikap dan pengetahuan ibu terhadap kejadian stunting pada anak baru masuk Sekolah Dasar di kecamanatan Nanggalo. *Jurnal Kesehatan Andalas*, *6*(3), 523-529. https://doi.org/10.25077/jka.v6i3.733

Palino, I. L., Majid, R. & Ainurafiq, A. (2017). *Determinan Kejadian Stunting pada Balita Usia 12-59 Bulan di Wilayah Kerja Puskesmas Puuwatu Kota Kendari Tahun 2016. Jurnal Ilmiah Mahasiswa Kesehatan Masyarakat Unsyiah, 2(6), 1-12*.

Pongrekun, P.S., Sunarsieh & Fatmawati. (2020). Faktor-Faktor Yang Berhubungan Dengan Kejadian Stunting Di Kabupaten Konawe Selatan: Factors That Are Related To Stunting Events In South Konawe District. *Jurnal Ilmiah Kebidanan (Scientific Journal of Midwifery)*, *6*(2), 95-104.

Pusmaika, R., Novfrida, Y., Simatupang, E. J., Djami, M. E., & Sumiyati, I. (2022). Hubungan Usia Ibu Saat Hamil dengan Kejadian Stunting Pada Balita di Kabupaten Tangerang. *Indonesian Health Issue*, *1*(1), 49-56. https://doi.org/10.47134/inhis.v1i1.11

Kementerian Kesehatan Republik Indonesia. (2018). *Hasil Utama Riset Kesehatan Dasar 2018*. Jakarta: Kementerian Kesehatan Republik Indonesia.

Rohmawati, W., Wintoro, P. D., & Sari, T. W. (2020). Hubungan Kekurangan Energi Kronik pada Ibu Hamil dengan Kejadian Stunting di Klaten. *MOTORIK Jurnal Ilmu Kesehatan*,

3(1), 39–44.
Ruaida, N., & Soumokil, O. (2018). Hubungan status KEK ibu hamil dan BBLR dengan kejadian stunting pada balita di puskesmas Tawiri kota Ambon. *Jurnal Kesehatan Terpadu (Integrated Health Journal)*, *9*(2), 1-7. https://doi.org/10.32695/jkt.v2i9.12
Safitri, A., & Djaiman, S. P. H. (2021). Hubungan hipertensi dalam kehamilan dengan kelahiran prematur: Metaanalisis. *Media Penelitian dan Pengembangan Kesehatan*, *31*(1), 27–38. https://doi.org/10.22435/mpk.v31i1.3881
Samiati, Amin F.A. & Ramadhaniah. (2022). Hubungan Pola Asuh, Pendidikan Ibu, Pengetahuan Ibu Dan Riwayat Penyakit Infeksi Dengan Kejadian Stunting Pada Balita Usia 12-24 Bulan Di Wilayah Kerja Puskesmas Rundeng Kota Subulussalam Tahun 2021. *Journal of Health and Medical Science*, 1(4), 216-223.
Sani, M., Solehati, T., & Hendrawati, S. (2019). Hubungan usia ibu saat hamil dengan stunted pada balita 24-59 bulan. *Holistik: Jurnal Kesehatan*, *13*(4), 284-291.
Saragih, F. L., Simanjuntak, Y. T., & Hutajulu, J. (2020). Hubungan Pengetahuan Keluarga Dengan Tindakan Pencegahan Stunting Di Desa Perk. Aek Tarum Kecamatan Bandar Pulau Kabupaten Asahan Tahun 2020. *Jurnal Teknologi Kesehatan Dan Ilmu Sosial (Tekesnos)*, *2*(2), 20-29.
Sari, K., & Sartika, R. A. D. (2021). The effect of the physical factors of parents and children on stunting at birth among newborns in indonesia. *Journal of Preventive Medicine and Public Health*, *54*(5), 309–316. https://doi.org/10.3961/jpmph.21.120
Selvia, D., & Wahyuni, A. (2022). Wahyuni, A. (2021). Manajemen General Anestesi Pada Pasien Splenomegali. *Jurnal Kesehatan Saintika Meditory*, 4(2), 78-84. http://dx.doi.org/10.30633/jsm.v4i2.1270
Tobing, M. L., Pane, M., & Harianja, E. (2021). Pola Asuh Ibu Dengan Kejadian Stuntingpada Anak Usia 24–59 Bulan di Wilayah Kerja Puskesmas Kelurahan Sekupang Kota Batam. *Jurnal Kesehatan Masyarakat*, *5*(1), 448-465. https://doi.org/10.31004/prepotif.v5i1.1630
UNICEF. (2021). *UNICEF-WHO-World Bank: Joint Child Malnutrition Estimates—2021 Edition Interactive Dashboard*. UNICEF. Retrieved from https://data.unicef.org/resources/joint-child-malnutrition-estimates-interactive-dashboard-2021
Wanimbo, E., & Wartiningsih, M. (2020). Wanimbo, E., & Wartiningsih, M. (2020). Hubungan karakteristik ibu dengan kejadian stunting baduta (7-24 bulan). *Jurnal Manajemen Kesehatan Yayasan RS. Dr. Soetomo*, *6*(1), 83. https://doi.org/10.29241/jmk.v6i1.300
Wardani, D. K. (2022). Pengaruh Faktor Maternal Ibu terhadap Kejadian Stunting pada Balita Usia 24-59 Bulan di Wilayah kerja UPT Puskesmas Sopaah Kabupaten Pamekasan The Influence of Maternal Factors on The Incidence of Stunting among Toddlers Aged 24–59 Months in Working Area of Sopaah Primary Health Care, Pamekasan District. *Media Gizi Kesmas*, 11(02), 386-393. https://doi.org/10.20473/mgk.v11i2.2022.386-393
Western Health. (2020). *Western Health Research Reports*. Western Health.
Widyaningsih, W., & Dewi, I. P. (2021). Hubungan Tekanan Darah Tinggi Dengan Kejadian Stunting Pada Anak. *MAHESA: Malahayati Health Student Journal*, *1*(4), 333-344. https://doi.org/10.33024/mahesa.v1i4.5476
Zahrawani, T. F., Nurhayati, E., & Fadillah, Y. (2022). Hubungan kondisi jamban dengan kejadian stunting di Puskesmas Cicalengka Tahun 2020. *Jurnal Integrasi Kesehatan dan Sains (JIKS)*, *4*(1), 1–5. https://doi.org/10.29313/jiks.v4i1.7770

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 864-874
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1203*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

The "HeForshe" Approach Model to The Elimination of Violence Against Women and Children

Mariana Ngundju Awang[1a*], Matje M Huru[1b], Odi Namandjabar[1c], Wilhelmina A A Woda[2d]

[1] Department of Midwifery, Poltekkes Kemenkes Kupang, Kupang, East Nusa Tenggara Province, Indonesia
[2] Prof. Dr. W. Z. Johannes Hospital Kupang, Kupang, East Nusa Tenggara Province, Indonesia

[a] Email address: ramyakeyken1711@gmail.com
[b] Email address: matjeh@gmail.com
[c] Email address: odi069@gmail.com
[d] Email address: hwpunk86@gmail.com

Received: 26 May 2023 Revised: 13 December 2023 Accepted: 31 December 2023

Abstract

The pandemic causes the risk of gender-based violence to increase, one of which is domestic violence. It is because many women as mothers are workers, so they also have to do waiting office tasks, as well as do household work which is frequently burdened by women. Based on data from the Online Information System for the Protection of Women and Children (understood as Sistem Informasi Online Perlindungan Perempuan dan Anak/SIMFONI PPA) in October 2022, 19,613 cases of violence occurred, with details of 3,164 male victims and 17,960 victims, specifically for NTT (East Nusa Tenggara) Province as many as 895 cases of violence. Percentage of Women Victims of Violence by Type of Violence in the Province of NTT of abuse 44.03%, humiliation 65.01%, harassment 7.12%, neglect 12.71%, and others 13.02%. Perpetrators 68.85% are parents and victims of violence against women 1.91% in rural areas and 2.23 in urban areas. The Research Objective is to identify the 'HeForShe" Approach Model to the Involvement of Men in the Elimination of Violence against Women and Children in Kupang City and Kupang Regency, NTT Province in 2022. The research Method is a Mixed Method, Qualitative with Phenomenological Method and Quantitative Descriptive Survey Method. The population in the study were informants encompassing married men and women aged <55 years with the sample criteria being wife/husband status, and living together for more than 1 year. Female and male aged 18 years and unmarried, living with their parents. Religious leaders, midwives, teachers, and local government. Purposive sampling. Collecting data was performed by in-depth interviews and FGD in groups of 10-15 people, analysis was carried out descriptively, and a way ANOVA test to compare the three models. Research Results: From the 3 proposed models, it was discovered that 65 percent of respondents agreed with model 2, and the results of the one-way ANOVA test were obtained the p-value is 0.002 or smaller than alpha 5%, Conclusion: One model was obtained, namely the Network Coordination Model for the Office of Health, Education and Local Government in Empowering Youth in Primary Health Units and schools in Action to Prevent Violence against Women and Children. Recommended as one of the HeForShe models that is more appropriate to apply in the case of the Approach to the Elimination of Violence Against Women and Children by involving teenagers.

Keywords: HeForShe, Violence Against Women and Children, Kupang City, Kupang Regency.

Corresponding Author:
Mariana Ngundju Awang
Department of Midwifery, Poltekkes Kemenkes Kupang, Kupang, East Nusa Tenggara Province, Indonesia
Email: ramyakeyken1711@gmail.com

1. INTRODUCTION

The pandemic has increased the risk of Gender-Based Violence (GBV) cases, one of which is domestic violence (DV). This is due to the fact that many women as mothers are workers, who have to do office tasks as well as do household work which is frequently burdened by women. Based on data from the Online Information System for the Protection of Women and Children (SIMFONI PPA), there have been 105 cases of violence against women, with 106 victims, 67 of whom experienced domestic violence (Kementerian Pemberdayaan Perempuan dan Perlindungan Anak Republik Indonesia, 2019). There are four factors that cause domestic violence against women, especially physically and sexually by partners, which are individuals, partners, socio-cultural, and economic (Pramudya, 2014; Koalisi Perempuan Indonesia, 2017)

East Nusa Tenggara Province is recorded as a province in Eastern Indonesia which has the highest number of violence against women cases with 677 cases. Based on 2023 SIMFONI PPA violence data, in NTT there were 339 psychological violence, 411 physical violence and 348 sexual violence. National Commission on Women perceives that the high number is related to the number of service providers in the province, and the public's trust to complain. Past; The patriarch's large household consisting of women, young men, children, slaves, and domestic servants who are all under the rule of the male ruler and today men's power is the relationship that causes men to dominate women or 85 percent of power on the father (Patriachi) (Awang et al., 2022). Cases of violence against women and children occurred in East Nusa Tenggara (NTT), from 2002 to 2017, there have been 3,621 cases of violence, perpetrators are parents and victims of violence against girls 1.91% in rural areas and 2.23 in urban areas (Komnas Perempuan, 2019; Missa, 2010; Susanty & Julqurniati, 2019; Simaibang & Bajari, 2019). The number of cases of violence against women in the distribution area is 93 cases (49%) in the city of Kupang and 83 cases in the regency of Kupang, while 17 cases (9%) were spread in other districts. There were 5 cases of male perpetrators of domestic violence who received counseling out of 79 cases of domestic violence. The number of cases of violence against children as many as 98 cases (50%) cases accompanied by Rumah Perempuan in 2019 the victims were children with details of 40 (41%) occurring in boys and 58 (59%) occurring in girls (Antara News, 2022).

The concrete steps include the "HeForShe" campaign or increasing men's participation on women's and children's issues to increase women's participation and representation in politics and development and protect women, children, and marginalized groups through 3 (three) focus areas, which are: Increasing women's participation in politics and decision-making, Reducing Maternal Mortality Rate (MMR) in childbirth; and Elimination of all forms of violence against women and girls (Sakina, 2017; Suri & Noerzaman, 2020).

The research aims to identify the "HeForShe" Approach Model - Involvement of Men in the Elimination of Violence against Women and Children in Kupang City and Kupang Regency, NTT Province in 2022.

2. RESEARCH METHOD

The type of research used in this study is the Mixed Method, which is a type of qualitative research with the phenomenological method that will explore data to identify the meaning of the basic and essential things from phenomena, reality, or experiences experienced by the object of research. Quantitative research with descriptive method is a method in examining the status of a group of people, an object, a set of conditions, a system of thought or a class of events in the present with the aim of making a systematic, factual and accurate description, picture, or painting of the facts, the properties and relationships between the investigated phenomena (Sugiyono, 2019). Location and time of the research were conducted in 2022 - 2023 in Kupang

City and Kupang Regency, NTT Province. The population in the study were informants consisting of married men and women aged <55 years with the sample criteria being wife/husband, not widow/widower, divorced, living/died, living together for more than 1 year. Girls and boys aged 7 – 18 years and not yet married, live with their parents, religious leaders, midwives, teachers and local government. The sampling method employed was purposive sampling based on sample data obtained from the midwife in the village and the village head and sub-village head according to the criteria above and collected in groups of 10 – 15 people to be interviewed at the house of one of the residents. Total sample 100. In addition, there are personal interviews with individuals who are victims of violence to examine the causes and as material in FGDs to identify solutions or policy models for preventing cases of violence.

The research variable is the HeforShe Approach Model – Involvement of Men in the Prevention of Violence against Women and Children, which is the Approach Model that is performed by involving men in preventing violence against women based on the results of a study of 7 root causes of violence problems conducted in 2021 using 10 methods of preventing violence against women in the form of models or policies. The study also employed nominal variable scale - questionnaire measuring instrument.

This research was performed by conducting in-depth interviews (in-depth interview) and FGD (Focus Group Discussion) using a questionnaire that had been prepared by the researcher on the involvement of men in preventing violence against women and children based on the results of the study of 7 Root causes of violence problems from men using the Model Approach. Model 1: Model 1: Networking approach with local government, police in preventing violence against women and children (PKPA)

Model 2: Coordination of Networks of Health, Education and Local Government agencies in Empowering Adolescent Girls Involving Boys in Actions for the Prevention of Violence against Women and Children, Model 3: Model of Handling Women and Children Based on Local Wisdom.

The data that has been collected is then administered data processing, the research data processing process is performed by editing stages; checking the contents of the questionnaire or question guidelines whether the existing answers are complete, clear, relevant and consistent., Coding: Code marking for each respondent data that belongs to the same category, to facilitate data analysis. In this study, the researcher provided a code for answers to interviews and FGDs. Tabulating is the processing of data that has been obtained which is compiled and displayed in the form of a frequency distribution table or a narrative of results. Data were analyzed manually and computerized by employing descriptive analysis, inference analysis was carried out one way ANOVA test to compare the three models and content analysis. This research has received ethical approval from the Health Research Ethics Committee of the Kupang Ministry of Health Polytechnic No.LB.02.03/1/0001/2022 (Description Of Ethical Exemption, 2022)

3. RESULTS AND DISCUSSION

Table 1. Frequency distribution of data on age, gender, education and occupation of respondents.

Age (year)		**Gender**		**Education**		**Employment**	
18-24	25-55	Male	Female	Junior-Senior High	University	Employed	Unemployed
43 (43%)	57 (57%)	40 (40%)	60 (60%)	49 (49%)	51 (51%)	90 (90%)	10 (10%)

The table above shows that the respondents in this study were aged 18 and over, the majority were women, most had undergraduate education levels and worked as farmers, traders,

fishermen, civil servants, police and private employees, but there were also those who did not have a job, even though it was small, but this supported occurrence of domestic violence.

Table 2. Types and Impacts of Violence.

Experiencing violence	Witnessing violence	Perpetrators of violence	Form of violence	
			Physical & Psychological	Sexual
50 (50%)	15 (15%)	35 (35%)	79 (79%)	21 21%)

This table shows that most of the respondents had witnessed cases of violence and were perpetrators of violence, and the majority were physical and psychological violence but not a few were also sexual violence.

Table 3. Types of Physical and Psychological Violence.

Types of Physical and Psychological Violence	Total	Percentage
Angry/get angry	35	44.3
Being snapped in a public place	11	13.9
Evicted from home	5	6.2
Beaten/kicked/slapped	25	31.7
Doused with water	3	3.9
Total	79	100

This table describe that most of the physical and psychological violence experienced was anger or yelling and being beaten/kicked/slapped.

Conducting a test analysis to compare the 3 (three) models of approaches studied in this research, after data processing and data analysis of model types 1, 2 and 3 in the prevention of violence against women and children, the result is that model 2, namely the Network Coordination model of Health, Education and Local Government agencies in Youth Empowerment in Primary Health Unit and schools in the Action for the Prevention of Violence against Women and Children are more appropriate to apply according to the results of the One way ANOVA test, namely:

Model 2	ANOVA				
	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.006	1	.006	.064	.002
Within Groups	4.494	48	.094		
Total	4.500	49			

Based on the table above, the p-value is 0.002 or smaller than alpha 5%, thus the test decision is to reject H0, that is, at least there is one model, namely model 2 which has different results compared to models 1 and 3 or it can be said that there are different results. significant among respondents in determining a more appropriate model to be applied in preventing cases of violence against women and children against model 1, model 2 and model 3.

Results of FGD on 2 Representative Groups of Kupang City and Kupang Regency.

Model 1. Networking approach with local government, police in preventing violence against women and children (PKPA). According to 10 respondents, this approach is appropriate, if there are perpetrators of violence, firm and consistent action must be given in accordance with applicable regulations through the cooperation of the local government starting from the RT, RW, Sub-Village, Village, District and Regency/City levels and the police so that there is a deterrent effect for the perpetrator. Then the victim must be given protection,

given treatment related to the trauma experienced both physically, psychologically and sexually.

Model 2. Network Coordination model of Health, Education and Local Government agencies in Youth Empowerment in Primary Health Unit and schools in the Action for the Prevention of Violence against Women and Children. The network coordination referred to for health agencies is more focused on Empowering Primary Health Unit Cadres, adolescent boys and girls and educational institutions through education in the form of counseling and training in schools ranging from elementary, junior high and high school levels, which will automatically involve the Village Government/District and Staff.

As many as 65 respondents reported that so far there have been acts of violence, physically, psychologically and sexually. We have reported them to the authorities starting from the RT, RW, Sub-village, Village, District and Regency/City levels and the Police, but the actions always end in mediation, peaceful, there are not strict actions against the perpetrators, in fact, there are cases that are not processed due to insufficient evidence such as the absence of witnesses in cases of sexual violence. It causes the victims to be lazy to report cases of violence, just keep quiet, if it is too much, they report to the family which is also resolved in a peaceful manner. If it cannot change, they continue to experience acts of violence, finally getting divorced and even then, it is difficult, it requires a long process, it is not easy to get divorced, even if it is not permissible to divorce because there are religious rules that bind oaths and promises during marriage.

Opinion of Female Respondents, Husbands are the most dominant perpetrators of domestic violence, especially against wives and sometimes children are victims only because of the following: wives are not quick to serve in preparing food and drink, children also come home from school and do not help their parents with chores, refusing to have sexual intercourse regardless of the reason the wife just came home from work and feels tired or is getting her period. It takes sometimes a long time to serve because the food ingredients at home run out (gas, kerosene, coffee, sugar, rice, cooking oil, etc.). Most husbands do not want to help just sit and watch television, play cellphones, and just wait to be served by their wives. What is worse is that the husband does not work, but only goes out every day drinking drunkenly, gambling, so that when he returns home because he loses gambling and is drunk, his wife and children become victims of violence if they are slow to open the door, slow to serve for drink, do not have food or are not cooked. Moreover, the husband will seize the wife's valuables to be sold or pawned in order to get money for gambling and buying liquor.

There are confessions from girls who are victims of sexual violence by their biological fathers only because their wives refuse to have sex when they are sick and during menstruation. This child hates his father until now because she was raped since she was in second grade of junior high school. When her mother wanted to help her child not to be raped by her husband, her mother was kicked until she fainted and then her daughter screamed but the neighbors did not help because they were afraid as the father was known as a notorious drunkard in the neighborhood surroundings. After the incident, the mother and child reported the incident to the family, both male and female, religious leaders (the Congregational Council and Pastor) but it ended peacefully and promised not to do it again. The fact is that the father always commits acts of violence against both mother and child.

In connection with the above, 65 percent of respondents agree more if given early understanding to teenagers both boys and girls about violence, the impact, prevention and handling of violence against women and children by empowering the activities of the Youth Primary Health Unit in the family and community, and involve local cadres and traditional leaders so that they can speak out about violence that is not in accordance with local culture,

values and norms. Adolescents, after knowing and understanding, are expected to be able to break the chain of violence because men and women already have the same concept of acts of violence violating human rights. There is protection for victims and also sanctions both socially, customary and legal. These youths will become extension workers or informers to their peers in order to attempt to prevent violence and become reporters if there are cases of violence.

In the opinion of the respondents, it is more effective and efficient because it continues as long as the youth Primary Health Unit is activated. This information will continue to be echoed so that the teenagers develop properly in a healthy environment that does not witness any more cases of violence. Because many also commit violence during marriage because they were victims of violence as a child or teenager or witnessed neighbors committing violence without understanding that it is wrong, not good and not right or violates applicable laws and regulations.

Model 3. Model of Handling Women and Children Based on Local Wisdom. According to 25 respondents, the handling of cases of violence against women and children based on local wisdom is still very good to be used in solving problems of domestic violence through a family approach, which involves parents of marriage witnesses, customary witnesses and biological people from both husband and wife's families. Peace is just the same case of violence over and over again. There is no deterrent effect because they only forgive each other but there is no change in the attitudes and actions of the perpetrators of violence. The bad impact is that children follow what their parents do or they are afraid every time they see their parents, unable to express opinions or problems experienced by children at school or in the learning process. In fact, it is not uncommon for children to become perpetrators of violence again when they grow up because they feel that what their parents are doing is right. Thus, perhaps, it can be combined with the second approach model, which is the Coordination of Networks of Health and Education Institutions in Empowering Adolescent Girls Involving Boys in the Action for the Prevention of Violence against Women and Children. With hope, the community is educated from an early age so that it can prevent cases of violence that occur in the household.

DISCUSSION

Violence against women and children is a phenomenon that occurs around the world and requires attention and commitment from all parties to overcome and this is stated in the fifth SDGs goal. Achieving gender equality and empowering all women and girls has a target by 2030, that is ending all forms of discrimination against all women and girls everywhere and eliminating all forms of violence against women and girls in public and private spaces, including trafficking and sexual and other forms of exploitation (Kurniasi, Sumardi & Sakharina, 2022) Violence occurs due to various differences that exist such as differences in attitudes and feelings, cultural backgrounds, changes in interests, and rapid and sudden changes in values in society that lead to conflicts or disputes between individuals in the family. As the smallest unit of society, the family has a very important role in the growth and development of children, in this case, the family plays a role in various functions, such as the function of love, education, protection, to economic functions. Every family must have problems, therefore, it is crucial for parents to be more sensitive to problems that exist in a family such as: lack of communication in the family, parents who frequently fight, each family member does not know each other's conditions, violence and pressure between family members (Keating et al., 2013). The results presented that 65 percent of cases of violence occurred due to disharmony in family relationships, economic factors or conflicts that could not be resolved properly and ended in domestic violence.

Conflict resolution that leads to violence will usually be resolved in one of the following four ways: Obedient, it is a condition where one party decides to give in and follow the wishes of the other party. Compromise; A condition in which both parties give in a little and take a middle ground that is acceptable to both parties. Dodge; A condition in which both parties decide to end the conflict without a resolution, frequently both parties agree to disagree on the matter. Withdraw; A condition where only one of the parties decides not to continue the interaction which leads to unresolved problems, frequently, it will make the relationship between the two parties worse and how family conflicts will be resolved depends on the communication that exists in the relationship. If communication between family members is not good, it is not easy to discuss the root of the problem and find a solution. In addition, communication in the family is also colored by other aspects such as dominance, daily communication patterns, or culture. However, the fact is that based on the results of the research above, the problem is not resolved, even though it is repeated and it has done the things mentioned above so that it requires another policy model to overcome cases of violence by educating and training teenagers from an early age how to prevent and overcome violence that occurs in the family involving elements of education, health and local government periodically and continuously (Purnama & Syam, 2020; Suri and Noerzaman, 2020)

The assertive training can help women and victims of sexual violence to have the courage to refuse and express their feelings in the right way. Meanwhile, according to (Mutiara, 2020) said that the collaboration of stakeholders in overcoming acts of violence against women and children in the city of Padang has gone quite well which is manifested through a network structure of stakeholders that is equal in obligations, mutual trust between stakeholders in preventive, curative and rehabilitative efforts. This collaboration also has good governance, and is based on clear standard operating procedures. The role of a leader that unites stakeholders so that members have a clear division of tasks. There is information sharing between members and the public. In connection with the above, the Coordination of Networks of Health, Education and Local Government agencies in Empowering Adolescent Girls Involves Boys in the Action to Prevent Violence against Women and Children in Primary Health Unit and schools as a proposed policy model to be applied in the resolution and prevention of cases of violence in the city and regency of Kupang according to the objective of this study.

According to (Suri & Noerzaman, 2020; Vasquez, 2021; Kurniasi, Sumardi & Sakharina, 2022) one of 10 ways to help end violence against women, even during a pandemic is to teach the next generation and learn from them. The examples we provide to young people is by shaping the way they think about gender, respect and human rights, starting conversations about gender roles early, and challenging the traditional features and characteristics assigned to both men and women, pointing out the stereotypes kids always face, whether in the media, on the street or at school, and let them know that it is okay to be different, encouraging a culture of acceptance, talking about consent, bodily autonomy and accountability to boys and girls, and also listening to what they have to say about their experiences in the world. By empowering young advocates with information, and educating them about women's rights, we can build a better future for all.

It is in accordance with the results of the study that 65 percent of respondents agreed more if given early understanding to adolescent boys and girls about violence, impacts, prevention and handling of violence against women and children by empowering the activities of the Youth Primary Health Unit in the family and community, as well as involving local cadres and traditional leaders to be able to voice about violence that is not in accordance with local culture, values and norms. Adolescents, after understanding, are expected to be able to break the chain of violence because men and women already have the same concept of acts of

violence violating human rights. There is protection for victims and also sanctions both socially, customary and legally. These teenagers will become extension workers or convey information to their peers in order to attempt to prevent violence and become reporters if there are cases of violence.

In this regard, early youth empowerment in Primary Health Unit and schools regarding their involvement in preventing violence against women and children is important as part of the role of parents or families in the community. Each member is encouraged to think independent., There is openness that will help them solve problems and build positive relationships. Families continue to support each other and try to resolve conflicts in a positive way (Keating et al., 2013; Ramadhana et al., 2019; Szkody & Mckinney, 2021). Instead of using protective communication patterns emphasize conformity and obedience, where one family member who is considered dominant will make a decision or problem solving that feels good, and other family members must follow. This pattern of communication gives rise to a lot of negative emotions and ineffective conflict resolution. As a result, in addition to unresolved problems, relationships in the family also have the potential to be damaged due to feelings of dislike. In comparison, children from protective families tend to have difficulty separating from decision-making figures. They are angry because they are required to always obey, feel very guilty due to unresolved problems, and have difficulty adapting to lectures. It is what respondents have encountered so far, thus, they think early education and training for teenagers (Rahmawati & Gazali; Renie Tri, 2019; Saputri, Khutobah & Risqiana, 2020).

How families apply communication patterns to resolve family conflicts will affect how their children build relationships with other people. The results of the study show that happy couples have satisfying communication with their partners. Happy couples report that their partners understand their feelings and are good listeners. Happy couples also report that it is easy for them to share their true feelings with their partner. Research results also present that unhealthy communication between husband and wife predicts the occurrence of tension in marriage and divorce, as well as domestic violence. The studies above reveal that communication is vital in building a happy marriage (Koerner & Fitzpatrick, 2006).

Communication appears to be something simple, but in reality, many married couples have difficulty in doing so, in the end, they choose to remain silent and avoid feelings of hurt, and avoid prolonged conflict, finally husband and wife relations become cold and tasteless. Given that communication is the key to the intimacy of a husband-and-wife relationship. It is significantly crucial to learn and practice effective and healthy communication. Communication is a dynamic process in which there is a transfer of meaning from one party to another. Therefore, effective communication involves the art of speaking to convey messages and meanings, and the art of listening to capture messages and meanings. The art of speaking: First, convey the message specifically and concretely. Second, convey your hopes, feelings, needs, thoughts to your partner frankly. Third, convey the things you do not like carefully, avoid attacking or blaming. Effective communication is the key to resolving conflict. Conflict is an unavoidable human phenomenon when humans interact with each other, there is certainty in the end that at some point in time, different personal preferences, ideas, likes and dislikes will create some level of conflict. Conflict can actually be positive. That is not to say that such occurrences are always negative, that conflict is frequently needed when helping to raise and resolve problems; energize the work to address the most appropriate issues; help motivate people to participate; and help people recognize and benefit from their differences. “Conflict is not the same as discomfort, conflict is not the problem it is when conflict is not managed properly, that is the problem (Ghaffar, 2019; Marfu’ah, Rofi’ah & Maksun, 2021; Tanskanen & Kivivuori, 2021)

The direct involvement of government organizations, indigenous peoples' organizations, religious organizations, educational organizations, health and legal service institutions has a strategic position in the campaign against violence against women and children. The campaign is a concrete step in preventing acts of violence against women and children which modes and numbers are increasing throughout Indonesia. Based on data collected by the Ministry of PPPA, violence against children in 2019 occurred as many as 11,057 cases, 11,279 cases in 2020, and 12,566 cases until November 2021 data. In children, the most cases experienced were sexual violence by 45 percent, psychological violence 19 percent, and physical violence around 18 percent. Other types of violence against children in the form of neglect, trafficking, economic exploitation, and others. Meanwhile, in cases of violence experienced by women, the Ministry of PPPA noted that it also experienced an increase. In the last three years, there were 26,200 cases of violence against women. In 2019, there were around 8,800 cases of violence against women, then in 2020, it had dropped to 8,600 cases, and again increased based on data until November 2021 at 8,800 cases. The type of violence experienced by women is mostly physical violence reaching 39 percent. Besides, there is 29.8 percent psychological violence, and 11.33 percent sexual violence. Violence Against Children; The 2021 SNPHAR results demonstrate a decrease in the prevalence of violence against children, compared to the 2018 SNPHAR results. Although both boys and girls experienced a decrease in prevalence, violence was still more experienced by girls. Based on the results of the SNPHAR in 2021, it was recorded that 34 percent or 3 out of 10 boys and 41.05 percent or 4 out of 10 girls aged 13-17 years had experienced one or more types of violence in their lifetime. Meanwhile, in 2018, 62.31 percent or 6 out of 10 boys and 62.75 percent or 6 out of 10 girls experienced one or more types of violence in their lifetime (Susanty & Julqurniati, 2019).

4. CONCLUSION

According to the results of the analysis of the three models, one model was obtained, namely the Network Coordination Model for the Office of Health, Education and Local Government in Empowering Youth in Primary Health Units and schools in Action to Prevent Violence against Women and Children as one of the HeForShe models is more appropriate to be applied in the Elimination Approach cases of Violence Against Women and Children in the City and District of Kupang, NTT Province in 2022 and will be studied and applied at a later stage in this research. The suggestion is to apply the model from the initial study so that it can produce an approach in the form of public policy that must be implemented in the context of preventing cases of violence against women and children.

REFERENCES

Antara News. (2022) *Rumah Perempuan: Kasus kekerasan perempuan-anak di NTT didominasi KDRT*. Antara News. Available at https://www.antaranews.com/berita/3175889/rumah-perempuan-kasus-kekerasan-perempuan-anak-di-ntt-didominasi-kdrt

Awang, M. N., Woda, W. A. A., & Kristin, D. M. (2022). Causes of Violence Against Women and Children Based On 7 (Seven) Root Causes of Violence According to Kauffman, 1999 & Nur Iman Subono, 2018. *Eduvest-Journal of Universal Studies*, *2*(6), 1184-1194. https://doi.org/10.59188/eduvest.v2i6.489

Ghaffar, A. (2009). Conflict in Schools: Its Causes & Management Strategies. *Journal of Managerial Sciences*, *3*(2), 212–227.

Keating, D. M., Russell, J. C., Cornacchione, J., & Smith, S. W. (2013). Family communication patterns and difficult family conversations. *Journal of Applied Communication*

Research, *41*(2), 160-180. https://doi.org/10.1080/00909882.2013.781659

Kementerian Pemberdayaan Perempuan dan Perlindungan Anak Republik Indonesia. (2019). *Kajian Partisipasi Organisasi Perempuan Dalam Menurunkan Angka Kematian Ibu di Propinsi Jawa Barat*. Kementerian Pemberdayaan Perempuan dan Perlindungan Anak Republik Indonesia.

Koalisi Perempuan Indonesia. (2017). *Survey Pengalaman Hidup Perempuan Nasional*. Koalisi Perempuan Indonesia.

Koerner, A. F., & Fitzpatrick, M. A. (2006). Family conflict communication. *The Sage handbook of conflict communication: Integrating theory, research, and practice*, 159-183.

Komnas Perempuan. (2019). *Catahu 2019: Korban Bersuara, Data Bicara Sahkan RUU Penghapusan Kekerasan Seksual sebagai Wujud Komitmen Negara: Catatan Kekerasan terhadap Perempuan Tahun 2018.* Komnas Perempuan.

Kurniasi, N. F., Sumardi, J., & Sakharina, I. K. (2022). Elimination of Violence Against Children During the Covid-19 Pandemic based on the United Nations Convention on the Rights of the Child (UNCRC 1989). *Khazanah Hukum*, *4*(2), 154-169.

Marfu'ah, U., Rofi'ah, S., & Maksun, M. (2021). Sistem Pencegahan dan Penanganan Kekerasan Seksual di Kampus UIN Walisongo Semarang. *Kafaah: Journal of Gender Studies*, *11*(1), 95-106.

Missa, L. (2010). *Studi kriminologi penyelesaian kekerasan dalam rumah tangga di wilayah Kota Kupang Propinsi Nusa Tenggara Timur*. *Master thesis.* Universitas Diponegoro.

Mutiara, S. (2020). *Kolaborasi Stakeholders dalam Mengatasi Tindak Kekerasan Terhadap Perempuan dan Anak di Kota Padang. Diploma thesis.* Universitas Andalas.

Pramudya, P. (2014). Mencari Akar Penyebab Kekerasan Dalam Rumah Tangga Terhadap Perempuan Tionghoa Di Jawa Tengah. *Jurnal Dinamika Hukum*, *14*(1), 151-161.

Purnama, S. E., & Syam, M. H. (2020). Perlindungan Korban Kekerasan Fisik terhadap Perempuan dalam Rumah Tangga Ditinjau dari Declaration On The Elimination Of Violence Against Women (Devaw) dan Undang-Undang Nomor 23 Tahun 2004 tentang Penghapusan Kekerasan dalam Rumah Tangga. *Prosiding Ilmu Hukum*, *6*(2), 458-465.

Ramadhana, M. R., Karsidi, R., Utari, P., & Kartono, D. T. (2019). Role of family communications in adolescent personal and social identity. *Journal of Family Sciences*, *4*(1), 1-11. https://doi.org/10.29244/jfs.4.1.1-11

Rahmawati, R., & Gazali, M. (2018). Pola komunikasi dalam keluarga. *Al-Munzir*, *11*(2), 327-245.

Renie Tri, H. (2019). Pola Komunikasi Keluarga Dalam Membangun Karakter Anak Berbasis Gender. *Ups Tegal*.

Sakina, A. I. (2017). Menyoroti budaya patriarki di Indonesia. *Share: Social Work Journal*, *7*(1), 71-80. https://doi.org/10.24198/share.v7i1.13820

Saputri, S. W. D., Khutobah, K., & Risqiana, D. (2020). Mother-Child Communication Pattern on Awe-Awe Doer Family: A Study in Kalibaru Manis Village Banyuwangi Regency. *Pancaran Pendidikan*, *9*(4), 65–74. https://doi.org/10.25037/pancaran.v9i4.316

Simaibang, E.W.A & Bajari, A. (2019). Representasi Male Feminist oleh Aliansi Laki-laki Barudi Media Sosial (Studi Etnografi VirtualLaki-laki Feminis oleh Aliansi Laki-laki Baru di Twitter @lakilakibaru). *Linimasa: Jurnal Ilmu Komunikasi*, 2(2), 1-21, https://doi.org/10.23969/linimasa.v2i2.1685

Sugiyono. (2019). *Buku Metode Penelitian Kuantitatif Kualitatif dan R&D*. Bandung : Alfabeta.

Suri, G. A., Hamka, H., & Noerzaman, A. (2020). Peranan United Nations Women Dalam Mengatasi Tindak Kekerasan Seksual Terhadap Perempuan Di Indonesia Tahun 2016-2017. *INDEPENDEN: Jurnal Politik Indonesia dan Global*, *1*(1), 30-40.

Susanty, D. I., & Julqurniati, N. (2019). Kekerasan Terhadap Perempuan Dalam Rumah Tangga (Studi Kasus Di Kota Larantuka Kabupaten Flores Timur). *Sosio Konsepsia: Jurnal Penelitian dan Pengembangan Kesejahteraan Sosial*, *8*(2), 139-156.

Szkody, E., & McKinney, C. (2021). Family communication patterns and relationship quality between emerging adults and their parents. *Journal of Social and Personal Relationships*, *38*(11), 3177-3197. https://doi.org/10.1177/02654075211027217

Tanskanen, M., & Kivivuori, J. (2021). Understanding intimate partner violence in context: social and community correlates of special and general victimization. *Nordic Journal of Criminology*, *22*(1), 72-89. https://doi.org/10.1080/2578983X.2021.1904605

Vasquez, P. T. (2021). The Impact of COVID-19 on Criminal Justice System Responses to Gender-based Violence Against Women. Austria: UNODC

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 875-885
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1164*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Comparison of Indicators of Families at Risk of Stunting in High-Income Regencies and Low-Income Regencies in East Nusa Tenggara Province

Mona Lydia[1a*], Christina Olly Lada[1b], Anderias Umbu Roga[1c]

[1] Master of Public Health Study Program, Faculty of Public Health, Nusa Cendana University, Kupang, East Nusa Tenggara, Indonesia

[a] Email address: monalydia1977@gmail.com
[b] Email address: christina_o_l@yahoo.com
[c] Email address: anderias_umburoga@staf.undana.ac.id

Received: 24 April 2023 Revised: 30 August 2023 Accepted: 21 September 2023

Abstract

Stunting is a condition of failure to thrive in children due to chronic malnutrition. Early detection of various indicators of families at risk of stunting is an important effort in preventing stunting in the community. This research aims to analyze the comparison of indicators of families at risk of stunting in districts with high per capita income and districts with low per capita income. The Method is secondary data research. The data source is the results of the 2021 National Population and Family Planning Agency (BKKBN) Survey of East Nusa Tenggara Province. The sample size is 878 families divided into 439 families at risk of stunting from high-income districts per capita, and 439 families at risk of stunting from low-income districts. Sampling was carried out by stratification sampling technique or layered sampling. The independent variable is an indicator of a family at risk of stunting, namely the age of the mother, education, fixed income, number of children, sources of drinking water, proper latrines, and habitable houses, and the dependent variable is income per capita in the district where the family lives. The data were identified and statistically analyzed using bivariate Chi-Square test and multivariate logistic regression with a significant p-value <0.05. The result show that the chi-square test mother's age (p = 0.31), mother's education (p=0.77), fixed family income (p=0.00), number of children (p=0.17), availability of water sources clean (p=0.67), healthy latrine ownership (p=0.82), and healthy home ownership (p=0.03). Logistic regression test results for family fixed income (p=0.00), healthy home (p=0.07). The Conclusion is mother's age, mother's education, number of children, availability of clean water sources, ownership of latrines, and healthy homes are the main indicators of the risk of stunting in families. This indicator has no difference between families living in areas with low per capita income, and families living in areas with high incomes.

Keywords: Stunting, Family Indicators at Risk of Stunting, Per Capita Income.

Corresponding Author:

Mona Lydia
Master of Public Health Study Program, Faculty of Public Health, Nusa Cendana University, Kupang, East Nusa Tenggara, Indonesia
Email: monalydia1977@gmail.com

1. INTRODUCTION

Stunting is a condition of failure to thrive in toddlers due to long-term malnutrition, exposure to repeated infections, and lack of stimulation which is influenced by various risk factors, namely the condition of pregnant women, toddlers' eating patterns, family economic conditions, social culture, and environmental factors such as sanitation and access to health services (Kementerian Kesehatan Republik Indonesia, 2022a). Stunting occurs as a result of malnutrition which mainly occurs during the first 1000 days of life (HPK). The condition of stunting will affect the level of intelligence of children and the health status of children during the period of growth and development into adulthood (Kementerian Kesehatan Republik Indonesia, 2018). The family has a very important role in fulfilling the nutritional intake of toddlers in preventing stunting (Wiliyanarti, Israfil, and Ruliati 2020). The incidence of stunting is very high in families who are at risk of stunting. Families at risk of stunting are families that have one or more risk factors for stunting, including having children aged 0-23 (twenty three) months, poor families, low parental education, poor environmental sanitation, and inadequate drinking water (Kemenko PMK, 2022).

The results of a study on the nutritional status of Indonesia in 2021 found that approximately 5 million Indonesian children are stunted, where one in four Indonesian children is stunted (Kementerian Kesehatan Republik Indonesia, 2022a). Indonesia is targeting the stunting rate to fall by 14% in 2024, while the stunting rate in 2021 will reach 24% (Kementerian Kesehatan Republik Indonesia, 2022a). The results of the 2022 Indonesian Nutrition Status Survey (SSGI) found that the national prevalence of stunting reached 21.6%, where the Province of East Nusa Tenggara (NTT) was found to be the province with the highest prevalence of stunting in Indonesia, namely 35.3% (Kementerian Kesehatan Republik Indonesia, 2022b). The NTT Province National Population and Family Planning Agency (BKKBN) continues to monitor and evaluate efforts to accelerate stunting reduction, especially in the first 10 regencies, namely West Sumba, Central Sumba, Southwest Sumba, East Sumba, West Manggarai, Manggarai, East Manggarai, Ngada , Ende and Nagekeo (BKKBN, 2022a) .

Gross Regional Domestic Product (GRDP) is an indicator that can be used to view the economic condition of a region in the Province of NTT. East Manggarai Regency is one of the districts with low per capita income in NTT, while East Sumba Regency is one of the districts with high per capita income (Badan Pusat Statistik, 2022a) . Total Gross Regional Domestic Product (GRDP) of East Sumba district is 16227256.00 in 2020 and 16 255 932.00 in 2021, while East manggarai district is 7416 826.00 in 2020 and 7 509 926.00 in 2021 (Badan Pusat Statistik, 2022b). The prevalence of stunting in East Manggarai Regency in 2021 was found to be 14%, and the prevalence of stunting in East Sumba Regency in 2021 was 19% (Badan Pusat Statistik, 2022a).

Stunting is a serious problem that interferes with the growth and development of children due to chronic malnutrition and recurrent infections and is a threat to the future of Indonesia (BKKBN, 2022a) . Stunting is a health problem that is higher than the national average in addition to the high problems of anemia, zinc deficiency and vitamin A in children (Miller et al., 2013) . One of the efforts to accelerate the reduction of stunting in the community is to optimize family empowerment (BKKBN, 2022b). A study found that around 76% of stunted children under five came from families whose income was below the regional minimum wage, and family income was found to be significantly related to the incidence of stunting in the community (Agustin and Rahmawati, 2021) . Determinants or family indicators related to stunting include low education, low household welfare, malnutrition during pregnancy, poor sanitation, inadequate water supply, fathers who smoke, young mothers and poor parenting (Syofyanengsih , Fajar, and Novrikasari 2022) . The purpose of this study was to analyze the comparison of indicators of families at risk of stunting in Families at Risk of Stunting in

Districts with high incomes (East Sumba Regency) and Low-income Districts (East Manggarai Regency).

2. RESEARCH METHOD

This research is secondary data research using data from the survey results of the National Population and Family Planning Agency (BKKBN) for East Nusa Tenggara Province in 2021. The population is 138,331 families. The sample in this study is a family at risk of stunting in the East Sumba and East Manggarai Regencies. The two districts selected based on the high per capita income are East Sumba District and the low per capita income are East Manggarai District. The samples were taken using the slovin formula and obtained 439 families, the total sample for the two districts was 878 families. Sampling was carried out using a stratified sampling technique or layered sampling which separated the population into two or more levels and then took samples from each level by tracing families at risk of stunting from districts, sub-districts, to sub-districts. The independent research variables are indicators of mother's age , education, fixed income, number of children, availability of clean water, healthy latrines, and healthy homes, and the dependent variable is income per capita in the district where families at risk of stunting live.

Data collection was carried out by identifying indicators of families at risk of stunting in families in the 2021 National Population and Family Planning Agency (BKKBN) data. The data was then tabulated and analyzed statistically with three stages, namely univariate analysis to describe each indicator and presented in the form of a frequency distribution table. Bivariate analysis to determine the effect of each independent and dependent variable used the *Chi Square statistical test* (X^2) with a confidence level of *ρ-value* < 0.05. Multivariate analysis was carried out to determine differences in indicators of families at risk of stunting in low-income districts (East Manggarai) and high-income districts (East Sumba). Multivariate analysis was performed using the Logistic Regression statistical test with a significant p-value <0.05.

3. RESULTS AND DISCUSSION

Table 1. Distribution of the frequency of indicators of families at risk of stunting in low-income districts (East Manggarai) and high-income districts (East Sumba) (n=878).

Indicators of Families at Stunting Risk	Regency				Amount	%
	Low Income (East Manggarai)		High Income (East Sumba)			
	n	%	n	%		
Mother's Age						
< 20 years	2	0.5	0	0.0	2	0.2
20 – 35 years	214	48.7	207	47.2	421	47.9
≥35 years old	223	50.8	232	52.8	455	51.8
Total	439	100	439	100	878	100
Mother's Education						
< SLTP	281	64.0	277	63.1	558	63.6
> SLTP	158	36.0	162	36.9	320	36.4
Total	439	100	439	100	878	100
Fixed income						
There is	398	90.7	366	83.4	764	87.0
No	41	9.3	73	16.6	114	13.0
Total	439	100	439	100	878	100
Number of children						
< 3 people	230	52.4	210	47.8	440	50.1

≥ 3 people	209	47.6	229	52.2	438	49.9
Total	439	100	439	100	878	100
Availability of Clean Water Sources						
Yes	277	63.1	271	61.7	548	62.4
No	162	36.9	168	38.3	330	37.6
Total	439	100	439	100	878	100
Ownership of Healthy Latrines						
Yes	145	33.0	142	32.3	287	32.7
No	294	67.0	297	67.7	591	67.3
Total	439	100	439	100	878	100
Healthy Home Category						
Yes	62	14.1	42	9.6	104	11.8
No	377	85.9	397	90.4	774	88.2
Total	439	100	439	100	878	100

Secondary Data, BKKBN 2021

Table 1 shows that the majority of mothers from the two districts are ≥ 35 years old with a total percentage of 51.8%, the education of mothers from the two regions is mostly low-educated < junior high school with a total percentage of 63.6%, the majority of family income from the two regions is mostly have a fixed income with a total percentage of 87.0%, the category of the number of children in families in the East Manggarai Regency area is the category < 3 people, namely 52.4%, and the highest percentage in East Sumba Regency is ≥ 3 children or 52.2%, the majority Families from the two districts have access to clean water sources with a total percentage of 62.4%, families from the two districts do not have healthy latrines with a total percentage of 67.3% and have houses that do not meet the healthy housing category with a total percentage of 88.2%. .

Table 2. Bivariate Chi-Square Test Comparison of Indicators of Families at Risk of Stunting in High-Income Districts (East Sumba) and Low-Income Districts (East Manggarai) (n=878).

Indicators of Families at Stunting Risk	**District area**				**∑**	**%**	**Pearson Chi-Square (X^2)**	**p-values**
	Low Income (East Manggarai)		**High Income (East Sumba)**					
	n	**%**	**n**	**%**				
Mother's Age								
< 20 years	2	0.5	0	0.0	2	0.2		
20 – 35 years	214	48.7	207	47.2	421	47.9	2.294	0.318
≥35 years old	223	50.8	232	52.8	455	51.8		
Total	439	100	439	100	878	100		
Mother's Education								
< SLTP	281	64.0	277	63.1	558	63.6		
> SLTP	158	36.0	162	36.9	320	36.4	0.079	0.779
Total	439	100	439	100	878	100		
Family Income								
There is	398	90.7	366	83.4	764	87.0		
No	41	9.3	73	16.6	114	13.0	10.323	0.001*
Total	439	100	439	100	878	100		

Indicators of Families at Stunting Risk	District area				∑	%	Pearson Chi-Square (X^2)	p-values
	Low Income (East Manggarai)		High Income (East Sumba)					
	n	%	n	%				
Number of children								
< 3 people	230	52.4	210	47.8	440	50.1		
≥ 3 people	209	47.6	229	52.2	438	49.9	1.822	0.177
Total	439	100	439	100	878	100		
Availability of Clean Water Sources								
Yes	277	63.1	271	61.7	548	62.4		
No	162	36.9	168	38.3	330	37.6	0.175	0.676
Total	439	100	439	100	878	100		
Ownership of Healthy Latrines								
Yes	145	33.0	142	32.3	287	32.7		
No	294	67.0	297	67.7	591	67.3	0.047	0.829
Total	439	100	439	100	878	100		
Healthy Home Category								
Yes	62	14,1	42	9,6	104	11,8		
No	377	85.9	397	90.4	774	88.2	4.363	0.037*
Total	439	100	439	100	878	100		

**Significant value < 0.05*

Table 2 shows that there is no difference in the indicators of mother's age, mother's education, number of children, availability of clean water, and ownership of healthy latrines in families at risk of stunting in high-income districts (East Sumba) and low-income districts (East Manggarai) with values p-Value > 0.05. There are differences in indicators of family income and healthy homes for families at risk of stunting in high-income districts (East Sumba) and low-income districts (East Manggarai) with a p-value <0.05.

Table 3. Multivariate Logistic Regression Test Comparison of Indicators of Families at Risk of Stunting in Low-Income Districts (East Manggarai) and High-Income Districts (East Sumba) (n=878).

Indicators of Families at Stunting Risk	District area				∑	%	Ods Ratio (Exp.B)	*p-Value*
	Low Income (East Manggarai)		High Income (East Sumba)					
	n	%	n	%				
Family Fixed Income								
There is	398	90.7	366	83,4	764	87.0		
No	41	9.3	73	16.6	114	13.0	1,876	0.003*
Total	439	100	439	100	878	100		
Healthy Home Ownership								
Yes	62	14.1	42	9,6	104	11.8		
No	377	85.9	397	90.4	774	88.2	1,471	0.071
Total	439	100	439	100	878	100		

**Significant value < 0.05*

Table 3 shows that based on the results of the multivariate test statistical logistic regression on the family income indicator and the criteria for a healthy home, the Ods value.

The ratio and p-value of each indicator is family income (Exp.B = 1.876, p-value = 0.003*), healthy home criteria (Exp.B=1.471, p-value =0.071). The results of this statistical test show that there is no difference in the criteria for healthy homes for families at risk of stunting in high-income districts (East Sumba) and low-income districts (East Manggarai). There are differences in family income indicators for families at risk of stunting in high-income districts (East Sumba) and low-income districts (East Manggarai) with a p-value <0.05.

Stunting is a serious nutritional problem and has an impact on the quality of human resources. Stunting prevention is the responsibility of all parties, not only the government but also all families throughout Indonesia (Kementerian Kesehatan Republik Indonesia, 2018). Family factors are known to have a large influence on the incidence and prevention of stunting. The family has an important role in the toddler's diet in preventing stunting (Wiliyanarti, Israfil, and Ruliati, 2020). The results of this study found no differences in indicators of mother's age, mother's education, number of children, availability of clean water, healthy latrines, and healthy homes for families at risk of stunting in low-income districts (East Manggarai) and high-income districts (East Sumba).

Age is a risk factor for stunting in toddlers. Various research results have found that there is a significant relationship between maternal age during pregnancy and the incidence of stunting in toddlers (Junus et al., 2022) . Research on the incidence of stunting in children aged 7-24 months was found to be significantly related to the age of the mother during pregnancy (Wanimbo and Wartiningsih 2020). The results of the study prove that pregnant women at a young age have a significant relationship with the incidence of stunting (Pamungkas, WD, and Nurbaety, 2021). Pregnant women at a very young age (adolescents) are closely related to the incidence of stunting in children aged 7-24 months (Wanimbo and Wartiningsih 2020) . The incidence of stunting increases when the mother's age during pregnancy is <20 or ≥35 years, the mother's upper arm circumference during pregnancy is ≥23.5cm, pregnancy is in her teens, and the mother's height is low (Nirmalasari 2020). Pregnant women with a risk age of <20 years or > 35 years have a high risk of giving birth to babies with low birth weight which will predispose to stunting in toddlers (Junus et al., 2022).

The mother's education level and knowledge about nutrition has a relationship with the incidence of stunting in toddlers (Dasril and Annita, 2019). The results of the study prove that there is a significant relationship between family income, mother's education and knowledge of mother's nutrition with the incidence of stunting in toddlers (Zurhayati and Hidayah, 2022). Previous research in the East Sumba region found that the determinants of stunting were family income, knowledge of mother's nutrition, mother's upbringing, history of disease infection, history of immunization, protein intake and mother's education (Picauly and Toy, 2013) .

The level of education and knowledge of mothers about toddler nutrition influences attitudes and behavior in choosing food ingredients which will further affect the nutritional state of toddlers (Zurhayati and Hidayah, 2022). Mothers who have a high level of education can have the ability to understand more broadly about healthy child care practices (Zurhayati and Hidayah, 2022). Mother's knowledge about good nutrition will result in a good ability to prepare healthy food for consumption. The better the mother's knowledge about toddler nutrition, the better understand mothers about the type, quantity and quality of food consumed by all family members including toddlers (Bulu, Picauly, and Sir, 2022) .

The number of family members (more than 4 people) and third-order children increases the risk of stunting in toddlers with families of low socioeconomic status (Rahmawati, Fajar, and Idris 2020). The large number of children can affect the family's ability to meet various types of food needs and appropriate nutritional intake for each child. The way people know and provide healthy food for children and the habit of eating healthy food available in the family is found to have a significant relationship with the incidence of stunting in children (Nugraha

2019). Low family income, low mother's education and knowledge of nutrition are factors that aggravate the condition of families with a large number of children to meet the nutritional needs of children in an effort to prevent stunting (Zurhayati and Hidayah, 2022). It is important to monitor the nutritional status of the mother before becoming pregnant and provide nutritional interventions in the early 1000 days of life for the risk of stunting and other health problems such as cardiometabolic risk later in life (Lada, et al., 2018).

The availability of clean water is one of the factors related to the prevention of stunting. The results of the study found that drinking water that was not treated had an influence on the incidence of stunting (Nirmalasari 2020). The availability of clean drinking water is related to the adequacy of water and minerals, and the provision of micronutrients and macronutrients during critical growth periods in toddlers which are needed during the process of metabolizing nutrients for growth and development (Beal et al. 2018). Children from families or households with unhealthy latrines and clean drinking water that is not properly treated have a higher risk of stunting (Beal et al. 2018). This condition is related to the presence of E Coli bacteria in the water which is one of the one cause of gastrointestinal infections in children. Research has shown that clean water samples from PADAM and well water that have not been properly treated for drinking have a high content of Escherichia coli bacteria (Restina et al., 2019). A study of bacteria in stunted patients found that the number of E. coli bacteria in the stunted toddler group was higher than the normal toddler group (Helmyati et al., 2017) . Water factors (inappropriate drinking water sources, drinking water treatment), sanitation factors (use of toilet facilities, open defecation behavior, improper disposal of toddler feces in latrines) are important factors related to the incidence of stunting in children under five in families in Indonesia. Water and sanitation are important factors related to stunting among toddlers in Indonesia (Olo, Mediani, and Rakhmawati 2021).

The use of latrines that do not meet health requirements, the practice of open defecation, and the disposal of children's feces not in the latrines cause children to be contaminated with environmental pollution, making it easier for the transmission of pathogens originating from feces and at risk of increasing the prevalence of diarrhea, intestinal worms and the incidence of stunting in children under five (Olo, Mediani, and Rakhmawati, 2021). In a study of toddlers in one of the districts in NTT, it was found that 36% of children had anemia (Hb level <11 mg/100 mL), 68% lacked vitamin A (level plasma vitamin A < 0.8 mumol/L) and 50% zinc deficiency (plasma zinc <9.94 mumol/L).All children except one were positive for intestinal parasites (Lada, 2018).

The habit of defecating in open places such as rivers or gardens or inadequate latrines has an influence on the risk of stunting (Nirmalasari, 2020) . This condition occurs because human feces can become a medium for various insects to spread bacteria. The spread of bacteria by insects that contaminate food or eating utensils for toddlers is at risk of causing diarrhea. A history of frequent diarrhea in the last 3 months and poor hygiene practices increases the risk by 3.619 and 4,808 times the incidence of stunting in toddlers aged 24-59 months (Desyanti and Nindya 2017). Diarrhea that occurs repeatedly causes toddlers to lose electrolyte fluids and adequate nutrition for growth and ultimately increases the risk of stunting (Nirmalasari, 2020). The results of the study have proven that in addition to increasing knowledge of mothers and families about nutrition, efforts to reduce the incidence of stunting in families at risk also require interventions to improve environmental sanitation, construct latrines that meet health requirements, carry out health promotion efforts with education to increase public awareness (Olo, Mediani , and Rakhmawati 2021).

A healthy house is a house that meets health standards with good management of basic sanitation. The results of the study found that there was a significant relationship between basic sanitation in the household and the incidence of stunting (Fibrianti, Thohari, and Marlik, 2021). Basic sanitation meant in a healthy household is having clean water facilities, having latrines,

waste water management, waste management, clean and healthy food management (Fibrianti, Thohari, and Marlik, 2021). Research proves that there is a significant relationship between the availability of latrines, sources of clean water and the incidence of stunting in the family (Zairinayati and Purnama, 2019). The availability of basic sanitation in healthy homes is the basis for efforts to prevent various types of infectious diseases that are at risk of causing stunting in toddlers. Management of drinking water in the household to prevent high Escherichia coli bacterial infections (Restina et al., 2019), (Helmyati et al. 2017). Availability of healthy latrines in the household to prevent the spread of bacteria causing diarrhea which is at risk of causing stunting (Desyanti and Nindya, 2017), (Nirmalasari 2020).

The results of this study found that there were differences in indicators of fixed family income for families at risk of stunting in low-income districts (East Manggarai) and high-income districts (East Sumba). Family income or economic status is one of the main causes of stunting in the community. Family socioeconomic factors are significantly related to the incidence of stunting, namely family income and parental education (Oktavia 2021). Around 76% of families with stunted toddlers are families with incomes below the regional minimum wage (Agustin and Rahmawati, 2021). The incidence of stunting which is influenced by family income has a 7 times greater risk in families with incomes less than the regional minimum wage (Agustin and Rahmawati, 2021). Unfavorable economic status will have an impact on the nutritional status of children where children will have disrupted growth and development such as being thin or short (Agustin and Rahmawati, 2021). Increasing family income will be able to increase family opportunities to buy food with good quality and better quantity, conversely a decrease or low family income will also cause a decrease in the purchasing power of good food for family members both in quality and quantity (Wahyuni and Fitrayuna 2020). One of the nutrient-rich plants that is actually affordable in the community is Moringa leaves (Moringa oleifera). Aside from being a vegetable, Moringa leaves can be processed into pudding or cakes as additional snacks for toddlers. The results of the study found that there were more changes in nutritional status in elementary school children who had been given pudding made from processed moringa leaves (Meko et al., 2019).

Families or households with low and poor economic income have a higher probability of having a stunted toddler. This condition is related to the availability of food in the household (Laksono, Kusrini, and Megatsari, 2021). However, these factors still depend on how the family implements the income they have in meeting the nutritional needs of their children. This condition will be influenced by various factors including education or family knowledge (Oktavia, 2021) . High income which is not matched by adequate knowledge of nutrition can also cause families to become consumptive with eating patterns that do not match the quality and quantity of nutrition expected for the health of toddlers (Wahyuni and Fitrayuna 2020).

4. CONCLUSION

There are no differences in the indicators of mother's age, mother's education, number of children, availability of clean water sources, ownership of latrines and healthy homes for families at risk of stunting in districts with high per capita income and in districts with low per capita income. Mother's age, mother's education, number of children, availability of clean water sources, latrines, and healthy homes are the main indicators of the risk of stunting in families, both in families living in areas with low per capita income, and in families living in areas with high incomes. Health promotion in increasing family knowledge about the risk of stunting must be continuously improved for both family members who live in areas with low per capita income and families who live in areas with high per capita income.

REFERENCES

Agustin, L., & Rahmawati, D. (2021). Hubungan Pendapatan Keluarga dengan Kejadian Stunting. *Indonesian Journal of Midwifery (IJM)*, *4*(1), 30-34. https://doi.org/10.35473/ijm.v4i1.715

Beal, T., Tumilowicz, A., Sutrisna, A., Izwardy, D., & Neufeld, L. M. (2018). A review of child stunting determinants in Indonesia. Maternal & child nutrition, 14(4), e12617. https://doi.org/10.1111/mcn.12617

BKKBN. (2022a). Satu dari Dua Balita Stunting, NTT Perlu Kerja Keras Turunkan Prevalensi. *Media Center BKKBN*. Retrieved from https://www.bkkbn.go.id/berita-satu-dari-dua-balita-stunting-ntt-perlu-kerja-keras-turunkan-prevalensi

BKKBN. (2022b). Stunting Tertinggi di Indonesia, NTT Optimalkan Kampung KB untuk Percepat Penurunan. *Media Center BKKBN*. Retrieved from https://www.bkkbn.go.id/berita-stunting-tertinggi-di-indonesia-ntt-optimalkan-kampung-kb-untuk-percepat-penurunan

Badan Pusat Statistik. (2022a). Jumlah Balita Stunting Menurut Kabupaten/Kota (Jiwa), 2022. *Badan Pusat Statistik Nusa Tenggara Timur*. Retrieved from https://ntt.bps.go.id/indicator/30/1489/1/nomor-balita-stunting-according to-kabupaten-kota.html

Badan Pusat Statistik. (2022b). Produk Domestik Regional Bruto Perkapita Atas Dasar Harga Konstan 2010 Menurut Kabupaten/Kota (Ribu Rupiah), 2020-2022.Badan Pusat Statistik Nusa Tenggara Timur. Retrieved from https://ntt.bps.go.id/indicator/156/1383/1/-seri-2010-product-domestik-regional-bruto-perkapita-atas-dasar-harga-konstan-2010-menurut-kabupate

Bulu, D., Picauly, I., & Sir, A. B. (2022). Factors Related to The Incidence of Stunting at The Watukawula Puskesmas, Southwest Sumba Regency. *Lontar: Journal of Community Health*, *4*(3), 214-222. Retrieved from https://ejurnal.undana.ac.id/index.php/LJCH/article/view/5042

Dasril, O., & Annita. (2019). Karakteristik Keluarga Terhadap Kejadian Stunting Pada Anak Sekolah Dasar di Kecamatan Nanggalo Kota Padang. *Jurnal Sehat Mandiri*, 14(2): 48–56. Retrieved from https://jurnal.poltekkespadang.ac.id/ojs/index.php/jsm/article/view/116

Desyanti, C., & Nindya, T. S. (2017). Hubungan Riwayat Penyakit Diare dan Praktik Higiene dengan Kejadian Stunting pada Balita Usia 24-59 Bulan di Wilayah Kerja Puskesmas Simolawang, Surabaya. *Amerta Nutrition*, *1*(3), 243–251. https://doi.org/10.20473/amnt.v1i3.2017.243-251

Fibrianti, E. A., Thohari, I., & Marlik, M. (2021). Hubungan sarana sanitasi dasar dengan kejadian stunting di Puseksmas Loceret, Nganjuk. *Jurnal Kesehatan*, *14*(2), 127-132.

Helmyati, S., Yuliati, E., Wisnusanti, S. U., Maghribi, R., & Juffrie, M. (2017). Keadaan mikrobiota saluran cerna pada anak sekolah dasar yang mengalami stunting di Lombok Barat. *Jurnal Gizi dan Pangan*, *12*(1), 55-60. https://doi.org/10.25182/jgp.2017.12.1.55-60

Junus, R., Langi, G. K., Paruntu, O. L., & Ranti, I. N. (2022, June). Usia Saat Hamil dan Lila Dengan Kejadian Stunting Pada Anak Balita Di Wilayah Kerja Puskesmas Ratatotok. *E-PROSIDING Seminar Nasional 2022*, 1(02), 381-391.

Kementerian Kesehatan Republik Indonesia. (2022a). *Cegah Stunting itu Penting*. Jakarta: Kementerian Kesehatan Republik Indonesia. Retrieved from https://ayosehat.kemkes.go.id/cegah-stunting-itu-penting

Kementerian Kesehatan Republik Indonesia. (2022b). *Hasil Survei Status Gizi Indonesia (SSGI) 2022*. Jakarta: Kementerian Kesehatan Republik Indonesia. Retrieved from https://ayosehat.kemkes.go.id/pub/files/files46531._MATERI_KABKPK_SOS_SSGI.p

df

Kementerian Kesehatan Republik Indonesia. (2018). *Buletin Stunting*. Jakarta: Kementerian Kesehatan Republik Indonesia

Kemenko PMK. (2022). Keluarga Berisiko Stunting. Kemenko PMK. Retrieved from https://satudata.kemenkopmk.go.id/metadata_indikator/detail_indikator/89

Lada, C. O. (2018). Faktor Predisposisi Intrauterin, Ekstrauterin, Stres Oksidatif dan Adaptasi Metabolik serta Risiko Kardiometabolik pada Anak Stunting Usia 6-24 bulan= Intrauterine, Extrauterine Predisposing Factors, Oxidative Stress and Metabolic Adaptation and Cardiometabolic Risk in Stunting Children Aged 6-24 Months. *Disertasi*. Universitas Indonesia. Retrieved from https://lontar.ui.ac.id/detail?id=20480902

Laksono, A. D., Kusrini, I., & Megatsari, H. (2021). Stunting di Provinsi Nusa Tenggara Timur: Apakah status bekerja ibu berpengaruh?. *Research Gate*, 1-11.

Meko, M. M., Koamesah, S. M., Woda, R. R., & Lada, C. O. (2020). Pengaruh pemberian puding sari daun kelor terhadap perubahan status gizi anak di SD inpres noelbaki kabupaten kupang. *Cendana Medical Journal (CMJ)*, *8*(1), 521-527.

Miller, J., Ritchie, B., Tran, C., Beggs, S., Lada, C. O., Whetter, K., & Cobiac, L. (2013). Seasonal variation in the nutritional status of children aged 6 to 60 months in a resettlement village in West Timor. *Asia Pacific journal of clinical nutrition*, *22*(3), 449-456.

Nirmalasari, N. O. (2020). Stunting Pada Anak: Penyebab dan Faktor Risiko Stunting di Indonesia. *Qawwam: Journal For Gender Mainstreming*, 14 (1), 19–28.

Nugraha, M. A. (2019). Analisis situasi stunting di Kabupaten Manggarai Timur: Focus group study terhadap kebiasaan makan yang sehat untuk menggali peluang dan tantangan mendukung aksi konvergensi pencegahan stunting Stunting situation analysis in East Manggarai Regency. *FLOBAMORA* 2(2): 61–67.

Oktavia, R. (2021). Hubungan Faktor Sosial Ekonomi Keluarga Dengan Kejadian Stunting. *Jurnal Medika Hutama*, *3*(01 Oktober), 1616-1620.

Olo, A., Mediani, H. S., & Rakhmawati, W. (2021). Hubungan Faktor Air dan Sanitasi dengan Kejadian Stunting pada Balita di Indonesia. *Jurnal Obsesi: Jurnal Pendidikan Anak Usia Dini*, *5*(2), 1113-1126.

Pamungkas, C. E., WD, S. M., & Nurbaety, B. (2021). Hamil usia muda dan stunting pada balita usia 12-59 bulan di Kabupaten Lombok Timur. *Jurnal Kebidanan*, *10*(2), 141-148. https://doi.org/10.26714/jk.10.2.2021.141-148

Picauly, I., & Toy, S. M. (2013). Analisis determinan dan pengaruh stunting terhadap prestasi belajar anak sekolah di Kupang dan Sumba Timur, NTT. *Jurnal gizi dan pangan*, *8*(1), 55-62. https://doi.org/10.25182/jgp.2013.8.1.55-62

Rahmawati, N., Fajar, N., & Idris, H. (2020). Faktor sosial, ekonomi, dan pemanfaatan posyandu dengan kejadian stunting balita keluarga miskin penerima PKH di Palembang. Jurnal Gizi Klinik Indonesia, 17(1), 23-33. https://doi.org/10.22146/ijcn.49696

Restina, D., Ramadhian, M. R., Soleha, T. U., & Warganegara, E. (2019). Identifikasi Bakteri Escherichia coli pada Air PDAM dan Air Sumur di Kelurahan Gedong Air Bandar Lampung. *Jurnal Agromedicine*, *6*(1), 58-62.

Syofyanengsih, S., Fajar, N. A., & Novrikasari, N. (2022). Hubungan Peran Keluarga terhadap Kejadian Stunting: Literature Review. *Jurnal Ilmiah Universitas Batanghari Jambi*, *22*(2), 1167-1171. http://dx.doi.org/10.33087/jiubj.v22i2.2399

Wahyuni, D., & Fitrayuna, R. (2020). Pengaruh sosial ekonomi dengan kejadian stunting pada balita di desa kualu tambang kampar. *PREPOTIF: Jurnal Kesehatan Masyarakat*, *4*(1), 20-26.

Wanimbo, E., & Wartiningsih, M. (2020). Hubungan Karakteristik Ibu Dengan Kejadian Stunting Baduta (7-24 Bulan) Di Karubaga. *Jurnal Manajemen Kesehatan Yayasan RS. Dr. Soetomo*, *6*(1), 83-93.

Wiliyanarti, P.F., Israfil, & Ruliati. (2020). Peran Keluarga dan Pola Makan Balita Stunting. *Journal of Muhammadiyah Nursing*, 5(1). https://doi.org/10.30651/jkm.v5i1.4299

Zairinayati, Z., & Purnama, R. (2019). Hubungan hygiene dan sanitasi lingkungan dengan kejadian stunting pada balita. *Babul Ilmi Jurnal Ilmiah Multi Science Kesehatan*, *10*(1).

Zurhayati, Z., & Hidayah, N. (2022). Faktor Yang Berhubungan Dengan Kejadian Stunting Pada Balita. *JOMIS (Journal of Midwifery Science)*, *6*(1), 1-10. https://doi.org/10.36341/jomis.v6i1.1730

Jurnal Info Kesehatan
Vol. 21, No. 4, December 2023, pp. 886-895
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol21Iss4.1183*
Journal homepage:*http://jurnal.poltekeskupang.ac.id/index.php/infokes*

RESEARCH **Open Access**

Pesticide Exposure and Increased Liver Enzyme Activity among Suburban Horticultural

Ahmad Dahlan[1a], James Perdinan Simanjuntak[1b*], Raden Mustopa[1c], Devi Oktarina Putri[1d], Putrilia Amanda[1e], Adinda Cahyaning Ratri[1f], Ahmad Syathibi[1g], Sabarudin[1h], Haflin[1i]

[1] Department of Environmental Health, Poltekkes Kemenkes Jambi, Jambi City, Jambi Province, Indonesia

[a] Email address: dahlan1961@poltekkesjambi.ac.id
[b] Email address: james.p.simanjuntak@poltekkesjambi.ac.id
[c] Email address: mustopa.rm@poltekkesjambi.ac.id
[d] Email address: devioktarinap@gmail.com
[e] Email address: putriliaamanda25@gmail.com
[f] Email address: adindacahyaningratri@gmail.com
[g] Email address: syarthibiahmad@gmail.com
[h] Email address: sabarudin.ahmad@gmail.com
[i] Email address: drshaflinapt@gmail.com

Received: 14 May 2023 Revised: 23 September 2023 Accepted: 24 September 2023

Abstract

Horticultural farmers use chemicals such as pesticides to increase productivity and also product quality. Exposure to pesticides can cause health problems, especially in the liver. A reference for evaluating liver function is blood test results for ALT, AST, ALP, and GGT activity. The objective of this study was to characterize the transaminase enzyme activity in horticultural farmers in the southern ring road area of Jambi city, based on the risk factors associated with pesticide exposure. This study employed a cross-sectional study approach in conjunction with a descriptive method. A total of thirty-four participants were involved, and blood samples were obtained from each for analysis in a lab. A photometer was utilized in the Medical Laboratory Technology department at Health Polytechnic of Jambi to measure the activity of liver enzymes. This study found some respondents who experienced increased enzyme activity, namely ALT: 8 people (23.5%), AST: 3 people (8.8%), ALP: 1 person (2.9%), and GGT: 1 person (2.9%.). Based on the risk description observed, it was known that the intensity of pesticide exposure showed a significant increase only in ALT enzyme activity (p=0.0048), while adherence to mask-wearing increased ALT (p=0.0018) and GGT (p=0.0134). This study discovered that wearing a mask and the amount of pesticide exposure can increase enzyme activity, which may be a sign of liver impairment in the horticultural farmers under observation. It is anticipated that workers will pay greater attention to workplace safety by wearing masks and applying pesticides in the recommended dosages.

Keywords: Horticultural Farmers, Pesticide, Liver Enzyme Activity.

Corresponding Author:

James Perdinan Simanjuntak
Department of Environmental Health, Poltekkes Kemenkes Jambi, Jambi City, Jambi Province, Indonesia
Email: james.p.simanjuntak@poltekkesjambi.ac.id

1. INTRODUCTION

Indonesia is a productive country in the agricultural sector. Horticulture is one of the commodities produced by this sector. Considering that horticulture has characteristics that are easily damaged, managing pests and plant diseases has a significant impact on productivity (Amilia, Joy, and Sunardi., 2016). In reality, a large number of horticultural farmers continue to use excessive amounts of chemicals, such as pesticides, to enhance yields and product quality, which can have negative effects on health (Agustina & Norfai, 2018; Hassaan & El Nemr, 2020; Mrema et al., 2017).

According to data from the World Health Organization (WHO), there are between one and five million cases of poisoning among agricultural laborers annually, varying in severity and potentially affecting vital organs like the kidneys, lungs, or heart. An estimated 11,000 people die globally each year as a result of unintentional pesticide poisoning (Boedeker et al., 2020; Tostado & Bollmohr, 2022). Meanwhile, the Food and Drug Supervisory Agency reported that there were 344 cases of pesticide poisoning in Indonesia in 2019; 41.7% of those cases were associated with agricultural pesticides (BPOM, 2020)

Pesticides are generally absorbed by farmers through inhalation, digestion, or dermal, and distributed through the circulatory system to affect various organs, particularly the liver and kidneys involved in detoxification. The health of the farmers themselves may be adversely affected by this exposure condition (Boedeker et al., 2020; Jamal et al., 2015). ALT (alanine aminotransferase), also known as SGPT (serum glutamic Pyruvic transaminase), AST (aspartate aminotransferase), also known as SGOT (serum glutamic Oxaloacetic transaminase), GGT (gamma-glutamyl transaminase), and ALP (alkaline phosphatase), are manifestations of the enzymes connected to these organs and can be utilized to demonstrate the presence of liver dysfunction (Lala et al., 2022). Through measuring the activity of these enzymes in horticultural farmers in Jambi City's South Rim neighborhood who frequently come into contact with pesticides at work, a picture of the health of their livers was intended to be obtained.

The analysis was conducted using the following criteria: how long the research participants had been farmers, how frequently they implemented pesticides at work, and whether they employed masks, or personal protective equipment, to protect themselves from herbicide and insecticide exposure while spraying pesticides. Concerning farmers' attitudes and practices regarding the use of pesticides, as well as their elevated enzyme activities, which are considered to be an index marker of hepatotoxicity, these studies were conducted.

2. RESEARCH METHOD

Descriptive research utilizing a cross-sectional approach is the methodology employed. In Paal Merah, Jambi's Lingkar Selatan Village, sampling was conducted. The clinical chemistry laboratory of the Department of Medical Laboratory Technology at Health Polytechnic of Jambi is where the activity of the enzymes ALT, AST, ALP, and GGT was evaluated.

Horticultural farmers in Jambi's Lingkar Selatan Paalmerah Village who employed herbicides and insecticides contributed to the study's sample. Thirty-four farmers who belonged to Gapoktan Tani Makmur were the samples employed for this study. Purposive sampling was the method utilized for sampling, and 10 to 14 willing respondents from each group were selected to constitute the sample. The Health Polytechnic of Jambi's Research Ethics Committee granted ethical approval for this study, with approval number LB.02.06/2/353/2022.

Blood specimens from each subject were taken using a closed system with a yellow lid vacutainer tube filled with a gel separator.

To extract serum for testing, the frozen blood was centrifuged for five minutes at 3000 RPM. Using BioSystems reagent and the BTS-350 semi-automatic photometer, the kinetic method was used to measure the activity of the enzymes ALT, AST, ALP, and GGT.

After the enzyme activity was determined, the data was examined to discover how it related to the respondents' attributes, particularly those that were directly connected to their risk of pesticide exposure. The average value of enzyme activity and the frequency, or percentage, of instances of high enzyme activity detected are displayed in tabulations and graphs containing the data. Statistical different tests (ANOVA test and independent t-test) were performed using the Medcalc ver. 19.0.7 for Windows with a significance level of 0.05.

3. RESULTS AND DISCUSSION

Table 1. Characteristics of demographic and enzyme activity test results

Characteristics		Total	Percentage
Gender	Male	22	64.7%
	Female	12	35.3%
Age	Mean (± SD) *	41.6	(± 10.8)
	Adult	18	52.9%
	Pre-elderly	14	41.2%
	Elderly	2	5.9%
Length of time as a farmer	Mean (± SD) *	14.8	(± 8.7)
	<10 years	12	35.3%
	11-20 years	12	35.3%
	>20 years	10	29.4%
Intensity of pesticide using	Very rarely	15	44.1%
	Rarely	13	38.2%
	Often	6	17.6%
Mask-wearing adherence	Very rarely	2	5.9%
	Rarely	9	26.5%
	Always	23	67.6%
Alanine transaminase (ALT)	Mean (± SD) *	30.3	(± 16.4)
	Normal	26	76.5%
	High	8	23.5%
Aspartate transaminase (AST)	Mean (± SD) *	23.6	(± 8.6)
	Normal	31	91.2%
	High	3	8.8%
Alkaline Phosphatase (ALP)	Mean (± SD) *	70.2	(± 25.1)
	Normal	33	97.1%
	High	1	2.9%
Gamma-glutamyl transferase (GGT)	Mean (± SD) *	22.7	(± 12.8)
	Normal	31	91.2%
	High	1	2.9%

** Mean and standard deviation (enzyme activity in IU/L; age & length of being a farmer in years)*

The study's samples' clinical laboratory and demographic characteristics are displayed in Table 1. The Indonesian Ministry of Health categorized age characteristics into three groups: adults (19–44 years), pre-elderly (45–60 years), and elderly (>60 years) (Dahlan et al., 2018).

The duration of employment as a farmer was also classified into three groups according to the respondents' statements about the date of their initial horticultural employment. The predefined range in this study is every ten years. The frequency with which respondents administered pesticides while at work was divided into three categories: very rare (less than three times per month), rare (one to two times per week), and frequent (more than two times per week). Furthermore, data were also obtained on the level of respondents' compliance in wearing a good mask as a piece of personal protective equipment (PPE) when spraying pesticides in the categories of very rarely (never or only occasionally wearing a mask), rarely (sometimes wearing a mask), and often (almost always or always wearing a mask).

Table 1. illustrates that most of the respondents are male with the criteria of mature and pre-elderly age. The respondents' duration of farming is equitably distributed according to the three observed criteria. Based on the description of the intensity of spraying and the use of masks obtained, it appeared that the majority of respondents also had a relatively low risk of pesticide exposure. The average value of the test results for each of the observed laboratory parameters is also provided, and it is still within the normal range. The graph in Figure 1 below demonstrates how each enzyme activity test result was distributed among the 34 horticultural farmer respondents who were observed.

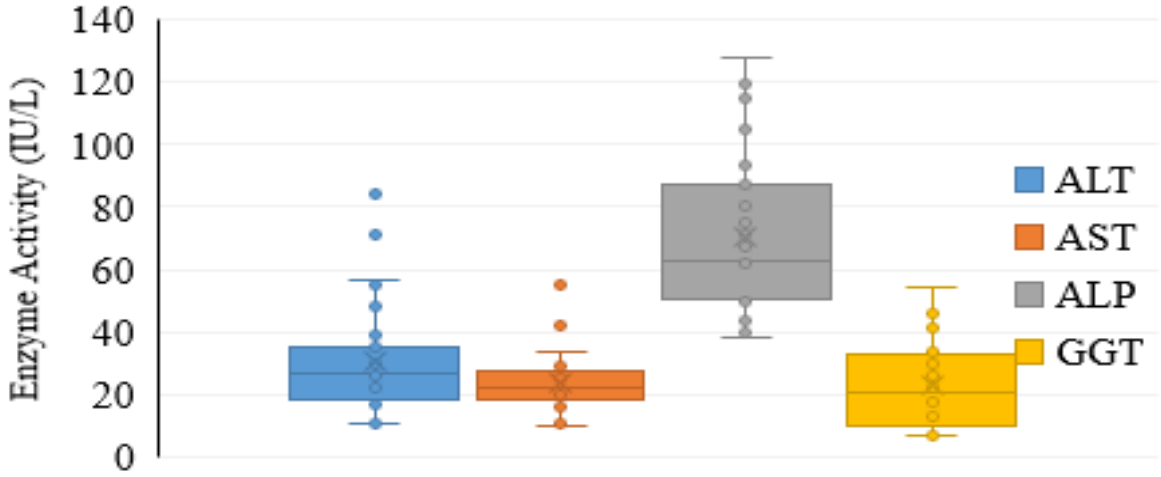


Figure 1. Boxplot graph of the results of measuring enzyme activity in horticultural farmers' liver function tests

The majority of the findings from the analysis of the four enzyme activities identified in this investigation decreased within the typical range for each parameter. Lala et al. (2022) provided the normal values for this study, which are as follows: GGT: 6-50 IU/L; AST: 5-30 IU/L; ALP: 30-120 IU/L; and ALT: 4-36 IU/L. Various frequencies of enzyme activity descending into the high category (exceeding the normal value) were observed for each enzyme test parameter. The largest proportion was identified in 8 respondents (23.5%) with high ALT activity test parameter results. ALP had one respondent (2.9%), GGT had one respondent (2.9%), and AST had three (8.8%) respondents. In the meantime, these were the other three parameters.

Based on the results of the demographic features of the study participants, the percentage of high-activity events in the four enzymes that were observed was subsequently examined (figure 2). The group of respondents who did not wear protective equipment (PPE) included individuals with high ALT and AST activities. In contrast to variations from other characteristics, respondents with the characteristic of the intensity of pesticide spraying that

was included in the frequent category had the highest percentage of high ALP and GGT enzyme activities. Based on the characteristics of each respondent group examined in this study, overall ALT has the highest percentage when compared to other parameters.

Toxic chemical compounds can enter the human body in several ways, encompassing absorption through the skin, orally, or inhalation, either intentionally or unintentionally. These dangerous materials are a potential workplace risk for many different professions worldwide. The detrimental effects of pesticide exposure on liver disorders, which are in charge of neutralizing dangerous substances that enter the body, have been documented in a number of long-running studies (Colombo et al., 2019; Luo et al., 2005; Malaguarnera, 2012; Redlich, 1988). Prospective cohort studies have also reported on discussions regarding different pesticide types that affect human health. These studies state that, despite not having a high and consistent potential, this hazardous material is predicted to be one of the triggers of cancer in a person, involving bladder and liver cancer (Koutros et al., 2016; Rapisarda et al., 2016; VoPham et al., 2017).

Studies on various types of farmers have also reported pesticide exposure. The liver eventually suffers chronic damage from the accumulation of this exposure (Melaram, 2021; Damalas & Koutroubas, 2016). Based on the results of the study's analysis of the respondents' demographic features, the percentage of high activity occurrence in each of the four enzymes that were identified was further examined (Figure 2). The "very rarely" category of respondents' mask-wearing compliance displayed the highest percentage (100%) for the ALT and AST parameters. In contrast to other risk variations or characteristics, the highest percentage (50%) of respondents with pesticide spraying intensity in the "frequent" category had high activity of ALP and GGT enzymes.

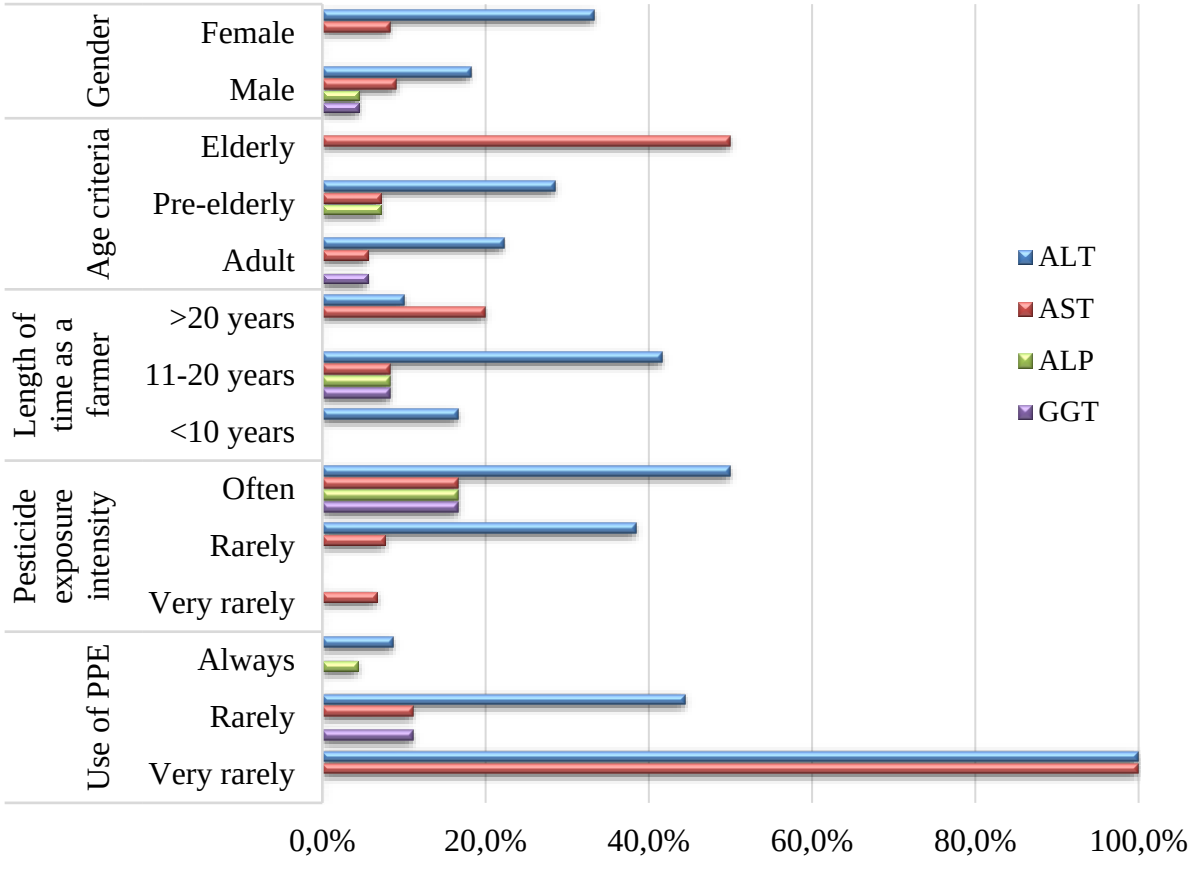


Figure 2. Graph of the percentage of high enzyme activity based on the characteristics of horticultural farmers.

Statistical analysis was administered to show differences in the results of the four parameters of measurement of enzyme activity based on each variable group of respondent characteristics. There were no discernible differences between the respondents' age, gender, or length of time employed as farmers for any of the enzyme activities. Stated differently, there was no observed increase in enzyme activity among the respondents as a result of these three variables. There was a difference in the ALT enzyme activity measurements according to the degree of pesticide exposure (p=0.0048) and farmers' adherence to wearing masks when spraying (p=0.0018). Furthermore, this significance was also demonstrated by the GGT enzyme activity, but only in the variable mask use (p=0.0134). In contrast, AST and ALP activities did not provide a significant difference in each of the variations of these two variables.

Table 2. Analysis of the characteristics of farmers on the results of enzyme activity tests.

Characteristic	**ALT**			**AST**			**ALP**			**GGT**		
	N	**H**	**Mean**	**N**	**H**	**Mean**	**N**	**H**	**Mean**	**N**	**T**	**Mean**
Gender												
Male	18	4	27.3	20	2	23.3	21	1	69.5	21	1	20.7
Female	8	4	35.8	11	1	24.2	12	0	72.1	12	0	26.4
p-value			0.125			0.3295			0.705			0.1251
Age group												
Adult	14	4	29.7	17	1	21.7	18	0	73.3	17	1	21.5
Pre-elderly	10	4	32.4	13	1	24.9	13	1	66.1	14	0	23.9
Elderly	2	0	21	1	1	32	2	0	74.5	2	0	25.5
p-value			0.6511			0.2173			0.7307			0.8354
Length of time as a farmer												
<10 years	10	2	29	12	0	20.7	12	0	74.1	12	0	20.2
11-20 years	7	5	35	11	1	23.3	11	1	69.5	11	1	26.3
>20 years	9	1	26.2	8	2	27.4	10	0	67.1	10	0	25.1
p-value			0.4456			0.1917			0.819			0.4822
Intensity of pesticide-using												
Very rarely	15	0	21.4	14	1	20.7	15	0	67.3	15	0	17.9
Rarely	8	5	33.9	12	1	25.7	13	0	73.5	13	0	25.9
Often	3	3	44.7	5	1	27.5	5	1	71.9	5	1	27.8
p-value			0.0048 **			0.1138			0.8206			0.1462
Mask-wearing adherence												
Very rarely	0	2	25.3	0	2	21.5	2	0	69.4	2	0	19.2
Rarely	5	4	35.8	8	1	28.2	9	0	69.4	8	1	27.1
Always	21	2	63	23	0	26.5	22	1	87.2	23	0	43.5
p-value			0.0018 **			0.1252			0.6496			0.0134 *

*Note: N = number of respondents with normal enzyme activity; H = the number of respondents with high enzyme activity; Mean= average value of enzyme activity (IU/L); P-value is significant at the level of: *= 0.05 & **= 0.01*

In comparison to other parameters, overall ALT is also the one that frequently demonstrates the highest percentage, particularly when it comes to respondent characteristics associated with pesticide exposure risk factors. Although pesticide poisoning also increases other enzyme activities present in farmers' blood, this is very consistent with the phenomenon

found in several previous studies in several countries that showed an increase in the same enzyme in cases of pesticide poisoning (Damalas & Koutroubas, 2016; Freire et al., 2015; Jamal et al., 2015). When Lozano-Paniagua et al., (2021) observed greenhouse farmers in Spain who were exposed to pesticides, they discovered that workers who had high exposure periods had higher levels of ALT and ALP. Bernieri et al., (2021) observed that although AST enzyme activity increased significantly following high pesticide exposure in Brazilian farmers, ALT and GGT did not increase. In the past, Manfo et al., (2020) used a case-control methodology to track the prevalence of kidney and liver diseases among farmers in Buea, Cameroon. The study revealed that exposure to pesticides increased the activity of the ALT enzyme significantly, but not that of the AST, creatinine, or uric acid. Nevertheless, because the majority of these enzymes are produced in the liver (hepatic cells), ALT is recognized as the most specific enzyme to indicate impaired liver function when compared to other enzymes (Aulbach & Amuzie, 2017).

Freire et al., (2015) who observed Brazilians who were heavily exposed to organochlorine pesticides also gathered that there was an increase in liver enzyme activity due to these compounds. Moreover, other parameters such as bilirubin, which is also the main marker of liver function abnormalities, were successfully evidenced to possess a significant relationship with beta-hexachlorocyclohexane levels unveiled in the blood of respondents. Furthermore, from the hematological aspect, eosinophilia was also reported, as well as decreased hemoglobin levels and erythrocyte counts in the blood.

Several factors, including age, length of employment, use of personal protective equipment (PPE), pesticide dosage, wind direction during spraying, and frequency of spraying, can affect how severe liver function disorders caused by pesticide exposure can be. Because farmers are more susceptible to come into direct contact with pesticides, including both herbicides and insecticides, the length of time they work can raise their risk of pesticide poisoning (Andarini & Rosanti, 2018). Farmers frequently disregard the importance of wearing personal protective equipment (PPE), such as masks, even though it can lessen the negative health effects of pesticide exposure. Numerous studies conducted on lab animals have demonstrated the hepatotoxic effects of pesticides (Nieradko-Iwanicka & Borzęcki, 2015; Rizzati et al., 2016). Meanwhile, Yokoyama et al., (2019) asserted that exposure to pesticides provided to animals tested in his study did not cause an increase in ALP enzyme activity. This is similar to the facts uncovered in this study on ALP enzyme activity which also did not perform any significant difference from each risk group observed.

Bayili et al., (2020) performed a longitudinal study on 113 farmers in two phases: the first phase occurred during the harvest period, and the second phase was conducted six months after the harvest period ended. The second phase's ALT and AST activity significantly decreased ($p<0.01$), according to the results. Although ALP's average value decreased as well, there was no discernible change. On the other hand, GGT activity rose from 40.5 ± 30.68 U/L in the first phase to 63.0 ± 67.07 U/L in the second phase ($p < 0.0001$). This demonstrates how heavily farmers' exposure to pesticides during their work affects abnormalities in liver function; the less intensely farmers are exposed, the lower the results of the measurement of liver enzyme activity that exceeds normal values.

In a study conducted in Indonesia, Sukmayanti et al., (2020) concluded that gender and age affect ALT and cholinesterase enzyme activity. Male farmers in Bali's Tabanan district had higher levels of enzyme activity than female farmers, according to observations made of them growing vegetables. This contrasts with the phenomenon uncovered when ALT activity was measured in farmers in Jambi City's South Ring, where nearly all of the enzymes discovered had mean values that were higher in the female group than the male group. In the same way, the researchers identified no statistically significant differences in the age group of farmers in

this study, even though the observed enzyme activity values in the South Ring of Jambi City tended to increase with farmer age.

Meanwhile, research conducted by Tsani et al., (2017) revealed that 29 out of 43 farmers (67.4%) in Sumberejo village, Magelang had impaired liver function. The study ultimately concluded that a working period can have an impact on liver function impairment and lead to an accumulation of pesticides in the body. It was determined that there is little correlation between PPE use and the prevalence of liver function disorders. This is conceivable because there was only one farmer respondent in the study who fully utilized PPE. The results of a study on farmers in Jambi City's South Ring demonstrate a lower percentage—just 9 out of 34 farmers, or 26.5 percent. Since the length of service as a farmer generated no statistically significant results in this study, it can be assumed that it is not a significant factor in determining the onset of liver function disorders. The high intensity of pesticide use and not followed by the use of good PPE is proven to cause the accumulation of pesticides in the body to increase and cause impaired liver function.

4. CONCLUSION

Within the southern ring road of Jambi City, nine out of the horticultural farmers who used pesticides (26.5%) had high enzyme measurement results, according to this study. The most frequently encountered enzyme with elevated activity above normal values was alanine aminotransferase (ALT). This study has demonstrated that the intensity of pesticide spraying and mask use by horticultural farmers are risk factors that may lead to elevated liver enzyme activity, particularly ALT and GGT.

REFERENCES

Agustina, N., & Norfai, N. (2018). Paparan Pestisida terhadap Kejadian Anemia pada Petani Hortikultura. *Majalah Kedokteran Bandung*, *50*(4), 215–221. https://doi.org/10.15395/mkb.v50n4.1398

Amilia, E., Joy, B., & Sunardi, S. (2016). Residu Pestisida pada Tanaman Hortikultura (Studi Kasus di Desa Cihanjuang Rahayu Kecamatan Parongpong Kabupaten Bandung Barat). *Agrikultura*, *27*(1), 23-29. https://doi.org/10.24198/agrikultura.v27i1.8473

Andarini, Y. D., & Rosanti, E. (2018). Kajian toksisitas pestisida berdasarkan masa kerja dan personal hygiene pada petani hortikultura di Desa Demangan. *An-Nadaa: Jurnal Kesehatan Masyarakat (e-Journal)*, *5*(2), 82-89. https://doi.org/10.31602/ann.v5i2.1655

Aulbach, A. D., & Amuzie, C. J. (2017). Biomarkers in Nonclinical Drug Development. In *A Comprehensive Guide to Toxicology in Nonclinical Drug Development*, pp. 447–471. Elsevier. https://doi.org/10.1016/B978-0-12-803620-4.00017-7

Bayili, B., Da, O., Ilboudo, S., Ouedraogo, R., Coulibaly, V. P., Bationo, J. F., ... & Ouedraogo, G. A. (2020). Study of biochemical parameters in farmers exposed to pesticides used in cotton growing around the Bala hippopotamus pond. *GSC Biological and Pharmaceutical Sciences*, *13*(1), 111-122. https://doi.org/10.30574/gscbps.2020.13.1.0323

Bernieri, T., Rodrigues, D., Randon Barbosa, I., Perassolo, M. S., Grolli Ardenghi, P., & Basso da Silva, L. (2021). Effect of pesticide exposure on total antioxidant capacity and biochemical parameters in Brazilian soybean farmers. *Drug and Chemical Toxicology*, *44*(2), 170–176. https://doi.org/10.1080/01480545.2019.1566353

Boedeker, W., Watts, M., Clausing, P., & Marquez, E. (2020). The global distribution of acute unintentional pesticide poisoning: Estimations based on a systematic review. *BMC Public Health*, *20*(1), 1875. https://doi.org/10.1186/s12889-020-09939-0

BPOM. (2020). *Laporan Tahunan Pusat Data dan Informasi Obat dan Makanan tahun 2019*. Badan Pengawasan Obat dan Makanan.

Colombo, M., La Vecchia, C., Lotti, M., Lucena, M. I., Stove, C., Paradis, V., & Newsome, P. (2019). EASL Clinical Practice Guideline: Occupational liver diseases. *Journal of Hepatology*, *71*(5), 1022–1037. https://doi.org/10.1016/j.jhep.2019.08.008

Dahlan, A. K., Umrah, A. S., & Abeng, T. (2018). Kesehatan Lansia: Kajian Teori Gerontologi dan Pendekatan Asuhan pada Lansia. Malang: Intimedia.

Damalas, C., & Koutroubas, S. (2016). Farmers' Exposure to Pesticides: Toxicity Types and Ways of Prevention. *Toxics*, *4*(1), 1. https://doi.org/10.3390/toxics4010001

Freire, C., Koifman, R. J., & Koifman, S. (2015). Hematological and Hepatic Alterations in Brazilian Population Heavily Exposed to Organochlorine Pesticides. *Journal of Toxicology and Environmental Health, Part A*, *78*(8), 534–548. https://doi.org/10.1080/15287394.2014.999396

Hassaan, M. A., & El Nemr, A. (2020). Pesticides pollution: Classifications, human health impact, extraction and treatment techniques. *The Egyptian Journal of Aquatic Research*, *46*(3), 207–220. https://doi.org/10.1016/j.ejar.2020.08.007

Jamal, F., Haque, Q. S., Singh, S., & Arshad, M. (2015). The Influence of Pesticides on Hepatic and Renal Functions in Occupational Sprayers of Rural Malihabad, Lucknow (India). *Toxicology: Open Access*, *1*(01). https://doi.org/10.4172/2476-2067.1000106

Koutros, S., Silverman, D. T., Alavanja, M. C., Andreotti, G., Lerro, C. C., Heltshe, S., Lynch, C. F., Sandler, D. P., Blair, A., & Beane Freeman, L. E. (2016). Occupational exposure to pesticides and bladder cancer risk. *International Journal of Epidemiology*, *45*(3), 792–805. https://doi.org/10.1093/ije/dyv195

Lala, V., Zubair, M., & Minter, D. A. (2022). *Liver Function Tests*. StatPearls. Treasure Island (FL). Retrieved from https://pubmed.ncbi.nlm.nih.gov/29494096/

Lozano-Paniagua, D., Parrón, T., Alarcón, R., Requena, M., López-Guarnido, O., Lacasaña, M., & Hernández, A. F. (2021). Evaluation of conventional and non-conventional biomarkers of liver toxicity in greenhouse workers occupationally exposed to pesticides. *Food and Chemical Toxicology*, *151*, 112127. https://doi.org/10.1016/j.fct.2021.112127

Luo, J.-C., Cheng, T.-J., Kuo, H.-W., & Chang, M. J. W. (2005). Abnormal liver function associated with occupational exposure to dimethylformamide and glutathione *S* -transferase polymorphisms. *Biomarkers*, *10*(6), 464–474. https://doi.org/10.1080/13547500500333648

Malaguarnera, G. (2012). Toxic hepatitis in occupational exposure to solvents. *World Journal of Gastroenterology*, *18*(22), 2756. https://doi.org/10.3748/wjg.v18.i22.2756

Manfo, F. P. T., Mboe, S. A., Nantia, E. A., Ngoula, F., Telefo, P. B., Moundipa, P. F., & Cho-Ngwa, F. (2020). Evaluation of the Effects of Agro Pesticides Use on Liver and Kidney Function in Farmers from Buea, Cameroon. *Journal of Toxicology*, *2020*, 1–10. https://doi.org/10.1155/2020/2305764

Melaram, R. (2021). Environmental Risk Factors Implicated in Liver Disease: A Mini-Review. *Frontiers in Public Health*, *9*, 683719. https://doi.org/10.3389/fpubh.2021.683719

Mrema, E. J., Ngowi, A. V., Kishinhi, S. S., & Mamuya, S. H. (2017). Pesticide Exposure and Health Problems Among Female Horticulture Workers in Tanzania. *Environmental Health Insights*, *11*, 117863021771523. https://doi.org/10.1177/1178630217715237

Nieradko-Iwanicka, B., & Borzęcki, A. (2015). Effect of 28-Day Exposure to Fenpropathrin on the Activities of Serum Alanine Transaminase and Liver Antioxidant Enzymes in Mice. *Bulletin of the Veterinary Institute in Pulawy*, *59*(1), 165–169. https://doi.org/10.1515/bvip-2015-0025

Rapisarda, V., Loreto, C., Malaguarnera, M., Ardiri, A., Proiti, M., Rigano, G., Frazzetto, E., Ruggeri, M. I., Malaguarnera, G., Bertino, N., Malaguarnera, M., Catania, V. E., Di Carlo, I., Toro, A., Bertino, E., Mangano, D., & Bertino, G. (2016). Hepatocellular

carcinoma and the risk of occupational exposure. *World Journal of Hepatology*, *8*(13), 573. https://doi.org/10.4254/wjh.v8.i13.573

Redlich, C. A. (1988). Liver Disease Associated with Occupational Exposure to the Solvent Dimethylformamide. *Annals of Internal Medicine*, *108*(5), 680. https://doi.org/10.7326/0003-4819-108-5-680

Rizzati, V., Briand, O., Guillou, H., & Gamet-Payrastre, L. (2016). Effects of pesticide mixtures in human and animal models: An update of the recent literature. *Chemico-Biological Interactions*, *254*, 231–246. https://doi.org/10.1016/j.cbi.2016.06.003

Sukmayanti, N. L. P. A., Artini, N. P. R., & Yanti, N. P. W. (2020). Analisis Kadar SGPT (Serum Glutamic Pyruvic Transaminase) Dan Kholinesterase Pada Petani Sayur Di Desa Riang Gede, Kecamatan Penebel, Kabupaten Tabanan. *THE JOURNAL OF MUHAMMADIYAH MEDICAL LABORATORY TECHNOLOGIST*, *3*(2), 25. https://doi.org/10.30651/jmlt.v3i2.5841

Tostado, L., & Bollmohr, S. (2022). Facts and figures about toxic chemicals in agriculture 2022. *Creative Commons*, *1st edition*. Retrieved from https://eu.boell.org/PesticideAtlas

Tsani, R. A., Setiani, O., & Dewanti, N. A. Y. (2017). Hubungan Riwayat pajanan pestisida dengan gangguan fungsi hati pada petani di desa sumberejo kecamatan ngablak kabupaten magelang. *Jurnal Kesehatan Masyarakat*, *5*(3), 411-419. https://doi.org/10.14710/jkm.v5i3.17258

VoPham, T., Bertrand, K. A., Hart, J. E., Laden, F., Brooks, M. M., Yuan, J.-M., Talbott, E. O., Ruddell, D., Chang, C.-C. H., & Weissfeld, J. L. (2017). Pesticide exposure and liver cancer: A review. *Cancer Causes & Control*, *28*(3), 177–190. https://doi.org/10.1007/s10552-017-0854-6

Yokoyama, Y., Ono, A., Yoshida, M., Matsumoto, K., & Saito, M. (2019). Toxicological significance of increased serum alkaline phosphatase activity in dog studies of pesticides: Analysis of toxicological data evaluated in Japan. *Regulatory Toxicology and Pharmacology*, *109*, 104482. https://doi.org/10.1016/j.yrtph.2019.104482