Volume 17, Issue 4, November 2022

p-ISSN 1907-7505
e-ISSN 2460-0601

Kesmas

Jurnal Kesehatan Masyarakat Nasional
(National Public Health Journal)

Quarterly Journal

Invited Article:

Research Articles:

Nationally accredited and indexed in SINTA-S1 by Ministry of Education and Culture of the Republic of Indonesia & SCOPUS coverage years from 2016 - present

Kesmas
Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Volume 17, Issue 4, November 2022

p-ISSN 1907-7505
e-ISSN 2460-0601

TABLE OF CONTENT

Nationally accredited and indexed in SINTA-S1 by Ministry of Education and Culture of the Republic of Indonesia & SCOPUS coverage years from 2016-present

Kesmas
Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Volume 17, Issue 4, November 2022

p-ISSN 1907-7505
e-ISSN 2460-0601

TABLE OF CONTENT

Nationally accredited and indexed in SINTA-S1 by Ministry of Education and Culture of the Republic of Indonesia & SCOPUS coverage years from 2016-present

Kesmas

Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Volume 17, Issue 4, November 2022

p-ISSN 1907-7505
e-ISSN 2460-0601

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal) is a quarterly published journal containing both research and invited review articles in the field of public health.

Published by
Faculty of Public Health Universitas Indonesia
G301 Building G 3rd Floor
Kampus Baru UI, Depok 16424
Mobile Phone: +62815-1141-6600
E-mail: jurnalkm@ui.ac.id or jurnalkesmas.ui@gmail.com
Website: http://journal.fkm.ui.ac.id/kesmas

READER MAIL

Dear Editorial Team, Authors, Viewers, Subscribers, and Readers

By the time I write this reader mail, the implementation of restrictions on community activities or *Pemberlakuan Pembatasan Kegiatan Masyarakat* (PPKM) in Jakarta has been set to level 1 again. Even when the activity in the community is running as usual, I should remind myself that this pandemic is not over yet. Luckily, Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal) Volume 17-3 is still covering the COVID-19 articles, so I can refer to the sources about facing this never-ending COVID-19 pandemic. Even though this coronavirus disease is living with us in society, I hope there will still be articles discussing this pandemic in the future. **(Aloysius, Jakarta)**

INFORMATION

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal) editorial team accepts any criticism, feedback, and recommendation related to published articles and the progress of the journal which can be submitted through e-mail: jurnalkesmas.ui@gmail.com. Please kindly inform your name, affiliation, and address. We will publish the criticism, feedback, and recommendation received on Reader Mail section in the next edition. We will provide an interesting souvenir for the reader whose criticism/feedback/recommendation is published on the reader mail. Thank you. **(Editorial Team)**

Every article published is charged an Article Processing Charge (APC) since Volume 16 Issue 3 (August 2021) of USD 450 (*four hundred and fifty the United States dollars*)

Please make a payment to the following account:
UNIVERSITAS INDONESIA BHPP
Bank BNI UI Depok
Account Number: 1273000568
Swift Code: BNINIDJA

Please send the receipt to:
Secretariat of Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)
Faculty of Public Health Universitas Indonesia
G301 Building G 3rd Floor
Kampus Baru UI, Depok 16424
or e-mail: jurnalkm@ui.ac.id or jurnalkesmas.ui@gmail.com

AUTHOR GUIDELINES

1. **Kesmas:** Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal) publishes articles in the field of public health that includes Biostatistics, Epidemiology, Health Policy and Administration, Occupational Health and Safety, Environmental Health, Health Education and Behavioral Science, Public Health Nutrition, and Sexual and Reproductive Health.
2. Submitted articles must be research articles and invited review articles that should not have been previously published or be currently under consideration for publication anywhere else and free of plagiarism. Each submitted article will be checked by Ithenticate, an application for detecting plagiarism.
3. Components of Articles:
   - The title is written in English with a maximum of 20 words.
   - The author's identity is written under the title, including name, affiliation, correspondence address, phone number, and e-mail.
   - Abstract is written in English with a maximum of 200 words. The abstract should be one paragraph covering introduction, aim, method, results, and conclusion with a maximum of 5 (five) keywords separated by a comma.
   - Introduction contains background, brief and relevant literature review and the aim of study.
   - Method includes design, population, sample, data sources, techniques/ instruments of data collection, data analysis procedure, and ethics.
   - Results are research findings and should be clear and concise.
   - Discussion should properly and argumentatively define results of study with any relevant theory and prior finding.
   - Tables should be single-spaced and numbered consecutively in accordance with a presentation in the text. Figures, pictures, or formulas should be original. Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (not on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used. Then, for resolution, rasterized based files (e.g., with .tiff or .jpeg extension) require a resolution of at least 1000 dpi (dots per inch). Line art should be supplied with a minimum resolution of 1000 dpi. Tables and/or figures should be no more than 6 (six) as presented in Result.
   - Conclusion and Recommendation (if any), should answer problems of study not exceeding the capacity of finding. Recommendation should refer to the aims and conclusion in form of narration, be logical and effective.
4. Abbreviations consist of abbreviations mentioned in the article (from Abstract to Conclusion).
5. Ethics Approval and Consent to Participate inform license obtained from institution and research subject.
6. Competing Interest stated whether the author(s) have interest in research.
7. Availability of Data and Materials clarifies sources of data or information used as study materials.
8. Authors' Contribution explain about contribution done by each author to the study.
9. Acknowledgment mention thank-you note to all components supporting the study, including funding (grant).
10. Additional Information confirms the names and institutions of authors if the study consist of more than 6 (six) of it and/or other additional information if necessary.
11. References should be written with Vancouver style.
    - Please ensure that every reference cited in the text is also present in the reference list (and vice versa).
    - Reference number must be numbered consecutively in accordance with the whole text and recent journal references are preferred.
    - For the author's name, please write the last name and the first name, and initials if any, with a maximum of 6 (six) names of authors. If more than 6 (six) authors, the following author should be written with "et al".
    - The first letter of reference tittle should be capitalized and the remaining should be written in lowercase letters, except name of person, place and time. Latin terms should be written in italics. Title should not be underlined and written in bold.
    - Please provide the URL of the referred article.
    - When referencing in the body of text use superscript after full stop (.), e.g.: ..... .[10]. If the sentence stating the other author's name as reference, use the reference number by the end of the author`s name then continue the sentence till full stop (.), e.g.: Abood,[2]...; or Latief, *et al*,[1]...).

    Example of References :
    - Journal Article :
      Hoq MN. Effects of son preference on contraceptive use in Bangladesh. Kesmas: National Public Health Journal. 2019; 14 (1): 21-7. Available from : http://dx.doi.org/10.21109/kesmas.v14i1.2848
    - Book :
      Grech ED. ABC of interventional cardiology. 2nd ed. Chichester: Wiley blackwell; 2011. Available from: https://ebookcentral.proquest.com/lib/imperial/detail.action?docID=822522
    - Online article :
      Pullen LC. Antibiotic resistance continues to be a problem in children. Medscape; 2017. Available from: https://www.medscape.com/viewarticle/860801
    - Thesis and Dissertation :
      Slawsky E. An evaluation of greenspace exposure as a protective factor in dementia risk among U.S adults 75 years or older [Thesis]. University of Washington; 2019.
12. Manuscript should be typed using word processors (Microsoft Word or Open Office) software. The font type for the paper is Times New Roman with font size 12. The paper size is A4 (e.g., 210 x 297 mm). Then it should be one-column format with all margin 3 cm, double spaced and maximum at 5,000 words. Manuscript must be submitted via website http://journal.fkm.ui.ac.id/kesmas. Please include Covering Letter and Statements and Ethics Approval Form in a separated document file containing the summary of scientific finding and uploaded on Supplementary Files in PDF format.

Achmy, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 235-242
DOI: 10.21109/kesmas.v17i4.6209

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Factors Influencing Handwriting Development among Preschool Children: A Systematic Review

Zati Izni Achmy, Masne Kadar, Nor Afifi Razaob*, Farahiyah Wan Yunus

Program of Occupational Therapy, Center for Rehabilitation and Special Needs Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Abstract

Handwriting development is essential for academic performance, yet the research on the factors contributing to it is scant. This systematic review aimed to provide a comprehensive overview of the factors contributing to handwriting development among preschool children that may benefit public health knowledge, especially among teachers, parents, and therapists. A systematic search was conducted using four databases: PubMed, ERIC, CINAHL, and Google Scholar. During the preliminary search, 565 relevant studies were found. Screening, review selection, and characterization were performed based on the inclusion and exclusion criteria. The inclusion criteria included preschool children, quantitative, written in English, and published in January 2012–January 2022. The exclusion criteria were studies involving children with specific diagnoses. A consensus agreement was obtained, and ten studies were eventually selected for the comprehensive review. Executive function, letter knowledge, motor skills, and writing surface were identified. These factors indicated that handwriting was not an independent process, as its acquisition involved numerous components. This systematic review confirmed that executive function, letter knowledge, motor skills, and writing surface influenced handwriting development. More randomized controlled trials should be conducted to provide more conclusive and exhaustive evidence.

Keywords: handwriting acquisition, handwriting development, handwriting skills, kindergarten children, preschool children

Introduction

Handwriting is a medium of communication that allows users to project thoughts and ideas. During childhood, handwriting is a significant occupation required for classroom participation as it is part of the educational component and represents children's understanding of subjects during learning sessions and examinations. Handwriting development begins with children scribbling on paper before prewriting skills evolve, and over time they master handwriting skills.[1] In preschool, children are exposed to prewriting activities such as tracing and coloring; over time, they learn writing alphabets and simple words such as names. The acquisition of letter writing occurred between the ages of 6 and 7, while at the age of 8, children focused more on improving movement control and further achieved writing automation at the age of 10.[2]

Handwriting is vital and must not be underestimated, even in a world dominated by computers and keyboards. It could contribute to developing other skills such as reading skills,[3] recognition skills,[4] and visual-spatial skills.[4] The neural activation in the left inferior frontal gyrus (IFG), also known as Broca's area, and left anterior cingulate cortex, was observed to be more significant after writing than typing.[3] Therefore, the study suggests that handwriting development during early childhood could aid in developing reading skills.[3] Compared to typing by keyboard, handwriting could also encourage learning letters and improve visuospatial skills.[4] In addition, a study found that handwriting fostered letter recognition and highlighted that hand production or handwriting encourages letter knowledge compared to visual study alone.[5]

Handwriting becomes increasingly important and intricate with increasing age. A review by Dinehart,[6] elucidates how good handwriting can influence academic performance. According to the review study, first, teachers tend to give more marks to legible assignments. Second, children who struggle with handwriting are more likely to focus on the act of writing rather than on the content of their composition.[6] Last, children who are frustrated with their handwriting are less likely to write more and

Correspondence:* *Nor Afifi Razaob, Program of Occupational Therapy, Center for Rehabilitation and Special Needs Studies, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Raja Muda Abdul Aziz Street, Kuala Lumpur, Malaysia 50300, E-mail: fifie.razaob@ukm.edu.my, Phone: +60 3928 97350*

Received : September 06, 2022
Accepted : November 19, 2022
Published : November 30, 2022

tend to feel awful about their handwriting, which, consequently, affects their content.[6] Furthermore, poor handwriting negatively affects students' academic performance in terms of time management, work completion, writing compliance, and legibility.[1]

Difficulty in handwriting is also a specific learning disability, referred to as dysgraphia, a disorder that entails the inability to write; it encompasses acquired and developmental dysgraphia.[7] Acquired dysgraphia is when brain pathways are disrupted, causing the loss of previously acquired skills, possibly due to brain injury or degenerative disease.[8] Developmental dysgraphia entails difficulty in developing handwriting skills regardless of adequate learning opportunities and cognitive skills; this type of dysgraphia is common among children.[7] Nevertheless, compared to dyslexia, which is more frequently highlighted in terms of specific learning disabilities, awareness and knowledge of dysgraphia are still scant. No gold standard is available to diagnose dysgraphia.[8] A study conducted to assess the knowledge of specific learning disabilities among teachers in Ethiopia showed that teachers exhibited poor knowledge regarding specific learning disabilities.[9] This is significantly alarming as teachers responsible for children's learning demonstrated poor knowledge of dysgraphia; the public presumably had poor or no knowledge at all. This lack of knowledge among teachers and the public, particularly parents, may lead to late diagnosis, which consequently affects children's learning performance. Public health awareness is important for educating people about dysgraphia and seeking early intervention.

Previous literature showed that about 6% to 33% of children had handwriting difficulties.[10] Commonly, occupational therapists use handwriting assessments to identify the problems and guide the intervention. Standardized assessments are beneficial in assessing handwriting performance and factors that influence handwriting, as well as monitoring progress.[11] However, there are discrepancies across handwriting assessments used by occupational therapists. Some available handwriting assessments, such as the Minnesota Handwriting Assessment and Test of Handwriting Skills–Revised, focus solely on performance tasks. In contrast, handwriting assessments, such as shore handwriting screening and print tools, incorporate both performance tasks and underlying factors. Performance tasks include copying, writing, and tracing, while underlying factors include fine motor, cognitive, and gross motor skills. Studies on early handwriting acquisition tend to focus more on the product than on the process underlying these skills, which may account for these discrepancies.[12]

According to Case-Smith and O'Brien,[1] alphabet writing, copying, composition, writing speed, legibility, and biomechanical factors need to be examined when evaluating handwriting. However, some components proposed by Case-Smith and O'Brien,[1] are unsuitable for assessing preschool children. For instance, composition and writing speed are important because preschool children are still in the handwriting development phase. Therefore, factors influencing handwriting development in preschool children must be identified so that occupational therapists and educators can provide interventions for children. Occupational therapists are health care professionals working with individuals to achieve optimal health and well–being through participation in life occupations. In the pediatric population, occupations from an occupational therapist's perspective are activities of daily living, education, social participation, and play.[1]

Understanding the factors that affect handwriting performance could assist occupational therapists in providing interventions to help children improve.[13] These factors may be biomechanical, sensorimotor, or teaching-learning perspectives. This review aimed to clarify and identify factors in terms of skills or components that might influence handwriting development among preschool children. Hence, the findings of this review would benefit therapists, educators, and parents as public persons in delivering the best intervention to improve handwriting acquisition and mitigate the risk of handwriting difficulties among preschool children. This review also might benefit public health by gaining more information on the factors influencing handwriting development.

Method

This review was conducted following the updated preferred reporting items for systematic reviews and meta-analyses (PRISMA).[14] First, this review formulated the research question based on the PICO model, where P, I, C, and O denoted the patient/population, intervention, comparison, and outcome, respectively. As this review involved observational studies and no comparison of interventions, only P and O were used to formulate the research question.[15] The target population was preschool children, and the outcome measured was the factors influencing handwriting development. Therefore, the research question of this review was "What are the factors that influence handwriting development among preschool children?" This review identified the existing evidence to answer this question.

The next step was to identify the relevant studies. The search strategy involved the search for potential studies, and the study selection was based on the inclusion and exclusion criteria. The search strategy, inclusion and exclusion criteria, study selection, and data extraction are explained below.

Search Strategy

A comprehensive search of electronic databases,

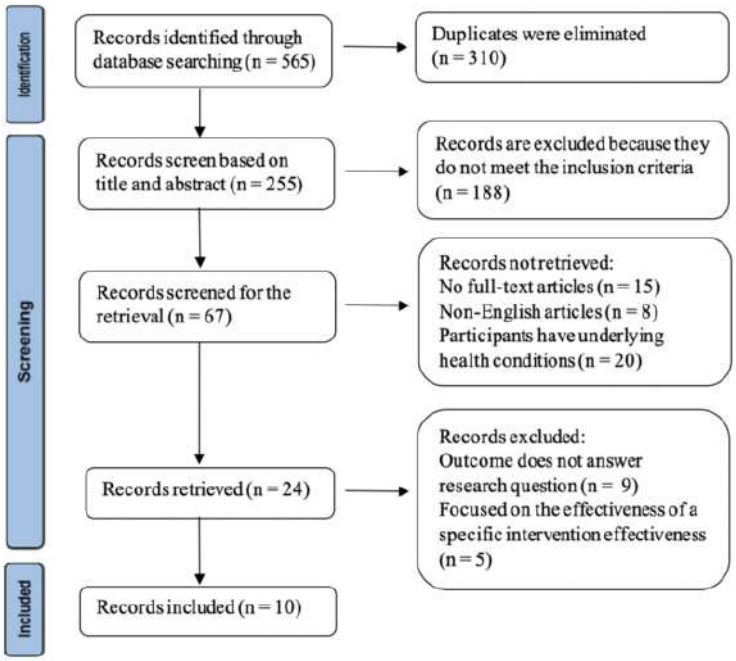


Figure 1. The Flowchart for the Studies Selection

including PubMed, ERIC, CINAHL, and Google Scholar, through the first 20 pages, was conducted from August 2021 to January 2022. The authors devised search terms refined through discussions with experienced librarians. The search strings including Boolean operators were used for combining the search terms; ("Factors" OR "associated factors" OR "components") AND ("handwriting development" OR "handwriting acquisition" OR "handwriting readiness" OR handwriting skills) AND ("preschool children" OR "kindergarten children" OR "children aged 4-6 years"). The same search strategy was used for all databases (Figure 1).

Inclusion and Exclusion Criteria

This review comprised studies related to handwriting development among preschool children. The inclusion criteria in this study were studies involving preschool children, quantitative, written in English, and published in January 2012–January 2022. The exclusion criteria were studies whose participants had specific diagnoses such as dyslexia, autism spectrum disorder (ASD), and cerebral palsy.

Study Selection

A total of 565 articles were identified based on the inclusion and exclusion criteria. The study selection involved several critical steps. The first step was eliminating duplicate or similar documents, leaving 255 articles for subsequent phases. The screening of titles and abstracts of the studies selected was independently done. Of the 255 articles, 67 were selected for retrieval based on articles that met the inclusion criteria. Of the 67 articles, 15 were eliminated as no full-text articles were available, and 20 were eliminated as the participants had underlying health conditions, such as ASD and developmental coordination disorder (DCD).

In addition, non-English articles were eliminated, as the translation process might influence the exact meaning of the articles and the comprehension of authors, 24 selected articles were then reviewed; and discussions were held to reach a consensus on the final selection. Of the 24 retrieved studies, nine were eliminated as the outcome did not answer the research question, and five were eliminated as the studies examined the effectiveness of a specific intervention. For instance, a study measured the effectiveness of a specific handwriting curriculum, such as handwriting without tears. Since this review aimed to ascertain the influential factors to handwriting development, the intervention study did not answer the research question accurately. Finally, only 10 articles were selected for this review study.

Data Extraction

A standardized data extraction form was developed.

The selected studies were reviewed, and all relevant data were extracted independently. Two or three reviewers were suggested for the data extraction process to reduce bias and error.[15] Relevant data, including author, year of publication, study design, sample size, country of population studies, and study findings, were extracted.

Results

Clinical Appraisal of the Studies

Table 1 shows the study appraisal using the McMaster Critical Review Form. The included studies were independently reviewed and discussed until reaching a consensus. All the included studies had a clear purpose, relevant literature, reliable and valid outcome measures, appropriate conclusions, and implications. However, none of the studies justified the sample size used. Moreover, five studies did not report dropouts.

Study Characteristics

This review included 10 articles from four databases; three studies were conducted in the United States, two in South Korea, two in Germany, and one in Brazil, Australia, and Egypt. Each study was published in 2012, 2014, 2015, 2016, 2017, and 2020, except for 2018 and 2021, two studies were published (Table 2). The studies listed were observational studies with a sample size ranging from 25 to 166 preschool children. Two studies compared other populations, including elementary-aged children and adults. Therefore, only data pertaining to preschool children were included in this review, which focused on preschool children. Four factors, including letter knowledge, motor skills, executive functions, and writing surface, were identified in the included articles.

Letter Knowledge (n = 4)

Letter knowledge was assessed in terms of letter recognition,[16] and letter naming,[16-18] copying familiar letters, as well as unfamiliar symbols.[18] Letter recognition was influenced by handwriting fluency,[12,16,18] and name-writing,[17] in preschool children. Reutzel, *et al.*,[18] found that letter-naming and letter-writing fluency were associated. The study further suggested that competent retrieval of letter names contributes to the rapid and legible writing among kindergarten children. According to Fears and Lockman,[12] this fluency is attributed to a reduction in the information-gathering process prior to handwriting. This study required children to copy three familiar English letters and three unfamiliar Cyrillic symbols. The findings revealed that all the children required additional time to copy unfamiliar Cyrillic symbols. In addition, younger children needed more time than older children during the information-gathering phase.[18] Letter knowledge affected the phase of writing the letter rather than the fluency of movement while drawing letter features. Therefore, it was concluded that a lack of letter knowledge causes disfluency in handwriting.[16] According to Gerde, *et al.*,[17] the most important predictor of children's name writing was letter knowledge, specifically capital letters.

Motor Skills (n = 3)

Motor skills were categorized into fine and gross motor skills. A study identifying the relationship between handwriting and fine motor skills found that fine motor

Table 1. Study Appraisal using McMaster Critical Review

	Fears and Lockman[12]	Fitjar, *et al.*,[16]	Gerde, *et al.*,[17]	Reutzel, *et al.*,[18]	Seo[19]	Dayem, *et al.*,[20]	Pazeto, *et al.*,[21]	Valcan, *et al.*,[22]	Gerth, *et al.*,[23]	No and Choi[24]
Study purpose										
Was the purpose clearly stated?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Literature										
Was relevant background literature review?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Sample										
Was the sample described in detail?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Was the sample size justified?	x	x	x	x	x	x	x	x	x	x
Outcomes										
Were the outcome measures reliable?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Were the outcome measures valid?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Results										
Results were reported in terms of statistical significance?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Were the analysis method(s) appropriate?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Clinical importance was reported.										
Dropouts were reported?	✓	✓	x	x	✓	x	✓	✓	✓	x
Conclusions and implications										
Conclusions were appropriate given study methods and results.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Table 2. Descriptive Summary of Reviewed Studies

Author	Year	Country	Design	Sample Size	Participant Characteristics	Key Findings
Fears and Lockman[12]	2018	United States	Observational	n = 40	Mean age: 69.60 months	Children copied familiar English words more efficiently than unfamiliar Cyrillic symbols. Unfamiliar Cyrillic symbols needed more regathering information process during the act of writing than familiar English letters.
Fitjar, *et al.,*[16]	2021	Germany	Observational	n = 176	Mean age: 74.6 months Sex: 90 boys, 86 girls	Pen control ability (garlands and figure eights) could predict the fluency of copying characters. Good letter knowledge (phoneme to grapheme encoding) allowed children to copy letters and symbols proficiently.
Gerde, *et al.,*[17]	2012	United States	Observational	n = 103	Mean age: 47.35 months Sex: 59 boys, 44 girls	Letter knowledge and fine motor skills were more significant predictors of name writing than the other factors analyzed.
Reutzel, *et al.,*[18]	2017	United States	Observational	n = 48	Sex: 23 boys, 25 girls	A high correlation between letter naming and letter-writing fluency.
Seo[19]	2018	South Korea	Observational	Preschool children n = 52	Mean age: 69.19 months Sex: 23 boys, 29 girls	Fine motor precision and in-hand manipulation skills were found as components that could influence handwriting legibility.
Dayem, *et al.,*[20]	2015	Egypt	Observational	Group A n = 54 Group B n = 46	Group A Mean age: 56.7 months Sex: 29 boys, 25 girls Group B Mean age: 64.1 months Sex: 28 boys, 18 girls	Gross motor skills were strongly correlated to the speed of handwriting.
Pazeto, *et al.,*[21]	2014	Brazil	Observational	Kindergarten I n = 37 Kindergarten II n = 53	Kindergarten I Mean age: 4.35 years Sex: 19 boys, 18 girls Kindergarten II Mean age: 5.30 years Sex: 27 boys, 26 girls	In the field of executive function, only attention was significantly affected by the school level. Executive function correlated with handwriting in both groups of kindergarten.
Valcan, *et al.,*[22]	2020	Australia	Observational	T1 n = 166 T2 n = 155	T1 Mean age: 5 years 8 months Sex: 81 boys, 85 girls T2 Mean age: 6 years 5 months Sex: 74 boys, 81 girls	Executive function could predict academic achievement, specifically reading and writing. Immediate effects pathway supported in handwriting automaticity and writing quality. The growth potential model supported reading and writing quality.
Gerth, *et al.,*[23]	2016	Germany	Observational	Preschool children n = 25	Mean age: 5.4years Sex: 8 boys, 17 girls	Better handwriting quality during paper writing. Better velocity was found for tablet writing compared to paper.
No and Choi[24]	2021	South Korea	Observational	n = 97	Mean age: 79.06 months Sex: 39 boys, 58 girls	A larger print was recorded on the tablet. Writing speed improved on the tablet. Lesser pressure on the tablet.

precision, in-hand manipulation skills, and handwriting legibility were related.[19] This study concluded that fine motor precision and in-hand manipulation skills contribute to handwriting legibility and that in-hand manipulation skills should be included once children learn how to write. A study by Gerde, *et al.*,[17] discovered fine motor skills to be the most crucial predictor of name-writing skills in the development of children's handwriting. A study on gross motor activities reported that gross motor activities influence handwriting, especially handwriting speed, in both copying and dictation skills.[20]

Executive Function (n = 2)

Two studies reported the relationship between executive function and handwriting.[21,22] Executive function was measured via activities involving working memory, shifting ability,[22] inhibition,[21,22] cognitive flexibility, and selective attention.[21] Based on the two reviewed articles, the executive function had the ability to predict children's handwriting achievement.[21,22] A related study described the relationship between executive function and handwriting in two groups of kindergartners: kindergarten I and kindergarten II.[21] The findings showed that executive function correlated with the handwriting of both groups of children, and the study recommended executive function as a target of intervention to improve academic achievement.[21] Another study investigated the mechanisms that enabled executive function to predict later academic success.[22] The findings indicated that executive function could predict handwriting automaticity via the immediate effects pathway and writing quality via both the immediate effects pathway and growth potential

pathway.[22]

Writing Surface (n = 2)

Two studies had identified the effects of the writing surface on handwriting by comparing writing on tablets and paper.[23,24] One study investigated the effect of the writing surface using three tasks: graphomotor abilities, visuomotor abilities, and automatic handwriting abilities.[23] Visuomotor is the coordination of visual perception and motor movements, whereas the task involved in this study was copying geometric forms. The study's findings indicated that children had better handwriting quality while writing on paper because they were not automatized in their writing actions, which made writing on tablets difficult due to the lack of proprioceptive feedback.[23] Regarding the handwriting process, tablet writing was found to be faster than paper writing because of the smoother surface of the tablet. Therefore, a smoother surface requires additional control and challenges the learners' handwriting.[23] In their study, No and Choi,[24] evaluated three factors: print size, writing speed, and writing pressure. The study explained that a larger print was recorded on the tablet, and the pen was found to move faster and applied less pressure on the tablet.[24] This is consistent with Gerth, *et al.*,[23] reporting that writing on a tablet reduces handwriting clarity while increasing the writing speed and print size.

Discussion

Of 10 quantitative studies on handwriting development in preschool children in this review, there were four factors: executive function, letter knowledge, motor skills, and writing surface, were discovered. Generally, all the factors discovered in this review were interconnected and consequently contributed to handwriting development.

Executive function is a cognitive process involving working memory, inhibitory control, and cognitive flexibility.[25-27] This review showed that executive function contributed to the prediction of children's handwriting development. Executive function facilitated children memorizing what they learned, shifting and controlling attention, and responding to stimulation appropriately. In line with Rosenblum,[28] efficient handwriting performance required components of executive function, including shifting, working memory, planning and organization, monitoring, and material organization. Moreover, executive function was found to be significantly associated with the growth of letter knowledge.[29]

Letter knowledge facilitated automaticity in handwriting. Inadequate letter knowledge disrupts automaticity because children cannot automatically retrieve letters from memory.[12] A study found that improving handwriting automaticity could contribute to longer and better text writing.[30] Therefore, lack of handwriting automaticity reduced writing speed as children might require references to write the letters. When the children used references, their gaze will frequently shift from the reference to the writing surface. Hence, letter knowledge significantly contributes to facilitating the handwriting process. Moreover, good executive function encouraged the learning and memorization of letter knowledge.

Motor skills were further divided into gross and fine motor skills; gross motor skills involved large muscle groups, and fine motor skills involved small muscle groups. Both fine and gross motor skills were necessary for handwriting acquisition.[31] Gross motor skills were necessary for maintaining a stable and correct posture while writing in a classroom.[20] Fine motor skills were equally important and necessary to hold and manipulate writing tools during the handwriting process.[26] Writing tools, such as crayons, pencils, and pencils color, are usually small. Therefore, fine motor precision and hand manipulation skills were required to manipulate small writing tools. In addition, the writing surface could influence fine motor skills. Smoother writing surfaces required children to have good fine motor skills to manipulate writing tools effectively.

The handwriting process was guided by proprioceptive feedback. However, low-friction writing surfaces such as tablets reduce proprioceptive feedback, causing writers to rely more on visual feedback.[32] According to dynamic system theory, sensory perception and motor systems are coupled and continually interact to acquire new skills.[6] Generally, sensory input is transmitted to the brain to generate motor commands before producing written output. A study comparing the effect of a smooth tablet surface on handwriting quality and kinematics in children in grades 9 and 2 found that handwriting on a tablet reduced letter legibility and augmented letter size in both age groups.[33] The smoother surface demanded greater graphomotor control due to the lower proprioceptive feedback.[23]

The findings coincided with the conceptual framework of Malay language handwriting.[34] This framework explains that neuromotor development (fine and gross motor skills), ergonomics (writing surface), orthography (letter knowledge), and cognitive factors all contribute to Malay handwriting (executive function).[34] According to the framework, neuromotor development and ergonomic factors are acquired from the occupational therapy discipline.[34] While, the education discipline lays out most information on linguistic and memory factors. Hence, the involvement of multidisciplinary teams is essential for handwriting development.[34]

According to Dinehart,[6] the best strategy for teaching handwriting among young children before schooling was unclear; thus, this study encouraged practitioners to de-

velop effective handwriting strategies. Accordingly, the findings from this review could guide teachers, parents, and occupational therapists to implement effective strategies in teaching handwriting. For instance, as the review explained, smoother writing surfaces demand more graphomotor control and provide lower proprioceptive feedback; therefore, teaching handwriting using pencils and paper promises more benefits. Moreover, pencils and paper have been extensively used in classroom learning. Additionally, based on both gross and fine motor skills review explains that teachers, parents, or occupational therapists should focus on both skills and not only on fine motor skills.

Furthermore, these findings encouraged the public to obtain more information on the influential factors to handwriting development. Awareness of these factors could make the public realize that handwriting is a complex task that depends on multiple components. The public could be aware of the possibility for children to face handwriting difficulty, even though the writing task could be perceived as easy for adults. Therefore, less awareness about this issue may cause people to think they are lazy. Awareness and understanding of this issue could prevent late intervention programs and negative perceptions towards children with handwriting difficulty.

The strength of this review was that it might be the first systematic review to examine the factors influencing handwriting development among preschool children. Children begin learning handwriting at an early age; thus, the factors discovered may be beneficial for improving handwriting acquisition among preschool children. However, this review does not include a study of ergonomic factors. According to Case-Smith and O'Brien,[1] ergonomics factor, such as sitting postures and desk and chair height, should be analyzed. Second, this review also incorporated a study involving the Korean (non–English alphabet). The Korean and English alphabets have distinct features. Therefore, it would be ideal for explaining this distinct feature and its relationship with handwriting development in children.

Conclusion

Overall, this review explains the four factors influencing handwriting development and provides an understanding of the relationship between all the factors discovered. This review supports the notion that handwriting depends on various components, including executive function, letter knowledge, motor skills, and the writing surface. Occupational therapists, educators, and parents may implement the factors discovered to facilitate handwriting acquisition among preschool children. For instance, before handwriting learning, educators may implement letter knowledge activities such as alphabet flashcards, and tablet use may be avoided to teach handwriting among preschool children.

These findings also help raise public awareness of the factors influencing handwriting development. Therefore, more people would be aware of this issue, and more strategies could be developed to support handwriting development among children. However, as most handwriting studies examine school-aged children, the findings are insufficient to make definitive clinical recommendations. More Randomized Controlled Trials studies examining handwriting development among preschool children should be conducted to provide more conclusive and comprehensive evidence.

Abbreviations

IFG: Inferior Frontal Gyrus; PRISMA: Preferred Reporting Items for Systematic Review and Meta-analyses; PICO: Patient/population, Intervention, Comparison, Outcome; ASD: Autism Spectrum Disorder; DCD: Developmental Coordination Disorder.

Ethics Approval and Consent to Participate

The ethical approval was granted by the Medical Research and Innovation Secretariat, Universiti Kebangsaan Malaysia (JEP-2021-474).

Competing Interest

The authors declare that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

This review used four databases: The data PubMed, ERIC, CINAHL, and Google Scholar.

Authors' Contribution

ZI contributed substantially to the concept, work design, and manuscript drafting. ZI and NAR screened the title and abstract. ZI, NAR, MK, and FWY were involved in reviewing 24 articles to reach a final consensus. ZI and NAR reviewed the final ten articles. NAR, MK, and FWY were involved in critically reviewing the manuscript's content, and NAR revised the final version to be published.

Acknowledgment

The authors wish to thank everyone who contributed to this study, especially Universiti Kebangsaan Malaysia and the Ministry of Higher Education, for providing research funding (FRGS/1/2020/SSI0/UKM/03/2).

References

1. Case-Smith J, O'Brien J. Occupational therapy for children and adolescents. 7th ed. St Louis: MI: Elsevier Mosby; 2015.
2. Thibon LS, Gerber S, Kandel S. The elaboration of motor programs for the automation of letter production. Acta Psychologica. 2018; 182: 200-11.
3. James KH, Engelhardt L. The effects of handwriting experience on

functional brain development in pre-literate children. Trends in Neuros Edu. 2012; 1 (1): 32-42.
4. Mayer C, Wallner S, Budde-Spengler N, Braunert S, Arndt PA, Kiefer M. Literacy training of kindergarten children with pencil, keyboard or tablet stylus: the influence of the writing tool on reading and writing performance at the letter and word level. Front Psychol. 2020; 10.
5. Zemlock D, Vinci-Booher S, James KH. Visual-motor symbol production facilitates letter recognition in young children. Read Writ. 2018; 31 (6): 1255-71.
6. Dinehart LH. Handwriting in early childhood education: current research and future implications. J Early Childhood Literacy. 2014; 15 (1): 97-118.
7. Chung PJ, Patel DR, Nizami I. Disorder of written expression and dysgraphia: definition, diagnosis, and management. Translational Pediatrics. 2020; 9 (S1).
8. Biotteau M, Danna J, Baudou E, Puyjarinet F, Velay JL, Albaret JM, et al. Developmental coordination disorder and dysgraphia: signs and symptoms, diagnosis, and rehabilitation. Neuropsychiatric Disease and Treatment. 2019; 15: 1873–85.
9. Mekonnen AM. Specific learning disabilities in the eyes of school-teachers in Ethiopia. Read Writ Quarterly. 2022; 1–11.
10. Duiser I, Ledebt A, van der Kamp J, Savelsbergh G. Persistent handwriting problems are hard to predict: a longitudinal study of the development of handwriting in primary school. Research In Developmental Disabilities. 2020; 97: 103551.
11. Piller A, Torrez E. Defining occupational therapy interventions for children with fine motor and handwriting difficulties. J Occup Ther, Sch, Early Interv. 2019; 12 (2): 210-24.
12. Fears NE, Lockman JJ. How beginning handwriting is influenced by letter knowledge: visual-motor coordination during children's form copying. J Exp Chil Psyc. 2018; 171: 55-70.
13. Asaba E, Nakamura M, Asaba A, Kottorp A. Integrating occupational therapy specific assessments in practice: exploring practitioner experiences. Occup Ther Int. 2017; 2017: 1-8.
14. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The Prisma 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021; 372: n71.
15. Tawfik GM, Dila KAS, Mohamed MYF, Tam DNH, Kien ND, Ahmed AM, et al. A step-by-step guide for conducting a systematic review and meta-analysis with simulation data. Trop Med Heal. 2019; 47 (1): 46.
16. Fitjar CL, Rønneberg V, Nottbusch G, Torrance M. Learning handwriting: factors affecting pen-movement fluency in beginning writers. Front Psychol. 2021; 12.
17. Gerde HK, Skibbe LE, Bowles RP, Martoccio TL. Child and home predictors of children's name writing. Chil Dev Res. 2012; 2012: 1-12.
18. Reutzel P, Mohr KA, Jones CD. Exploring the relationship between letter recognition and handwriting in early literacy development. J Earl Chil Lit. 2017; 19 (3): 349-74.
19. Seo SM. The effect of fine motor skills on handwriting legibility in preschool age children. J Physic Ther Sci. 2018; 30 (2): 324-7.
20. Dayem T, Salem E, Hadidy E. Correlation between gross motor activities and hand writing skills in elementary school children. Trends in Applied Sciences Research. 2015; 10 (5): 259-69.
21. Pazeto T, Seabra A, Dias N. Executive functions, oral language and writing in preschool children: development and correlations. Paidéia (Ribeirão Preto). 2014; 24 (58): 213-22.
22. Valcan D, Davis H, Pino-Pasternak D, Malpique A. Executive functioning as a predictor of children's mathematics, reading and writing. J App Dev Psychol. 2020; 70: 101196.
23. Gerth S, Klassert A, Dolk T, Fliesser M, Fischer M, Nottbusch G, et al. Is handwriting performance affected by the writing surface? Comparing preschoolers', second graders', and adults' writing performance on a tablet vs. paper. Front Psychol. 2016; 7: 1308.
24. No B, Choi N. Differences in graphomotor skills by the writing medium and children's gender. Edu Sci. 2021; 11 (4): 162.
25. Fang Y, Wang J, Zhang Y, Qin J. The relationship of motor coordination, visual perception, and executive function to the development of 4–6-year-old Chinese preschoolers' visual motor integration skills. BioMed Res Int. 2017; 2017: 1-8.
26. McClelland M, Cameron C. Developing together: the role of executive function and motor skills in children's early academic lives. Early Childhood Research Quarterly. 2019; 46: 142-151.
27. Zelazo P. Executive function: reflection, iterative reprocessing, complexity, and the developing brain. Dev Rev. 2015; 38: 55-68.
28. Rosenblum S. Inter-relationships between objective handwriting features and executive control among children with developmental dysgraphia. PLOS ONE. 2018;13 (4): e0196098.
29. Zhang C, Bingham G, Quinn M. The associations among preschool children's growth in early reading, executive function, and invented spelling skills. Read Writ. 2017; 30 (8): 1705-28.
30. Alves RA, Limpo T, Fidalgo R, Carvalhais L, Pereira LA, Castro SL. The impact of promoting transcription on early text production: effects on bursts and pauses, levels of written language, and writing performance. J Edu Psychol. 2016; 108 (5): 665–79.
31. Cameron CE, Brock LL, Murrah WM, Bell LH, Worzalla SL, Grissmer D, et al. Fine motor skills and executive function both contribute to kindergarten achievement. Child Development. 2012; 83 (4): 1229-1244.
32. Guilbert J, Alamargot D, Morin M. Handwriting on a tablet screen: role of visual and proprioceptive feedback in the control of movement by children and adults. Human Move Sci. 2019; 65: 30-41.
33. Alamargot D, Morin M. Does handwriting on a tablet screen affect students' graphomotor execution? A comparison between Grades Two and Nine. Human Move Sci. 2015; 44: 32-41.
34. Lee AS, Lee LW, Low HM, Ooi SC. Revisiting handwriting fundamentals through an interdisciplinary framework. Malays J Med Sci. 2022; 29 (1): 18-33.

Faradilah, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 243-250
DOI: 10.21109/kesmas.v17i4.6218

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Breastfeeding Duration More than 18 Months Possibly Lowers the Risk of Language Development Delay in Children Aged 18–35 Months

Andi Faradilah[1,2*], Andi Musafir Rusyaidi[3], Syatirah Jalaluddin[4], Ary I Savitri[5]

[1]Department of Nutrition, School of Medicine, Universitas Islam Negeri Alauddin, Makassar, Indonesia, [2]Department of Nutrition, Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia, [3]Department of English Language Teaching, Institut Agama Islam Negeri, Palopo, Indonesia, [4]Department of Pediatric, School of Medicine, Universitas Islam Negeri Alauddin, Makassar, Indonesia, [5]Clinical Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center, Utrecht, the Netherlands

Abstract

Studies have demonstrated the benefits of breastfeeding (BF) on children's cognitive function and language development. However, most cognitive and language tools used in these studies have limited ability to identify children's language development delays. The Language Development Survey (LDS) is expected to provide detailed information on children's language development. This study aimed to examine the association between BF duration and children's LDS. A questionnaire was administered to 286 BF mothers to obtain information on their BF duration, and LDS was employed to assess children's language development. Language delays were detected in 91 (31.8%) children (LDS-vocabulary) and 35.7% children (LDS-phrase). This study also found that children who were breastfed for ≤6 months and 7–18 months had an adjusted OR (AOR) of 0.86 of LDS-vocabulary, and 0.8 of LDS-phrase, whereas children who were breastfed for >18 months had AOR's LDS-vocabulary of 0.57 and LDS-phrase of 0.46. This study found no significant association between BF duration and LDS score. Nevertheless, BF duration of >18 months possibly lowers the risk of children's language development delay. More studies are required to investigate this observation's relationship with children's language development.

Keywords: breastfeeding, language development survey, phrase, vocabulary

Introduction

Breastfeeding (BF) benefits children's immune systems and determines their health and physical growth. Regarding cognitive development, the impact of BF duration on children's language development remains an ongoing debate. A study in Korea argues that the apparent advantages of "longer breastfeeding duration" on language development are often confounded by factors such as sociodemographic contexts, which should be considered in the analysis.[1] Furthermore, children's language development has rarely been assessed thoroughly.[2] Although some studies have extensively explored the relationship between BF and children's development, they focused less on language development.[3,4]

Pre-screening Developmental Questionnaire (PDQ) or Denver Developmental Screening Test (DDST) is the most widely applied assessment tool to assess children's cognitive and language development, especially in Indonesia.[5] However, some scholars in a review study have criticized the tool's limitation in determining comprehensive language assessment.[6] This tool assesses children's language development using only 1-2 questions, resulting in vague diagnoses and recommendations about children's language ability. Consequently, the diagnosis of children's language development problems may be delayed. The limitations of the DDST indicate that employing a more comprehensive method to assess, diagnose, and further provide recommendations on children's language development is crucial in assessing children's cognitive and language development.

To address this concern, this study employed the Language Development Survey (LDS), known for its excellent test-retest reliability and internal consistency, along with its high sensitivity and specificity in identifying language delays in children through detailed and specific words or vocabulary lists.[2] Furthermore, the LDS's advantages in identifying children's language development have been confirmed by several studies in various contexts, including in Korea,[7] Italy,[8] and Poland.[9] By employing LDS, this study was expected to provide comprehensive data on children's language development in the Indonesian context, which remains underexplored,

Correspondence: Andi Faradilah, Department of Nutrition, School of Medicine, Universitas Islam Negeri Alauddin, Sultan Alauddin Street No. 63, Makassar, South Sulawesi, Indonesia, 90222, E-mail: a.faradilah@uin-alauddin.ac.id, Phone: +62 852 4203 2134*

Received : September 08, 2022
Accepted : October 19, 2022
Published : November 30, 2022

especially when the development is attached to BF practices. Therefore this study primarily focused on the association between BF duration and children's language development using LDS.

Method

A cross-sectional study was consecutively conducted at four primary health care (PHC) in South Sulawesi Province, Indonesia: Samata Primary Health Care in Gowa District, Wara Primary Health Care in Palopo City, Bulukunyi Primary Health Care in Takalar District, and Bontomate'ne Primary Health Care in Jeneponto District. All children in this study were the age of 18-35 months and breastfed or being breastfed during the data collection period (December 2016 to January 2017 in Gowa District and Palopo City; and November to December 2019 in Takalar and Jeneponto Districts). Children diagnosed with delayed development were excluded from the study. Written informed consent was obtained from the mothers to participate in the study (Figure 1). A total of 286 children were included: 76 from Samata PHC Gowa District; 94 from Wara PHC Palopo City; 70 from Bulukunyi PHC Takalar District; and 46 from Bontomate'ne PHC Jeneponto District.

Data on BF duration were obtained from a questionnaire distributed among the mothers. The BF duration was categorized into three parts: ≤6 months, 7–18 months, and >18 months. A separate questionnaire was used to obtain demographic data, including mother and children status. Mothers' information including age, occupation, family income, family language, health condition during BF (diseases or illnesses [yes/no]), pregnancy information (frequency, number of antenatal care visits [sufficient if ≥3 visits or insufficient if <3 visits during pregnancy] and method of pregnancy delivery),[10,11] as well as information regarding whether family support was provided during BF,[12,13] was obtained.

Information on their breastmilk production was also gathered (yes/no).[14] Formula promotion was determined based on mothers' awareness of infant formula, based on the information from health care professionals. Maternal knowledge of BF was grouped into sufficient (>5 correct answers) and insufficient knowledge (≤5 correct answers).[12] Additionally, mothers' BF practice was categorized into good (performing 3 or 4 BF practice components), average (performing 2 BF practice components), and poor (performing only 1 BF practice component).[15] Family's smoking habits were classified into yes or no, whether a family member is a smoker. Additional information on children, such as their birth weight, health status, birth order among the siblings, and the total number of children in the family, were obtained from the questionnaire. Further, children were classified based on whether they fell ill during the BF period. All questionnaires were filled out with the assistance of a skilled enumerator.

Maternal weight and height were measured using the Omron digital weight scale and GEA medical microtoise stature meter, respectively. Maternal body mass index (BMI) was calculated using the BMI formula (BMI =

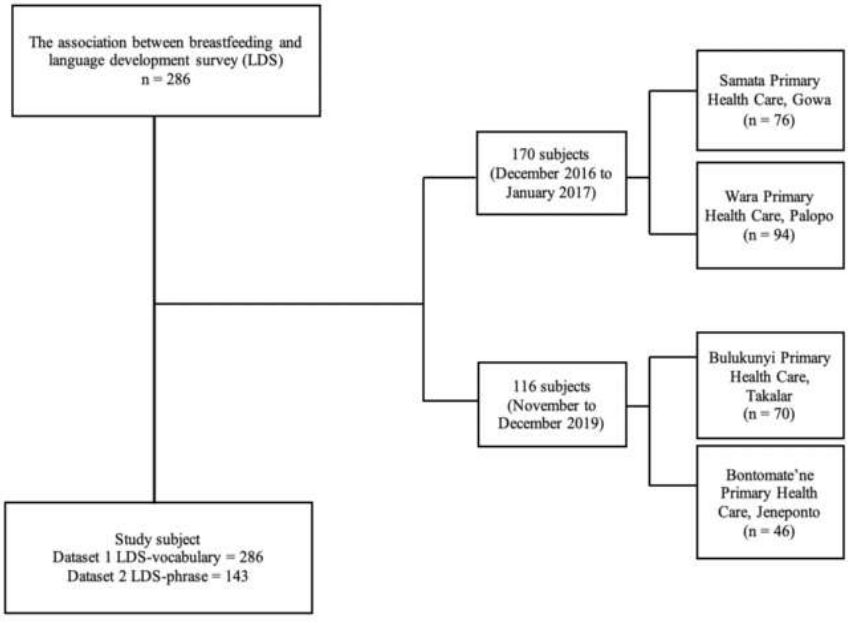


Figure 1. Participation Recruitment Flow

kg/m2), where kg represents maternal weight in kilograms and m2 represents their height in meters squared.[16] Children's nutritional status was classified into severely underweight (< −3SD), underweight (−3SD to < −2SD), normal (−2SD to 1SD), and at risk of being overweight (> 1SD) using the weight-for-age Z-Score Table based on the Regulations of the Minister of Health of the Republic of Indonesia Number 2 of 2020 concerning Child Anthropometry Standards.[17]

To identify children's language abilities, the LDS was employed and adapted. The survey was developed by Rescorla in 1989 as an alternative to previously designed language assessment tools, which were inefficient and inadequate to measure children's language ability.[8] The survey, designed as a screening tool and had to be completed by parents (especially mothers), can identify children's language (vocabulary and phrase productions) and predict a potential language delay in children aged 18–35 months. The validation studies of LDS were conducted and showed a high correlation with three other similar assessment tools.[18]

The LDS-vocabulary contains 310 vocabulary words arranged by semantic category. Parents' answers in the survey represent words or vocabulary uttered by their children. The total number of words or vocabulary was summarized by a skilled enumerator to calculate the LDS-vocabulary score. Parents with children aged 24 months or older were asked to list the five longest and best phrases their children could produce. The average number of words for the five phrases was calculated to assess their LDS-phrase score. Interpretations of LDS scores—vocabularies and phrases—were conducted by grouping children according to age and sex. Children's LDS-vocabulary was scored on the basis of their age groups (e.g., 18–23 months, 24–29 months, or 30–35 months). Similarly, children's LDS-phrase was scored on the basis of their age groups (e.g., 24–29 months and 30–35 months). Furthermore, a mean score technique was applied to asses children's LDS-phrase production.[2]

The data were presented descriptively as mean ± standard deviation (SD) for normally distributed data, median (interquartile range/IQR) for non-normally distributed data. While, data with frequency was presented as percentage of collected data. The prevalence rate among different BF groups was compared and calculated using Pearson's Chi-square test. The association between BF and LDS score (vocabulary and phrase) was examined using logistic regression analysis (univariate and multivariate). First, Model 1 (crude model) was conducted to identify whether an unadjusted association exists between the determinant and the outcome. Then, several potential confounder factors (maternal age) were consecutively included in Model 2; Model 3 was augmented (Model 2 + occupation), and Model 4 was further augmented (Model 3 + family income + the number of children). Model 4 was considered the fully adjusted model. The changes in the odds ratio were evaluated using the adjustments from Models 1 to 4, and the results were considered significant at p-value<0.05. All statistical analyses were conducted using the IBM Statistical Package for Social Sciences (IBM SPSS Statistics for Windows; IBM Corp., Armonk, New York, USA) Version 26.

Results

Among the 286 children in this study, the majority (55.2%) were breastfed for >18 months. The number of children who were breastfed for 7–18 months and six months were 78 (27%) and 50 (17.5%), respectively. The mean age of the children was 26.51±5.1 months. Most mothers were housewives with a low to moderate family income (less than one million and up to three million rupiahs per month) and had normal BMI (24.88±12.65) with a mean age of 30±6.1 years. The overall prevalence of underweight and severely underweight children was 18.8% and 6.5%, respectively. The proportion of severely underweight children was the highest in those with a BF duration of 7–18 months (13%), whereas overweight was 6.1% in children with a BF duration of six months. In line with family support during BF, most mothers (57.7%) confirmed receiving support, and their BF practices were predominantly classified as good (45.8%) (Table 1).

Moreover, mothers receiving less infant formula promotion and having adequate milk production appeared to have the longest BF duration (>18 months). During the BF period, the health status of the mothers was similar across the BF duration groups and the children's health status. Apparently, having only one child in the family influenced the BF duration. In a two-children family, the highest prevalence of BF duration was 7–18 months, whereas, in a single-child family, the BF duration was longer. However, the birth order of children did not differ among the BF duration groups (Table 1).

Association of Breastfeeding Duration and Children's Language Development (Vocabulary Score and Phrase Score)

The LDS-vocabulary scores of the 286 children revealed that 91 children (31.8%) experienced language delays. Children who were breastfed for 7–18 months had the highest percentage (33.3%) of delayed vocabulary development, according to their age. Data analysis on the association between BF-group and LDS-vocabulary score revealed a similar prevalence in normal vs. delayed LDS-vocabulary scores across different BF duration groups (p-value = 0.937) (Table 2). The LDS-phrase score was assessed in the subset of children (24–35

months). The prevalence of delayed LDS-phrase score was 35.7%, consistent with LDS-vocabulary; the highest delayed LDS-phrase was observed in the BF group of 7–18 months (39.5%). The association between BF duration and the event of delayed LDS-phrase score was similar within BF groups (p-value = 0.849) (Table 2).

Association of Breastfeeding Duration and Language Development (Vocabulary Scores)

The association of BF duration and delayed vocabulary development was analyzed using logistic regression with adjustments for the maternal age, occupation, family income, and the number of children. The result showed

Table 1. Subject Characteristics

Variable	Category	≤6 months (n = 50)	7–18 months (n = 78)	>18 months (n = 158)	p-value
Maternal and family characteristics					
Age (median, IQR)		31 (19–48)	30 (17–50)	30 (18–75)	0.23[a]
BMI (median, IQR)		22.7 (15–35)	23.3 (15–160)	23.15 (9.5–157.5)	0.76[a]
Maternal occupation (n, %)	Civil servant	3 (10.7)	3 (7.3)	6 (6.3)	0.04[b]
	Self-employed (business)	0	2 (4.9)	6 (4.7)	
	Housewife	24 (85.7)	35 (85.4)	87 (68.5)	
	Laundress, laborer, domestic assistant	1 (3.6)	1 (2.4)	26 (20.5)	
Family income (n, %)	<1 million (IDR)	16 (32)	30 (38.5)	63 (40.1)	0.28[b]
	1–3 million (IDR)	21 (42)	34 (43.6)	74 (47.1)	
	>3 million (IDR)	13 (26)	14 (17.9)	20 (12.7)	
Maternal health status (n, %)	Healthy	15 (53.6)	16 (39)	48 (47.1)	0.47[b]
	Sick	13 (46.4)	25 (61)	54 (52.9)	
Pregnancy record					
Number of antenatal care visits (n, %)	Sufficient	24 (88.9)	35 (89.7)	80 (80.8)	0.33[b]
	Insufficient	3 (11.1)	4 (10.3)	19 (19.2)	
Number of pregnancies (n, %)	1	4 (14.3)	5 (12.2)	29 (28.4)	0.22[b]
	2	13 (46.4)	14 (34.1)	38 (37.8)	
	3	5 (17.9)	12 (29.3)	20 (19.6)	
	>3	6 (21.4)	10 (24.4)	15 (14.7)	
Method of delivery (n, %)	Vaginal birth	24 (85.7)	33 (80.5)	91 (89.2)	0.38[b]
	C-section	4 (14.3)	8 (19.5)	11 (10.8)	
Children's characteristics					
Sex (n, %)	Male	28 (56)	39 (50)	74 (46.8)	0.52[b]
	Female	22(44)	39(50)	84(53.2)	
Birth weight in grams (median, IQR)		3,000 (1,900–3,800)	3,000 (2,500–4,500)	3,000 (1,450–4,200)	0.54[a]
z-weight-age (n, %)	Normal	40 (81.6)	50 (64.9)	108 (70.5)	0.07[b]
	Underweight	5 (10.2)	17 (22.1)	56 (19.9)	
	Severely underweight	1 (2)	10 (13)	23 (8.2)	
	Overweight	3 (6.1)	0	4 (1.4)	
Number of siblings (n, %)	1	14 (28)	17 (21.8)	53(33.5)	0.45[b]
	2	20 (40)	32 (41)	54(34.2)	
	≥3	16 (32)	29 (37.2)	51(32.3)	
Children's birth order (n, %)	1	19 (38)	24 (30.8)	54 (34.3)	0.94[b]
	2	15 (30)	28(35.9)	52 (32.9)	
	≥3	16 (32)	26 (33.3)	52 (32.9)	
Children's health status (n, %)	Healthy	9 (32.1)	11 (26.8)	23 (22.8)	0.58[b]
	Sick	19 (67.9)	30 (73.2)	78 (77.2)	
Breastfeeding record					
Perceived breastmilk production (n, %)	Sufficient	24 (85.7)	39 (95.1)	96 (94.1)	0.25[b]
	Insufficient	4 (14.3)	2 (4.9)	6 (6.59)	
Maternal knowledge of BF (n, %)	Sufficient	27 (96.4)	40 (97.6)	98 (97)	0.96[b]
	Insufficient	1 (3.6)	1 (2.4)	3 (3)	
Exposure to infant formula promotion (n, %)	No	15 (53.6)	27 (65.9)	74 (72.5)	0.16[b]
	Yes	13 (46.4)	14 (34.1)	28 (27.5)	
Maternal practice of BF (n, %)	Good	22 (48.9)	28 (35.9)	81 (51.3)	0.15[b]
	Average	10 (22.2)	24 (30.8)	44 (27.8)	
	Poor	13 (28.9)	26 (33.3)	33 (20.9)	
Family support (n, %)	Yes	26 (92.9)	38 (92.7)	101 (99)	0.09[b]
	No	2 (7.1)	3 (7.3)	1 (1)	
Maternal and family's language (n, %)	Native language	30 (60)	37 (47.4)	73 (47.4)	0.51[b]
	Local language	9 (18)	20 (25.6)	44 (28.6)	
	Mix language	11 (22)	21 (26.9)	37 (24.0)	
Smoking status of family members (n, %)	Smoker	7 (25)	9 (22.5)	24 (23.8)	0.97[b]
	Non-smoker	21(75)	31(77.5)	77(76.5)	

Notes: [a]Kruskal Wallis for numerical data, [b]Pearson's Chi-square for categorical data
IQR = Interquartile Range, IDR = Indonesian Rupiah, z-weight-age = z Score Weight per Age, BF = Breastfeeding.

Table 2. Language Development Survey Scores by Breastfeeding Duration Groups

Variable	Category	Total	≤6 months	7–18 months	>18 months	p-value
LDS-vocabulary (n = 286)	Normal	195 (68.2)	34 (68)	52 (66.7)	109 (69.0)	0.937
	Delayed	91 (31.8)	16 (32)	26 (33.3)	49 (31.0)	
LDS-phrase[b,c] (n = 143)	Normal	92 (64.3)	19 (65.5)	23 (60.5)	50 (65.8)	0.849
	Delayed	51 (35.7)	10 (34.5)	15 (39.5)	26 (34.2)	

Notes: LDS = Language Development Survey.
Interpretation of LDS-vocabulary and LDS-phrase scores were adjusted on the basis of children's sex and age. Percentages are mentioned within parentheses.
[a]LDS-vocabulary categories were based on the analysis of all subjects (n = 286), [b]LDS-phrase categories were based on the analysis of children aged 24–35 months (n = 143), [c]Missing data for the total phrase was 30%.

Table 3. Association of Breastfeeding Duration and Language Development (Vocabulary Scores)

Model (n = 286)	Category	Odds Ratio (95% CI)	p-value
Model 1 (Crude OR)	≤6 months	Reference	
	7–18 months	1.06 (0.50–2.27)	0.88
	>18 months	0.95 (0.48–1.89)	0.89
Model 2 (Model 1 + maternal age)	≤6 months	Reference	
	7–18 months	1.01 (0.47–2.17)	0.98
	>18 months	0.89 (0.45–1.78)	0.74
Model 3 (Model 2 + maternal occupation)	≤6 months	Reference	
	7–18 months	1.00 (0.37–2.76)	0.99
	>18 months	0.68 (0.28–1.65)	0.39
Model 4	≤6 months	Reference	
(Model 3 + family income + number of children)	7–18 months	0.86 (0.30–2.47)	0.79
	>18 months	0.57 (0.23–1.42)	0.23

Note: CI = Confidence Interval

that the risk of delayed LDS-vocabulary score was lower in the BF duration group of >18 months as compared to the BF duration group of ≤6 months, although it was not statistically significant (OR [95% CI] = 0.57 [0.23–1.42]; p-value = 0.23) (Table 3, Model 4). Model 4 was the fully adjusted model for the association between BF duration and delayed vocabulary development (measured by the LDS-vocabulary score). Although insignificant, the analysis showed that a longer BF duration (>18 months) could effectively reduce the risk of delayed vocabulary development.

Association of Breastfeeding Duration and Language Development (Phrase Scores)

In line with the findings on LDS-vocabulary, this study also calculated the association between BF duration and delayed LDS-phrase scores in children aged 24–35 months. Similarly, children with a longer BF duration had a lower risk of delayed phrase development than the reference group (BF ≤6 months). In the fully-adjusted model, the risk of delayed phrase development in children with a BF duration of >18 months was less than half the odds of those with a BF duration of ≤6 months (OR [95% CI] = 0.46 [0.14–1.67]; p-value = 0.25) (Table 4, Model 4). A huge decline in OR was observed when maternal employment status variable was entered into the model. Data analysis showed a clear trend toward lower odds ratios, as shown in Model 1 to Model 4, suggesting that longer BF duration might prevent delayed phrase development.

Following the missing data in this study, a sensitivity analysis was performed to calculate the estimated coefficients of the complete data (n = 171), and a similar result was found with the total sample (n = 286). The results of the fully adjusted model of LDS-vocabulary unveiled that the risk of BF duration >18 months was less than the ≤6 months one (OR [95% CI] = 0.61 [0.24–1.57]; p-value = 0.78). Along with this result, the risk of the LDS-phrase score of BF duration of >18 months (OR [95% CI] = 0.28 [0.62–1.23], p-value = 0.09) were revealed to be less than the ≤6 months.

Discussion

Although this study found no association between BF duration and LDS scores, the adjustments for confounders revealed that a longer BF duration might prevent delayed language development. Maternal age, working status, family income, and children's number of siblings might affect the relationship between BF duration and language development. The above variables were po-

Table 4. Association of Breastfeeding Duration and Language Development (Phrase Score)

Model (n = 143)	Category	Odds Ratio (95% CI)	p-value
Model 1 (Crude OR)	≤6months	Reference	
	7–18 months	1.24 (0.45–3.38)	0.68
	>18 months	0.99 (0.40–2.43)	0.98
Model 2 (Model 1 + maternal age)	≤6 months	Reference	
	7–18 months	1.17 (0.42–3.25)	0.76
	>18 months	0.95 (0.38–2.36)	0.92
Model 3 (Model 2 + maternal occupation)	≤6 months	Reference	
	7–18 months	0.71 (0.17–2.91)	0.64
	>18 months	0.55 (0.17–1.79)	0.32
Model 4	≤6 months	Reference	
(Model 3 + family income + number of children)	7–18 months	0.80 (0.18–3.55)	0.78
	>18 months	0.46 (0.14–1.67)	0.25

Note: CI = Confidence Interval

tential confounders that must be considered to reveal the relation between BF duration and language development, including vocabulary improvement.[19]

Children's language development was determined by two main factors: internal and external factors.[20] The internal factors were related to children's genetics, health status, and nutritional status. In contrast, the external factors were linked to family environment, parents' level of education, children's school environment, and parenting patterns. Although some aspects of the internal and external factors had been included in this study, family environment and parenting patterns factors that specifically describe mother-child closeness were not studied.

Studies on BF duration yielded mixed results regarding the best BF duration influencing cognitive and language ability. These studies vary widely, ranging from less than six months, exclusive BF (6 months), more than six months, 12 months, to more than 12 months. Interestingly, a BF duration of 3–6 months was sufficient to support early and late childhood language development.[1,21-23] Moreover, mothers who breastfed for six months promoted continuous improvement in their children's intelligence (including vocabulary development) until they reached 15 years old.[24] Conversely, a study in Balochistan about the association between BF and cognitive and language development stated a need to lengthen BF duration to more than 12 months to enhance cognitive and language development significantly.[25]

Similar to a study in Balochistan, although this study's data were not statistically significant, a BF duration of >18 months appeared to prevent language development delay in children. While, a study examining children's cognitive and noncognitive development found no association once the children reached the age of five.[26] The results also highlighted mothers' educational background as a significant factor in children's cognitive development.[26,27]

Two mechanisms were attributed to the correlation between BF duration and improvement of cognitive ability, which included children's language development. First, human milk contains a specific fatty acid known as Polyunsaturated Fatty Acid (PUFA), consisting of Docosahexaenoic acid (DHA) and Arachidonic Acid (ARA) that aids in the myelination of brain neurons, thereby supporting cognitive development.[28,29] Second, BF fosters emotional intimacy between mother and child, stimulating positive emotions and reducing antisocial and aggressive behaviors associated with children's cognitive development.[28]

The LDS score is not commonly administered to assess language development for medical and health studies. For example, several studies preferred other tools, including Receptive and Expressive Vocabulary Tests (REVT), DDST, Early Language Milestones (ELM), and the Receptive-Expressive Emergent Language Scale (REEL), to assess children's language development.[26,30] However, these language screening tools have been broadly used in pediatric settings, and it is important to note that "they are not without limitations." Some of the questions in these assessment tools may be overly vague and leave out critical information regarding children's language development. For example, in ELM, which seeks children's word production, the tools only ask parents or guardians whether their children can produce a minimum of 50 words without requiring them to provide examples of such words or vocabulary.[6] The LDS has demonstrated a much more advanced technique in identifying, capturing, and analyzing information regarding children's language development compared to other assessment tools.[31]

However, given that information is solely acquired from parents or guardians (rather than children themselves), observations of children's daily interactions are crucial. Parents or guardians can provide the LDS with a wealth of information regarding their children's language development if they have made accurate and thorough

observations. Hence less input from the parents or guardians may leave out sensitive information that can be useful in predicting whether children experience mild language delays. For example, when this study requested information on their children's phrase production, roughly 30% of the participants failed to provide detailed information regarding their children's phrase ability. Consequently, although their children performed well in vocabulary production, the inadequate information from phrase productions might indicate other implications.

Strength and Limitation

This study emphasized language development by introducing the LDS as an assessment tool to reveal comprehensive information on the language development of children aged 18–35 months. Particularly, LDS can identify specific language delays, that is, words and phrases, that can guide the effectiveness of children's language therapy. Furthermore, LDS is considered the best tool for measuring children's language because of its efficacy in the assessment and data analysis process. It can be personally conducted and analyzed by parents, guardians, or others interested in children's language development.

Nevertheless, this study had some limitations, such as the limited number of subjects and insufficient data on how the length and frequency of each BF duration influence the effect of BF duration on language development. Moreover, the study did not obtain data regarding mothers' direct versus indirect BF practices, which may affect children's language development. Lastly, this study employed a cross-sectional data approach, which only described a single shoot on both variables with no further follow-up data.

Conclusion

This study lends support to the role of BF duration in the language development of children aged 18–35 months, specifically by employing the LDS tool. It also finds no significant association between BF duration and LDS score. Nevertheless, a trend towards longer BF duration seems able to prevent delayed language development problems. This study encourages further exploration on children's language development and the use of LDS as a specific assessment tool to evaluate it.

Abbreviations

BF: Breastfeeding; LDS: Language Development Survey; AOR: Adjusted Odds Ratio; PDQ: Pre-screening Developmental Questionnaire; DDST: Denver Developmental Screening Test; PHC: Primary Health Care; BMI: Body Mass Index; SD: Standard Deviation; IQR: Interquartile Range; IDR: Indonesian Rupiah; OR: Odds Ratio; PUFA: Polyunsaturated Fatty Acid; DHA: Docosahexaenoic Acid; ARA: Arachidonic Acid; REVT: Receptive and Expressive Vocabulary Tests; ELM: Early Language Milestones; REEL: Receptive-Expressive Emergent Language Scale.

Ethics Approval and Consent to Participate

Ethical approval for the study was obtained from the ethical committees of the Faculty of Medicine, Universitas Hasanuddin, Indonesia (ref: no.176/H4.8.35.31/PP36_KOMETIK/2017) for study sites in Gowa District and Palopo City and the ethical committees of the Faculty of Medicine and Health, Universitas Islam Negeri Alauddin, Indonesia (ref: no. E.010/KEPK/FKIK/XII/2019) for study sites in Jeneponto and Takalar Districts and all participants provided written informed consent.

Competing Interest

The authors declare that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The generated dataset is available to share from the corresponding author upon a reasonable request.

Authors' Contribution

AF designed the study, collected samples, conducted quantitative data analyses, and drafted the manuscript. AMR collected samples, interpreted the LDS score, and drafted the manuscript. SJ gave feedback and revised the manuscript. AIS analyzed the data and provided input, and revised the manuscript. The author(s) read and approved the final manuscript.

Acknowledgment

This study abstract was presented at the 15th Symposium on Nutri Indonesia in conjunction with the 7th International Nutrition Symposium 2020.[32] This article has been published in Research Square as preprint with DOI: https://doi.org/10.21203/rs.3.rs-580559/v1 consisted only a preliminary report that has not undergone peer review. It should not be considered conclusive, used to inform clinical practices, or referenced by the media as validated information. Dr. Faradilah is supported by grant 585898-EPP-1-2017-1-NL-EPPKA2-CBHE-JP from the HEALTH-I project. The HEALTH-I project is epidemiology blended learning and capacity building program in Indonesia, funded by the European Commission under the Erasmus+ Capacity Building in Higher Education grant program. The sponsor had no role in the design, collection, analysis, manuscript preparation, or the decision to submit for publication.

References

1. Kim KM, Choi JW. Associations between breastfeeding and cognitive function in children from early childhood to school age: a prospective birth cohort study. Int Breastfeed J. 2020; 15: 83.
2. Beaulieu-Poulin C, Simard M-N, Babakissa H, Lefebvre F, Luu TM. Validity of the language development survey in infants born preterm. Early Hum Dev. 2016; 98: 11–6.
3. Achenbach TM, Ivanova MY, Verhulst FC. In memoriam: Leslie Altman Rescorla. J Clin Child Adolesc Psychol. 2021; 50 (5): 547–50.

4. Law J, Charlton J, Dockrell J, Gascoigne M, McKean C, Theakston A. Early language development: needs, provision, and intervention for preschool children from socio-economically disadvantaged background. London: Public Health England; 2017.
5. Lutfiya I, Irwanto, Purnomo W. Identification validity early detection of child development using Indonesian mch handbook. Indian J Public Heal Res Dev. 2019; 10 (8): 1819–24.
6. Larson AL. Language screening for infants and toddlers: a literature review of four commercially available tools. Commun Disord Q. 2016; 38 (1): 3–12.
7. Rescorla L, Cathy Lee YM, Oh KJ, Kim YA. Lexical development in Korean: vocabulary size, lexical composition, and late talking. J Speech Lang Hear Res. 2013; 56 (2): 735–47.
8. Rescorla L, Frigerio A, Sali ME, Spataro P, Longobardi E. Typical and delayed lexical development in Italian. J Speech Lang Hear Res. 2014; 57 (5): 1792–803.
9. Rescorla L, Constants H, Białecka-Pikul M, Stepien-Nycz M, Ochal A. Polish vocabulary development in 2-year-olds: comparisons with English using the language development survey. J Speech Lang Hear Res. 2017; 60 (4): 1029–35.
10. Atabik A. Faktor ibu yang berhubungan dengan praktik pemberian ASI eksklusif di wilayah kerja Puskesmas Pamotan. Unnes J Public Heal. 2014; 3 (1).
11. Astuti F, Faradilah A, Yunus P. Karakteristik faktor-faktor yang berhubungan dengan lama menyusui anak. Moluc Medic. 2021; 14 (1): 36-43.
12. Mamangkey SJF, Rompas S, Masi G. Hubungan dukungan Keluarga dengan pemberian ASI eksklusif pada bayi di Puskesmas Ranotana Weru. J Kep. 2018; 6 (1).
13. Sarina S, Amiruddin A, Darlian L. Faktor-faktor yang berhubungan dengan lama pemberian ASI eksklusif pada bayi (0-6 Bulan) di wilayah kerja Puskesmas Mokoau Kota Kendari. AMPIBI J Alumni Pendidik Biol. 2017; 2 (1): 11–20.
14. Rahmawati A, Prayogi B. Analisis faktor yang mempengaruhi produksi air susu ibu (ASI) pada ibu menyusui yang bekerja. J Ners dan Kebidanan. 2017; 4 (2): 134–40.
15. Tiruye G, Mesfin F, Geda B, Shiferaw K. Breastfeeding technique and associated factors among breastfeeding mothers in Harar City, Eastern Ethiopia. Int Breastfeed J. 2018; 13 (1): 5.
16. Par'i HM, Wiyono S, Harjatmo TP. Penilaian status gizi. 2017th ed. Jakarta: Pusat Pendidikan Sumber Daya Manusia Kesehatan, Badan Pengembangan dan Pemberdayaan Sumber Daya Manusia Kesehatan.
17. Menteri Kesehatan Republik Indonesia. Peraturan Menteri Kesehatan Nomor 2 Tahun 2020 tentang Standar Antropometri Anak. Jakarta: Kementerian Kesehatan Republik Indonesia; 2020.
18. McDuffie Andrea, Haebig E. Language development survey. In: Volkmar FR, editor. Encyclopedia of autism spectrum disorders. Cham: Springer International Publishing; 2021. p. 2631–4.
19. Walfisch A, Sermer C, Cressman A, Koren G. Breast milk and cognitive development-the role of confounders: a systematic review. BMJ Open. 2013; 3 (8): e003259.
20. Fitria NI. Factors affecting children's language development. In: 5th ASEAN Conference on Psychology, Counselling, and Humanities (ACPCH 2019). Dordrecht, The Netherlands: Atlantis Press; 2020.
21. Guzzardi MA, Granziera F, Sanguinetti E, Ditaranto F, Muratori F, Iozzo P. Exclusive breastfeeding predicts higher hearing-language development in girls of preschool age. Nutrients. 2020; 12 (8): 1–12.
22. Novayelinda R, Rahmadhani N, Hasanah O. Does exclusive breastfeeding correlate with infant's early language milestone? Enferm Clin. 2019; 29: 49–51.
23. Choi HJ, Kang SK, Chung MR. The relationship between exclusive breastfeeding and infant development: a 6- and 12-month follow-up study. Early Hum Dev. 2018; 127: 42–7.
24. Boutwell BB, Young JTN, Meldrum RC. On the positive relationship between breastfeeding & intelligence. Dev Psychol. 2018; 54 (8): 1426–33.
25. Iqbal M, Rafique G, Ali SA. The effect of breastfeeding on the cognitive and language development of children under 3 years of age: results of 'Balochistan-Early Childhood Development Project.' J Gen Pract. 2017; 5 (2).
26. Girard LC, Doyle O, Tremblay RE. Breastfeeding, cognitive and noncognitive development in early childhood: a population study. Pediatrics. 2017; 139 (4): e20161848.
27. Stelmach I, Kwarta P, Jerzyńska J, Stelmach W, Krakowiak J, Karbownik M, et al. Duration of breastfeeding and psychomotor development in 1-year-old children – Polish mother and child cohort study. Int J Occup Med Environ Health. 2019; 32 (2): 175–84.
28. Krol KM, Grossmann T. Psychological effects of breastfeeding on children and mothers. Bundesgesundheitsblatt - Gesundheitsforsch - Gesundheitsschutz. 2018; 61 (8): 977–85.
29. Deoni S, Dean D, Joelson S, O'Regan J, Schneider N. Early nutrition influences developmental myelination and cognition in infants and young children. Neuroimage. 2018;178: 649—59.
30. Lee H, Park H, Ha E, Hong YC, Ha M, Park H, et al. Effect of breastfeeding duration on cognitive development in infants: 3-year follow-up study. J Korean Med Sci. 2016; 31 (4): 579–84.
31. Sansavini A, Favilla ME, Guasti MT, Marini A, Millepiedi S, Di Martino MV, et al. Developmental language disorder: early predictors, age for the diagnosis, and diagnostic tools. A scoping review. Brain Sci. 2021; 11 (5): 654.
32. Faradilah A, Rusyaidi AM. The association between breastfeeding duration and language development survey score in children. World Nutr J. 2020; 4 (1-3): 46.

Nursasi, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 251-256
DOI: 10.21109/kesmas.v17i4.5927

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Impact of Instrumental Support from Family on Medication Adherence among Tuberculosis Patients

Astuti Yuni Nursasi[1*], Mega Hasanul Huda[2,3], Syifa Widya Rahmasari[1]

[1]Department of Community Health Nursing, Faculty of Nursing, Universitas Indonesia, Depok, Indonesia, [2]Research and Development Hermina Hospitals Group, Jakarta, Indonesia, [3]Preclinic and Clinic Medical Research Center, Health Research Organization, National Research and Innovation Agency, Jakarta, Indonesia

Abstract

Instrumental support is concrete and tangible, for instance, helping in providing food or accompanying patients to health care facilities. Its impact on medication adherence among tuberculosis (TB) patients in Indonesia needs to be explored. This study aimed to examine the instrumental support impact from family on TB patients' adherence to medication in Bogor City, West Java Province, Indonesia. A cross-sectional study involving 106 participants with an age average of 39.7 was conducted in 12 primary health cares (PHCs). The independent variables (age, sex, education, employment status, wealth index, and the distance between home and PHC) of instrumental support from family were assessed using MMAS-8. The dependent variable of medication adherence was assessed using a self-reported instrument. Multivariate binary logistic regression was used in the analysis and indicated that participants receiving family support were more likely to adhere to medication protocol (95% CI = 1.1–6.3; p-value = 0.029). Instrumental support from family was associated with medication adherence among tuberculosis patients in Bogor City, West Java Province, Indonesia. It is necessary to design further comprehensive interventions in the community setting to encourage the family to support tuberculosis patients following medication protocol.

Keywords: family support, instrumental support, medication adherence, tuberculosis

Introduction

Tuberculosis (TB) has become one of the top ten causes of death, with the number of cases reaching 10 million globally in 2018.[1] In Indonesia, where the third highest incidence of cases in the world occurs and increases every year, the number reached 563,879 in 2018.[1,2] Bogor City, located in West Java Province, Indonesia, shared 1,059 cases of positive pulmonary TB in 2018.[3] TB cases in Indonesia are still relatively high, with Bogor City contributing to the total figure.

As the number of TB cases increases annually, the world has attempted to find means to reduce the TB incidence rate. "The End TB Strategy" program is one such effort. The program has three indicators of success: the annual TB mortality, incidence of TB cases, and the percentage of households affected by financial problems due to TB.[1] Indonesia also has several programs to control TB, including the Directly Observed Treatment Short-Course (DOTS),[4] initiated by World Health Organization (WHO) and *Temukan Obati Sampai Sembuh* (TOSS).[2] DOTS focuses on finding and healing patients, while the TOSS focuses on finding, diagnosing, and treating TB patients to reduce the risk of TB transmission in the community.

The accomplishment of the DOTS and TOSS programs is indicated by the success rate of TB treatment in Indonesia (87.5%), which has reached the global target (85%) set in 2017.[2] However, the treatment success rate differs from the cure rate, indicating that only 42% of the Indonesian TB patients were cured in 2017.[2] Bogor City, which has a relatively high incidence of TB cases, has not yet reached the target for TB cure rates. In 2018, the TB cure rate only reached 81.22% compared to a target of 90%.[3] The number of TB cases and the cure rate in Bogor City between 2014 and 2018 are indicators of patients' medication adherence. The data from Bogor City Health Office showed a lower cure rate than the target, indicating that not all TB patients in Bogor City adhered to their medication regimen.[3]

TB treatment takes at least six months, and the medication should be taken throughout this time.[5] It means surveillance of TB drug consumption is needed to maintain treatment adherence. Adherence is the extent to which a person follows an agreed series of actions.[6] A

Correspondence:* *Astuti Yuni Nursasi, Department of Community Health Nursing, Faculty of Nursing, Universitas Indonesia, Prof. Dr. Bahder Djohan Street, Depok, West Java, Indonesia 16424, E-mail: ayunin@ui.ac.id, Phone: +62 856 7891 775*

Received : May 31, 2022
Accepted : November 26, 2022
Published : November 30, 2022

study indicated that one factor affecting adherence to TB medication is the involvement of a drug ingestion supervisor (DIS).[7] The DIS is a component of the DOTS program, and its role can be carried out by the family member of TB patients undergoing treatment.[8] Another study showed a significant relationship between the role of the family as DIS and the success rate of patients undergoing pulmonary TB treatment.[9] The forms of support that can be provided are accompanying TB patients to the health care facilities for routine checks and taking TB medication, which is usually given once a week; preparing and reminding patients to take their TB medicament each day; and providing encouragement to increase TB patients' self-efficacy and confidence that they will recover.[9,10]

The role of DIS in TB patients' families is a form of family support. A study showing a significant relationship between family support and medication adherence identified four types of family support: instrumental, emotional, informational, and rewarding.[11] Instrumental support from family is simple support given through direct assistance, such as material aid or service.[7] Instrumental support from family, which family members often provide during episodes of illness, can be financial, homework, and transportation assistance.[12] This support is proven to increase TB patients' adherence to their treatment.[9] Although the instrumental support provided by family is usually less noticed than other forms of support (informational, emotional, and reward) given to TB patients, this type of support substantially increases patients' adherence to TB medication.[13]

Usually, instrumental support involves material provision. Therefore, as the family needs to have a certain amount of money, its financial circumstances may affect its provision of instrumental support.[12] Poor financial circumstances, for example, affect a family's ability to buy medicine, fulfill daily needs such as food and clothing, and access health facilities.[12,14,15] Most TB patients come from the middle to lower economic class.[2] It is perceived that TB patients from families with low socioeconomic status may encounter obstacles to providing instrumental support from family, which may affect their adherence. TB patients mostly lack awareness of the fact that their instrumental support from family may influence their adherence. It is also known that the family's financial circumstances can lead to their inability to provide good instrumental support, which can be examined further. This study aimed to examine the impact of instrumental support from family, including financial support, homework and transportation assistance, and medication adherence among TB patients in Bogor City.

Method

This cross-sectional study was conducted between June and July 2021 in Bogor City, West Java Province, Indonesia. Participants were included in the study if they met the following criteria: (a) TB patients who had received TB treatment for two months or more; and (b) living with their families in Bogor City. The participants who had communication problems and could not read, write, or speak in Indonesian language were excluded. The medical records were used to select participants who met the eligibility criteria. The study was conducted in 12 primary health cares (PHCs) with high TB cases in Bogor City.[6] Purposive sampling was used to determine the respondents from each PHC. The sample size of 106 participants was required for logistic regression to detect the correlation of 0.5 with an alpha of 0.05. Considering a non-completion rate of 30%, a total of 106 participants was included in this study.

The data were collected by inviting participants to come to the PHC and complete questionnaires whose items related to the participants' characteristics, instrumental support from family, and adherence to TB medication. However, a home visit was conducted for those participants who found it difficult to visit the PHC. A structured questionnaire about instrumental support from family was developed based on a previous study, including age, sex, education, employment status, wealth index, and distances between home and PHC,[11,16-18] and then combined and modified into 20 items. A 4-point Likert scale was used, with a categorical division using quartiles: the "Poor" category includes any score in the 0–60 range, the "Moderate" category comprises the 61–74 range, and the "Good" ranges from 75 to 80. This study's questionnaire was highly reliable, with a Cronbach's alpha value of 0.743.

A patient is considered to meet medication adherence by the American Medical Association if they take 80% of their prescribed medicine(s).[19] Patients taking less than 80% of their prescribed medication(s) are considered nonadherent.[19] This outcome was based on self-reported data concerning whether the patients still took TB medication.[19] A Morisky Medication Adherence Scale (MMAS) questionnaire was used to measure medication adherence. This instrument consisted of eight items. The scale was categorized as "high adherence" (total score of 8), "moderate adherence" (total score of 6–7), and "low adherence" (total score of 0–6). An Indonesian language version of the MMAS was found to have good reliability with a Cronbach's alpha of 0.731.[20]

Data were analyzed using SPSS Version 23 (IBM Corp. 2020). Descriptive analyses were carried out on the variables, including participants' characteristics, instrumental support from family, and medication adherence, using means and standard deviation (SD) for continuous data and frequencies and percentages for categorical data. Bivariate analysis was performed to deter-

mine the relationship between the dependent variable (medication adherence) and the independent variable (instrumental support from family) using the univariate logistic regression model. To examine the relationship of participants' characteristics with instrumental support from family and medication adherence, multivariable logistic regression modeling was used. The adjusted odds ratio (AOR) was calculated to examine the strength of the association by entering the variables one by one into the model to avoid the collinearity of all factors.

Result

A total of 106 individuals participated in the survey, with a response rate of 100%. Overall, the mean age of participants was 39.7, with a standard deviation (SD) of 14.9. More than half the participants were males and attending primary education (≤senior high school). Most participants were unemployed and did earn less than the regional minimum wage in Bogor City (<IDR3,843,000). Over half the participants lived more than five kilometers from the PHC (Table 1). The results indicated that more than half the participants received instrumental support from their families. The analysis also found that 76 participants (71.7%) were adherent to the medication protocol (Table 1).

Participants' Characteristics, Instrumental Support from Family, and Medication Adherence

The univariate model indicated that none of the participants' characteristics (age, sex, education, employment status, wealth index, and distance from home to PHC) were associated with medication adherence. The findings showed that participants receiving instrumental support from family had a higher AOR of following the medication protocol (Table 2).

Instrumental Support from Family Associated with Medication Adherence

The findings of this study stated that most TB patients in Bogor City earned less than the regional minimum wage (Table 1); hence, individuals from families with low economic levels were at an increased risk of TB infection. After all, it was possible that these individuals' needs, such as nutrition or adequate housing, were not met. The low economic level could affect medication adherence among TB patients because they could not access treatment. The multivariate analysis indicated that instrumental support from family was associated with medication adherence. From the analysis, participants receiving support from their families were more likely to adhere to the medication protocol, with an odds ratio of 2.7 (95% CI = 1.1–6.3; p-value = 0.029).

Table 1. Distribution of Participants' Characteristics (n = 106)

Variable	Category	n	%	Mean (SD)
Age				39.7 (14.9)
Sex	Male	61	57.5	
	Female	45	42.5	
Education	≤Senior high school	101	95.3	
	Higher education	5	4.7	
Employment status	Employed	41	38.7	
	Unemployed	65	61.3	
Wealth index	<IDR3,843,000	98	92.5	
	≥IDR3,843,000	8	7.5	
Distance from home to PHC	≥5 kilometers	43	40.6	
	<5 kilometers	63	59.4	
Instrumental support from family	Support	57	53.8	
	Not support	49	46.2	
Medication adherence	Adhere	76	71.7	
	Not adhere	30	28.3	

Notes: SD = Standard Deviation, IDR = Indonesian Rupiah PHC = Primary Health Care

Table 2. The Relationship of Participant Characteristics and Instrumental Support from Family with Medication Adherence (n = 106)

Variable	Category	n (%)	Medication Adherence			
			Crude OR	AOR	95% CI	p-value
Age			0.024	1.024	0.993–1.056	0.126
Sex	Male	61 (57.5)				
	Female	45 (42.5)	0.414	1.513	0.650–3.522	0.337
Education	≤Senior high school	101 (95.3)				
	Higher education	5 (4.7)	0.477	1.611	0.173–15.03	0.676
Employment status	Employed	41 (38.7)				
	Unemployed	65 (61.3)	0.271	0.763	0.323–1.802	0.537
Wealth index	<IDR3,843,000	98 (92.5)				
	≥IDR3,843,000	8 (7.5)	1.079	2.942	0.346–24.998	0.323
Distance from home to PHC	≥5 kilometers	43 (40.6)				
	<5 kilometers	63 (59.4)	0.033	0.968	0.409–2.291	0.941
Instrumental support from family	Support	57 (53.8)				
	Not support	49 (46.2)	0.974	2.648	1.106–6.344	0.029

Notes: SD = Standard Deviation, OR = Odds Ratio, AOR = Adjusted Odds Ratio, IDR = Indonesian Rupiah, PHC = Primary Health Care

Discussion

Most TB patients earned less than the minimum wage in Bogor City (IDR3,843,000), and previous study showed that most TB patients earned less than the minimum wage.[7,11] The monthly income earned by an individual can determine their economic level. A study identified that individuals with low economic levels have a higher risk of TB infection.[21] The low individual economic level is closely related to a family's ability to carry out economic functions, meaning that their ability to fulfill family needs is also low.[21] Fulfilling family needs can mean fulfilling healthy nutrition requirements or having a decent place to live in a fair and healthy physical condition.[7] This study found that a lower income affected an individual's economic level in such a way that it affected their ability to meet family needs. If a family's needs, such as their nutritional and living condition requirements, cannot be fulfilled, their vulnerability to being infected with TB will increase.[18,21-23]

The comparative analysis of family income to instrumental support from family obtained in this study found that TB patients earning higher than the regional minimum wage of Bogor City (≥IDR3,843,000) had better instrumental support from family than those earning less. Tuberculosis patients with a low economic level have a lower level of family support than those with a higher economic level.[24] On the basis of this explanation, the form of instrumental support provided can be assumed. For example, to meet TB patients' nutritional needs, a family needs to provide high-protein food. However, some families had economic limitations on what food they could provide, meaning that they could not fulfill the nutritional needs of TB patients. Insufficient nutrition can have a negative impact on the healing process.[25-27]

This study also analyzed the ratio of income to medication adherence in TB patients. The analysis showed that TB patients earning greater than the regional minimum wage (≥IDR3,843,000) adhered more closely to treatment than those who earned less. Tuberculosis patients earning less than the minimum wage were 1.7 times less likely to comply than those earning greater than the minimum wage.[7] However, income is not a benchmark for medication adherence because TB treatment at the PHCs is granted free of charge.[11] In light of this explanation, a high adherence by TB patients with a high income might occur because those patients have better facilities for their treatment process. For example, it assumed that TB patients earning greater than or equal to the regional minimum wage had private vehicles, making it easier for them to obtain their TB medicament at the PHC, which might reduce the risk of skipping drug-taking if the patient runs out of drugs.

The results showed that some TB patients had not received optimal instrumental support from family. A study stated that TB patients with a low economic level had a low level of family support, which could obstruct the healing process.[7] The provision of suboptimal instrumental support could be seen in the family's ability to carry out family functions, including effective, economic, and family care functions. When an effective function is carried out correctly, each family member supports the TB patient, one aspect of which is instrumental support.[14] The family's economic functions, if executed well, can provide TB patients with good nutrition, helping people with TB in the healing process.[28,29] The family care function is tied to instrumental support from family for TB patients, including the family's contribution to care during TB treatment.[30] Therefore, the family's function is closely related to instrumental support.

Most TB patients had moderate or high adherence level, which means that TB patients were adhering to treatment. This finding was in line with two studies reporting that more than 60% of TB patients complied with treatment.[16,31] In contrast, another study found that only 48.9% of TB patients complied with treatment.[11] This difference occurs because medication adherence is influenced by several factors, including factors relating to the TB patients themselves, health care facilities, medication, and sociocultural features.[7,15,32] However, the results also showed that there were still TB patients with a low adherence level. The failure of TB patients to adhere to their treatment could occur because the family had not performed its family functions optimally.[7] Among the family's useful functions, medication adherence is helped by supporting and motivating TB patients.[30] The family care function can be executed to maintain a TB patient's medication adherence by reminding them to take their medication on time.[17] Concerning the family's economic function, a high economic level can provide facilities for better treatment processes, such as facilitating transportation for health check-up.[29]

This study proved a significant relationship between instrumental support from family and medication adherence by TB patients (p-value = 0.022, $\alpha = 0.05$). The results of this study were in line with three studies that indicated a significant relationship between family support and medication adherence.[11,16,31] However, two studies showed that instrumental support from family does not have a significant relationship with medication adherence.[13,18] This difference might arise because each patient has different family conditions and backgrounds. At the same time, the provision of instrumental support can depend on the availability of materials, services, or time available for TB patients.[13] Most participants in this study stated that families often perform instrumental support (Table 1), which included reminding patients to take their medicine, preparing the medicine, delivering,

or getting medicine at the health center facilities, and accompanying patients to take medication. Therefore, the better the instrumental support from family provided, the higher the level of compliance by TB patients.

Strength and Limitations

Family functions and the family's role as DIS were referred to most often in this study, suggesting that these two factors were related to instrumental support from family and medication adherence among TB patients. Further study may explore the relationship between the family's role as DIS and the ability to provide family support to TB patients. However, this study had some limitations. First, the COVID-19 pandemic made the schedule for TB patients to take their medication change from once a week to once every two weeks, so that fewer TB patients would visit the PHC. Therefore, visiting each patient's house was needed to collect the data. Another limitation was that the addresses of TB patients in the PHC records sometimes differed from the patients' residential addresses, which made data on the distance between home and PHC must be double-checked.

Conclusion

This study reveals that good family support will elevate TB patients' adherence. Tuberculosis patients in Bogor City mostly live close to PHC, and many of them receive good support from their families. Therefore, most TB patients in Bogor City adhere to their treatment.

Recommendation

The findings may have implications for the nursing service concerning the provision of education regarding the importance of the family's role in providing instrumental support for medication adherence by TB patients. Efforts to increase instrumental support can be made by increasing the family's role as DIS in monitoring TB patients' ingestion of drugs. The instrumental support provided can be adjusted to the economic level of the patient's family; for example, when delivering education on providing nutritious food, health care providers can talk about nutritious food which is available at an affordable price. The form of instrumental support provision can be adjusted to the family's financial circumstances, so that the need for instrumental support can be fulfilled.

Abbreviations

TB: Tuberculosis; DOTS: Directly Observed Treatment Short-Course Strategy; WHO: World Health Organization; TOSS: Temukan Obati Sampai Sembuh; DIS: Drug Ingestion Supervisor; PHC: Primary Health Care; MMAS: Morisky Medication Adherence Scale; SD: Standard Deviation; AOR: Adjusted Odds Ratio; IDR: Indonesian Rupiah; COVID-19: coronavirus disease 2019.

Ethics Approval and Consent to Participate

This study protocol was reviewed by the ethical test by the school administration number UN2.F12.D/HKP.02.07/2019. The ethical test carried out has met the established criteria. The criteria referred to include, among others, accompanying an explanation of the benefits of research, explaining the rights of the respondent, maintaining the privacy of the respondent, holding the aspect of justice, and upholding the principle of openness by explaining the research procedure and informed consent. In this study, written informed consent was obtained from the participants who agreed to participate after the authors had explained the purposes of the study.

Competing Interest

The authors declare that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The generated dataset is available to share from the corresponding author upon a reasonable request.

Authors' Contribution

AYN participated in conceptualizing, designing, analyzing, and revising the manuscript. SWR participated in collecting the data, analyzing, and writing the manuscript. MHH participated in analyzing and writing the result in manuscript. The authors discussed the results of the study. All authors read and approved the final manuscript.

Acknowledgment

The authors thank the participants who agreed to complete the questionnaire and the Health Office and Primary Health Care of Bogor City for cooperating with us in selecting the participants.

References

1. World Health Organization. Global tuberculosis report 2022. Geneva: World Health Organization; 2022.
2. Kementerian Kesehatan Republik Indonesia. Infodatin tuberkulosis 2018 - Dicari para pemimpin untuk dunia bebas TBC. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018.
3. Dinas Kesehatan Kota Bogor. Profil Kesehatan 2018. Bogor; Dinas Kesehatan Kota Bogor; 2019.
4. World Health Organization. Communicable diseases cluster. What is DOTS?: a guide to understanding the WHO-recommended TB control strategy known as DOTS. Geneva: World Health Organization; 1999.
5. World Health Organization. Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update. Geneva: World Health Organization; 2017.
6. Chapman H. Nursing theories 4: adherence and concordance. Nursing Times. 2018; 114 (2): 50.
7. Wulandari DH. Analisis faktor-faktor yang berhubungan dengan kepatuhan pasien tuberkulosis paru tahap lanjutan untuk minum obat di RS Rumah Sehat Terpadu tahun 2015. Jurnal Arsi. 2015; 2 (1): 17–28.
8. Menteri Kesehatan Republik Indonesia. Peraturan Menteri Kesehatan

Nomor 67 Tahun 2016 Tentang Penanggulangan Tuberkulosis. Jakarta: Kementerian Kesehatan Republik Indonesia; 2016.
9. Jufrizal J, Hermansyah H, Mulyadi M. Peran keluarga sebagai pengawas minum obat (PMO) dengan tingkat keberhasilan pengobatan penderita tuberkulosis paru. J Ilmu Keperawatan. 2016; 4 (1): 25–36.
10. Jakaria. Keberhasilan pengobatan dalam kepatuhan minum obat TB paru di Puskesmas Dramaga Kabupaten Bogor Provinsi Jawa Barat [Undergraduate Thesis]. Depok: Universitas Indonesia; 2017.
11. Sutini E. Hubungan dukungan keluarga terhadap kepatuhan minum obat pada klien TB di Puskesmas Pancoran Mas [Undergraduate Thesis]. Depok: Universitas Indonesia; 2016.
12. Chen LC, Chen TC, Huang Y Bin, Chang CS. Disease acceptance and adherence to imatinib in Taiwanese chronic myeloid leukaemia outpatients. Int J Clin Pharm. 2014; 36 (1): 120–7.
13. Arifin VN, Juariah, Nur A, Uzair FM. The relationship of social support with medication adherence pulmonary tuberculosis patients through DOTS strategy in Pidie Aceh Indonesia. In IOP Conference Series: Materials Science and Engineering. IOP Publishing Ltd; 2019; 4691.
14. Cross CJ, Nguyen AW, Chatters LM, Taylor RJ. Instrumental social support exchanges in African American extended families. J Fam Issues. 2018; 39 (13): 3535–63.
15. Goldsmith LJ, Kolhatkar A, Popowich D, Holbrook AM, Morgan SG, Law MR. Understanding the patient experience of cost-related non-adherence to prescription medications through typology development and application. Soc Sci Med Internet. 2017; 194: 51–9.
16. Maulidia DF. Hubungan antara dukungan keluarga dan kepatuhan minum obat pada penderita tuberkulosis di wilayah Ciputat tahun 2014 [Undergraduate Thesis]. South Tangerang: Universitas Islam Negeri Syarif Hidayatullah Jakarta; 2014.
17. Tamamengka D, Kepel B, Rompas S. Fungsi afektif dan perawatan keluarga dengan kepatuhan pengobatan TB paru. J Keperawatan. 2019; 7 (2): 1-10.
18. Chen X, Du L, Wu R, Ji H, Zhang Y, Zhu X, et al. The effect of family, society and national policy support on treatment adherence among newly diagnosed tuberculosis patients: a cross-sectional study. BMC Infectious Diseases. 2020; 20: 623.
19. Hugtenburg JG, Timmers L, Elders PJ, Vervloet M, van Dijk L. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. Patient Prefer Adherence. 2013; 7: 675-82.
20. Riani DA. Validasi 8-item morisky medication adherence scale versi Indonesia pada pasien hipertensi dewasa di Puskesmas Kabupaten Sleman dan Kota Yogyakarta [Thesis]. Yogyakarta: Universitas Gadjah Mada; 2017.
21. Masithoh AR. Hubungan tingkat ekonomi dengan kejadian tuberkulosis paru di Puskesmas Kaliwungu Kecamatan Kaliwungu Kabupaten Kudus. J Ilmu Keperawatan Kebidanan. 2013; 4 (2): 35–44.
22. Narasimhan P, Wood J, MacIntyre CR, Mathai D. Risk factors for tuberculosis. 2013; 2013: 828939.
23. Nurjana MA. Faktor risiko terjadinya tubercolosis paru usia produktif (15-49 tahun) di Indonesia. Media Penelitian dan Pengembangan Kesehatan. 2015; 25 (3): 163–70.
24. Manan, I. Gambaran dukungan dan peran keluarga sebagai PMO dalam pencegahan TB MDR di wilayah kerja Puskesmas Gang Kelor Kota Bogor Tahun 2017. 2018; 10 (2).
25. Kant S, Gupta H, Ahluwalia S. Significance of nutrition in pulmonary tuberculosis. Crit Rev Food Sci Nutr. 2015; 55 (7): 955–63.
26. Ren Z, Zhao F, Chen H, Hu D, Yu W, Xu X, et al. Nutritional intakes and associated factors among tuberculosis patients: a cross-sectional study in China. BMC Infect Dis. 2019; 19: 907.
27. Samuel B, Volkmann T, Cornelius S, Mukhopadhay S, MejoJose, Mitra K, et al. Relationship between nutritional support and tuberculosis treatment outcomes in West Bengal, India. J Tuberc Res. 2016; 4 (4): 213–9.
28. Deshmukh RD, Dhande DJ, Sachdeva KS, Sreenivas AN, Kumar AMV, Parmar M. Social support a key factor for adherence to multidrug-resistant tuberculosis treatment. Indian J Tuberc. 2018; 65 (1): 41–7.
29. Sanusi GN, Satus AS, Karso I. Hubungan tingkat ekonomi dengan kepatuhan minum obat penderita TB paru BTA positif di wilayah kerja Puskesmas Cukir Kabupaten Jombang. JIKep. 2017; 3 (1).
30. Iksan RR, Muhaimin T, Anwar S. Fungsi-fungsi keluarga dengan hasil pengobatan tuberculosis program DOTS. J Keperawatan Silampari. 2020; 3 (2): 638–47.
31. Septia A, Rahmalia S, Sabrian F. Hubungan dukungan keluarga dengan kepatuhan minum obat pada penderita TB paru. JOMPSIK. 2014; 1 (2).
32. Gugssa Boru C, Shimels T, Bilal AI. Factors contributing to non-adherence with treatment among TB patients in Sodo Woreda, Gurage Zone, Southern Ethiopia: a qualitative study. J Infect Public Health. 2017; 10 (5): 527–33.

Mokoagow, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 257-263
DOI: 10.21109/kesmas.v17i4.6301

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Factors Associated with Depression among Type 2 Diabetes Mellitus Patients at a Tertiary Hospital during the COVID-19 Pandemic

Muhammad Ikhsan Mokoagow[1,2]*, Dian Pitawati[3], Ditya Nona Arisandy[4], Nadya Magfira[2], Pratiwi Indah Palupi[2], Jerry Nasarudin[1,2], Marina Epriliawati[1,2], Ida Ayu Kshanti[1,2]

[1]Division of Endocrinology, Metabolism, and Diabetes, Department of Internal Medicine, Fatmawati General Hospital, Jakarta, Indonesia, [2]Diabetes Integrated Care Center, Fatmawati General Hospital, Jakarta, Indonesia, [3]Department of Psychiatry, Fatmawati General Hospital, Jakarta, Indonesia, [4]Department of Research and Development, Fatmawati General Hospital, Jakarta, Indonesia

Abstract

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia that can cause various complications, economic burdens, and psychosocial issues that eventually lead to depression. This study aimed to describe the prevalence of depression among type 2 diabetes mellitus patients in the Internal Medicine Outpatient Clinic of a South Jakarta tertiary hospital during the COVID-19 pandemic. This cross-sectional study was conducted from May to July 2021. The data were collected consecutively from 100 patients aged 18 years or older who came for regular consultation. The instrument used for determining depression is Beck Depression Inventory-II. The prevalence of depression, a correlation between depression and participant's characteristics, and multivariate analysis for risk factors were determined. The results showed that the prevalence of mild to severe depression based on the BDI-II classification was 17%. Screening showed mild to severe depression predominantly in females above 60 years old, with higher levels of education, obesity grade I, individuals with one or more comorbidities, and those who had diabetes for more than ten years. In this study, having one or more comorbidities was associated with an increased risk of depression in people with diabetes.

Keywords: Beck Depression Inventory-II, depression screening, diabetes mellitus, prevalence of depression

Introduction

Noncommunicable Diseases (NCDs) are by far the leading causes of death globally. According to global trends, the World Health Organization (WHO), stated that NCDs contributed to 71% (41 million) of 57 million deaths that occurred globally in 2016.[1] NCDs include cardiovascular disease, cancer, chronic respiratory disease, and diabetes. Based on WHO data in 2020, Indonesia, with an estimated population of 261,100,000, has a 1,365,000 total death rate caused by NCDs or approximately 73%, with diabetes as one of the etiologies.[2]

In 2019, according to International Diabetes Federation (IDF), 463 million adults aged 20–79 years old worldwide had diabetes, with about 79.4% sufferers living in low and middle-income countries. Of that 463 million adults, 240.1 million (9.6%) are male, and 222.9 million (9.0%) are female. In 2019, IDF estimated that there would be 578.4 million diabetes patients in 2030. The total number will increase to 700.2 million in 2045.[3] The 2018 National Basic Health Research/*Riset Kesehatan Dasar* (Riskesdas) documented diabetes prevalence based on doctor's diagnosis in the population older than 15 years old is 2%. The highest prevalence of diabetes mellitus (DM) based on a doctor's diagnosis and more than 15 years old is in Jakarta, with a total percentage of 3.4%.[4]

Diabetes creates economic and health burdens and poses various psychosocial issues to people with diabetes (PWD), such as depression.[1,3,5] As the most common mental disorder, depression commonly affects PWD. It has a bidirectional relationship: diabetes increases the risk of future depression, and depression increases the risk of having diabetes.[5] Patients with diabetes need a comprehensive self-management plan (monitoring blood glucose, daily oral antidiabetic drugs and/or insulin injection, and committing to a healthy lifestyle, including a nutritional diet and physical activity).[3] Because of those things, they may have difficulties of accepting and adjusting a comprehensive self-management plan to different levels, which will pose a practical and psychological burden. In addition to psychological mechanisms, biological mechanisms, such as inflammation, may have a role in the relationship between depression and diabetes.[5]

Correspondence: Muhammad Ikhsan Mokoagow, Division of Endocrinology, Metabolism, and Diabetes, Department of Internal Medicine, Fatmawati General Hospital, West Cilandak, South Jakarta, 12430, Indonesia, E-mail: mimokoagow@gmail.com, Phone: +62 815 8414 9555*

Received : October 21, 2022
Accepted : November 26, 2022
Published : November 30, 2022

In 2017, WHO estimated 4.4% of the world's population suffered from depression.[6] While the prevalence of comorbid depression in adults with type 2 diabetes mellitus (T2DM) ranges from 10% to 15%.[7] Based on age predictor, the prevalence of depression heightens in adult-old age (more than 7.5% in women aged 55–74 years old, and more than 5.5% in men).[6] The 2018 Riskesdas documented that for three decades (1990–2017), depression was the first and most significant mental disorder that contributed to the burden of disease in Indonesia.[8]

The current COVID-19 pandemic that occurred globally has become a stressor for many individuals. It has changed people's lifestyles and threatens physical and mental health and well-being.[9] Stressors during this pandemic may arise from fear of transmission, inadequate information, loss of personal control and freedom, changes of plan in a shorter period or the future, concerns about the health and well-being of oneself, relatives, and family, negative stigma against COVID-19 sufferers, the quarantine period, loss of job, and financial insecurity.[9] These circumstances may increase predisposed individuals' risk of psychiatric ailments such as depression and anxiety.[9] Alessi, *et al.*, found a high prevalence of psychological distress among PWD during the COVID-19 pandemic.[10] Another study on T2DM patients treated in Egypt's Primary Health Care during the COVID-19 pandemic showed that 9.2% of the participants had a major depression.[11]

Due to the high prevalence of diabetes, which pose various burdens, and depression is a mental health disorder that often occurs in PWD, diabetes may increase the incidence of depression, especially during the COVID-19 pandemic. Therefore, this study aimed to determine the prevalence of depression among PWD who came for regular consultation in the Internal Medicine Outpatient Clinic of a tertiary hospital in South Jakarta Municipality, the Special Capital Region of Jakarta, Indonesia.

Method

This cross-sectional study was conducted at a tertiary hospital in South Jakarta from May to July 2021. The sample size for a single population was calculated to be a minimum of 80 participants to assess depression among T2DM patients (CI = 95%, Z = 1.96, power = 90%, d = 0.10, p-value = 0.292). A total of 100 participants were eligibly recruited. The inclusion criteria for this study were adults above 18 years old, diagnosed with T2DM, and who agreed to participate in this study. Adult T2DM patients who came for regular consultation at the Internal Medicine Outpatient Clinic consecutively between May and July 2021 were asked whether they agreed to participate in this study. Patients who agreed to participate would undergoing further history taking and review of their medical records to rule out any existing exclusion criteria.

The exclusion criteria were patients with a cognitive disorder, a severe visual impairment that caused an inability to fill in the questionnaire independently, and record of mental disorder treatment in the past three months of sampling time. All recruited participants agreed to sign a written informed consent before data collection. The data was collected by asking the participants to fill out Beck's Depression Inventory (BDI)-II questionnaire in Indonesian language. The BDI-II is one of the most widely used depression self-rating scales to assess depressive symptoms and their severity.[12,13] It consists of 21 items describing symptoms and categories reflecting over psychological and somatic symptoms of depression. Each item has four answers with a point weight of 0–3. All items are summed to create a total score, with higher scores indicating higher levels of depression.[12,13]

Demographical data (sex, age, education), duration of diabetes (less than 1 year, 1–5 years, 6–10 years, more than 10 years), the type of diabetes medication (without medical regiment, with one/two/three oral antidiabetic regiments, with insulin, with both insulin and oral antidiabetic), and the duration of the medication were obtained from taking and reviewing the patient's medical record. The nutritional status of participants was assessed with body mass index (BMI) and determined based on the WHO cut-off point for Asian-Pacific populations: less than 18.5 for underweight, 18.5–22.9 for normal weight, 23–24.9 for overweight, 25–29.9 for obesity grade I, more than or equal to 30 for obesity grade II. Diabetes was determined based on the patient's medical record and laboratory parameters, such as HbA1C higher than 6.5%, fasting blood glucose higher than 126 mg/dL, or random blood glucose higher than 200 mg/dL in two consecutive measurements.

Based on the patient's medical record, comorbidity was determined by whether there were other chronic conditions, such as hypertension, chronic kidney disease, cardiovascular disease, coronary artery disease, or congestive heart failure. Comorbidities were then classified into two groups: without comorbidity (no additional chronic disease) and the presence of one or more comorbidities. Record of diabetic foot ulcer (DFU) obtained from physical examination and medical records looking for unresolved foot ulcer or records of amputation related to diabetic foot and then classified into two groups: patient with a record of DFU and without a record of DFU. Total scores from the individual BDI-II questionnaire were classified into four groups: minimal (0–13), mild (14–19), moderate (20–28), and severe (29–63).[12,13]

Categorical data describing participants' characteris-

tics (sex, age, education, nutritional status, duration of diabetes, presence of comorbidities, record of DFU, diabetes treatment) and BDI-II score (minimal, mild, moderate, and severe) were presented as frequency and percent. The correlation between depression and respondent characteristics and the correlation between depression and diabetes treatment were also assessed using a bivariate Chi-square test. Statistical significance was determined if a p-value was less than 0.05. If the bivariate analysis found a p-value of less than 0.20, it would proceed to multivariate logistics regression analysis.

Results

During the study period from May to July 2021, 105 individuals with T2DM were consecutively approached to participate. Of 100 participants were subsequently enrolled; none had exclusion criteria and were eligible for the analysis (Figure 1).

Table 1 shows the participants' characteristics. The results showed 61 participants in this study were female, and the largest age group was more than 60. Most subjects had BMI within obesity grade 1 and had been diagnosed with T2DM for more than 10 years. Almost two-thirds of participants attended senior high school or higher (college or university). More than half of the subjects had hypertension as a comorbid (54%), and most had neither record of DFU nor amputation (81%). Most participants received pharmacological treatments with various regimens. More than a third of them were on a combination of insulin and oral antidiabetics (OAD), followed by only OAD, then only insulin-based treatment. More than two-thirds of the participants had a treatment duration of 1–5 years and more than ten years (31% and 37%, respectively).

The prevalence of depression is presented in Table 2.

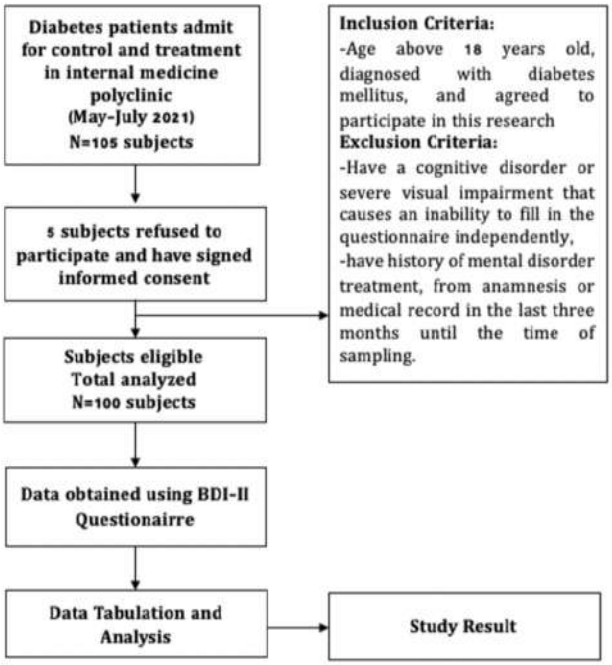


Figure 1. Diagram Depicting Participants and Study Flow

Table 1. Participants Characteristics

Variable	Category	n	%
Sex	Male	39	39
	Female	61	61
Age (Year)	18–39	6	6
	40–59	42	42
	60+	52	52
Education	<Senior high school	37	37
	≥Senior high school (University)	63	63
Nutritional status (BMI)	Underweight	4	4
	Normal	25	25
	Overweight	23	23
	Obesity grade I	32	32
	Obesity grade II	16	16
Duration of diabetes	<1 year	4	4
	1–5 years	23	23
	5–10 years	19	19
	10+ years	54	54
Comorbidity	Hypertension	54	54
	CKD	10	10
	CVD	10	12
	CAD	27	30
	CHF	11	11
Record of DFU	DFU	15	15
	Amputation	4	4
	No DFU or amputation	81	81
Type of medical regiment	No medical regiment	5	5
	OAD		42
	One regiment	20	20
	Two regiments	15	15
	Three regiments	7	7
	Insulin		18
	Basal	1	1
	Prandial	5	5
	Basal bolus	10	10
	Pre-mixed	2	2
	OAD + Insulin	35	35
Duration of treatment	<1 year	8	8
	1–5 years	31	31
	5–10 years	24	24
	10+ years	37	37

Notes: BMI = Body Mass Index, CKD = Chronic Kidney Disease, CVD = Cardiovascular Disease, CAD = Coronary Artery Disease, CHF = Congestive Heart Failure, DFU = Diabetic Foot Ulcer, OAD = Oral Antidiabetic Drug

Table 2. The Prevalence of Depression Based on Beck Depression Inventory-II

Depression	BDI-II Score	n	%
Minimal	0–13	83	83
Mild	14–19	8	8
Moderate	20–28	7	7
Severe	29–63	2	2

Note: BDI-II = Beck Depression Inventory-Second Edition

Table 3. Correlation between Depression and Respondent Characteristics

Variable	Category	Mild to Severe Depression	Minimal Depression	p-value
		n = 17 (17%)	n = 83 (83%)	
Sex	Male	7 (41.18)	32 (38.55)	0.840
	Female	10 (58.82)	51 (61.45)	
Age (year)	18–39	0 (0)	6 (7.23)	0.507
	40–59	8 (47.06)	34 (40.96)	
	60+	9 (52.94)	43 (51.81)	
Education	<Senior high school	8 (47.06)	29 (34.94)	0.346
	≥Senior high school (University)	9 (52.94)	54 (65.06)	
Nutritional status	Underweight	0 (0)	4 (4.82)	0.526
	Normal	2 (11.76)	23 (27.71)	
	Overweight	5 (29.41)	18 (21.69)	
	Obesity grade I	7 (41.18)	25 (30.12)	
	Obesity grade II	3 (17.65)	13 (15.66)	
Duration of diabetes	<1 year	2 (11.76)	2 (2.41)	0.135
	1–5 years	2 (11.76)	21 (25.3)	
	5–10 years	5 (29.41)	14 (16.87)	
	10+ years	8 (47.06)	46 (55.42)	
Comorbidity	No comorbid	1 (5.88)	28 (33.73)	0.036*
	One comorbid	8 (47.06)	31 (37.35)	
	Two comorbidities	7 (41.18)	14 (16.87)	
	Three or more comorbidities	1 (5.88)	10 (12.05)	
History of DFU	No DFU	14 (82.35)	67 (80.72)	0.848
	DFU	2 (11.76)	13 (15.66)	
	Amputation	1 (5.88)	3 (3.61)	
Type of medical regiment	No medical regiment	1 (5.88)	4 (4.82)	0.963
	Oral antidiabetic			
	One regiment	2 (11.76)	18 (21.69)	
	Two regiments	2 (11.76)	13 (15.66)	
	Three regiments	1 (5.88)	6 (7.23)	
	Insulin			
	Basal	0 (0)	1 (1.20)	
	Prandial	1 (5.88)	4 (4.82)	
	Basal bolus	2 (11.76)	8 (9.64)	
	Mixed	0 (0)	2 (2.41)	
	OAD + insulin	8 (47.06)	27 (32.53)	
Duration of Treatment	<1 year	3 (17.65)	5 (6.02)	0.281
	1–5 years	3 (17.65)	28 (33.73)	
	5–10 years	5 (29.41)	19 (22.89)	
	10+ years	6 (35.29)	31 (37.35)	

Notes: DFU = Diabetic Foot Ulcer, OAD = Oral Antidiabetic Drug

The screening conducted using the BDI-II instrument found that most participants scored 0–13 and were considered to have minimal depression. While, another 17% scored equal to or more than 14, classified as having mild to severe depression. Based on the BDI-II classification, 83% of participants had minimal depression, 8% mild depression, 7% moderate depression, and 2% severe depression, as shown in Table 2.

The correlation analysis between several variables and depression is presented in Table 3. From bivariate analysis, comorbidity correlated statistically with depression (p-value<0.036). While, other variables such as sex, age, education, nutritional status, duration of diabetes, and record of DFU were not statistically significant. No correlation was found significant for types of diabetes treatment or duration of treatment. Multivariate analysis in Table 4 showed factors associated with depression in T2DM patients with one or more comorbidities was eight times more likely to experience depression than those with none (adjusted PR of 8.09; 95% CI = 1.01–65.12).

Discussion

In this study, the prevalence of depression in DM patients during the COVID-19 pandemic was 17%. This data was higher than the prevalence of depression globally, as stated in 2017 WHO data (4.4%),[6] and 27 European countries collected data of 2013–2015 (6.38%).[14] While the prevalence of depression among PWD in general ranges from 10–15%.[15] These suggested that depression was more prevalent among DM patients compared to the general population. The current COVID-19 might also increase predisposed individuals' risk of psychiatric ailments. A survey by Ettman, *et al.*,[9] stated that the prevalence of depression (mild-severe) in-

Table 4. Multivariate Analysis Factors Associated with Depression in People with Diabetes

Variable	Category	Crude PR (95%CI)	Adjusted PR (95% CI)
Sex	Male	1.09 (0.42–2.88)	1.74 (0.61–4.95)
	Female	1.00	1.00
Age (year)	60+	01.04 (0.40–2.69)	1.13 (0.41–3.10)
	<60 years old	1.00	1.00
Education	≥Senior high school (University)	0.66 (0.26–1.71)	0.72 (0.25–2.06)
	<Senior high school	1.00	1.00
Nutritional status	Obesity	1.55 (0.59–4.07)	1.60 (0.58–4.41)
	No obesity	1.00	1.00
Duration of diabetes	10+ years	0.76 (0.29–1.96)	0.72 (0.14–3.74)
	<10 years	1.00	1.00
Comorbidity	1 comorbid+	6.53 (0.87–49.28)	8.09 (1.01–65.12)*
	No comorbid	1.00	1.00
History of DFU	Yes	0.91 (0.26–3.18)	1.36 (0.34–5.46)
	No	1.00	1.00
Type of medical regiment	Insulin	1.56 (0.58–4.21)	1.83 (0.63–5.36)
	Not Insulin	1.00	1.00
Duration of medication	10+ years	0.93 (0.34–2.51)	1.21 (0.23–6.41)
	<10 years	1.00	1.00

Notes: PR = Prevalence Ratio, DFU = Diabetic Foot Ulcer, CI = Confidence Interval
*Result of correlation test was expressed through measurement of prevalence ratio. People with diabetes who had >1 comorbid were at eight times greater risk for depression.

creased three times higher, from 8.5% before the COVID-19 pandemic to 27.8% during the COVID-19 pandemic. It is important to note that the COVID-19 pandemic may impact PWD. Care should be taken to detect early signs of depression in PWD.

Findings in this study revealed that women were highly likely to suffer from depression, with a percentage of 61%. Torre, *et al.*,[14] explained that in 27 European countries, the prevalence of depression in women was 7.74% and lowered in men, with a percentage of 4.89%. The study by Alonso-Moran, *et al.*,[15] in Spain reported that 9.8% of patients diagnosed with depression consist of 15.1% in women and 5.2% in men. These findings may indicate that women are more prone to depression than men and paying attention if there is depressive behavior in women might be necessary.

Another participants characteristic in this study showed that the biggest age group who experienced depression was older than 60 years. This result was similar to WHO data which reports that the prevalence of depression culminates in adult-old age (above 7.5% in women aged 55–74 years old and above 5.5% in men).[6] Older adults, in general, already have underlying conditions that are risk factors for depression. Those conditions are functional and cognitive impairment, comorbid medical conditions, social isolation, and widowed or separated marital status.[16] Diabetes could be one of the comorbid conditions in the elderly. In addition, social isolation during the COVID-19 pandemic might aggravate the risk of depression. The look Action for Health in Diabetes (AHEAD) study found that the prevalence of mild or greater depressive symptoms in older adults (mean [SD] age 75.6 [6.0] years) with diabetes was more than 1.6 times higher during COVID-19 than before the pandemic.[17]

Obesity in diabetes can escalate the risk of depression. Other findings in this study showed that most respondents, through measurement of BMI, have obesity grade 1. This result was similar to a meta-analysis study by Chauvet-Gelinier, *et al.*,[18] stated that obesity increases the risk of future depression (unadjusted OR = 1.55; 95% CI = 1.22-1.98; p-value<0.001). The underlying mechanism is the increase of adiponectin and accumulating adipose tissues that stimulate inflammatory cytokines, which can increase neuroinflammation and depressive behavior, endothelial dysfunction, and oxidative stress.[18] Obesity and depression in PWD are associated with hormonal dysregulation, including the hypothalamic-pituitary-adrenal (HPA) axis, cortisol, leptin, adiponectin, resistin, and insulin.[5,18] Those disruptions might lead to insulin resistance and depression.[18]

The Diabetes in Adolescence Engagement and Monitoring by Pharmacists (DIADEMA) study conducted by Salinero-Fort, *et al.*,[19] in Spain reported that insulin and oral antidiabetic are significantly related to depression (OR = 1.802; p-value≤0.001). Two points elucidate these conditions. First, frequent glucose measurements and insulin injections induce pain, distress, and depression. Second, insulin is commonly used in poor glycemic control, and non-optimal diabetes control leads to worse moods and tremendous stress.[20] Those conditions might elucidate the high prevalence of depression found in this study since more than a third of participants

(35%) were treated with a combination of oral antidiabetic and insulin.

This study found a more significant prevalence of mild to severe depression in T2DM patients diagnosed for at least five years or longer. This result was consistent with the study by Darwish, *et al.*,[21] showed that the duration of diabetes affects the development of depressive symptoms. In general, depressive symptoms immediately increase after people are diagnosed with diabetes, decrease over several years, and increase within a longer duration. Depression coincides with longer diabetes duration and has been proven to increase frailty score and cerebral macrovascular complications.[21] All those things contribute to depressive symptoms, for instance, anhedonia and apathy. It is necessary to be aware of these complaints in patients with a long record of diabetes.

A study by Ahmad, *et al.*,[22] reported that DFU patients are more likely to undergoing depression and anxiety. The likelihood of patients who have DFU for more than 7 months to suffer depression is 12.62-fold higher than less than 7 months (p-value = 0.001 95% CI = 1.48–4.67).[22] It was sensible that DFU disrupted a patient's daily life. These included changes in sleep patterns, impaired mobility, and disturbances in certain aspects of life, such as feelings of loneliness, helplessness, anxiety, and depression.[22] However, this study could not portray those findings because 81% of respondents had no record of DFU or amputation.

Although this study showed a higher prevalence of women in the mild to severe depression group, no significant correlation between participants' sex and depression was observed in this study. Demmer, *et al.*,[23] reported that depressive symptoms were associated with an increased risk of diabetes, particularly in women. This was proven by the risk ratio (RR) of depressive symptoms between men and women, which was 0.69 [0.43–1.10] and 2.11 [1.06–4.19], with a p-value of <0.007. It proved that men and women represented different ways of dealing with stress and adversity, which might contribute to different diabetes profiles. Men tend to be aggressive and engage in activities, while women are likely to think a lot, reduce physical activity, and eat more. In addition, women tend to have an exaggerated inflammatory response to chronic stress. Demmer, *et al.*,[23] reported that women with depressive symptoms favor consuming sugary and fast food more than fruits and vegetables, leading to increased adipose tissue, insulin resistance, metabolic disturbance, and mood disorder risk.

According to this study, comorbidities were significantly correlated with depression. Comorbidity is the coexistence of one or more additional diseases or disorders occurring concomitantly with a primary disease or disorder, whether noncommunicable, mental, or infectious.[24] The mechanism that could explain this is comorbidities such as hypertension and obesity caused by neurohormonal alteration by leptin. Leptin regulates appetite, stimulates sympathetic nerves, and increases insulin sensitivity, natriuresis, diuresis, and angiogenesis. Leptin normally is secreted to blood circulation in low concentrations.[5,18] However, in obese people, leptin resistance occurs, causing hypertension and depressive symptoms.[18]

This study had its limitation that must be acknowledged. As the hospital where the study took place was a tertiary hospital, most patients admitted already had multiple comorbidities. This situation could exacerbate the condition and lead to a higher prevalence. A single-center study's results might not represent other populations. However, this study might benefit future study as a reference point investigating other associated factors related to depression and diabetes, especially during the COVID-19 pandemic. The potential bias that might arise from self-completion questionnaires in crowded clinic settings run the risk of being biased by respondents' quick and disorganized responses. This condition can be mitigated by assisting in the less crowded area and ensuring the respondents are in their free time.

Conclusion

This study shows that the prevalence of depression among T2DM patients was 17% at a tertiary hospital during the COVID-19 pandemic. Amongst factors associated with depression, having one or more comorbidities is associated with an increased risk of depression in T2DM patients in this study. Due to a substantial proportion of PWD with complication in a tertiary hospital, this finding suggests that screening for depression in PWD is clinically beneficial. Early detection and prompt handling to address psychological ailments in PWD is essential to provide a comprehensive management of diabetes.

Abbreviations

NCDs: Noncommunicable Diseases; WHO: World Health Organization; IDF: International Diabetes Federation; Riskesdas: *Riset Kesehatan Dasar*; DM: Diabetes Mellitus, PWD: People with Diabetes; T2DM: Type 2 Diabetes Mellitus; COVID-19: coronavirus disease 2019; CI: Confidence Interval; BDI-II: Beck Depression Inventory-II; BMI: Body Mass Index; DFU: Diabetic Foot Ulcer; CKD: Chronic Kidney Disease; CVD: Cardiovascular Disease; CAD: Coronary Artery Disease; CHF: Congestive Heart Failure; OAD: Oral Antidiabetics; SHS: Senior High School; PR: Prevalence Ratio; AHEAD: Action for Health in Diabetes; SD: Standard Deviation; HPA: Hypothalamic-Pituitary-Adrenal; DIADEMA: Diabetes in Adolescence Engagement and Monitoring by Pharmacists; OR: Odds Ratio; RR: Risk Ratio.

Ethics Approval and Consent to Participate

Ethical approval was obtained from The Ethics Commission of

Fatmawati General Hospital (19/KEP/VI/2021).

Competing Interest

The author declares that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The data and materials in this study are available to the corresponding author upon request.

Authors' Contribution

All authors were involved in this study process. MIM and DP drafted the study topics, together with JN, ME, and IAK, who had a role in the intellectual content of the study, and provided final approval for publication. NM and DNA contributed to the study design, analysis, and interpretation of the data, along with PIP designing and preparing the manuscript.

Acknowledgment

This study received a grant from Fatmawati General Hospital. All the authors would like to thank all who have been involved and helped in the process of this study.

References

1. World Health Organization. Noncommunicable diseases: progress monitor 2020. Geneva: World Health Organization; 2020.
2. World Health Organization. Noncommunicable diseases country profiles 2018. Geneva: World Health Organization; 2018.
3. International Diabetes Federation. IDF diabetes atlas ninth edition 2019. Brussels: International Diabetes Federation; 2019.
4. Badan Penelitian dan Pengembangan Kesehatan. Hasil utama Riskesdas 2018. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018.
5. Moulton CD, Pickup JC, Ismail K. The link between depression and diabetes: the search for shared mechanisms. Lancet Diabetes & Endocrinology. 2015; 3 (6): 461-71.
6. World Health Organization. Depression and other common mental disorders: global health estimates. Geneva: World Health Organization; 2017.
7. Sartorius N. Depression and diabetes. Dialogues in Clinical Neuroscience. 2018; 20 (1): 47-52.
8. Pusat Data dan Informasi Kementerian Kesehatan Republik Indonesia. Situasi kesehatan jiwa di Indonesia. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018.
9. Ettman CK, Abdalla SM, Cohen GH, Sampson L, Vivier PM, Galea S. Prevalence of depression symptoms in US adults before and during COVID-19 pandemic. JAMA Netw Open. 2020; 3 (9): e2019686.
10. Alessi J, de Oliveira GB, Franco DW, do Amaral BB, Becker AS, Knijnik CP, et al. Mental health in the era of COVID-19: prevalence of psychiatric disorders in a cohort of patients with type 1 and type 2 diabetes during the social distancing. Diabetology & Metabolic Syndrome. 2020; 12: 76.
11. Ahmed HAS, Fouad AM, Elotla SF, Joudeh AI, Mostafa M, Shah A, et al. Prevalence and associated factors of diabetes distress, depression and anxiety among primary care patients with type 2 diabetes during the COVID-19 pandemic in Egypt: a cross-sectional study. Front Psychiatry. 2022; 13: 937973.
12. Garcia-Batista ZE, Guerra-Pena K, Cano-Vindel A, Herrera-Martinez XS, Medrano LA. Validity and reliability of the Beck Depression Inventory (BDI-II) in general and hospital population of Dominican Republic. PloS One. 2018; 13 (6): e0199750.
13. Gebrie MH. An analysis of Beck Depression Inventory 2nd Edition (BDI-II). Glob J Endocrinol Metab. 2018; 2 (3).
14. Arias-de la Torre J, Vilagut G, Ronaldson A, Serrano-Blanco A, Martin V, Peters M, et al. Prevalence and variability of current depressive disorder in 27 European countries: a population-based study. Lancet Public Health. 2021; 6 (10): e729-38.
15. Alonso-Moran E, Satylganova A, Orueta JF, Nuno-Solinis R. Prevalence of depression in adults with type 2 diabetes in the Basque Country: relationship with glycaemic control and health care costs. BMC Public Health. 2014; 14: 769.
16. Idaiani S, Indrawati L. Functional status in relation to depression among elderly individuals in Indonesia: a cross-sectional analysis of the Indonesian National Health Survey 2018 among elderly individuals. BMC Public Health. 2021; 21 (1): 2332.
17. Chao AM, Wadden TA, Clark JM, Hayden KM, Howard MJ, Johnson KC, et al. Changes in the prevalence of symptoms of depression, loneliness, and insomnia in U.S. older adults with type 2 diabetes during the COVID-19 pandemic: the look AHEAD study. Diabetes Care. 2022; 45 (1): 74-82.
18. Chauvet-Gelinier JC, Roussot A, Cottenet J, Brindisi MC, Petit JM, Bonin B, et al. Depression and obesity, data from a national administrative database study: geographic evidence for an epidemiological overlap. PLoS One. 2019; 14 (1): e0210507.
19. Salinero-Fort MA, Gomez Campelo P, San Andres-Rebollo FJ, Cardenas-Valladolid J, Abanades-Herranz JC, de Santa Pau EC, et al. Prevalence of depression in patients with type 2 diabetes mellitus in Spain (The DIADEMA STUDY): results from MADIABETES cohort. BMJ Open 2018; 8 (9): e020768.
20. Snoek FJ, Bremmer MA, Hermanns N. Constructs of depression and distress in diabetes: time for an appraisal. Lancet Diabetes & Endocrinology. 2015; 3 (6): 450-60.
21. Darwish L, Beroncal E, Sison MV, Swardfager W. Depression in people with type 2 diabetes: current perspectives. Diabetes Metab Syndr Obes. 2018; 11: 333-43.
22. Ahmad A, Abujbara M, Jaddou H, Younes NA, Ajlouni K. Anxiety and depression among adult patients with diabetic foot: prevalence of associated factors. J Clin Med Res. 2018; 10 (5): 411-8.
23. Demmer RT, Gelb S, Suglia SF, Keyes KM, Aiello AE, Colombo PC, et al. Sex differences in the association between depression, anxiety, and type 2 diabetes mellitus. Psychosom Med. 2015; 77 (4): 467-77.
24. World Health Organization. Regional Office for Europe. Addressing comorbidity between mental disorders and major noncommunicable diseases. Copenhagen: World Health Organization; 2017.

Lolo, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 264-269
DOI: 10.21109/kesmas.v17i4.6224

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Quality of Life of Hypertensive Patients Undergoing Chronic Disease Management Program during the COVID-19 Pandemic

Widya Astuty Lolo[1*], Gayatri Citraningtyas[1], Deby Afriani Mpila[1], Heri Wijaya[2], Sandeep Poddar[3]

[1]Study Program of Pharmacy, Faculty of Mathematics and Natural Sciences, Universitas Sam Ratulangi, Manado, Indonesia, [2]Sekolah Tinggi Ilmu Kesehatan Samarinda, Samarinda, Indonesia, [3]Research & Innovation Division, Lincoln University, Selangor, Malaysia

Abstract

The COVID-19 pandemic has restricted some common activities for hypertensive patients undergoing the Chronic Disease Management Program at primary health care, decreasing the quality of life. This study aimed to measure the quality of life of hypertensive patients undergoing the Chronic Disease Management Program at primary health care of Manado City, North Sulawesi Province, Indonesia, during the COVID-19 pandemic. Also to determine factors influencing hypertension such as sex, age, education, employment status, monthly income and duration of hypertension. This cross-sectional study was carried out on 150 hypertensive patients randomly sampled at primary health care from June to September 2021. The data were analyzed using the Mann-Whitney test. The utility value and the visual analog scale of hypertensive patients with and without complications were 0.808±0.13 and 80.2±8.16 and 0.761±0.17 and 75.1±7.56, respectively. The quality of life of hypertensive patients without complication is better than that of hypertensive patients with complication.

Keywords: Chronic Disease Management Program, COVID-19, hypertension, noncommunicable disease, quality of life

Introduction

By 2025, 1.56 billion adults are estimated to suffer from hypertension. The data from the 2018 Indonesian Basic Health Research/*Riset Kesehatan Dasar* (Riskesdas) showed an increase in the prevalence of hypertension in Indonesia from 2013 to 2018 by 25.8% to 34.11% and particularly in North Sulawesi Province in 2018 by 33.12%.[1] Hypertension was recorded as a comorbid condition, with the highest percentage of the incidence of COVID-19 patients at 49.8%.[2] Elderly patients and comorbid hypertension may be risk factors for a poor prognosis in patients with COVID-19. Therefore, the government should treat hypertensive patients because they are vulnerable to coronavirus infection.[2,3]

Since January 1, 2014, Healthcare and Social Security Agency/*Badan Penyelenggara Jaminan Sosial Kesehatan* (BPJS Kesehatan) has been committed to ensuring equitable health for all Indonesians by providing decent health care for the community. One of the government's health service systems is integrated between participants, health facilities, and BPJS Kesehatan in the form of the Chronic Disease Management Program/*Program Pengelolaan Penyakit Kronis* (Prolanis). Furthermore, it is designed to offer people with hypertension and type 2 diabetes mellitus an optimal quality of life at affordable healthcare costs. Activities included in Prolanis include medical/educational consultations, home visits, reminders, club activities, and monitoring of health status. However, the COVID-19 pandemic resulted in limited medical/educational consultations; hence, home visits and club activities were not carried out. This condition is because restrictions on community activities are being put in place following government regulations to prevent the spread of COVID-19.

The European Quality of Life-5 Dimensions (EQ-5D) consists of a short questionnaire and the determination of the Visual Analog Scale (VAS) value, which only takes a short time. The results of the questionnaire will give a clear picture of the participants' health condition.[4] The standard measure of health status developed by the EuroQol Group, European Quality of Life, can be used in clinical and economic assessments. The EQ-5D has been widely used to measure Health-Related Quality of Life (HRQoL), both in the general population and directly in patients.[4] It is also used to describe and assess the health status of various diseases. The European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) instrument is widely used and can measure HRQoL and

Correspondence:* *Widya Astuty Lolo, Study Program of Pharmacy, Faculty of Mathematics and Natural Sciences, Universitas Sam Ratulangi, Kleak, Manado City, North Sulawesi, Indonesia, 95115, Email: widyaastutylolo@unsrat.ac.id, Phone: +62 821 9353 6448*

Received : September 12, 2022
Accepted : November 27, 2022
Published : November 30, 2022

utility.[5] The EQ-5D-5L instrument consists of five dimensions describing individual health in walking ability (mobility), self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension has five severity levels: no problems, slight problems, moderate problems, severe problems, and extreme problems.[5] However, to accurately measure the quality of life (QoL) of Indonesians, it is better to use the Indonesian version of The EQ-5D-5L.[6-8]

However, cardiovascular disease and hypertension can significantly affect the QoL of patients, and a long-term reduction in cardiovascular risk is an important goal in treating high blood pressure.[6] A previous study tried to find ways to improve the QoL of people with high blood pressure so that they can do daily tasks better, have less physical and mental pain, and fully participate in family and social life.[9] In the context of health, the QoL is often equated with the length of life. In order to determine the general population and patients' health status and to measure the impact of health care interventions, an assessment of various elements affected physically, mentally, emotionally, and socially is used.[10] Hypertension is associated with a lower QoL, with patients scoring lower in almost all dimensions, including physical ability and vitality, compared to the general population. This disease affects patients' QoL in the form of headaches, dizziness, depression, anxiety, and fatigue as well as impaired vitality, social function, mental health, and psychological function.[11,12]

The prevalence of hypertension is increasing every year, specifically in North Sulawesi Province.[1] Further studies should be carried out to improve the QoL, the service, and the treatment system for patients suffering from the disease. Locally, the results of further studies can be a reference for the organizers to improve further the QoL of participants in the chronic disease management program. Globally, it can be used as information and reference material that a health service policy program existing in Indonesia through the Prolanis can improve the QoL of hypertensive patients. Therefore, this study aimed to measure the QoL of hypertensive patients undergoing Prolanis during the COVID-19 pandemic and determine the factors that significantly influenced it using the EQ-5D-5L instrument.

Method

This cross-sectional study was conducted during the COVID-19 pandemic from June to September 2021 at five primary health cares (PHCs) in Manado City, North Sulawesi Province, Indonesia. This city was selected due to a high prevalence of hypertension.[1] The subjects were 150 patients selected using a random sampling method divided into two categories: 75 hypertensives with complications and 75 hypertensives without complications. The selected participants fulfilled the established criteria: aged >18 years, agreed to participate, and had the adequate ability to complete the questionnaire in this study. The questionnaire data consisted of an agreement sheet, characteristic data, and EQ-5D-5L and VAS data. The characteristic data collected include sex, age, education, employment status, monthly income, and duration of hypertension. The stage of conducting the survey started by introducing the authors to the participants, explaining the aims of the study, and asking for willingness to fill out the questionnaire. The participants who agreed to complete the questionnaire were asked to fill out a consent form.

The patient's QoL was measured using the EQ-5D-5L instrument. The conversion of the state of health into the utility value was based on the Indonesian value system. The dimensions measured in the instrument included walking ability, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension was measured with five response levels, where the non-response was coded 1 to code 5 if it was very problematic. There were 3,125 possible state of health combinations to describe the level of each dimension, ranging from 11111 (perfect health) to 55555 (worst health). Furthermore, the value of the VAS was determined on a scale of 0–100, corresponding to the state of health observed by the participants during the study period. The number 0 represented the worst health status imaginable, while 100 represents the best health status imaginable,[5] and the questionnaire used was validated.[6-8]

The percentages of patient characteristics were calculated, which included sex, age, education, employment status, monthly income, and duration of hypertension. Furthermore, grouping was carried out based on the problem response in each EQ-5D-5L domain. The value for utility value conversion was based on the Indonesian value system. The data were analyzed using SPSS 22.0 for Windows (free version). Since the utility and VAS scores were not normally distributed, the Mann-Whitney test,[13] was used to observe the differences in each group of patients' QoL based on their characteristics.

Results

This study was conducted on 150 patients at five PHCs in Manado City that was committed to being a place for data collection during the COVID-19 pandemic from June to September 2021. The population was residents of Manado City, and the sample was those who came to the PHCs. According to the data, most participants with hypertension, with or without complications, were female, aged ≤50, not attending higher education, unemployed, earned the regional minimum wage (RMW), and had been suffering for more than a year (Table 1).

Table 1. Patients Characteristics

Variable	Category	Hypertension			
		Without Complication		With Complication	
		n = 75	%	n = 75	%
Sex	Male	24	32	30	40
	Female	51	68	45	60
Age	≤50 years	22	29.33	17	22.67
	>50 years	53	70.67	58	77.33
Education	≤Senior high school	42	56	46	61.33
	>Senior high school	33	44	29	38.67
Employment status	Employed	31	41.33	22	29.33
	Unemployed	44	58.67	53	70.67
Monthly income	≤RMW	48	64	52	69.33
	>RMW	27	36	23	30.67
Duration of hypertension	≤1 year	17	22.67	9	12
	>1 year	58	77.33	66	88

Note: RMW = Regional Minimum Wage

Table 2. Problem Responses in Each European Quality of Life-5 Dimensions-5 Levels Domain

EQ-5D-5L Domain	Category	Hypertension	
		Without Complication	With Complication
		n (%)	n (%)
Mobility	No Problem	51 (68%)	41 (54.67%)
	Problem	24 (32%)	34 (45.33%)
Self-care	No Problem	67(89.33%)	59 (78.67%)
	Problem	8 (10.67%)	16 (21.33%)
Usual activity	No Problem	65(86.67%)	56 (74.67%)
	Problem	10 (13.33%)	19 (25.33%)
Pain/Discomfort	No Problem	10 (13.33%)	8 (10.67%)
	Problem	65 (86.67%)	67 (89.33%)
Anxiety/Depression	No Problem	29 (38.67%)	30 (40%)
	Problem	46 (61.33%)	45 (60%)

Note: EQ-5D-5L = European Quality of Life-5 Dimensions-5 Levels

Table 2 describes the problem response data in each EQ-5D domain. The highest problem-free responses among participants without complications were reported with self-care (89.33%) and usual activities (86.67%). The same applied to participants with complications: self-care (78.67%) and usual activities (74.67%). The lowest problem response in hypertensive patients with and without complications was self-care and usual activities, at 21.33%, 25.3%, 10.67%, and 13.33%, respectively. In contrast, most problematic responses were reported in the pain/discomfort and anxiety/depression dimensions in hypertensive patients with or without complications. Hypertensive patients without complications reported pain/discomfort at 86.67% and anxiety/depression at 61.33%. For hypertensive patients with complications, the percentages of the pain/discomfort and anxiety/depression domains were 89.33% and 60%, respectively.

Data in Table 3 describes the utility and VAS values of hypertensive patients with and without complications. Hypertensive patients without complications had a utility value of 0.808±0.13 and VAS value of 80.2±8.16, while hypertensive patients with complications had a utility value of 0.761±0.17 and VAS value of 75.1±7.56. A comparison of the QoL in two groups of participants showed that the group of hypertensive patients without complications had a better QoL than those with complications based on utility and VAS values. The statistical utility value test with the Mann-Whitney test revealed significant differences in hypertensive patients without complications in age (p-value<0.001), monthly income (p-value<0.001), and duration of hypertension (p-value <0.001) but not in those with complications in age (p-value<0.001), education (p-value = 0.020), employment status (p-value = 0.001), and monthly income (p-value = 0.067). On the other hand, the VAS value showed a significant difference in patients' characteristics. In hyper-

Table 3. Value of Utility and Visual Analog Scale Based on Hypertensive Patients' Characteristics

Characteristic	Category	Utility						Visual Analog Scale					
		Without Complication			With Complication			Without Complication			With Complication		
		Average	SD	p-value	Average	SD	p-value	Average	SD	p-value	Average	SD	p-value
Total		0.808	0.13		0.761	0.17		80.2	8.16		75.1	7.56	
Sex	Male	0.847	0.03	0.090	0.774	0.18	0.559	82.1	3.88	0.047	0.774	0.18	0.955
	Female	0.791	0.16		0.753	0.17		79.3	9.44		0.753	0.17	
Age	<50 years	0.900	0.07	<0.001	0.886	0.07	<0.001	86.4	7.59	<0.001	0.886	0.07	<0.001
	≥50 years	0.770	0.14		0.725	0.18		77.6	6.98		0.725	0.18	
Education	≤SHS	0.816	0.11	0.960	0.735	0.18	0.020	79.9	6.58	0.909	0.735	0.18	0.151
	>SHS	0.799	0.16		0.807	0.15		80.6	9.90		0.807	0.15	
Employment status	Employed	0.819	0.15	0.419	0.863	0.08	0.001	81.1	9.46	0.660	0.863	0.08	0.010
	Unemployed	0.801	0.12		0.719	0.19		79.5	7.14		0.719	0.19	
Monthly income	≤RMW	0.769	0.15	<0.001	0.738	0.18	0.026	77.3	7.07	<0.001	0.738	0.18	0.076
	>RMW	0.879	0.07		0.813	0.16		85.4	7.46		0.813	0.16	
Duration of hypertension	≤1 year	0.907	0.06	<0.001	0.861	0.04	0.067	87.6	6.15	<0.001	0.861	0.04	0.891
	>1 year	0.780	0.14		0.747	0.18		78.0	7.37		0.747	0.18	

Notes: SHS = Senior High School, SD = Standard Deviation; RMW = Regional Minimum Wage

Table 4. Binary Logistic Regression Analysis on Factors Significantly Associated with Utility of Hypertensive Patients with Complication

Variable	p-value	Odds Ratio
Sex	0.362	0.560
Education	0.349	2.293
Employment status	0.011	14.253
Monthly income	0.672	0.724

Table 5. Binary Logistic Regression Analysis on Factors Significantly Associated with Utility of Hypertensive Patients without Complication

Variable	p-value	Odds Ratio
Age	0.023	10.611
Education	0.094	10.161
Employment status	0.541	0.460
Monthly income	0.087	0.110

tensive patients without complications, the characteristics were sex (p-value<0.047), age (p-value<0.001), monthly income (p-value<0.001), and duration of hypertension (p-value<0.001), while those with complications, the characteristics differed in age (p-value<0.001) and employment status (p-value<0.010). This significant difference indicated that there were differences in QoL in each group of participants according to these variables. Overall, age in each patient group showed a significantly different value (p-value<0.001).

The output results are presented in Table 4. Variables in the equation, with variable X4 (employment status) having a significant value of 0.011, which was less than 0.05 in this study. This variable partially had a significant effect on the Y (with complications) variable with an odds ratio (OR) value of 14.253. Table 5 describes that in this study, variable X2 (age) had a significant value of 0.023 and was smaller than 0.05. The age variable partially had a significant effect on the Y (without complications) variable, with an OR value of 10.611. Variable X5 (monthly income) had a significant value of 0.087, which was more than 0.05, so this variable partially had no significant effect on variable Y (without complications) with an OR value of 0.110.

Discussion

The distribution of participants' data according to sex showed that females were the majority of participants, with a proportion of 60% and 68% for hypertensive patients with and without complications, respectively. This result was in line with a study in Bandar Lampung City, Lampung Province, Indonesia, that 54.48% of 134 hypertensive patients were female.[14] A study in Yogyakarta City, Special Region of Yogyakarta Province, Indonesia, also stated that people suffering from hypertension were dominated by females (75%).[15] In terms of age, patients aged 50 years and above have the highest percentage of participants, both with (77.3%) and without complications (70.67%). A similar study by Kustanti, *et al.,*[16] also showed a high prevalence of hypertension in patients aged 65–80 years (60-80%). The utility and VAS values were higher in patients aged ≤50 years. A study by Xu, *et al.,*[17] supported this data and revealed that hypertensive patients aged ≤50 years had the highest average utility value.

Regarding the relationship between sex and age in terms of the prevalence of hypertension, women at the age of 40 should be aware of hypertension. They enter the premenopausal period at this age. Hence, estrogen and menstruation hormones will decrease until they fi-

nally experience menopause. The estrogen hormone helps control activities and protect against disease.[18] Therefore, when the amount decreases, the organs of the female body lose their capacity and become uncontrolled, which causes the atrial vessels to harden and become tense. Furthermore, it is more dangerous if hypertension occurs in postmenopausal women because endothelial cells will be destroyed due to reduced estrogen content. Damage to the endothelium will trigger the emergence of plaque in the blood and increase blood pressure.[19]

Most patients' education was still at a low level (≤senior high school). Education plays an important role in the therapeutic process as it relates to a person's ability to receive information on the disease and its treatment and can describe their level of understanding.[19] Xu, *et al.,*[17] reported that patients with higher levels of education tend to have a better QoL. A study by Anggara and Prayitno,[20] also found that the prevalence of hypertension tends to be higher in patients with low levels of education due to their ignorance of health and difficulty receiving information that affects their behavior and lifestyle. Furthermore, a low level of education is directly proportional to employment and income.

Most hypertensive patients were unemployed and had an income below the RMW. A low level of education indirectly related to poverty, having no place to live, and finding it difficult to find a permanent job, which eventually becomes a stressor.[21] Stress will cause cardiovascular disease through recurrent force per unit area elevations, as well as by stimulating the system to supply giant amounts of vasoconstriction hormones that increase force per unit area. Although stress does not directly cause cardiovascular disease, it does cause recurrent force per unit area elevations, which may eventually lead to cardiovascular disease.[21] Furthermore, a person's lack of activity impacts a higher heart rate. The higher the heart rate, the harder the heart contracts and the stronger the pressure on the artery walls.[22] Individuals with sufficient socioeconomic status will be able to fulfill their daily needs, and vice versa.

In this study, 77.33% of hypertensive patients did not have complications, and 88% had the disease for more than a year (Table 1). Hypertension is a chronic disease; therefore, measuring the length of the illness is an essential variable in measuring the QoL.[2] A person suffering from a disease for a long period, or in this case, a chronic disease such as hypertension, can affect the quality of their life as it can limit their activities. Patients suffering from this disease for longer than one year have a lower QoL (Table 4). In contrast, Hamida, *et al.,*[23] stated patients suffering from the disease for less than one year have a higher utility value.

The QoL of individuals with hypertension is worse than that of normotensive individuals.[17] Chronic disease is a factor that leads to a person's non-compliance with drug use, which can affect the QoL. Hypertension is one of the risk factors for this disease in which cells become insensitive to insulin and plays a role in increasing the glucose taken up by cells. On the other hand, hypertension can be caused by diabetes mellitus, which can trigger an increase in fluid volume that increases blood pressure, reduce the ability of blood vessels to expand, and cause changes in the body's ability to produce insulin, thereby increasing the rate of blood pressure.[24] The percentage of responses to the pain/discomfort and anxiety/depression domains exceeds half of the participants involved (Table 2). These results were in line with a study by Hamida, *et al.,*[23] which stating that hypertensive patients had the highest problem response in pain/discomfort (100%), followed by the anxiety/depression domain (84%).[23] The health status of hypertensive patients will deteriorate as they age, significantly impacting their poor QoL. All chronic diseases, including hypertension, significantly impact the patient's QoL.

Conclusion

The COVID-19 pandemic has negatively impacted on the QoL of hypertensive patients undergoing Prolanis because not all of the activities there can be implemented. Based on the results of this study, hypertensive patients without complications have a better QoL compared to those with complications. The most commonly-reported problems are in the pain/discomfort and anxiety/depression domains. Factors influencing the patient's low QoL are low level of education (not attaining higher education), unemployment, low monthly income.

Abbreviations

Riskesdas: *Riset Kesehatan Dasar*; BPJS Kesehatan: *Badan Penyelenggara Jaminan Sosial Kesehatan*; Prolanis: *Program Pengelolaan Penyakit Kronis*; EQ-5D: The European Quality of Life-5 Dimensions; VAS: Visual Analog Scale; HRQoL: Health-Related Quality of Life; EQ-5D-5L: The European Quality of Life-5 Dimensions-5 Levels; QoL: Quality of Life; Prolanis: Program Pengelolaan Penyakit Kronis; PHC: Primary Health Care; RMW: Regional Minimum Wage.

Ethics Approval and Consent to Participate

This study was carried out after receiving approval from the Health Research Ethics Committee of RSUP. Prof. Dr. R.D. Kandou, Manado City, North Sulawesi Province, Indonesia, Number 092/EC/KEPK-KANDOU/VI/2021.

Competing Interest

The authors declare that there is no significant competing financial, professional, or personal interest that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The data and materials in this study are available to the corresponding author upon request.

Authors' Contribution

WAL and GC were involved in conceptualizing the study design and contributed to data collection. DAM and HW analyzed the data. SP edited and supervised the work. All authors were involved in the manuscript's writing and final approval.

Acknowledgment

The authors express profound gratitude to the Universitas Sam Ratulangi Research and Community Service Institute for funding this research. The authors are also grateful to the parties who assisted in this research, particularly the primary health care in the Manado City area.

References

1. Badan Penelitian dan Pengembangan Kesehatan. Hasil utama Riskesdas 2018. Jakarta: Kementerian Kesehatan Republik Indonesia; 2018.
2. Hikmawati I, Setiyabudi R. Hipertensi dan diabetes mellitus sebagai penyakit penyerta utama COVID-19 di Indonesia Hypertension and diabetes mellitus as COVID-19 comorbidities in Indonesia. In PROSIDING SEMINAR NASIONAL LPPM UMP 2020. Purwokerto: Lembaga Penelitian dan Pengabdian pada Masyarakat Universitas Muhammadiyah Purwokerto. 2020; 95-100.
3. Zhou X, Zhu J, Xu T. Clinical characteristics of coronavirus disease 2019 (COVID-19) patients with hypertension on renin–angiotensin system inhibitors. Clinical and Experimental Hypertension. 2020; 42 (7): 656-60.
4. Devlin NJ, Brooks R. EQ-5D and the EuroQol Group: past, present and future. Appl Health Econ Health Policy. 2017; 15 (2): 127-37.
5. EuroQol Research Foundation. EQ-5D-5L: About. Rotterdam: EuroQol Research Foundation; 2022.
6. Purba FD, Hunfeld JAM, Iskandarsyah A, Fitriana TS, Sadarjoen SS, Ramos-Goñi JM, et al. The Indonesian EQ-5D-5L value set. PharmacoEconomics. 2017; 35 (11): 1153-65.
7. Sari A, Lestari NY, Perwitasari DA. Validasi ST European Quality of Life-5 Dimensions (EQ-5D) versi Indonesia pada pasien hipertensi di Puskesmas Kotagede II Yogyakarta. PharmaCiana. 2015; 5 (2).
8. Tondok SB, Watu E, Wahyuni W. Validitas instrumen European Qualitiy of Life (EQ-5D-5L) versi Indonesia untuk menilai kualitas hidup penderita tuberkulosis. Holistik Jurnal Kesehatan. 2021; 15 (2): 267-73.
9. Klocek M, Kawecka-Jaszcz K. Quality of life in hypertensive patients. health-related quality of life in cardiovascular patients. 2012; 9-29.
10. Saleem F, Hassali MA, Shafie AA. A cross-sectional assessment of health-related quality of life (HRQoL) among hypertensive patients in Pakistan. Health Expect. 2014; 17 (3): 388-95.
11. Chen L, Zong Y, Wei T, Sheng X, Shen W, Li J, et al. Prevalence, awareness, medication, control, and risk factors associated with hypertension in Yi ethnic group aged 50 years and over in rural China: the Yunnan minority eye study. BMC Public Health. 2015; 15: 383.
12. Ariffin AI, Sukandar H, Defi IR, Sofiatin Y, Roesly RMA. Quality of life among patients with hypertension type 1 in Jatinangor 2014. J Hypertens. 2015; 33: 36-42.
13. Yuswar MA, Susanti R, Az-zahra NS. Pengukuran kualitas hidup pasien pengguna antihipertensi dengan European Quality of Life 5 Dimensions (EQ5D) Questionnaire dan Visual Analog Scale (VAS). J. Sains Kes. 2019; 2 (2): 93-9.
14. Khoirunnisa SM, Akhmad AD. Quality of life of patients with hypertension in primary health care in Bandar Lampung. Indonesian Journal of Pharmacy. 2019; 30 (4): 309-15.
15. Sari A, Lolita L, Fauzia F. Pengukuran kualitas hidup pasien hipertensi di Puskesmas Mergangsan Yogyakarta menggunakan European Quality of Life-5 Dimensions (EQ5D) Questionnaire dan Visual Analog Scale (VAS). Jurnal Ilmiah Ibnu Sina. 2017; 2 (1): 1-12.
16. Kustanti N. Kualitas Hidup Lansia Dengan Hipertensi Di Wilayah Kerja Puskesmas Karangmalang Kabupaten Sragen [Undergraduate Thesis]. Surakarta: Universitas Muhammadiyah Surakarta; 2012.
17. Xu RH, Cheung AWL, Wong ELY. Examining the health-related quality of life using EQ-5D-5L in patients with four kinds of chronic diseases from specialist outpatient clinics in Hong Kong SAR, China. Patient Prefer Adherence. 2017; 11: 1565-72.
18. Majnarić LT, Martinović I, Šabanović Š, Rudan S, Babič F, Wittlinger T. The effect of hypertension duration and the age of onset on CV risk factors expression in perimenopausal women. International Journal of Hypertension. 2019; 2019.
19. Gholamaliei B, Karimi-Shahanjarini A, Roshanaei G, Rezapour-Shahkolaei F. Medication adherence and its related factors in patients with type II diabetes. J Educ Community Health. 2016; 2 (4): 3-12.
20. Anggara FHD, Prayitno N. Faktor-faktor yang berhubungan dengan tekanan darah di Puskesmas Telaga Murni, Cikarang Barat tahun 2012. Jurnal Ilmiah Kesehatan. 2013; 5 (1): 20–25.
21. Fuadina A, Arifin M. The correlation between stress and hypertension in society. In Strategi, Tantangan dan Peluang Tenaga Kesehatan di Era Society 5.0. Pekalongan: LPPM Universitas Muhammadiyah Pekajangan Pekalongan; 2019.
22. Tseng CD, Yen AMF, Chiu SYH, Chen LS, Chen HH, Chang SH. A Predictive model for risk of prehypertension and hypertension and expected benefit after population-based life-style modification (KCIS No. 24). American Journal of Hypertension. 2012; 25 (2): 171-9.
23. Hamida N, Ulfa M, Haris RNH, Endarti D, Wiedyaningsih C. Pengukuran kualitas hidup pasien program Pengelolaan Penyakit Kronis (Prolanis) di Puskesmas Menggunakan Instrumen EQ-5D-5L. Majalah Farmaseutik. 2019; 15 (2): 67-74.
24. Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. Can J Cardiol. 2018; 34 (5): 575-84.

Rachman, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 270-278
DOI: 10.21109/kesmas.v17i4.6303

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Cognitive Function in Type 2 Diabetes Mellitus Patients Taking Metformin and Metformin-Sulfonylurea

Abu Rachman[1], Rani Sauriasari[1*], Nadia Farhanah Syafhan[1], Pukovisa Prawiroharjo[2], Hindun Wilda Risni[1]

[1]Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia, [2]Department of Neurology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Abstract

The most prescribed antidiabetic drugs in Indonesian primary health care are metformin or a combination of metformin and sulfonylurea. Studies on metformin have shown various impacts on cognitive decline in patients with type 2 diabetes mellitus, whereas sulfonylurea has been shown to reduce this impact. This study aimed to compare the impacts of metformin and metformin-sulfonylurea on cognitive function and determine what factors affected it. This cross-sectional study was conducted at Pasar Minggu Primary Health Care involving 142 type 2 diabetes mellitus patients taking metformin or metformin-sulfonylurea for >6 months and aged >36 years. Cognitive function was assessed using the validated Montreal Cognitive Assessment Indonesian version. The effects of metformin and metformin-sulfonylurea on cognitive decline showed no significant difference, even after controlling for covariates (aOR = 1.096; 95% CI = 0.523–2.297; p-value = 0.808). Multivariate analysis showed age (OR = 4.131; 95% CI = 1.271–13.428; p-value = 0.018) and education (OR = 2.746; 95% CI = 1.196–6.305; p-value = 0.017) affected cognitive function. Since a lower education and older age are likely to cause cognitive decline, health professionals are encouraged to work with public health experts to address these risk factors for cognitive function.

Keywords: cognitive decline, cognitive function, diabetes mellitus, metformin, metformin-sulfonylurea

Introduction

Indonesia has 10.7 million people with diabetes mellitus (2% of its population), ranking it seventh in the world.[1] Type 2 diabetes mellitus (T2DM) is a metabolic disease that can cause various complications. Patients with diabetes mellitus (DM) have a one-and-a-half-fold risk of decreased cognitive function compared to those without it.[2] Declines in cognitive function interfere with self-care management behaviors, such as adherence to medication, seeking proper care, glycemic control,[3] and managing the adverse effects of diabetes medications.[4-6]

Various antidiabetic drugs have been evaluated and investigated for their relationship with cognitive function. Metformin is the first line of antidiabetic therapy and is often used alone or in combination with sulfonylurea.[7] Studies that have examined the effects of metformin on cognitive function have yielded different results.[8,9] One study showed that metformin could have a protective effect on cognitive function.[9] Another study showed that metformin causes cognitive decline by creating amyloid plaques in the brain,[10] and B12 deficiency.[6] Another antidiabetic drug, sulfonylurea, was found to reduce the occurrence of cognitive decline in patients with DM.[4] However, another study among diabetic patients found that sulfonylureas increase the risk of hypoglycemia, which increases the risk of cognitive decline.[11] While, the combined use of metformin-sulfonylurea was able to reduced cognitive decline and dementia.[12] Further study should be conducted due to the limited evidence of the effects of the combination of metformin and sulfonylureas on cognitive function.

Although T2DM patients are at high risk for cognitive decline, cognitive function assessments are rarely performed. People with cognitive decline are at risk of having other advanced neurocognitive disorders that can increase the public health burden.[13] Therefore, cognitive assessments can help health care providers address this problem. In addition, considerations in choosing only metformin or a combination need to include comprehensive assessments to optimize therapy for T2DM patients. Aside from drug indications, the effects of medications on cognitive function are of paramount importance in

***Correspondence**:* *Rani Sauriasari, Faculty of Pharmacy, Rumpun Ilmu Kesehatan A Building 3rd Floor Universitas Indonesia, Depok City, West Java, Indonesia, 16424, E-mail: rani@farmasi.ui.ac.id, Phone: +62 821 1425 2811*

Received : October 21, 2022
Accepted : November 27, 2022
Published : November 30, 2022

therapy considerations.[8] Moreover, it is important to explore other factors that can exacerbate declines in cognitive function so that appropriate intervention steps can be taken. Therefore, this study aimed to compare the effects of metformin and a combination of metformin-sulfonylurea on cognitive function and investigated other factors affecting cognitive function.

Method

This cross-sectional study was conducted at Pasar Minggu Primary Health Care in South Jakarta, Indonesia. Data collection took place between October and December 2021. The T2DM patients of Pasar Minggu Primary Health Care could participate in the study if they met the inclusion criteria, were not disqualified by the exclusion criteria, were willing to be interviewed, and signed an informed consent form. A total of 142 T2DM patients were included in this study. The minimum sample size was calculated using the formula in Formula 1.[14] The minimum sample size was 49 participants per group with a P_1 value of 0.67 and a P_2 value of 0.35.[15]

All samples in this study were taken from T2DM patients treated at the outpatient polyclinic for noncommunicable diseases at Pasar Minggu Primary Health Care. The data collection process was carried out via a consecutive sampling method. The participants in this study were selected based on the inclusion criteria: T2DM patients who used metformin alone or a combination of metformin and sulfonylurea for at least six months and aged 36 years and over. Metformin was primarily indicated for patients with an HbA1c value of less than 7.5%, while metformin-sulfonylurea was mainly given to patients with an HbA1c value of more than 7.5% or if monotherapy for three months resulted in an HbA1c value of more than 7%.[16]

The participants in their late adulthood were selected to distinguish the study subjects from type 1 diabetes mellitus (T1DM) patients, who are generally younger. Patients were then disqualified based on the exclusion criteria: used insulin, could not read or write, had difficulty in communicating, had mental disorders, diagnosed with dementia, and had mild depression as measured using the Indonesian version of the Beck Depression Inventory-II (BDI-II) questionnaire to reduce confounding factors that could affect the study variables. A flowchart of the participants' selection is shown in Figure 1.

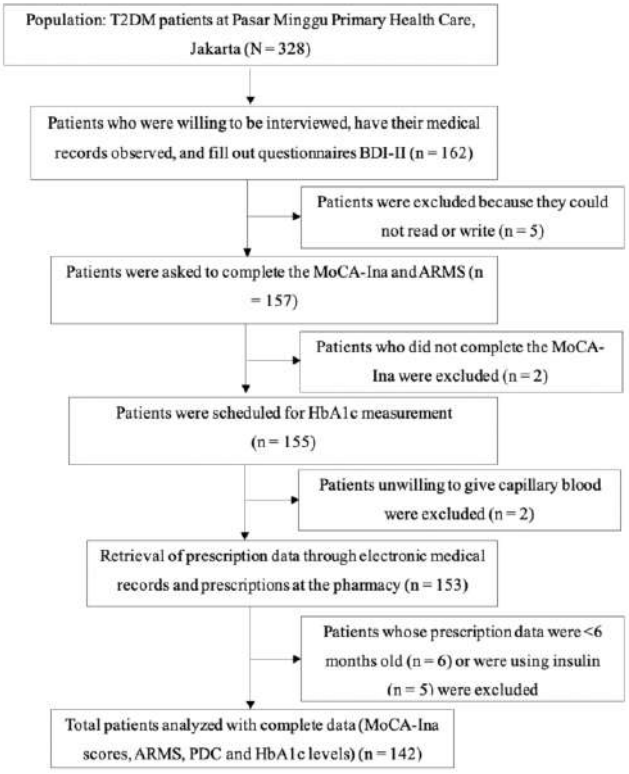
The outcome of this study was cognitive function. Cognitive function refers to problem-solving, learning, thinking, using stored information appropriately, remembering, and paying attention.[17] Cognitive function testing was carried out using the Montreal Cognitive Assessment Indonesian version (MoCA-Ina), which was previously validated.[18] Participants were considered to have not experienced a decline in cognitive function if they had a score ≥26.[19]

Patients who met the inclusion criteria were given the BDI-II questionnaire translated into the Indonesian language, which met validity and reliability tests. Patients with a BDI-II score above 17 were declared to have mild depression.[20] Based on the results of the BDI-II questionnaire, none of the patients in this study had mild depression. Patient demographic data were collected through

$$n = \frac{\left(z_{1-\alpha/2}\sqrt{2\bar{P}(1-\bar{P})} + z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)}\right)^2}{(P_1-P_2)^2}$$

Notes:
$Z_{1-\alpha/2}$ = the normal standard deviation (SD) (5% for type 1 error [p-value<0.05] is 1.96)
$Z_{1-\beta}$ = the normal SD for 90% power (10% for type 2 error is 1.2816)
$P = (P_1+P_2)/2$
P_1 = the proportion of patients using metformin with cognitive decline
P_2 = the proportion of patients using metformin-sulfonylurea with cognitive decline

Formula 1. Sample Size



Notes: T2DM = Type 2 Diabetes Mellitus, MoCA-Ina = Montreal Cognitive Assessment Indonesian Version, ARMS = Adherence to Refills and Medications Scale

Figure 1. Flowchart of Participants' Selection

observation of medical records (the use of drug therapy, weight, height, duration of DM, and disease comorbidities) and interviews with a questionnaire (age, sex, education, and smoking record).

Adherence was assessed by combining two measurement tools, the Indonesian version of the Adherence to Refills and Medications Scale (ARMS) and the proportion of days covered (PDC).[21,22] The participants were interviewed using the ARMS questionnaire. The PDC data were based on patients' visits over the last six months through the e-Puskesmas (an electronic system of patients' visits to primary health care).[22,23] Patients were considered adherent if their ARMS score was less than 12 and their PDC value was ≥80%. All the questionnaires (the Indonesian versions of ARMS, BDI-II, and the MoCA) had been through a translation and back-translation process were then tested for validity and reliability.[18,20,21] Peripheral blood samples were taken to measure HbA1c levels using the Abbott Afinion™ instrument. Hypertension and dyslipidemia were documented based on doctors' written statements in medical records, which means that the criteria for hypertension and dyslipidemia were not determine. Patients were considered smokers if they were current smokers at the time of the interview.

A comparison of the effects of metformin only and metformin-sulfonylurea on cognitive function was conducted. Univariate analysis was performed to describe patient's characteristics. To compare the impacts of the therapies on cognitive function, a Chi-square test was performed, where a p-value of <0.05 was considered significant. Variables with a p-value of <0.25 in the bivariate test or that theoretically had a significant effect on the function were included in the logistic regression. Logistic regression was used to control for confounding variables, and the last model was chosen based on the smallest precision value among all the models. To further identify the variables affecting cognitive function, predictive logistic regression using the backward elimination method was conducted. The variables were selected for the same reason as in the first logistic regression (control for variables). Variables with p-value<0.05 in the last model were considered factors affecting cognitive function. The data are expressed in proportions (n, %) for categorical variables and mean±SD or median (min-max) for numerical variables. The data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 28.0 ((IBM SPSS Statistics Grad Pack 28.0 for Windows or Mac; IBM Corp., Armonk, New York, USA).

Results

The participants in this study consisted of 142 T2DM patients at Pasar Minggu Primary Health Care. Females outnumbered males in each group, with 54 females (76.05%) in the metformin group and 55 males (77.47%) in the metformin-sulfonylurea group. There was a significant difference between the groups in terms of education (p-value = 0.044), as patients with more than 12 years of education were more dominant in the metformin group. Significant differences between groups were also seen in patients' HbA1c levels (p-value = 0.005), ARMS scores (p-value = 0.018), levels of adherence (p-value = 0.075), and vitamin B12 supplementation (p-value = 0.022). The mean age was 59.27 years (SD = 9.2) in the metformin group and 57.90 years (SD = 7.5) in the metformin-sulfonylurea group. There were no significant differences between the groups in age (p-value = 0.335), sex (p-value = 1.000), duration of diabetes (p-value = 0.063), PDC score (p-value = 0.707), body mass index (BMI) (p-value = 0.491), duration of drug consumption (p-value = 1.000), hypertension (p-value = 1.000), dyslipidemia (p-value = 0.595), or smoking (p-value = 1.000). The characteristics of the participants are shown in Table 1.

The participants who experienced a decline in cognitive function significantly outnumbered those who did not (66.90%; 95/142). The proportion of patients aged less than 65 years with normal cognitive function was significantly higher than that of patients aged older than 65 years (p-value = 0.022). Significantly different results were also found in terms of compliance (p-value = 0.024). Although a decline in cognitive function was predominantly observed among females, 71 (74.7%) patients, the difference between the sexes was insignificant. Differences in HbA1c levels were also insignificant despite participants with HbA1c levels of ≥7 being more likely to experience a decline in cognitive function. Education, duration of DM, ARMS score, PDC score, duration of drug consumption, vitamin B12 supplementation, BMI, hypertension, dyslipidemia, and smoking did not significantly increase the odds of cognitive decline (Table 2).

The metformin-sulfonylurea group had more participants who experienced cognitive decline than the metformin group. In the metformin group, the proportion of patients with decreased cognitive function was 63.4%, while that of patients with normal cognitive function was 36.6%. In the metformin-sulfonylurea group, 70.4% of the patients experienced decreased cognitive function. However, there was no significant difference between the two groups (OR = 1.376; 95% CI = 0.682–2.776; p-value = 0.373) (Table 3). To control confounding variables, a multivariate analysis was performed using logistic regression. Bivariate analysis was conducted to select variables that had p-value<0.25, which were age, education, adherence based on the ARMS questionnaire, and comorbid hypertension (Table 2). Sex, HbA1c, B12

Table 1. Participants' Characteristics

Variable	Category	Drug Consumption		n	p-value
		Metformin	Metformin-sulfonylurea		
		(n = 71)	(n = 71)		
Age, year	Mean±SD	59.27±9.2	57.90±7.5	-	0.335
Age, n (%)	6–65 years old	52 (73.2)	57 (80.3)	109	0.427
	>65 years old	19 (26.8)	14 (19.7)	33	
Sex, n (%)	Male	17 (23.94)	16 (22.53)	33	1.000
	Female	54 (76.05)	55 (77.47)	109	
Education, n (%)	>12 years	43 (60.6)	30 (42.3)	73	0.044
	≤12 years	28 (39.4)	41 (57.7)	69	
HbA1c, %	Mean±SD	7.64±1.4	8.85±1.8	-	<0.001
HbA1c level, n (%)	HbA1c<7	24 (33.8)	9 (12.7)	33	0.005
	HbA1c≥7	47 (66.2)	62 (87.3)	109	
Duration of DM, n (%)	≤5 years	46 (64.8)	34 (47.9)	80	0.063
	>5 years	25 (35.2)	37 (52.1)	62	
ARMS	≤12	38 (53.5)	23 (32.4)	61	0.018
	>12	33 (46.5)	48 (67.6)	81	
Proportion of days covered (PDC)	≥80%	50 (70.4)	53 (74.6)	103	0.707
	<80%	21 (29.6)	18 (25.4)	39	
Adherence, n (%)	Adherent	29 (40.8)	18 (25.4)	47	0.075
	Non-adherent	42 (59.2)	53 (74.6)	95	
Duration of drug consumption, n (%)	<12 months	2 (2.8)	3 (4.2)	5	1.000
	≥12 months	69 (97.2)	68 (95.8)	137	
Vitamin B12 supplementation	Yes	59 (83.1)	46 (64.8)	105	0.022
	No	12 (16.9)	25 (35.2)	37	
BMI, kg/m^2	Mean±SD	26.50±4.7	26.80±4.5	-	0.690
BMI in category, n (%)	Skinny–normal (≤25)	30 (42.3)	25 (35.2)	55	0.491
	Overweight–obese (>25)	41 (57.7)	46 (64.8)	87	
Hypertension	No	28 (39.4)	29 (40.8)	57	1.000
	Yes	43 (60.6)	42 (59.2)	85	
Dyslipidemia	No	26 (36.6)	22 (31.0)	48	0.595
	Yes	45 (63.4)	49 (69.0)	94	
Smoker	No	68 (95.8)	67 (94.4)	135	1.000
	Yes	3 (4.2)	4 (5.6)	7	

Notes: SD = Standard Deviation, HbA1c = Hemoglobin A1C, DM = Diabetes Mellitus, ARMS = Adherence to Refills and Medications Scale, BMI = Body Mass Index

supplementation, and BMI were still included in the multivariate analysis because they substantially affected cognitive function. The effect of cognitive function remained insignificant after controlling for confounding variables (Table 4).

Table 5 shows the last model of multivariate analysis using the predictive model. It shows that age (OR = 4.131; 95% CI = 1.271–13.428; p-value = 0.018) and education (OR = 2.746; 95% CI = 1.196–6.305; p-value = 0.017) affected cognitive function.

Discussion

Metformin is an antidiabetic drug widely used alone or in combination with sulfonylurea.[7,11] Both regimens can affect cognitive function, either positively or negatively.[8,11] In this study, the participants were predominantly females because they suffered from T2DM at a higher rate than males. Interestingly, males were 35.2% more at risk of experiencing cognitive decline than females, which is in line with the previous study.[1] However, a study found that women tend to experience more cognitive decline than men.[24] Therefore, more study is needed on sex and cognitive decline.[25]

Participants who suffered from T2DM for less than five years used metformin more (64.8%) than participants who suffered from T2DM for more than five years (35.2%). Participants with a T2DM duration of more than five years used metformin-sulfonylurea (52.1%) more than metformin only (47.9%). This condition was caused by uncontrolled blood sugar levels in more participants, so that the treatment target was not reached. The antidiabetic medicines of those patients were combined with therapy, following the guidelines which recommended metformin as the first line of antidiabetic therapy. If a patient's HbA1c value is more than 7.5% or monotherapy for three months results in an HbA1c value of more than 7%, then metformin-sulfonylurea will be prescribed with a different mechanism.[16]

This study's findings indicated no significant difference between metformin only and metformin-sulfonyl-

Table 2. Factors Increasing the Odds of Cognitive Function Decline

Variable	Category	Cognitive Function		p-value	OR (95% CI)
		Decline	Normal		
		(n = 95)	(n = 47)		
Age, year	Mean±SD	56.06±6.7	59.83±8.9	0.011	-
Age, n (%)	≤65 years old	67 (70.5)	42 (89.4)	0.022	Ref
	>65 years old	28 (29.5)	5 (10.6)		3.510(1.257–9.801)
Sex, n (%)	Male	24 (25.3)	9 (19.1)	0.548	Ref
	Female	71 (74.7)	38 (80.9)		0.701 (0.296–1.658)
Education, n (%)	>12 years	43 (45.3)	30 (63.8)	0.057	Ref
	≤12 years	52 (54.7)	17 (36.2)		2.134 (1.040–4.381)
HbA1c, %	Mean ± SD	8.3±0.9	8.2±0.1	0.896	-
HbA1c level, n (%)	HbA1c<7	24 (25.3)	9 (19.1)	0.548	Ref
	HbA1c≥7	71 (74.7)	38 (80.9)		0.701 (0.296–1.658)
Duration of DM, n (%)	≤5 years	50 (52.6)	30 (63.8)	0.277	Ref
	>5 years	45 (47.4)	17 (36.2)		1.588 (0.774–3.258)
ARMS	<12	35 (36.8)	26 (55.3)	0.062	Ref
	≥12	60 (63.2)	21 (55.3)		2.087 (1.025–4.249)
Proportion of days covered (PDC)	≥80%	70 (73.7)	33 (70.2)	0.813	Ref
	<80%	25 (26.3)	14 (29.8)		0.842 (0.388–1.826)
Adherence, n (%)	Adherent	25 (26.3)	22 (46.8)	0.024	Ref
	Non-adherent	70 (73.7)	25 (53.2)		2.464 (1.184–5.127)
Duration of drug consumption, n (%)	<12 months	2 (2.1)	3 (6.4)	0.414	Ref
	≥12 months	93 (97.9)	44 (93.6)		3.170 (0.511–19.661)
Vitamin B12 supplementation	Yes	67 (70.5)	38 (80.9)	0.264	Ref
	No	28 (29.5)	9 (19.1)		1.765 (0.754–4.128)
BMI, kg/m²	Mean±SD	27.27±4.3	26.34±4.7	0.254	-
BMI in category, n (%)	Skinny–normal (≤25)	38 (40.0)	17 (36.2)		Ref
	Overweight–obese (>25)	57 (60.0)	30 (63.8)	0.797	0.850 (0.413–1.751)
Hypertension	No	33 (34.7)	24 (51.1)		Ref
	Yes	62 (65.3)	23 (48.9)	0.092	1.960 (0.963–3.991)
Dyslipidemia	No	65 (68.4)	29 (61.7)		Ref
	Yes	45 (63.4)	49 (69.0)	0.543	1.345 (0.648–2.791)
Smoker	No	89 (93.7)	46 (97.9)		Ref
	Yes	6 (6.3)	1 (2.1)	0.501	3.101 (0.362–26.535)

Notes: OR = Odds Ratio, CI = Confidence Interval, SD = Standard Deviation, Ref = Reference, HbA1c = Hemoglobin A1C, DM = Diabetes Mellitus, ARMS = Adherence to Refills and Medications Scale, BMI = Body Mass Index

Table 3. Impacts of Metformin-Only and Metformin-sulfonylurea Use on Cognitive Function Decline

Variable	Category	Cognitive Function		p-value	OR (95% CI)
		Decline (<26)	Normal (≥26)		
Drug consumption	Metformin	45 (63.4)	26 (36.6)	0.373	Ref
	Metformin-sulfonylurea	50 (70.4)	21 (29.6)		1.376 (0.682–2.776)

Notes: OR = Odds Ratio, CI = Confidence Interval, Ref = Reference

urea on cognitive function (OR = 1.376; 95% CI = 0.682–2.776; p-value = 0.373). After controlling for education and adherence, there was still no significant difference (aOR = 1.214; 95% CI = 0.590–2.499; p-value = 0.598). These results were in line with several studies that found that these two therapies did not differ significantly regarding their impacts on cognitive function.[11,15] This condition can be caused by vitamin B12 supplementation; 59 patients (83.1%) and 46 patients (64.8%) consumed it in the metformin and metformin-sulfonylurea group, respectively. The use of long-term metformin has been shown to cause B12 deficiency.

B12 deficiency can affect the development and maintenance of the peripheral and central nervous systems. B12 deficiency also affects the blood-brain barrier and thus affects the small blood vessels in the brain. These conditions lead to cognitive decline.[26] B12 supplementation can help improve cognitive function.[27] However, not all T2DM patients took B12 supplements, which affected the results of this study. The ineffectiveness of treatment,

Table 4. Logistic Regression for Controlling Confounding Variables

Model	Confounding variable	Category	p-value	OR	95% CI
Crude	Drug consumption	Metformin	0.373	Ref	0.682–2.776
		Metformin-sulfonylurea		1.376	
Adjusted[a]	Drug consumption	Metformin	0.700	Ref	0.512–2.712
		Metformin-sulfonylurea		1.178	
	Age	≤65 years old	0.023	Ref	1.308–13.748
		>65 years old		4.240	
	Sex	Male	0.219	Ref	0.202–1.442
		Female		0.540	
	Education	>12 years	0.016	Ref	1.224–6.893
		≤12 years		2.904	
	BMI	Skinny–normal (≤25)	0.462	Ref	0.583–3.281
		Overweight–obese (>25)		1.383	
	HbA1c	HbA1c<7	0.320	Ref	0.222–1.635
		HbA1c≥7		0.603	
	ARMS	<12	0.682	Ref	0.395–5.912
		≥12		1.279	
	Adherence	Adherent	0.348	Ref	0.535–5.912
		Non-adherent		1.778	
	Hypertension	No	0.164	Ref	0.795–3.882
		Yes		1.757	
	B12 Supplementation	Yes	0.506	Ref	0.521–3.742
		No		1.397	
Adjusted[b]	Drug consumption	Metformin	0.808	Ref	0.523–2.297
		Metformin-sulfonylurea		1.096	
	Education	>12 years	0.098	Ref	0.890–3.949
		≤12 years		1.875	
	Adherence	Adherent	0.040	Ref	1.036–4.678
		Non-adherent		2.202	

Notes: OR = Odds Ratio, CI = Confidence Interval, HbA1c = Hemoglobin A1C, ARMS = Adherence to Refills and Medications Scale, BMI = Body Mass Index
[a]Adjusted for all variables that had p-value<0.25 in the bivariate analysis or that could theoretically affect cognitive function
[b]The most precise model.

Table 5. Effects of Variables on Decline in Cognitive Function

Variable	Category	p-value	OR	95% CI
Age	≤65 years old	0.018	Ref	1.271–13.428
	>65 years old		4.131	
Education	>12 years	0.017	Ref	1.196–6.305
	≤12 years		2.746	

Notes: OR = Odds Ratio, CI = Confidence Interval

which resulted in the treatment goals not being achieved, also affected the results. In this study, 67.6% of the metformin group and 87.6% of the metformin-sulfonylurea group had an HbA1c level ≥7. According to previous studies, high HbA1c levels result in cognitive function decline.[28,29]

The use of sulfonylureas has a high risk of causing hypoglycemia. Cognitive dysfunction in diabetes can be caused by repeated episodes of moderate to a severe hypoglycemia. During an episode of acute hypoglycemia, patients experience impaired global cognitive function and working memory, delayed verbal and visual memory, and impaired visual-spatial and visual-motor skills.[30] However, when combined with metformin, sulfonylureas reduce the occurrence of cognitive decline.[31] Sulfonylureas also have neuroprotective functions, modulating proinflammatory cytokine release and reducing neuronal loss and necrosis.[32] Although the use of sulfonylureas can cause hypoglycemia, which then triggers cognitive decline, supporting the higher proportion of patients with cognitive decline,[30] in the metformin-sulfonylurea group, its neuroprotective effects and the addition of metformin may have contributed to the insignificant difference between groups. Since data on which patients experienced hypoglycemia were unavailable, further study is needed to confirm this finding.

This study's results demonstrate that metformin only and metformin-sulfonylurea did not affect cognitive function. Therefore, to identify the factors that affect cognitive function, a predictive model was created, and a logistic regression was performed using the enter method. The result revealed that age and education affected cognitive function. Previous studies have found that education is a nonmedical protective factor against cognitive decline.[33,34] The lower the level of education, the higher the risk of cognitive decline. Individuals with higher le-

vels of education are not only at lower risk for cognitive distraction, but also show better cognitive performance than those with low education.[33]

Education is thought to play a role in increasing resistance to neurodegenerative processes. Experiences gained during education, such as continuous exposure to cognitive stimulation and opportunities to gain knowledge and skills, affect an individual's cognitive ability.[34] Furthermore, age is associated with physiological functional decline in various organ systems, including the psychomotor system and cognitive function in the brain. Changes in anatomy and physiology that inevitably occur during aging affect cognitive function.[35] The age difference between DM patients can also explain why some experience neurocognitive morbidity that is clinically significant while most are unaffected.

Cognitive decline has been shown to significantly increase morbidity and mortality and reduce the quality of life, increasing the public health burden.[36] People with cognitive decline are at risk of having other neurodegenerative diseases, such as Alzheimer's disease, which increases the cost burden per patient by as much as USD6,784.[37] A declines in cognitive function can interfere with self-care management behaviors, such as adherence to medication. As education and age can affect cognitive decline, people in the public health sector should be encouraged to pay more attention to nonmedical factors that affect cognitive decline. For populations with less than 12 years of education, special education sessions and health promotion can be implemented to develop knowledge, attitude, and behavior about the importance of good medication management.

Elderly patients need special attention from health professionals to manage their treatment. Collaboration between health professionals has been shown to improve the quality of patient care in the long term.[38] Programs in Indonesian primary health care, such as the Prolanis and Integrated Service Post for Older People/*Pos Pelayanan Terpadu Lansia* (Posyandu Lansia), can be a means for health providers to encourage the elderly with cognitive decline to visit primary health care facilities to monitor and treat their diseases and achieve optimal quality of life and prevent complications.[39,40] At any rate, health professionals are encouraged to work with public health experts to address the effect of medical and nonmedical factors on patient health status.

Strengths and Limitations

This study has some limitations, one of which is its cross-sectional design. A cross-sectional design cannot determine the causal factors of the study variables. Second, this study was only conducted at one primary helath care. Hence, selection bias might have affected the validity of the results, as the sample was not representative of the overall population in Indonesia. Moreover, the sample size was limited and predominantly comprised women, thus limiting statistical power.

However, the inclusion and exclusion criteria, including the minimum antidiabetic therapy duration, helped reduce the limitation. The MoCA-Ina instrument used to measure cognitive function also had high validity and reliability. The metformin and metformin-sulfonylurea groups, the most widely used therapies for T2DM in the primary health care, were examined. Therefore, the results could be useful for assessing the safety of antidiabetic therapies in the community. Given the limitations of the study and the widespread use of metformin and its combination with a sulfonylurea, further study is needed.

Conclusion

This study does not find a significant difference between the impacts of metformin only and the combination of metformin-sulfonylurea on cognitive function. Even though confounding variables are controlled for, the results are not statistically significant. The factors that most affect cognitive decline are education and age.

Abbreviations

T2DM: Type 2 Diabetes Mellitus; MoCA-Ina: Indonesian version of the Montreal Cognitive Assessment; BDI-II: Beck Depression Inventory-II; HbA1c: Hemoglobin A1C; PDC: Proportion of Days Covered, ARMS: Adherence to Refills and Medications Scale; BMI: Body Mass Index.

Ethics Approval and Consent to Participate

This study passed an ethical review conducted by the Health Research Ethics Committee in the Faculty of Medicine at Universitas Indonesia (KEPK FK UI; approval number KET-936/UN2.F1/ETIK/PPM.00.02/2021). Research approval was also given by the Special Capital Region of Jakarta Health Office and then forwarded to the South Jakarta Municipality Health Office and the Pasar Minggu Primary Health Care of South Jakarta.

Competing Interest

The authors declare that there are no significant competing financial, professional, or personal interests that might have affected the performance.

Availability of Data and Materials

The data were not made publicly available, as they contained information that could compromise the privacy of the research participants.

Authors' Contribution

RS contributed to conceptualization, data curation, funding acquisition, investigation, methodology, project administration, supervision, validation, writing, reviewing, and editing. AR contributed to conceptualization, data curation, formal analysis, methodology, supervision,

validation, investigation, writing, reviewing, and editing. All the authors discussed the final results and contributed to the final manuscript. NFS contributed to conceptualization, data curation, methodology, supervision, validation, investigation, writing, reviewing, and editing. PP contributed to conceptualization, methodology, supervision, validation, investigation, writing, reviewing, and editing. HWR contributed to data curation, formal analysis, supervision, writing, reviewing, and editing.

Acknowledgment

This study was funded and supported by a *Penelitian Disertasi Doktor* grant from the Ministry of Education, Culture, Research, and Technology, Republic of Indonesia (NKB-376/UN2.RST/HKP.05.00/2022). The authors gratefully acknowledged the supervisors and colleagues who facilitated this study from start to finish. The authors would also like to thank all the colleagues, respondents, and Pasar Minggu Primary Health Care staff who helped with the data collection.

References

1. Kementerian Kesehatan Republik Indonesia. Tetap produktif, cegah dan atasi diabetes mellitus. Pusat Data dan Informasi Kementrian Kesehatan RI; 2020.
2. Varghese SM, Joy N, John AM, George G, Chandy GM, Benjamin AI. Sweet memories or not? a comparative study on cognitive impairment in diabetes mellitus. 2022; 10 (February): 1–7.
3. Hopkins R, Shaver K, Weinstock RS. Management of adults with diabetes and cognitive problems. Diabetes Spectr. 2016; 29 (4): 224–37.
4. Biessels GJ, Nobili F, Teunissen CE, Simó R, Scheltens P. Series diabetes and brain health 3 understanding multifactorial brain changes in type 2 diabetes: a biomarker perspective. 2021; 19.
5. Moore EM, Mander AG, Ames D, Kotowicz MA, Carne RP, Brodaty H, et al. Increased risk of cognitive impairment in patients with diabetes is associated with metformin. Diabetes Care. 2013; 36 (10): 2981–7.
6. Porter KM, Ward M, Hughes CF, O'Kane M, Hoey L, McCann A, et al. Hyperglycemia and metformin use are associated with b vitamin deficiency and cognitive dysfunction in older adults. J Clin Endocrinol Metab. 2019; 104 (10): 4837–47.
7. Baker C, Retzik-Stahr C, Singh V, Plomondon R, Anderson V, Rasouli N. Should metformin remain the first-line therapy for treatment of type 2 diabetes? Ther Adv Endocrinol Metab. 2021; 12: 1–13.
8. Zhang QQ, Li WS, Liu Z, Zhang HL, Ba YG, Zhang RX. Metformin therapy and cognitive dysfunction in patients with type 2 diabetes. Medicine (Baltimore). 2020; 99 (10): e19378.
9. Samaras K, Makkar S, Crawford JD, Kochan NA, Wen W, Draper B, et al. Metformin use is associated with slowed cognitive decline and reduced incident dementia in older adults with type 2 diabetes: the Sydney memory and ageing study. Diabetes Care. 2020; 43 (11): 2691–701.
10. Picone P, Nuzzo D, Caruana L, Messina E, Barera A, Vasto S, et al. Metformin increases APP expression and processing via oxidative stress, mitochondrial dysfunction and NF-κB activation: use of insulin to attenuate metformin's effect. Biochim Biophys Acta - Mol Cell Res. 2015; 1853 (5): 1046–59.
11. Lee AK, Rawlings AM, Lee CJ, Gross AL, Huang ES, Sharrett AR, et al. Severe hypoglycaemia, mild cognitive impairment, dementia and brain volumes in older adults with type 2 diabetes: the Atherosclerosis Risk in Communities (ARIC) cohort study. Diabetologia. 2018; 61 (9): 1956–65.
12. Tumminia A, Vinciguerra F, Parisi M, Frittitta L. Type 2 diabetes mellitus and Alzheimer's disease: role of insulin signalling and therapeutic implications. Int J Mol Sci. 2018; 19 (11): 3306.
13. Olivari BS, Baumgart M, Taylor CA, McGuire LC. Population measures of subjective cognitive decline: a means of advancing public health policy to address cognitive health. Alzheimer's Dement Transl Res Clin Interv. 2021; 7 (1).
14. Ogston SA, Lemeshow S, Hosmer DW, Klar J, Lwanga SK. Adequacy of sample size in health studies. Biometrics. 1991; 47 (1): 347.
15. Wu CY, Ouk M, Wong YY, Anita NZ, Edwards JD, Yang P, et al. Relationships between memory decline and the use of metformin or DPP4 inhibitors in people with type 2 diabetes with normal cognition or Alzheimer's disease, and the role APOE carrier status. Alzheimer's Dement. 2020; 16 (12): 1663–73.
16. Perkumpulan Endokrinologi Indonesia. Pedoman pengelolaan dan pencegahan diabetes melitus tipe 2 dewasa di Indonesia 2015. PB Perkeni. 2020; 46.
17. Morley JE, Morris JC, Berg-Weger M, Borson S, Carpenter BD, del Campo N, et al. Brain health: the importance of recognizing cognitive impairment: an IAGG consensus conference. J Am Med Dir Assoc. 2015; 16 (9): 731–9.
18. Husein N, Lumempouw S, Ramli Y, Herqutanto. Montreal cognitive assessment versi Indonesia mocaina untuk skrining gangguan fungsi kognitif. Neurona. 2010; 27 (4).
19. Nasreddine ZS, Phillips NA, BÃ©dirian V, Charbonneau S, Whitehead V, Collin I, et al. The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005; 53 (4): 695–9.
20. Ginting H, Näring G, Van Der Veld WM, Srisayekti W, Becker ES. Validating the beck depression inventory-II in Indonesia's general population and coronary heart disease patients. Int J Clin Heal Psychol. 2013; 13 (3): 235–42.
21. Cahyadi H, Prayitno A, Setiawan E. Reliability and validity of adherence to refill and medication scale (ARMS) in Indonesian geriatric population with diabetes; 2015.
22. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Med Pharm Reports. 2019; 92 (2): 117–22.
23. Soraya IA, Sauriasari R, Prawiroharjo P, Risni HW. The association between adherence to oral antihyperglycemic agent and HbA1c level. Pharm Sci Res. 2022; 9 (2): 93–101.
24. Sohn D, Shpanskaya K, Lucas JE, Petrella JR, Saykin AJ, Tanzi RE, et al. Sex differences in cognitive decline in subjects with high likelihood of mild cognitive impairment due to Alzheimer's disease. Sci Rep. 2018; 8 (1): 7490.
25. Petersen RC, Roberts RO, Knopman DS, Geda YE, Cha RH, Pankratz VS, et al. Prevalence of mild cognitive impairment is higher in men. Neurology. 2010; 75 (10): 889 LP – 897.
26. Soh Y, Lee DH, Won CW. Association between vitamin B12 levels

and cognitive function in the elderly Korean population. Medicine (Baltimore). 2020; 99 (30): e21371.
27. Zhang Q, Li S, Li L, Li Q, Ren K, Sun X, et al. Metformin treatment and homocysteine: a systematic review and meta-analysis of randomized controlled trials. Nutrients. 2016; 8 (12): 798.
28. Silverman JM, Schmeidler J, Lee PG, Alexander NB, Beeri MS, Guerrero-Berroa E, et al. Associations of hemoglobin A1c with cognition reduced for long diabetes duration. Alzheimer's Dement Transl Res Clin Interv. 2019; 5: 926–32.
29. Zheng F, Yan L, Yang Z, Zhong B, Xie W. HbA1c, diabetes and cognitive decline: the English Longitudinal Study of Ageing. Diabetologia. 2018; 61 (4): 839–48.
30. Vijayakumar T, Sirisha G, Begam F. Mechanism linking cognitive impairment and diabetes mellitus. Eur J Appl Sci. 2012; 4 (1): 1–05.
31. Vijayakumar PRA. Comparison of different classes of oral antidiabetic. 2019; 10 (7): 3455–60.
32. Hussien NR, Al-Naimi MS, Rasheed HA, Al-Kuraishy HM, Ali AG. Sulfonylurea and neuroprotection: the bright side of the moon. J Adv Pharm Technol Res. 2018; 9 (4): 120–3.
33. Lövdén M, Fratiglioni L, Glymour MM, Lindenberger U, Tucker-Drob EM. Education and cognitive functioning across the life span. Psychol Sci Public Interes. 2020; 21 (1): 6–41.
34. Jansen MG, Geerligs L, Claassen JAHR, Overdorp EJ, Brazil IA, Kessels RPC, et al. Positive effects of education on cognitive functioning depend on clinical status and neuropathological severity. Front Hum Neurosci. 2021; 15: 1–10.
35. Kartikasari D, Ariwinanti D, Hapsari A. Gambaran pengetah kesehat reproduksi siswa SMK Wisnuwardhana Kota Malang. Preventia : The Indonesian Journal of Public Health. 2019; 4 (1): 34–41.
36. Paul KC, Ling C, Lee A, To TM, Cockburn M, Haan M, et al. Cognitive decline, mortality, and organophosphorus exposure in aging Mexican Americans. Environ Res. 2018; 160: 132–9.
37. Leibson CL, Long KH, Ransom JE, Roberts RO, Hass SL, Duhig AM, et al. Direct medical costs and source of cost differences across the spectrum of cognitive decline: a population - based study. Alzheimer's Dement. 2015; 11 (8): 917–32.
38. Sørensen M, Groven KS, Gjelsvik B, Almendingen K, Garnweidner-Holme L. The roles of healthcare professionals in diabetes care: a qualitative study in Norwegian general practice. Scand J Prim Health Care . 2020; 38 (1): 12–23.
39. Akbar JM, Gondodiputro S, Raksanagara AS. Elderly satisfaction on chronic disease management program at public health center, Bandung City, West Java, Indonesia. Int J Integr Heal Sci. 2020; 8 (1): 14–21.
40. Fatmah F. Training program to support posbindu cadre knowledge and community health centre staff in the Geriatric Nutrition Service. ASEAN J Community Engagem. 2020; 4 (2): 500–18.

Hasan, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 279-286
DOI: 10.21109/kesmas.v17i4.6214

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

The Potential of Private Health Insurance Ownership Based on the 2018-2020 National Socioeconomic Survey Data

Arief Rosyid Hasan, Adang Bachtiar, Cicilya Candi*

Department of Health Policy and Administration, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia

Abstract

In 2014, the Indonesian Government introduced a social security program in the health sector. However, Indonesia's out-of-pocket expenses remain high due to a lack of public interest in National Health Insurance services. Financing expensive health services with high out-of-pocket expenses has the potential to cause poverty. Private health insurance is considered a solution to this problem. This study aimed to determine the socioeconomic factors of private health insurance ownership and its potential in Indonesia. This study used secondary data from the 2018, 2019, and 2020 National Socioeconomic Surveys. Logistic regression analysis showed that the variables related to private health insurance ownership were age, sex, education, economic status, employment status, marital status, household status, and location of residence. The most dominant variable in 2018 was per capita expenditure (economic status), while education was the most dominant variable in 2019 and 2020. The result of this study can be used to formulate a strategy for increasing participation in private health insurance. The socioeconomic health sector should use this information to target specific markets for private health insurance.

Keywords: National Health Insurance, private health insurance, socioeconomic determinant

Introduction

The out-of-pocket (OOP) expenses for health insurance in Indonesia were more than 30% of total health expenditures in 2021.[1] High OOP in health financing can exacerbate the disease burden on individuals due to delayed or missing care, strained personal finances, and an increased likelihood of financial disaster, impoverishment, or deteriorating social determinants of health. The consequences experienced by the community are greater vulnerability to poverty and wider inequality in health.[2] Private health insurance is important in reducing OOP in health financing.[2] Several studies have found that private health insurance as additional insurance has a significant effect on reducing the burden of OOP payments.[4-8]

Although the National Health Insurance (NHI) program was introduced in 2014, public interest in NHI services tends to be low because the system is still considered unsatisfactory.[9] People from middle to upper economic statuses prefer OOP rather than using NHI. The small number of private health insurance providers in Indonesia is one of the reasons why private health insurance progress has been extremely slow in Indonesia.[10] Private health insurance companies must develop products that people need and know which potential customers to target.

This study aimed to provide a foundation for strengthening private health insurance in Indonesia by examining the characteristics of its users and analyzing its determinants so that private companies can know their marketing target. It is hoped that private health insurance companies will be interested in making health insurance services that strengthen private health insurance ownership in Indonesia. In addition, it is expected that the government will consider the results of this study when developing additional health insurance programs for NHI participants.

Method

This study used secondary data from the 2018, 2019, and 2020 National Socioeconomic Surveys (NSS)/*Survei Sosial Ekonomi Nasional* (SUSENAS). These data used the head-of-household level as the unit of research analysis. Univariate analysis was conducted to determine the characteristics of the head of household, and multivariate analysis was used to determine these characteristics' relationships to private health insurance ownership.

***Correspondence**:* *Cicilya Candi, Health Policy and Administration Department Faculty of Public Health Universitas Indonesia, F Building 1st Floor Kampus Baru UI Depok City, West Java, Indonesia, 16424, E-mail: cicilyacandi@ui.ac.id, Phone: +62 889 0619 9017*

Received : September 08, 2022
Accepted : November 28, 2022
Published : November 30, 2022

The univariate analysis in this study consisted of descriptive responses to the variables and examined the characteristics of 70,102,253 heads of households. The variables studied consisted of age (in years); sex, divided into two categories (male and female); educational background, divided into five categories (uneducated, elementary school/equivalent, junior high school/equivalent, senior high schools/equivalent, and higher education); and economic status or per capita expenditure (expenses per household per month) in Indonesian Rupiah (IDR). Employment status was divided into occupations (unemployed, informal, and formal) and types of occupations (extractives, manufacturing, and services).

Marital status was divided into single and married. Household status was divided into the number of household members, the number of household children under five were considered, the NHI ownership, private health insurance ownership, and insurance ownership (without

Table 1a. Variables and Operational Definitions

Variable	Category	Operational Definition	Unit/Scale	Value Range
Age		Head of household age	Years	Numeric (15–97 years old)
Sex	Male	Head of household sex is male	Nominal	1 if the head of the household is male 0 if the head of the household is female
	Female	Head of household sex is female Female is the base variable	Nominal	1 if the head of the household is female 0 if the head of the household is male
Education	Uneducated	The head of household never received a formal education or graduated from school Uneducated is the base variable	Ordinal	1 if the head of household never received an education or graduated from school 0 if other conditions (graduating elementary school, graduating from junior high school, graduating from high school, graduating from college)
	Elementary	The highest education of household head is an elementary school graduate	Ordinal	1 if the household head graduated only from elementary school 0 if other conditions (not going to school, graduating from junior high school, graduating from high school, graduating from college)
	Junior high school	The highest education of household head is a junior high school graduate	Ordinal	1 if the household head graduated only from junior high school 0 if other conditions (not going to school, graduating from elementary school, graduating from high school, graduating from college)
	Senior high school	The highest education of household head is a senior high school graduate	Ordinal	1 if the head of the household graduated only from senior high school 0 if other conditions (not going to school, graduating from elementary school, graduating from junior high school, graduating from college)
	Higher education	The highest education of household head is a college graduate	Ordinal	1 if the head of the household graduate from college 0 if other conditions (not going to school, graduating from elementary school, graduating from junior high school, graduating from senior high school
Occupation	Unemployed	The household head has no job Unemployed as the base variable	Ordinal	1 if the head of household has no job 0 if other conditions (informal worker or formal worker)
	Informal	The household head is a blue-collar worker	Ordinal	1 if the head of household is an informal worker 0 if other conditions (has no job or a formal worker)
	Formal	The household head is a white-collar worker	Ordinal	1 if the head of household is a formal worker 0 if other condition (has no job or an informal worker)
Types of occupation	Extractive	Head of household works in the extractive sector	Nominal	1 if the head of household works in the extractive sector (agriculture, plantation, fishery, forestry, mining) 0 if other conditions (not working, working in the manufacturing sector, working in the service sector)
	Manufacture	Head of household works in the manufacturing sector	Nominal	1 if the head of household works in the manufacturing sector (manufacturing, utilities, construction) 0 if other conditions (not working, working in the extractive sector, working in the service sector)
	Service	Head of household works in the service sector	Nominal	1 if the head of household works in the service sector (trade, services, communications, finance) 0 if other conditions (not working, working in the extractive sector, working in the manufacturing sector)
Marital status	Single	The head of household has never been married or is divorced Single is the base variable	Nominal	1 if the head of household is single 0 if head of household is married
	Married	The head of household is married	Nominal	1 if the head of household is married 0 if head of household is single

Table 1b. Variables and Operational Definitions

Variable	Category	Operational Definition	Unit/Scale	Value Range
Household status	Number of families	Number of household members	Numeric	(Total family members)
	Children under five	Number of children under five in the household	Nominal	1 if there are children under five (age 0–59 months) in the household 0 if there are no children under five in the household
	National Health Insurance (NHI) ownership	Household head membership status of NHI	Ordinal	1 if household head is a member of NHI 0 if household head is not a member of NHI
	Private health insurance ownership	Household head membership status of private health insurance	Ordinal	1 if household head is a member of private health insurance 0 if household head is not a member of private health insurance
	Insurance ownership	Household head membership status of any insurance	Nominal	1. No health insurance 2. NHI 3. Private health insurance 4. Both NHI and private health insurance
Area of residence	Rural	Household residence is in a rural area	Nominal	1 if the household is in a rural area 0 if the household is in an urban area
	Urban	Household residence is in an urban area	Nominal	1 if the household is in an urban area 0 if the household is in a rural area

health insurance, NHI only, only private health insurance, and ownership of both NHI and private health insurance). Area of Residence was classified as urban or rural (Table 1).

Multivariate analysis was performed after the logistic regression analysis to determine which variables significantly influenced the variable of private health insurance ownership. The logistic regression equation was used to estimate the probability of private health insurance ownership. Variables were selected by binary logistic analysis in advance of the logistic regression analysis, and it was used to select the correlated variable to the dependent variable (private health insurance ownership) with a significance level of 5%. The selected variables were then analyzed using logistic regression analysis. The coefficient in this analysis indicates the magnitude of the probability of a category, and a positive value indicates that the probability of a category is greater than that of the comparison category (the variable defined as a base). However, a negative coefficient means that the probability of the category is smaller than that of the comparison category. The results of the exponential estimated value of the regression coefficient (βi) obtained the value of the odds ratio, with a significance level of 5%.

Results

The univariate analysis in this study consisted of descriptive responses to the variables. Household characteristics are shown in Table 2. Based on sex, the 2018-2020 NSS was dominated by males. Based on the head of the household's type of work was dominated by work in the informal sector. The head of the household's occupation category was dominated by the service sector. The marital status of the head of the household was dominated by married status. Urban areas dominated the location of the household residences.

An average of four members dominated the number of household members. The distribution of the ownership of the NHI was dominated by members of the NHI. Private health insurance ownership distribution was dominated by households without it. The status of insurance ownership distribution was dominated by only NHI ownership.

The logistic regression equation estimated the opportunity for private health insurance ownership for NHI members with specific characteristics according to the abovementioned variables. The coefficient sign indicates the magnitude of the probability of a category; a positive sign indicates that the probability of a category is greater than the comparison category, while a negative coefficient sign means that the probability of the category is smaller than the comparison category. The base variable was used as the comparison variable.

The equation in Table 3 showed that the intercept value = -25.4885 when all independent variables are 0, including the ownership of additional private health insurance for NHI members, women living in a village, were uneducated, did not work, had never been married, family members less than four, and no children under five. The accuracy of the logistic regression model in predicting empirical data was seen in the classification table output, which was shown in the overall percentage value of 18%, meaning that the variation in the rate of additional private health insurance ownership among NHI members was only 18%, as determined by the overall predictor. It means that 82% of the additional private health

Table 2. Characteristics Based on Number of the Household Heads and Members in 2018, 2019, and 2020

Variable	Category	2018			2019			2020		
		n	Mean/Median	%	n	Mean/Median	%	n	Mean/Median	%
Age (years)		70,101,253	48.09/47		71,437,667	48.38/48		72,791,519	48.72/48	
Sex of household's head	Male	59,466,983		84.83	60,394,034		84.54	61,278,834		84.18
	Female	10,634,270		15.17	11,043,633		15.46	11,512,685		15.82
Education	Uneducated	3,596,168		5.13	3,322,611		4.65	3,108,850		4.27
	Elementary school	31,047,973		44.29	31,133,056		43.58	30,679,215		42.15
	Junior high school	11,388,111		16.25	11,915,752		16.68	11,643,284		16.00
	Senior high school	17,480,847		24.94	17,831,343		24.96	19,833,711		27.25
	Higher education	6,588,154		9.40	7,234,905		10.13	7,526,459		10.34
Occupation	Unemployed	9,216,811		13.15	9,235,641		12.93	15,992,886		21.97
	Informal	34,651,721		49.43	34,900,111		48.85	28,336,169		38.93
	Formal	26,232,721		37.42	27,301,915		38.22	28,462,464		39.10
Type of occupation	Extractive	21,983,372		36.11	21,653,901		34.81	21,869,141		34.67
	Manufacturing	7,121,559		11.70	7,357,645		11.83	7,482,068		11.86
	Service	31,779,511		52.20	22,190,480		53.36	33,729,040		53.47
Marital status of household's head	Single	13,667,696		19.50	14,655,780		20.52	15,332,509		21.06
	Married	56,433,557		80.50	56,781,887		79.48	57,459,010		78.94
Number of family members		70,101,253	3.77 of 4		71,437,667	3.74/4		72,791,519	3.71	4
Number of children under five in the household		70,101,253	0.34		71,437,667	0.33		72,791,519	0.31	0
NHI ownership	Head of household is not a member of NHI	25,114,341		35.83	26,856,398		37.59	22,032,519		30.27
	Head of household is a member of NHI	44,986,912		64.17	44,581,269	62.41		50,759,000		69.73
Private health insurance ownership	Household does not have private health insurance	66,837,063		95.34	68,381,939	95.72		69,908,963		96.04
	Household has private health insurance	3,264,190		4.66	3,055,728		4.28	2,882,556		3.96
Insurance ownership	No health insurance	22,716,338		32.41	24,690,896		34.56	19,984,421		27.45
	NHI	44,120,725		62.94	43,691,043		61.16	49,924,542		68.59
	Private health insurance	2,398,003		3.42	2,165,502		3.03	2,048,098		2.81
	NHI and private health insurance	866,187		1.24	890,226		1.25	834,458		1.15
Area of household residence	Rural	31,747,219		45.29	31,414,505		43.97	32,019,313		43.99
	Urban	38,354,034		54.71	40,023,162		56.03	40,772,206		56.01

Note: NHI = National Health Insurance

insurance ownership rate in NHI member households was determined by factors other than the analyzed predictors. From Table 3, the odds ratio value was indicated by the magnitude of the Exp(B) named coefficient value, which can be explained as follows:

Age

Older heads of households tended to have private health insurance coverage 0.145 times less. Health quality declines with age.

Sex

The male head of household participants tended to have private health insurance coverage 2.3 times greater than female participants in 2018, 1.1 times greater than females in 2019, and 2.6 times greater than females in 2020. Therefore, male heads of households tended to have insurance coverage. Overall, male private health insurance ownership was 2.03 times greater than that of females.

Education

In 2018, compared to uneducated heads of households, the participating heads of households with an elementary school education tended to have private health insurance coverage 4.2 times greater, and heads of households with a junior high school education tended to have private health insurance coverage 3.8 times greater. Heads of households with a senior high school education tended to have private health insurance coverage 9.5 ti-

Table 3. Logistics Regression Analysis Results

Logistic regression of private health insurance ownership		2018		2019		2020		all	
		Coefficient	Std. Error	Coefficient	Std. Error	Coefficient	Std. Error	Coefficient	Std. Error
Age (years)		0.0338	0.0007	0.0305	0.0007	0.0145	0.0007	0.0203	0.0004
Age_sq (years^2)		-0.00058	7.33E-06	-0.00049	6.90E-06	-0.00045	7.51E-06	-0.00045	4.15E-06
Sex	Base: Female								
	Male	0.2330	0.0041	0.1114	0.0038	0.2589	0.0042	0.2037	0.0023
Education	Base: Uneducated								
	Graduated from elementary school or equivalent	0.4248	0.0126	0.6899	0.0154	0.1327	0.0167	0.4468	0.0084
	Graduated from junior high school/equivalent	0.3848	0.0130	0.7977	0.0157	0.4374	0.0169	0.5540	0.0086
	Graduated from senior high school/equivalent	0.9508	0.0126	1.2873	0.0154	0.8647	0.0166	1.0497	0.0084
	Graduated from university or equivalent	1.2775	0.0128	1.5881	0.0155	1.4064	0.0167	1.4437	0.0085
Economic status	Per capita expenditure (ln)	1.3292	0.0018	1.3400	0.0018	1.3950	0.0019	1.3458	0.0011
Employment status	Base: Unemployed								
	Extractive sector	0.4759	0.0055	0.4531	0.0055	0.8249	0.0061	0.5691	0.0033
	Manufacturing sector	1.0486	0.0051	0.9925	0.0049	1.2925	0.0056	1.0997	0.0030
	Service sector	-0.0040	0.0047	0.0739	0.0045	0.2780	0.0052	0.1051	0.0028
Marital status	Base: Single								
	Married	0.6430	0.0064	0.4608	0.0057	0.7653	0.0058	0.6771	0,0034
Number of family members	Base: Household members ≤4								
	Household members > 4	0.2644	0.0028	0.1985	0.0029	0.3084	0.0028	0.2839	0.0016
Number of children under five years old	Base: No children under five in the household								
	At least 1 child under five in the household	0.2620	0.0028	0.2637	0.0029	-0.0620	0.0026	0.1192	0.0015
Area of residence	Base: Rural area (village)								
	Urban	0.5448	0.0033	0.6835	0.0035	0.4499	0.0035	0.5636	0.0020

Note: All variables are significant with a p-value<0.001

mes greater. Overall, heads of households with higher education tended to have private health insurance coverage 1.3 times greater than uneducated heads of households.

In 2019, compared to uneducated heads of households, participating heads of households with an elementary school education tended to have private health insurance coverage 6.9 times greater, and heads of households with a junior high school education tended to have private health insurance coverage 7.9 times greater. Heads of households with a senior high school education tended to have private health insurance coverage 1.3 times greater. Overall, participating heads of households with higher education tended to have private health insurance coverage 1.6 times greater than the uneducated heads of households.

In 2020, compared to uneducated heads of households, participating heads of households with an elementary school education tended to have private health insurance coverage 1.3 times greater, and heads of households with a junior high school education tended to have private health insurance coverage 4.4 times greater. Heads of households with a senior high school education tended to have private health insurance coverage 0.8647 times greater. Overall, heads of households with higher education tended to have private health insurance coverage 1.4 times greater than uneducated heads of households.

Over all three years, in comparison to uneducated heads of households, participating heads of households with an elementary school education tended to have private health insurance coverage 1.3 times greater, heads of households with a junior high school education tended to have private health insurance coverage 4.4 times greater, and heads of households with a senior high school education tended to have private health insurance coverage 8.6 times greater. Overall, heads of households with higher education tended to have private health insurance coverage 1.4 times greater than uneducated heads of households.

Economic Status

In 2018, concerning per capita expenditure, participant heads of households tended to have private health

insurance coverage 1.3 times greater; in 2019, heads of households tended to have private health insurance coverage 1.340 times greater; and in 2020, heads of households tended to have private health insurance coverage 1.345 times greater. Overall, from 2018–2020, heads of households tended to have private health insurance coverage 1.3 times greater concerning per capita expenditure.

Employment Status

In 2018, in comparison to unemployed heads of households, participating heads of households in the agriculture/mining sector tended to have private health insurance coverage 4.8 times greater, heads of households in the manufacturing sector tended to have private health insurance coverage 1.05 times greater, and heads of households in the service sector tended to have private health insurance coverage 0.0040 times less. In 2019, heads of households in the agriculture/mining sector tended to have private health insurance coverage 4.5 times greater than those who were unemployed, while heads of households in the manufacturing sector tended to have private health insurance coverage 9.9 times greater, and heads of households in the service sector tended to have private health insurance coverage 0.7 times less.

In 2020, heads of households in the agriculture/mining sector tended to have private health insurance coverage 8.2 times greater than those who were unemployed, while heads of households in the manufacturing sector tended to have private health insurance coverage 1.3 times greater, and heads of households in the service sector tended to have private health insurance coverage 2.8 times greater. Overall, from 2018–2020, household heads in the agriculture/mining sector tended to have private health insurance coverage 5.7 times greater than those who were unemployed, while heads of households in the manufacturing sector tended to have private health insurance coverage 1.1 times greater, and heads of households in the service sector tended to have private health insurance coverage 1.05 times greater. Hence, the results of this study indicated that working status greatly affected private health insurance coverage compared to unemployed people.

Marital Status

In 2018, heads of households who were single tended to have private health insurance coverage 6.4 times greater than their married counterparts. In 2019, heads of households tended to have private health insurance coverage 4.6 times greater than those who were single. In 2020, heads of households who were married tended to have private health insurance coverage 7.6 times greater than those who were single. Overall, from 2018–2020, heads of households who were married tended to have private health insurance coverage 6.7 times greater than those who had never been married.

Household Status

In 2018, households with more than four family members tended to have private health insurance coverage 2.6 times greater than households with fewer than four family members. In 2019, households with more than four family members tended to have private health insurance coverage 1.9 times greater than households with fewer than four family members. In 2020, households with more than four family members tended to have private health insurance coverage 3.08 times greater than households with fewer than four family members. Overall, from 2018–2020, households with more than four family members tended to have private health insurance coverage 2.8 times greater than households with fewer than four. Hence, the results of this study indicated that households with fewer than four family members were less likely to have private health insurance.

In 2018, households with one child under five tended to have private health insurance coverage 2.6 times greater than households without children under five. In 2019, households with one child under five tended to have private health insurance coverage 2.6 times greater than households without a child under five. In 2020, households with one child under five tended to have private health insurance coverage 0.6 times less than households without children under five. Overall, from 2018–2020, households with one child under five tended to have private health insurance coverage 1.2 times greater than those households without children under five.

Area of Residence

In 2018, households in urban area tended to have private health insurance coverage 5.4 times greater than households in rural area. In 2019, households in urban area tended to have private health insurance coverage 6.8 times greater than those in rural area. In 2020, households in urban area tended to have private health insurance coverage 4.5 times greater than those in rural area. Overall, from 2018–2020, households in urban area tended to have private health insurance 5.6 times greater than households in rural area.

Discussion

This study implied that older individuals tended to have health insurance more than younger ones. This result was in line with a study by Shao, *et al.,*[11] stated that the older someone is, the more they will be aware of health insurance.[11,12] People in the 40-44 and 45-49 age groups had an 11% and 8% higher likelihood of health insurance, respectively.[11]

Heads of households with higher education tended to

have private health insurance coverage 1.4 times greater than uneducated heads of households. This finding showed that education plays an important role, as it could enlighten individuals about the importance of health insurance coverage.[13] Education also helped individuals make informed choices about health issues, including purchasing health insurance to avoid huge health expenses when they were ill. People with higher education had a higher view of the need for health insurance to deal with unexpected health problems. In contrast, people with low education were unaware of the threat caused by unforeseen health problems.[11,14]

The higher economic status (seen from the level of expenditure) of the household's head in this study tended to have private health insurance coverage 1.3 times greater. Accordingly, the results of this study indicated that the tendency of per capita spending was highly influential in having private health insurance guarantees. Income is an important determinant of both the demand for health services and the decision to have health insurance.[8] Some studies have stated that the most critical factor affecting general insurance was income.[11,14,15] Regarding occupation, the employed status significantly affected private health insurance guarantees compared to those unemployed. Participation in the formal sector's health insurance was dominated by workers in the public sector (civil servants and armed forces), while health insurance participation in the informal sector was dominated by farmers, fishermen, and the like.[16,17] In terms of marital status, people who were single were less likely to have private health insurance ownership. The status of living together is likely to be greater than that of those who are divorced/dead.[16] Married women were more likely to have private coverage than the singles in almost all income groups.[11,12]

Households with one child under five tended to have private health insurance coverage 1.2 times greater than households without one. Thus, the results of this study indicated that households without a child under five were less likely to have private health insurance. A study in Bangladesh found that parents might have less capacity to pay premium health insurance than other family members.[16] Health insurance schemes sometimes view women as wives or mothers, rather than as individuals or workers, even though each individual's right to social insurance is fundamental. If women's access to social or health insurance comes through their husbands, this can protect the family, not women's autonomy.[8]

In this study, households in urban area were likelier to have private health insurance coverage than those in rural ones. Hence, an individual residing in a village was less likely to have private health insurance. The reason of that informal sector workers in rural areas had a lower chance of having health insurance compared to those living in urban areas was that public health insurance companies were mostly found in urban areas, and these companies adjusted their health insurance products to meet the needs of urban people.[17] The difficulty of access and the high cost of transportation also made health insurance less valuable because it was difficult to use; thus, informal sector workers in villages did not feel the need to have health insurance.[18] In brief, rural people did not consider health insurance a need because the product design did not match them.

Conclusion

The results of this study show a relationship between age, sex, education, economic status, employment status, marital status, household status, and location of residence with private health insurance ownership. Particularly, most households in this study do not enroll in private health insurance. The government should understand this situation and find the best solution to strengthen the health insurance ecosystem in Indonesia. These results can be used to formulate a strategy for strengthening private health insurance ownership. The health economic sector should use this information to expand the target market for private health insurance.

Abbreviations

OOP: Out-of-Pocket; NHI: National Health Insurance; NSS: National Socioeconomic Surveys; SUSENAS: Survei Sosial Ekonomi Nasional; IDR: Indonesian Rupiah.

Ethics Approval and Consent to Participate

The Research and Community Engagement Ethical Committee, Faculty of Public Health, Universitas Indonesia, granted ethical approval, No. Ket-558/UN2.F10.D11/PPM.00.02/2022.

Competing Interest

The authors declare that there are no significant competing financial, professional, or personal interests that might have affected the performance.

Availability of Data and Materials

Since this study used secondary data, it can be accessed through Statistics Indonesia.

Authors' Contribution

ARH conceptualized and designed the study, collected data, and analyzed and interpreted the results. AB guided data analysis, review, and manuscript approval. CC provided the latest research literature, prepared draft manuscripts, and served as the corresponding author.

Acknowledgment

The authors thanked Rully Endepe Al Faizin as a statistical analysis mentor.

References

1. World Health Organization Global Health Expenditure. Out-of-pocket expenditure (% current health expenditure). The World Bank; 2021.
2. Salari P, Di Giorgio L, Ilinca S, Chuma, J. The catastrophic and impoverishing effects of out-of-pocket healthcare payments in Kenya, 2018. BMJ Glob Health. 2019; 4: e001809.
3. Shin J. Private health insurance in South Korea: an international comparison. Health Pol. 2012; 108 (1): 76–85.
4. Paccagnella O, Rebba V, Weber G. Voluntary private health insurance among the over 50s in Europe. Health Econ. 2013; 22 (3): 289–315.
5. Duc Thanh N, Anh BTM, Thanh Hung P, Quynh Anh P, Huyen Xiem C. Impact of public health insurance on out-of-pocket health expenditures of the near-poor in Vietnam. Health Serv Insights. 2021; 14: 11786329211017411.
6. Harish R, Ranjana S, Rameesa S, Laiveishiwo PM, Loktongbam PS, Prajitha KC, et al. Health insurance coverage and its impact on out-of-pocket expenditures at a public sector hospital in Kerala, India. J Fam Med Prim Care. 2020; 9 (9): 4956–61.
7. Al-Hanawi MK, Mwale ML, Qattan AMN. Health insurance and out-of-pocket expenditure on health and medicine: heterogeneities along income. Front Pharmacol. 2021; 12: 638035.
8. Aji B, De Allegri M, Souares A, Sauerborn R. The impact of health insurance programs on out-of-pocket expenditures in Indonesia: an increase or a decrease? Int J Environ Res Pub Health. 2013; 10: 2995–3013.
9. Kurniawati W, Rachmayanti R. Identifikasi penyebab rendahnya kepesertaan JKN pada pekerja sektor informal di kawasan pedesaan. J Admin Kesehatan Indonesia. 2018; 6: 33.
10. Shao L, Wang Y, Wang X, Lu J, Huang R. Factors associated with health insurance ownership among women of reproductive age: a multi-country study in Sub-Saharan Africa. PLoS One. 2022; 17 (4).
11. Grossman M. On the concept of health capital and the demand for health. Determinants of health. Columbia University Press. 2017 p. 6–41.
12. Mulenga JN, Bupe BB, Gebremeskel Y. Demographic and socio-economic determinants of women's health insurance coverage in Zambia; 2017.
13. Al-Sanaani EA, Ismail A, Manaf MRA, Suddin LS, Mustafa N, Sukor N, et al. Health insurance status and its determinants among patients with type 2 diabetes mellitus in a tertiary teaching hospital in Malaysia. PLoS One. 2022; 17 (5).
14. Amu H, Dickson KS, Kumi-Kyereme A, Maafo Darteh EK. Understanding variations in health insurance coverage in Ghana, Kenya, Nigeria, and Tanzania: evidence from demographic and health surveys. PLoS One. 2018; 13 (8): e0201833.
15. Intiasari A, Aji B, Masfiah S, Trisnantoro L, Hendrartini J. Factors affecting delaying payment of National Health Insurance (BPJS Kesehatan) premium among participants of the informal sector in Banyumas Regency. Ann Trop Med Pub Health. 2019; 22: 485–91.
16. Fu D, Liu L, Zhang X, Yu C, Luo H, Li N. The relationship between urban and rural health insurance and the self-rated health of migrant workers in southwest China. BMC Health Serv Res. 2021; 21: 1–13.
17. Tana L. Faktor yang berperan pada lama rawat inap akibat cedera pada kelompok pekerja usia produktif di Indonesia. Buletin Penelitian Sistem Kesehatan. 2015; 19 (1): 75–82.
18. Ahmed S, Hoque ME, Sarker AR, Sultana M, Islam Z, Gazi R, Khan JAM. Willingness-to-pay for community-based health insurance among informal workers in urban Bangladesh. PloS One. 2016; 11 (2): e014821.

Muhammad, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 287-291
DOI: 10.21109/kesmas.v17i4.6216

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Medication Adherence and Self-Management Practices among Type 2 Diabetes Mellitus Patients in Jeli District, Kelantan, Malaysia

Marzuki Muhammad[1]*, Farzana Y[1], Alabed Ali A Alabed[1], Bibi Florina Abdullah[1], Sandeep Poddar[2]

[1]Faculty of Medicine, Lincoln University, Selangor, Malaysia, [2]Research & Innovation Division, Lincoln University, Selangor, Malaysia

Abstract

This study was carried out to investigate the level of medication adherence and diabetic knowledge among type 2 diabetes mellitus patients in Jeli District, Kelantan, Malaysia. This cross-sectional study was done from February to July 2019 by giving a questionnaire to 150 type 2 diabetes mellitus patients aged 40-80 years in three primary health cares in Jeli District, Kelantan, Malaysia. The quantitative descriptive method was used in this study. The findings of this study revealed that knowledge was significantly related to poor adherence. When sex, record of diabetes, and education were accounted for, patients with low diabetic knowledge had an odds ratio of 4.53 for poor adherence compared to those with high knowledge (adjusted 95% CI = 1.92–10.69; p-value = 0.001). To achieve the goal of regulating diabetes management in primary health care, a clinical supervision program should be implemented to improve staff competence in diabetes management and to empower patients through self-management.

Keywords: medication adherence, self-management practices, type 2 diabetes mellitus

Introduction

The World Health Organization (WHO) states that health is a stage or state in which a person has perfect mental, physical, and social well-being and is not just free from disease or helplessness.[1] Personal health is a valuable asset, but many are unaware of it until they are infected. Many also do not realize that improper living habits can contribute to harmful diseases. One of most feared diseases in the community is diabetes mellitus (DM).[2] It is not a new disease for the public, and it threatens humans through high blood glucose levels. If the increase in blood glucose levels persists over a long period, several sensitive cells, tissues, and organs will suffer damage due to the toxic effects caused by glucose, and the damage will be permanent.[2] According to the WHO, "Poor adherence to long-term therapies severely compromises the effectiveness of treatment," making this a critical issue in population health both from the perspective of quality of life and health economics.[3]

According to the 2019 National Health and Morbidity Survey (NHMS), 3.9 million Malaysians aged 18 years and above have diabetes; 9.4% are aware of the disease, but 8.9% are unaware they have it.[4] It also states that among diabetic patients receiving treatment at primary health care, 25.7% stated that they had insulin resistance, but 85.6% said they had taken oral anti-diabetic medications in the last two weeks.[4] This report also shows that 88% of patients practice a diabetic diet after consultation with health staff to control blood sugar and lose weight. In comparison, 75.4% of patients have undergone weight-loss exercise and are more physically active. Diabetic patients who received regular treatment at the Malaysian Ministry of Health (MOH) primary health care (PHC), hospital, private clinic, and private hospital are approximately 68.2%, 15%, 12.1%, and 2.8%, respectively. Furthermore, approximately 0.4% of people with diabetes (PWD) purchase their medications from a private pharmacy, while 0.2% take traditional medicine to treat their diabetes.[4]

Globally, about 1.8 million people have not been diagnosed, have never undergone a health screening, and did not realize the presence of DM.[5] This diabetic disease gives the patient many complications, including diabetic foot ulcer (DFU). If this condition is not treated, it will injure the wound and spread to the upper leg. Eventually, the amputation should be performed to save the healthy

Correspondence*: Marzuki M, Lincoln University, Wisma Lincoln, No.12-18 Off Perbandaran Street, 47301 Petaling Jaya, Selangor Darul Ehsan, Malaysia, E-mail: marzuki.mmd@gmail.com, Phone: +60 19 7590 092*

Received : September 08, 2022
Accepted : November 26, 2022
Published: November 30, 2022

feet.[3] Most cases of amputation and leg ulcers can be avoided with early treatment and proper foot care. Diabetic neuropathy and other diabetic conditions cause leg complications in patients with diabetes. The main aim of this study was to determine the level of knowledge and the medication adherence of PWD, primarily type 2 diabetes mellitus (T2DM) patients, in Jeli District, Kelantan, Malaysia.

Method

This cross-sectional study was conducted from February to July 2019 in Jeli District, Kelantan, Malaysia, using the quantitative method. There were 1,402 T2DM patients registered in three PHCs of Jeli District. The sample size was calculated using the Krejcie and Morgan formulas.[6,7] Based on the calculation, the sample size was 150 (95% confidence interval (CI) and a 5% error margin). The samples were randomly selected using the patient registration system available at PHC.

The data was collected by distributing a questionnaire following the instrument used by Aminde, *et al.*,[8] to 150 T2DM patients at three PHCs of Jeli District. The questionnaires consisted of two parts; part A covered participants' characteristics such as sex, age, ethnicity, education, employment status, and monthly income; while part B asked about the objective of the study and level of knowledge regarding DM. Each PHC was allotted four weeks for selecting and collecting patients, and data collection at three PHCs was completed in 12 weeks. The process of distributing the questionnaires and retrieving the survey forms took three months due to the distance between the PHCs involved.

Results

Table 1 shows the breakdown of participants by demographic variables. For sex, 63 (42%) were male, while 87 (58%) were female. The ethnicity data showed all T2DM patients in the study area were Malays because

Table 1. Diabetes Mellitus Patients' Demographic Data

Variable	Category	n	%	Median	IQR
Age				53.00	18
HbA1c				8.20	3.9
Duration of DM				5.00	6
Sex	Male	63	42.0		
	Female	87	58.0		
Ethnicity	Malay	150	100		
	Non-Malay	0	0.0		
Education	Uneducated	8	5.3		
	Primary	43	28.7		
	Secondary	92	61.3		
	Tertiary	7	4.7		
Employment status	Unemployed	89	59.3		
	Employed	61	40.7		
Monthly income	<1,000 MYR	5	3.3		
	1,000-3,000 MYR	46	30.7		
	3,000-4,000 MYR	92	61.3		
	>4,000 MYR	7	4.7		
Number of medication	1	67	44.7		
	2	83	55.3		
Family records of DM	Yes	67	44.7		
	No	83	55.3		
Receiving DM education	No	66	44.0		
	Yes	84	56.0		

Notes: DM = Diabetes Mellitus, MYR = Malaysian Ringgit, IQR = Interquartile Range

Table 2. Adherence and Knowledge Score Type 2 Diabetes Mellitus Patients

Variable	Category	n	%	Median	IQR
Knowledge score				58.33	33.33
Adherence score				50.00	50.00
Knowledge	Good	112	74.7		
	Poor	38	25.3		
Medication adherence	Good	112	74.7		
	Poor	38	25.3		

Note: IQR = Interquartile Range

most residents of Jeli District were Malays. Most T2DM patients in this study attained secondary education (61.3%) and only 4.7% attained tertiary education. A total of 46 participants had a monthly income in the middle range. While, the remaining 92 participants had the high monthly income group.

Table 2 displays the results of the medication adherence and knowledge score of T2DM patients in this study. Most T2DM patients in Jeli District had good knowledge and medication adherence. The knowledge score showed a median score of 58.33 and an interquartile range (IQR) of 33.33, while the adherence score showed a median of 50.00 and an IQR of 50.00. Most participants in this study had good knowledge and medication adherence (74.7%).

Based on Table 3, there was a significant association between poor knowledge and medication adherence (Crude OR 3.51, 95% CI: 1.58–7.78, p-value = 0.002), while remaining variables were insignificant. In the multivariate analysis (Table 4), first, all variables were selected for the selection process and applied forward logistic regression (LR), backward LR, and manual methods to determine a parsimonious model for the study. The final model consisted of the record of DM education, sex, and knowledge. Knowledge had a significant association with poor adherence. When sex and record of DM education were controlled, patients with poor knowledge had an odds ratio of 4.53 for poor adherence compared to patients with good knowledge (adj 95% CI = 1.92–10.69), p-value = 0.001). When sex and knowledge were controlled, patients with no record of DM education had a 2.40 chance of poor adherence compared to patients who received DM education (adj 95% CI = 1.04–5.57), p-value = 0.041). However, sex has no significant association with poor adherence, even when knowledge and record of receiving DM education were controlled.

Table 3. Factors Associated with Poor Medication Adherence Using Simple Logistic Regression (n = 150)

Variable	Category	Crude Odd Ratio	95% CI	p-value
Age		0.973	0.938–1.010	0.155
HbA1c		0.947	0.809–1.109	0.498
Duration of DM		0.961	0.880–1.049	0.374
Sex	Male	1.340	0.639–2.810	0.438
	Female	1		
Education	Uneducated	1		
	Primary	0.505	0.102–2.493	0.402
	Secondary	0.556	0.123–2.508	0.445
	Tertiary	0.667	0.076–5.878	0.715
Employment status	Unemployed	1		
	Employed	1.924	0.915–4.048	0.085
Monthly income	<1,000 MYR	1.667	0.147–18.874	0.680
	1,000–3,000 MYR	0.786	0.133–4.633	0.790
	3,000–4,000 MYR	0.833	0.151–4.591	0.834
	>4,000 MYR	1		
Number of medication	1	1.157	0.553–2.421	0.698
	2	1		
Family records of DM	Yes	0.713	0.870–0.414	1.830
	No	1		
Receiving DM education	No	1.594	0.761–3.340	0.217
	Yes	1		
Knowledge	Good	1		
	Poor	3.508	1.582–7.778	0.002

Notes: DM = Diabetes Mellitus, MYR = Malaysian Ringgit, CI = Confidence Interval

Table 4. Factors Associated with Poor Adherence Using Multiple Logistic Regression (n = 150)

Variable	Category	Adjusted OR	95% CI	p-value
Receiving DM education	No	2.401	1.035–5.571	0.041
	Yes	1		
Sex	Male	1.947	0.860–4.408	0.110
	Female	1		
Knowledge	Good	1		
	Poor	4.534	1.923–10.691	0.001

Notes: DM = Diabetes Mellitus, OR = Odd Ratio CI = Confidence Interval

Discussion

Diabetes care practices among T2DM patients in Jeli District remained satisfactory. Most participants in this study practiced diabetes care. Nevertheless, some did not know the correct way to practice because their knowledge was still limited in their basic understanding of diabetes. The results of this study revealed that patients with no record of receiving DM education (poor knowledge) would practice poor medication adherence. The last question for participants' level of knowledge related to whether DM patients could get information on diabetes care showed a significant difference in participants, with 84 participants saying "Yes" and 66 participants saying "No." Based on the analysis, participants still do not understand their diabetic care. A previous study stated that the record of receiving diabetic education has a significant association with poor adherence.[9]

The knowledge level of T2DM patients in this study was moderate, and many people still did not care about DM. This indifference to society is alarming, as it indirectly increases the number of patients with DM.[10] This condition is very concerning as people will take it lightly, not knowing the risk of DM. In addition, there are many other adverse effects of DM. A study by Leon and Maddox stated that DM caused many bad complications. The diabetic patients have not only twice the risk of heart disease, but also more likely to develop the disease at a younger age than those who do not have diabetes.[11] Diabetic patients' symptoms of heart disease are frequently undetectable, resulting in delays in diagnosing a heart attack and receiving timely treatment. Sudden cholesterol plaque breaking is the most common cause among diabetic patients with dyslipidemia (total fats or abnormal cholesterol in the blood), which causes a clogged artery that eventually causes a heart attack or stroke.[11]

Diabetes is a condition that lasts for a long time, and it is now considered one of the most severe threats and deaths to people's health in the 21st century.[12,13] Various campaigns have been organized to increase public awareness of DM. The drive and seminars are aimed at helping the community get the latest information on DM so that it can be prevented.[14] It fully supports the saying that prevention is better than cure. Therefore, awareness of the patient's attitude and responsibility is fundamental to ensuring that the information delivery objectives are met.[15] Knowledge of diabetes medication adherence is essential for PWD as it can control and prevent the disease from spreading and becoming more serious. Another study shows that greater adherence to the frequency of HbA1c testing advised in the guidelines was related to better glycemic management and a decreased risk of developing chronic kidney disease. These results may give valuable data to support the use of clinical recommendations to improve patient outcomes in T2DM patients.[16]

Various ways and recommendations can be made to address the problem of inadequate knowledge of DM in the population. Some practical suggestions are provided for elevating the knowledge level about DM. Comprehensive lectures or health education on DM can be held among all community groups. The lectures should also be applied to adolescents who do not have the opportunity to learn. The MOH must produce a total of pamphlets or promotional books related to DM and shall issue them from time to time. This pamphlet or leaflet is distributed to all sections, from the hospital outpatient department to the primary health care and the rural clinic.

Conclusion

Knowledge has a significant association with poor adherence. If T2DM patients have no history of receiving DM education, it can influence their medication adherence. Even though T2DM patients in this study have already practiced diabetes care, the number of DM patients can still increase if they do not practice it right. From the above discussion, it can be said that medication adherence is essential for people with DM; however, many groups still do not even care about DM. It is possible to start the clinical supervision program so that Malaysian people are aware of the value of DM information. This issue will be able to be avoided, which will indirectly lower the number of individuals to suffer from DM.

Abbreviations

WHO: World Health Organization, DM: Diabetes Mellitus; NHMS: National Health and Morbidity Survey, MOH: Ministry of Health; PHC: Primary Health Care; PWD: People with Diabetes; DFU: Diabetic Foot Ulcer; T2DM: Type 2 Diabetes Mellitus; CI: Confidence Interval; IQR: Interquartile Range, MYR: Malaysian Ringgit; MLR: Multiple Logistic Regression, SLR: Simple Logistic Regression.

Ethics Approval and Consent to Participate

An ethical clearance approval letter was received from Pejabat Kesihatan Daerah of Jeli Primary Health Care with reference number: (Ruj. Kami: PKDJ.2022/1/3) dated February 14, 2022.

Competing Interest

The authors declare that no significant competing financial, professional, or personal interests might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The data and materials in this study are available to the corresponding author upon request.

Authors' Contribution

MM contributed to the development of the detailed research, the analysis of the methods, the implementation of the methods, and the writing of the manuscript. FY and AAA verified, guided, and supervised this study's findings. BFA and SP reviewed, edited, and provided valuable feedback for this study.

Acknowledgment

The authors are thankful to Lincoln University, Malaysia, for the academic support.

References

1. World Health Organization. Health and Well-Being. Geneva: World Health Organization; 2022.
2. Balasubramaniam S, Lim SL, Goh LH, Subramaniam S, Tangiisuran B. Evaluation of illness perceptions and their associations with glycaemic control, medication adherence and chronic kidney disease in type 2 diabetes mellitus patients in Malaysia. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019; 13 (4): 2585-91.
3. World Health Organization. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization; 2003.
4. National Institute of Health. National Health And Morbidity Survey 2019: Non-communicable diseases, healthcare demand, and health literacy—Key Findings. Selangor: Ministry of Health Malaysia; 2020.
5. American Diabetes Association. 11. Microvascular complications and foot care: standards of medical care in diabetes—2019. Diabetes Care. 2019; 42 (Supplement_1): S124-38.
6. Krejcie RV, Morgan DW. Determining sample size for research activities. Educational and Psychological Measurement. 1970; 30; 607–10.
7. Ahmad, Ramli A, Islahudin F, Paraidathathu T. Medication adherence in patients with type 2 diabetes mellitus treated at primary health clinics in Malaysia. Patient Prefer Adherence. 2013; 7: 525-50.
8. Aminde LN, Tindong M, Ngwasiri CA, Aminde JA, Njim T, Fondong AA, et al. Adherence to antidiabetic medication and factors associated with non-adherence among patients with type-2 diabetes mellitus in two regional hospitals in Cameroon. BMC Endocr Disord. 2019; 19 (1): 1-9.
9. Chew BH, Vos RC, Pouwer F, Rutten GEHM. The associations between diabetes distress and self-efficacy, medication adherence, self-care activities and disease control depend on the way diabetes distress is measured: Comparing the DDS-17, DDS-2 and the PAID-5. Diabetes Research and Clinical Practice. 2018; 142: 74-84.
10. Gholamaliei B, Karimi-Shahanjarini A, Roshanaei G, Rezapour-Shahkolaei F. Medication adherence and its related factors in patients with type II diabetes. J Educ Community Health. 2016; 2 (4): 3-12.
11. Leon BM, Maddox TM. Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research. World Journal of Diabetes. 2015; 6 (13): 1246.
12. Kamillah S, Panduragan SL, Poddar S, Abdullah BF. Patients' experiences in using diabetes self-management application: a scoping review. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal). 2022; 17 (Special Issue 1): 67-73.
13. Zaman Z, Shohas MAAA, Bijoy MH, Hossain M, Al Sakib S. Assessing machine learning methods for predicting diabetes among pregnant women. International Journal of Advancement in Life Sciences Research. 2022; 5 (1): 29-34.
14. Epstein LH, Jimenez-Knight T, Honan AM, Paluch RA, Bickel WK. Imagine to remember: an episodic future thinking intervention to improve medication adherence in patients with type 2 diabetes. Patient Prefer Adherence. 2022; 16: 95.
15. Zamanillo-Campos R, Serrano-Ripoll MJ, Taltavull-Aparicio JM, Gervilla-García E, Ripoll J, Fiol-deRoque MA, Boylan AM, et al. Patients' views on the design of DiabeText, a new mHealth intervention to improve adherence to oral antidiabetes medication in Spain: a qualitative study. Int J Environ Res Public Health. 2022; 19 (3): 1902.
16. Imai C, Li L, Hardie RA, Georgiou A. Adherence to guideline-recommended HbA1c testing frequency and better outcomes in patients with type 2 diabetes: a 5-year retrospective cohort study in Australian general practice. BMJ Quality & Safety. 2021; 30 (9): 706-14.

Lestari, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (4): 292-296
DOI: 10.21109/kesmas.v17i4.6290

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

SO_2 Concentration and the Occurrence of Acute Respiratory Infection in Children Under Five

Puji Amrih Lestari[1], Budi Haryanto[1,2*]

[1]Department of Environmental Health, Faculty of Public Health, Universitas Indonesia, Depok, Indonesia, [2]Research Center for Climate Change, Universitas Indonesia, Depok, Indonesia

Abstract

Jakarta is the capital city of Indonesia, with 10.7 million inhabitants with poor air quality as of 2020. Higher levels of pollution often come with an increase in the number of health risks and pneumonia cases. This study aimed to determine the association between SO_2 concentration and the occurrence of acute respiratory infection (ARI) in children under five. An ecological time series design was implemented during the study by utilizing secondary data of SO_2 concentrations and ARI from the Indonesian Agency for Meteorological, Climatological, and Geophysics, the Special Capital Region of Jakarta Environmental, and Health Office. Statistical correlation tests were performed to analyze the association between SO_2 concentration and ARI prevalence in five municipalities cities in Jakarta from 2018-2021 based on the rainy and dry seasons. The average concentration of SO_2 was 18.06–20.89 μg/m^3. The SO_2 concentration and the occurrence of ARI in children under five in Jakarta from 2018 to 2021 showed a weak relationship (r = 0.24). It seems that children under five in Jakarta spent their time indoors rather than outdoors; therefore, they were exposed to fewer transportation emissions.

Keywords: acute respiratory infection, air pollution, children under five, SO_2 concentration

Introduction

Acute respiratory infection (ARI) is a major cause of morbidity and mortality from infectious diseases worldwide. The mortality rate due to ARI has reached 4.2 million annually worldwide, 98% of which are caused by respiratory infections.[1] High mortality rates due to ARI have been observed in infants, children, and the elderly, especially in countries with low and middle incomes per capita.[2] The World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) call ARI or pneumonia "the forgotten killer of children" or a forgotten pandemic because of the large number of deaths from ARI.[3]

The 2017 Indonesian Demographic and Health Survey (IDHS) stated that the child mortality rate was 32 per 1,000 live births.[4] Pneumonia was the second most common cause of death after diarrhea in 2019, with 314 (10.7%) deaths from 2,927 deaths occurring between 12–59 months.[5] Data from the Directorate General of Disease Prevention and Control Services, Ministry of Health of the Republic of Indonesia, in 2020, showed an increment in the coverage of toddler pneumonia cases throughout Indonesia from 51.2% in 2017 to 56.5% in 2018 and 52.9% in 2019.[5] The death rate from pneumonia in the infant group was almost twice for a group of children aged 1–4 years.[5]

Based on the 2019 Health Profile reported by the Special Capital Region of Jakarta Health Office, the observation of morbidity from year to year showed an increment in the percentage of pneumonia cases in Jakarta, as many as 45.301 cases or 121.9% compared to the 2018 report which was 217.5% of the total 14,629 cases.[6] Air pollution can be caused by humans or occur naturally in the environment.[7] Other factors at risk of increasing the occurrence of ARI in children under five are environmental conditions (such as air pollution, the density of household members, cleanliness, humidity, temperature, and season) and the availability and effectiveness of public health services.[2]

Jakarta's air pollution is caused by several factors, such as air pollutant emissions. The pollutant emissions degrade air quality in Jakarta.[8] Air pollution in Jakarta is increasing from year to year. As a developing city, Jakarta produces more and more air pollution, which causes air quality degradation because of population activities, industrial activities, and transportation. One factor that

Correspondence:* *Budi Haryanto, Department of Environmental Health, Building C 2nd Floor, Faculty of Public Health, Universitas Indonesia, Kampus Baru UI Depok, Depok City, West Java, Indonesia, 16424, E-mail: bharyanto@ui.ac.id, Phone: +62 855 7896 968*

Received : October 17, 2022
Accepted : November 28, 2022
Published : November 30, 2022

causes ARI increment is the high levels of ambient air sulfur dioxide (SO_2) and particulates (PM_{10}) concentrations. The Special Capital Region of Jakarta Environmental Office monitors the levels of primary pollutants, such as nitrogen dioxide (NO_2), SO_2, ozone (O_3), carbon monoxide (CO), and PM_{10} with the Air Quality Monitoring System (AQMS) in five municipalities cities in the Special Capital Region of Jakarta.[5] It is estimated that there were more than 5.5 million air pollution-related disease cases in Jakarta in 2010, including 2.45 million cases of ARI.[9]

A previous study has discussed that ambient air pollutants have an essential role in contributing to the high respiratory infection ratio by making people more vulnerable to the virus.[10] The WHO also reported that seven million die annually because of fine particles in the polluted air.[8] Two previous studies recognized that environmental temperature significantly impacts the prevalence of childhood respiratory diseases.[11,12] In contrast to exposure to moderate and comfortable temperatures, exposure to extreme hot and cold weather is associated with increased ARI morbidity. Therefore, current evidence suggests that ARI increases in temperate climates during the colder months of the year.[13] Indonesia's tropical climate is divided into two seasons in one year: the rainy and dry seasons. As a tropical country, there is a change of seasons every six months.[13] This study aimed to determine the association between SO_2 concentrations and the occurrence of ARI in children under five in Jakarta in 2018-2021.

Method

This study used an ecological design with aggregated data by time to assess the association between monthly numerical data in both SO_2 concentrations and the occurrence of ARI in children under five. This study was conducted in five municipalities cities (Central, North, West, South, and East Jakarta) of the Special Capital Region of Jakarta Province. The study population consisted of children under five in Jakarta who had ARI during the study period. The data used were from January 2018 to March 2021 and grouped into rainy and dry seasons. The monthly average SO_2 data for Jakarta for January 2018-March 2021 were accessed online through the Special Capital Region of Jakarta Environmental Office website (*https://lingkunganhidup.jakarta.go.id/publikasi/laporanudara*). These data were based on daily measurements from January 2018 to March 2021 from five AQMS in the Special Capital Region of Jakarta. Statistical correlation tests were performed to analyze the association between SO_2 concentration and ARI prevalence in five municipalities cities of the Special Capital Region of Jakarta over the last four years based on the rainy and dry seasons.

Results

The ARI variable had a minimum value of 708 cases, a maximum value of 6,347 cases, and a median value of 3,133 cases. The ARI variable had a standard deviation (SD) of 1,624, a mean of 2,948, and a 95% confidence interval (CI) of 2,422–3,475, indicating that 95% believe that the number of ARI cases was 2,948 in the range of 2,422–3,475 cases. The normality test results using the Kolmogorov-Smirnov test showed a p-value of 0.145 (>0.05), indicating that the ARI data were normal. Furthermore, the distribution was skewed to the right (positive skewed) based on the skewness value of +0.136 (Table 1).

The SO_2 concentration variable had a minimum value of 13.22 g/m^3, a maximum value of 31.46 g/m^3, and a median value of 19.31 g/m^3. The SO_2 concentration variable had an SD of 4.37, a mean SO_2 concentration of 19.31, and a 95% CI of 18.06–20.89). The normality test results using the Kolmogorov–Smirnov test showed a p-value of 0.259 (> 0.05), indicating that the SO_2 concentration data were normal. The distribution was skewed to the right (positive sloping) based on the skewness value of +1,154 (Table 1).

The number of ARI cases of children under five included in this study was between 708 and 6,347 occurrences (mean = 2,948, SD = 1,624). The data were normally distributed (Kolmogorov–Smirnov normality test with a p-value of 0.145; the distribution was skewed to the right). The mean SO_2 concentration was 19.31 g/m^3 (18.06–20.89 g/m^3, SD = 4.37). The results of the normality test using the Kolmogorov–Smirnov test showed a p-value of 0.259 (>0.05), which indicated that the SO_2 concentration data were normal, with a distribution

Table 1. Distribution of Acute Respiratory Infection in Children under Five and SO_2 Concentration in the Special Capital Region of Jakarta in 2018-2021

Variable	n	Min-Max	Mean	Median	SD	95% CI	p-value*	Skewness
ARI in children	39	708–6,347	2,948	3,133	1,624	2,422–3,475	0.145	0.136
SO_2 concentration	39	13.2–31.5	19.48	19.31	4.37	18.06–20.89	0.259	1.154

Notes: SO_2 = Sulfur Dioxide, SD = Standard Deviation, CI = Confidence Interval, ARI = Acute Respiratory Infection
*Test for normality with a one-sample Kolmogorov–Smirnov test

skewed to the right (+1.154) (Table 1).

The number of ARI cases of children under five during January 2018-March 2021 showed a fluctuating trend, with some periods showing a significantly high number of cases, namely: February 2018 (almost 5,000 cases), February 2019 (> 6,000 cases), and March 2020 (> 6,000 cases). In the other months, the number of cases was approximately 2,000–4,000 and sharply decreased to approximately 1,000 in May 2020-March 2021 (Figure 1).

The SO_2 concentrations in the Special Capital Region of Jakarta from January 2018 to March 2021 showed a fluctuating trend, with some showing significantly high concentrations, especially in January 2018, December 2020, February 2021, and March 2021 (Figure 2). The SO_2 concentrations in the Special Capital Region of Jakarta in 2018-2021 were higher during the months of November and December 2020 and January, February, and March 2022 and tended to decrease from April to October. This pattern showed that higher SO_2 concentrations occurred more frequent in the rainy season (Figure 3).

Analysis of the relationship between SO_2 concentration and the incidence of ARI in infants using the Spearman's correlation test between SO_2 concentrations and the incidence of ARI in children under five in the Special Capital Region of Jakarta in 2018-2021 showed a significant relationship (r = 0.241; p-value = 0.139) at a 1-month lag (Table 2). The relationship was negative, indicating that an increase in one variable was not followed by an increase in another. It means that if there is an increase in the monthly SO_2 concentration, it will not be followed by an increase in the number of ARI occurrences monthly in children under five in the following month (Figure 4).

The ARI's occurrence related to exposure to air pollution might have a delay of up to 14 days due to the variation of incubation periods, especially among children under five. Therefore, this study analyzed the association between SO_2 concentration and the number of ARI cases using the lag = 1 month data for the ARI cases, given that it might explain the association between SO_2 concentration and the occurrence of ARI cases in children under five more accurately. Furthermore, to provide

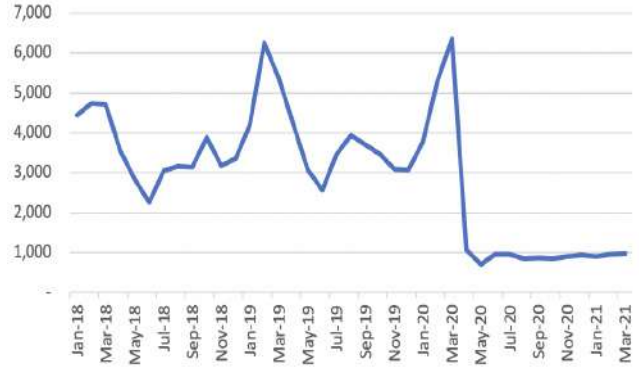


Figure 1. Monthly Cases of ARI in Children Under Five in the Special Capital Region of Jakarta in 2018-2021

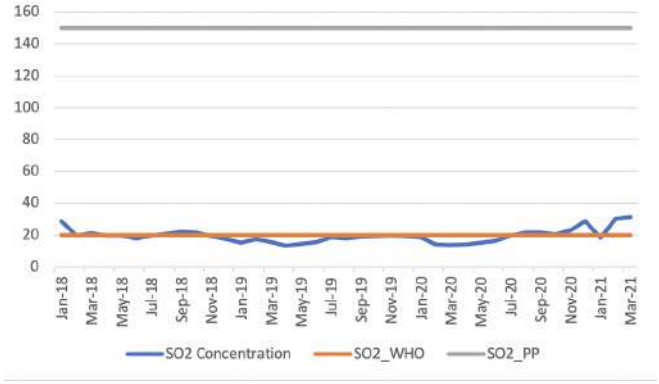


Figure 2. Monthly SO_2 Concentrations in the Special Capital Region of Jakarta in 2018-2021

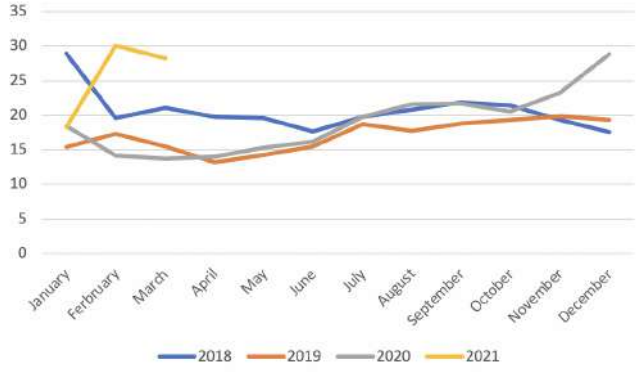


Figure 3. Seasonal SO_2 Concentrations in the Special Capital Region of Jakarta in 2018-2021

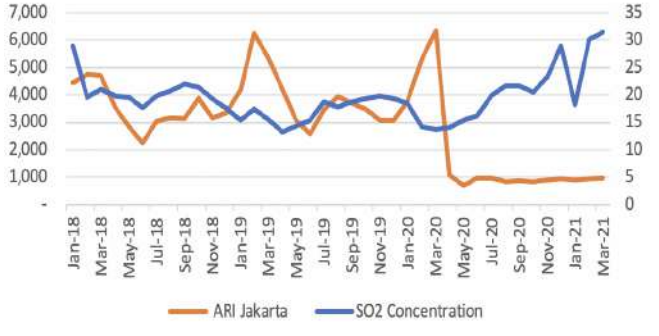


Figure 4. Relationship between SO_2 Concentration and ARI in Children under Five in the Special Capital Region of Jakarta by Season in 2018-2021

Table 2. Association between SO_2 Concentration and Acute Respiratory Infection in Children under Five in Jakarta at Lag 0 Month and Lag 1 Month by Seasons in 2018-2021

Year	Lag = 0			Lag = 1		
	r	p-value	Statistic test	r	p-value	Statistic test
2018	-0.32	0.32	Spearman	0.52	0.02	Spearman
Rainy season	0.67	0.15	Pearson	0.34	0.52	Pearson
Dry season	-0.43	0.39	Pearson	0.84	0.04	Pearson
2019	-0.05	0.87	Pearson	0.05	0.87	Pearson
Rainy season	0.07	0.89	Pearson	0.64	0.17	Pearson
Dry season	-0.97	0.001	Pearson	0.83	0.04	Spearman
2020	-0.57	0.05	Spearman	0.35	0.26	Spearman
Rainy season	-0.25	0.64	Pearson	0.22	0.67	Pearson
Dry season	0.85	0.03	Pearson	0.20	0.7	Pearson
2021	1	-	Spearman	0.5	0.67	Spearman
2018-2021	-0.34	0.04	Spearman	0.24	0.14	Spearman

more insights from the analysis, the data of lag = 0 was provided for comparison. The lag = 1 correlation test between SO_2 concentrations and the number of cases of ARI in 2018 showed a moderate positive relationship (r = 0.52; p-value = 0.02) for the entire year and a solid positive relationship for the dry season (r = 0.84; p-value = 0.04). In 2019, a solid positive relationship was found in the dry season (r = 0.83; p-value = 0.04) (Table 2).

Discussion

This study showed that the highest monthly cases of ARI in children under five from January 2018 to March 2021 occurred in March 2020. In contrast, the highest monthly SO_2 concentration occurred in March 2021. The SO_2 concentration was shown to have an insignificant relationship with the occurrence of ARI in children at lag = 1 month in Jakarta in 2018-2021. The SO_2 concentration significantly correlated with the incidence of ARI in children in 2018. This study was in parallel with a study conducted in Shenzhen, China, which showed no association between monthly SO_2 concentrations and monthly ARI incidence.[14] This pattern of events followed fluctuations and meteorology for SO_2 in the previous month (lag = 1 month).[15] In contrast, this finding was not in line with a study conducted in Hong Kong, which showed a significant association between the number of daily ARI consultations at health services and the concentration of SO_2, even though air pollution may cause substantial morbidity and increase the burden of health services.[16]

The burden of morbidity and mortality caused by air pollution is costly because most pollution-related deaths occur within 1–2 years of exposure.[17] Based on the Regulation of the Minister of Health of the Republic of Indonesia Number 1077 of 2011 Concerning Guidelines for Sanitary Air in Home Spaces, the maximum level of SO_2 required is 0.1 ppm or 261.75 g/Nm.[18] SO_2 is associated with several adverse effects on the respiratory system and other environmental issues.[19] Children are exposed to air containing SO_2 gas daily, which can irritate the respiratory system.[3] This study showed a monthly concentration average SO_2 of 19.48 g/m^3, with the lowest concentration of 13.22 g/m^3 and the highest concentration of 31.46 g/m^3. However, this average concentration of SO_2 was below the air quality standard for SO_2 (150 g/m^3) according to the Indonesian Government Regulation Number 22 of 2021 Concerning the Implementation of Environmental Protection and Management.[20] A study by Putra, *et al.*, stated that SO_2 pollution significantly correlated with the incidence of ARI, with a solid positive relationship.[21] A study conducted in 32 major cities in China also reported that air pollution had a significant relationship with the incidence of respiratory mortality.[22] Another study also revealed an association between air pollution levels and cardiovascular and respiratory disease mortality.[23] In brief, SO_2 pollution will impact respiratory tract irritation.

Conclusion

The number of ARI cases in children under five in Jakarta from January 2018 to March 2021 is sloping in 2021. Males are found to suffer from ARI compared to females. The SO_2 concentration and the occurrence of ARI in children under five in Jakarta from 2018 to 2021 showed a weak relationship. It may be because children under five in Jakarta spent their time indoors rather than outdoors, exposing them to fewer transportation emissions.

Abbreviations

ARI: Acute Respiratory Infection; WHO: World Health Organization; UNICEF: United Nations International Children's Emergency Fund; IDHS: Indonesian Demographic and Health Survey; AQMS: Air Quality Monitoring System; SD: Standard Deviation; CI: Confidence Interval.

Ethics Approval and Consent to Participate

This study was approved by the Research and Community Engagement Ethical Committee, Faculty of Public Health, Universitas Indonesia, No. 10/UN2.F10.D11/PPM.00.02/2021.

Competing Interest

The authors declare that there is no significant competing financial, professional, or personal interest that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The data available is only data that has been written in the manuscript, because other data are limited by research ethics.

Authors' Contribution

PAL conducted the data analysis, data interpretation, and drafting of the manuscript. BH contributed substantially to the concept, work design, and manuscript drafting. BH and PAL screened the title and abstract, and BH revised the manuscript critically for the important intellectual content of PAL. BH approved the final version to be published.

Acknowledgment

This research was supported by the International Indexed Publication Grant (PUTI) for Saintekes Fiscal Year 2020 Number: NKB-2379/UN2.RST/HKP05.00/2020, University of Indonesia.

References

1. Najmah. Epidemiologi penyakit menular. Jakarta Timur: CV. Trans Info Media; 2016.
2. Hill K, Zimmerman L, Jamison DT. Mortality risks in children aged 5-14 years in low-income and middle-income countries: a systematic empirical analysis. Lancet Glob Heal. 2015; 3 (10): e609–16.
3. World Health Organization & United Nations Children's Fund (UNICEF). Pneumonia: the forgotten killer of children. Geneva: World Health Organization; 2006.
4. National Population and Family Planning Board, Statistics Indonesia, Ministry of Health, ICF. Indonesia demographic and health survey 2017. Jakarta: National Population and Family Planning Board, Statistics Indonesia, Ministry of Health, ICF; 2018.
5. Kementerian Kesehatan Republik Indonesia. Profil kesehatan Indonesia tahun 2019. Jakarta: Kemeterian Kesehatan Republik Indonesia; 2020.
6. Dinas Kesehatan Provinsi DKI Jakarta. Profil kesehatan Provinsi DKI Jakarta tahun 2019. Jakarta: Dinas Kesehatan Provinsi DKI Jakarta; 2019.
7. United Nations Children's Fund. Clear the air for children: the impact of air pollution on children. UNICEF; 2016.
8. World Health Organization. Pencegahan dan pengendalian infeksi saluran pernapasan akut (ISPA) yang cenderung menjadi epidemi dan pandemi di fasilitas pelayanan kesehatan. WHO; 2007.
9. Rendana M, Komariah LN. The relationship between air pollutants and COVID-19 cases and its implications for air quality in Jakarta, Indonesia. J Pengelolaan Sumberd Alam dan Lingkung (Journal Nat Resour Environ Manag). 2021; 11 (1): 93–100.
10. Slama A, Śliwczyński A, Woźnica-Pyzikiewicz J, Zdrolik M, Wiśnicki B, Kubajek J, et al. The short-term effects of air pollution on respiratory disease hospitalizations in 5 cities in Poland: comparison of time-series and case-crossover analyses. Environ Sci Pollut Res. 2020; 27 (19): 24582–90.
11. Xu Z, Etzel RA, Su H, Huang C, Guo Y, Tong S. Impact of ambient temperature on children's health: a systematic review. Environ Res. 2012; 117: 120–31.
12. Deng SZ, Jalaludin BB, Antó JM, Hess JJ, Huang CR. Climate change, air pollution, and allergic respiratory diseases: a call to action for health professionals. Chinese Medical Journal. 2020; 133 (13): 1552–60.
13. Ariffin. Metode klasifikasi iklim di Indonesia. UB Press; 2019.
14. Xia X, Zhang A, Liang S, Qi Q, Jiang L, Ye Y. The association between air pollution and population health risk for respiratory infection: a case study of Shenzhen, China. Int J Environ Res Public Health. 2017; 14 (9).
15. Irawan A, Sutomo AH, Sukandarrumidi. Indeks standar pencemar udara, faktor meteorologi dan kejadian ISPA di Pekanbaru. J Community Med Public Heal. 2017; 33 (1): 15–32.
16. Tam WWS, Wong TW, Ng L, Wong SYS, Kung KKL, Wong AHS. Association between air pollution and general outpatient clinic consultations for upper respiratory tract infections in Hong Kong. PLoS One. 2014; 9 (1): 1–6.
17. Juginović A, Vuković M, Aranza I, Biloš V. Health impacts of air pollution exposure from 1990 to 2019 in 43 European countries. Sci Rep. 2021; 11 (1): 1–15.
18. Kementerian Kesehatan Republik Indonesia. Peraturan Menteri Kesehatan Republik Indonesia nomor 1077/Menkes/Per/V/2011 tentang pedoman penyehatan udara dalam ruang rumah.Kemenkes RI; 2011.
19. Roy P, Sardar A. SO2 emission control and finding a way out to produce sulphuric acid from industrial SO2 emission. J Chem Eng Process Technol. 2015; 06 (02).
20. Presiden Republik Indonesia. Peraturan Pemerintah Republik Indonesia nomor 22 tahun 2021 tentang penyelenggaraan perlindungan dan pengelolaan lingkungan hidup. Presiden RI; 2021.
21. Putra AF, Sulityorini L. Kadar SO2 dan kejadian ISPA di Kota Surabaya menurut tingkat pencemaran yang berasal dari kendaraan bermotor. IPTEK J Proc Ser. 2017; 3 (5).
22. Zhou M, He G, Liu Y, Yin P, Li Y, Kan H, et al. The associations between ambient air pollution and adult respiratory mortality in 32 major Chinese cities, 2006-2010. Environ Res. 2015; 137: 278–86.
23. Khanjani N, Hashemi SY. Air pollution and cardiovascular mortality in Kerman, Iran; from 2006 to 2011. ISEE Conf Abstr. 2014; 2014 (1): 2533.

Reviewer Acknowledgment

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Volume 17, February - November 2022

Acim Heri Iswanto
Anies Irawati
Aria Kusuma
Atikah Adyas
Budi Anna Keliat
Çağdaş Salih Meriç
Chatarina Umbul Wahyuni
Chigozie Gloria Anene-Okeke
Chotib
Dini Rahma Bintari
Djazuly Chalidyanto
Ede Surya Darmawan
Fransisca Andreani
Gita Miranda Warsito
H. J. Mukono
Hacı Ömer Yılmaz
Hari Basuki Notobroto
Helen Andriani
Helwiah Umniyati
I Made Djaja
I Made Susila Utama
Imami Nur Rachmawati
Indang Trihandini
Indri Hapsari Susilowati
Indri Safitri Mukono
Kemal Nazarudin Siregar
Laily Hanifah
Maya Ivanova
Meily Kurnia Wijaya
Mila Tejamaya
Minarto
Mochammad Bagus Qomaruddin
Mohd Faizal Bin Mohd Zulkifly
Novrikasari
Nurhayati Adnan Prihantono
Nurjazuli
Ponnusamy Subramaniam
Rahayu Lubis
Rani Sauriasari
Ratna Djuwita
Ririh Yudhastuti
Sandra Fikawati
Santi Martini
Septian Rahardiantoro
Setya Haksama
Setyowati
Sri Achadi Nugraheni
Sri Rahayu Sanusi
Stefanus Supriyanto
Suci Sandi Wachyuni
Sulistiyani
Suriah
Tiopan Sipahutar
Tri Joko
Tri Yunis Miko Wahyono
Tris Eryando
Trisari Anggondowati
Wah Yun Low
Wahyu Sulistiadi
Yasep Setiakarnawijaya
Zarfiel Tafal

Author Index

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Volume 17, February - November 2022

Subject Index

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Volume 17, February - November 2022

SUBSCRIPTION FORM

The undersigned:

Name : .....
Address : .....
.....
.....
Phone Number : .....
E-mail : .....
Edition : .....

is willing to be Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal) customer, and will be paying the cost of IDR 400,000,-/year/4 edition (exclude delivery cost).

....., ...

(.....)

Please make a payment to the following account:
UNIVERSITAS INDONESIA BHPP
BANK BNI UI DEPOK
ACCOUNT NO. 1273000568
SWIFT CODE: BNINIDJA

Please send the receipt to:
Secretariat of Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)
G301 Building G 3rd Floor
Faculty of Public Health Universitas Indonesia
Kampus Baru UI Depok 16424
Mobile Phone: +62815-1141-6600
or email: jurnalkm@ui.ac.id or jurnalkesmas.ui@gmail.com