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ORIGINAL RESEARCH

# Chemotherapy-Induced Nausea and Vomiting (CINV) Based on Blood Types among Cancer Patients in Yogyakarta, Indonesia



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## Abstract

**Background:** Studies related to blood type in cancer patients have been conducted extensively, but they are inclined to cancer incidence or survival rate. Meanwhile, there is limited research on Chemotherapy-Induced Nausea and Vomiting (CINV), the most disturbing side effect of chemotherapy, in relation to blood type.

**Purpose:** This study aimed to compare CINV frequency in cancer patients by blood groups in Yogyakarta, Indonesia.

**Methods:** A descriptive comparative study with a cross-sectional approach was conducted purposively on 70 chemotherapy patients in two hospitals in Yogyakarta. Patients with anticipatory CINV and brain cancer (primary or metastases) were excluded. The data were collected between July and November 2020 using a sheet for patient characteristics and a filled-in diary from the first to the seventh day post-chemotherapy to collect CINV data. The descriptive statistics and Kruskal Wallis test were used to analyze the data.

**Results:** Of 70 total samples, most of them were breast cancer (71.4%) and were in stage IV (50%). They received chemotherapy alone as their primary therapy (94.3%) and received moderate to high emetogenic agents (31.4% and 35.7%). Samples mostly had A blood type (34.3%) and had undergone chemotherapy for 3-18 months (min-max). As many as 64.6% of patients experienced CINV with a delayed type and experienced moderate severity (52.9%). The bivariate test showed no difference in CINV frequencies based on blood groups in general ( $p=0.068$ ). However, based on the CINV onset, there was a significant difference in CINV frequencies in the A blood group against other blood groups ( $p=0.020$ ) on the fourth post-chemotherapy day.

**Conclusions:** Unless the fourth-day post-chemotherapy, the frequency of CINV based on blood groups showed no difference. Since CINV incidence is still high, the provision of both pharmacological and non-pharmacological therapy to treat CINV has to be given to patients after chemotherapy. Blood group factors can be considered for more extensive management, especially in delayed CINV cases.

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## 1. Introduction

Non-communicable diseases (NCDs) are currently considered the most significant cause of death worldwide. Cancer, one of the NCDs, is the most significant barrier to increasing life expectancy in almost all countries in the 21st century (Bray et al., 2018). Lung, colorectal, and breast cancer have the most considerable incidence and are among the top five causes of death worldwide (International Agency For Research of Cancer, 2018). Cancer prevalence in Indonesia increased from 1.4‰ in 2013 to 1.49‰ in 2018. Among the provinces, Yogyakarta has the highest prevalence, with 4.86‰ in 2018 (Ministry of Health The Republic of Indonesia, 2019). From 2019 to 2020, there was a total of 9,333 cancer cases recorded in Yogyakarta province (Solikhah et al., 2022).

Cancer patients experience many problems that arise due to their illness. Cancer-related complaints are fatigue, pain, anxiety, and depression. Complaints are also still reported even though the patient has undergone surgery, radiotherapy, hormone therapy, and chemotherapy to treat the disease (Do et al., 2015; Habibi et al., 2016). Surgery in cancer cases aims to remove the patient's tumor mass or tissue (Angahar, 2017). For example, breast cancer patients undergoing mastectomy usually complain of sequelae due to the procedure, including limitations in the shoulder joints, arm and hand weakness, lymphedema, pain, and sensory disturbances (Do et al.,

2015). Meanwhile, other adjuvant therapies, such as hormone therapies, radiotherapies, and chemotherapies in breast cancer patients aim to reduce recurrence and death rates, although these therapies cause side effects that can harm the quality of life (Angahar, 2017; Do et al., 2015).

The radiotherapy has short-term side effects such as fatigue and skin rash. Long-term effects of radiotherapy are lymphedema, cardiopulmonary toxicity, and brachial nerve palsy. However, of the several side effects of adjuvant therapies, chemotherapy has the most dominant side effect because it has a toxic effect on healthy cells and tissues. Short-term adverse effects of chemotherapy include nausea, vomiting, diarrhea, headache, thrombosis, muscle aches, neuropathic problems, and fatigue (Do et al., 2015). Meanwhile, the long-term side effects of chemotherapy include bone marrow suppression, neuropathies, gastrointestinal disorders, hair loss, fatigue, and skin disorders (Chan & Ismail, 2014). Among the side effects caused by chemotherapy, nausea and vomiting are the most disturbing and debilitating effects for cancer patients (Dranitsaris et al., 2017). Nausea and vomiting caused by chemotherapy are known as chemotherapy-induced nausea and vomiting (CINV), which affects almost 70-80% of chemotherapy patients (Levine & Shega, 2013). If CINV is not controlled, it can lead to dehydration, anorexia, weight loss, electrolyte disturbances, and reducing the patient's quality of life. Fear of CINV can also delay chemotherapy, reduce chemotherapy dosages, and even discontinue chemotherapy. All of these things can result in reduced benefits from the therapy in the form of symptom control and prolonging the patient's life (Do et al., 2015).

CINV occurs when the medulla oblongata, the vomiting center (VC) that controls the vomiting response in humans is stimulated. The vomiting center integrates various inputs from both peripheral and central parts of the body, eliciting an emetic reflex in response. The peripheral pathway originates from the gastrointestinal tract, where stimuli are transmitted via the abdominal vagal afferents (Aapro, 2018). Vagal afferent fibers in the stomach express various receptors (e.g., 5-HT<sub>3</sub>, neurokinin 1, and cholecystokinin-1) that can trigger an emetic response when stimulated, with 5-HT<sub>3</sub> as the primary mediator. Vagal afferent fibers terminate in the dorsal vagal complex, which consists of the nucleus tractus solitarius (NTS), the area postrema, and the dorsal motor nucleus. In turn, the NTS and the area postrema (also known as the chemoreceptor trigger zone) transmit impulses to the vomiting center (Aapro, 2018; Gupta et al., 2021). Meanwhile, the central emesis pathway describes how brain input to the vomiting center will evoke an emetic response. The vomiting center receives direct cholinergic and histaminic input in response to pain, vestibular disturbances, or emotional factors. The vomiting center also receives input from the chemoceptor trigger zone or postrema area in response to endogenous toxins and other chemical stimuli (e.g., chemotherapy or other drugs) (Gupta et al., 2021; Shankar, 2015).

Several risk factors influence the incidence and severity of CINV in cancer patients undergoing chemotherapy, and these risk factors come from the treatment and patient characteristics (Navari & Rapoport, 2016). Risk factors derived from the given treatments include emetogenic agents, dosage, route of administration, duration of infusion, and combination of chemotherapeutic agents. Risk factors derived from patient characteristics were gender (women are more at risk), age being less than 50 years, an alcohol-free history, a history of previous chemotherapy-induced emesis, and a history of being a non-smoker (Navari & Rapoport, 2016; Sekine et al., 2013). However, the blood group factor is rarely mentioned among the various factors typically discussed.

The relationship between blood type and nausea and vomiting was previously studied by Habibi et al. (2016) in a different setting. They examined the relationship between the ABO blood group system and the incidence of nausea and vomiting in cancer patients receiving radiotherapy. The theoretical basis of this study was that the ABO blood type system could affect the condition of radiotherapy-induced nausea and vomiting (RINV) through its capacity to modulate the hemostatic system and the inflammatory response that would stimulate the nausea center in the medulla oblongata. The results indicated that blood type is significantly related to RINV conditions, where patients with blood type A are the most affected by RINV (Habibi et al., 2016). Other studies related to blood type in cancer patients have been conducted several times but tend to be more about the relationship between blood type and cancer incidence or with the survival rate of cancer patients. The relationship between blood type and cancer incidence has been meta-analyzed by Zhang et al. (2014), who stated that there is a relationship between blood types and cancer risks where A blood type is the most at risk for cancer, and O blood type is the least at risk

of developing cancer. This was also reinforced by research conducted by Meo et al. (2017), who found that there was a relationship between ABO blood type and the incidence of breast cancer in women, where people in the A blood group had the highest and people in AB blood group had the lowest incidence of breast cancer. It can, therefore, be concluded that research on the relationship or comparison between ABO blood groups and CINV is still scarce, even in Yogyakarta, which has the highest cancer prevalence rate in Indonesia. Therefore, this study aimed to compare CINV frequency based on blood types in cancer patients in Yogyakarta.

## **2. Methods**

### *2.1 Research design*

The study was a comparative descriptive study with a cross-sectional approach to find the differences in the incidence of CINV in cancer patients based on blood types.

### *2.2 Setting and samples*

The study was conducted in two hospitals (a public and a private hospital) in Yogyakarta from July to November 2020. The inclusion criteria were adult cancer patients (age 18 years or older) undergoing chemotherapy and receiving standard hospital antiemetic drugs and being able to communicate both verbally and in writing. The exclusion criteria were patients that had nausea and vomiting one day before chemotherapy (anticipatory CINV) and had a brain tumor (primary or metastasized). The study did not control for confounding factors such as a history of gastrointestinal irritation, chemotherapy dosage, chemotherapy emetogenicity, and the type of therapy given. However, the data on confounding factors would be used as enrichment material during the discussion.

This study used a Slovin formula (Adhikari, 2021) for sample size calculation with a 95% confidence level. The population of cancer patients undergoing chemotherapy in 2020 at the two hospitals was 107, and the measurement, according to the formula, determined that 84 was the minimum sample. Out of those eligible to be in the sample at the public hospital, only 35 participated, while five refused to take part in the study. Those eligible in the private hospital were 43, while three people did not return the diary. Therefore, the total sample obtained comprised 70 respondents rather than the 84 respondents needed for the minimum sample.

### *2.3 Measurement and data collection*

This study used a checklist and diary as tools for data collection. The checklist collected demographic data such as age, gender, marital status, educational background, monthly income, and blood group. It also collected data related to the disease and its therapies, such as primary cancers, stages, metastasis conditions, therapy types, history of gastrointestinal irritation, emetogenic agents, how long they had been diagnosed, and chemotherapy.

For the incidence of CINV, the study used a diary that used questions adopted from two similar previous studies in India and Iran (Habibi et al., 2016; Kapoor et al., 2020). The diary contained questions about the incidence of CINV, frequency of nausea/vomiting, onset of nausea/vomiting, duration of nausea/vomiting, time of severe nausea/vomiting, severity of nausea/vomiting, usage of antiemetics, and types of antiemetics used. The severity of nausea/vomiting in the study was measured using the Baxter Animated Retching Faces (BARF) nausea scale that was recommended for use with children and adults (Sisman et al., 2016). The scale ranged from 0 to 5, for an assessment of 0=no nausea to 5=very severe nausea (Sisman et al., 2016). The intra-class coefficient (95% CI) of BARF scores was 0.88 (0.76-0.94) (Watcha et al., 2018), and 9/10 (90%) experts agreed that the faces on the BARF scale represented the increasing intensity of nausea (Sisman et al., 2016), so it proved that the BARF nausea scale was a valid and reliable tool. The nausea/vomiting severity data were then coded into 0-1 as mild, 2 as moderate, 3-4 as severe, and 5 as very severe.

The data collection process gathered both primary and secondary data. Primary demographic data were collected through interviews with COVID-19 precautions approved by the hospitals, while secondary data were collected from medical records related to treatments and to confirm demographic data that may have been dubious. CINV data were obtained using the CINV diaries, which were distributed and taken home by each patient to be filled out from day 1 (after leaving the chemotherapy room for up to 24 hours) up to day 7 with a total of 7 days. CINV symptoms could appear at different stages of the chemotherapy. Acute CINV is predominantly mediated by

5-HT<sub>3</sub> and occurs within 24 hours of the start of chemotherapy (Aapro, 2018). Meanwhile, delayed CINV occurs between 24 hours and 7 days following treatment (Gupta et al., 2021; Hayashi et al., 2021). Patients were considered to have CINV if, within 7 days, they experienced at least 1 occurrence of CINV. Patients filled out their CINV diaries independently for 7 days following the instructions. The completed diaries were then returned to the researchers when they visited for the next chemotherapy session. The researchers periodically followed up if there were difficulties while filling out the diary and reminded patients to return the completed diaries.

#### 2.4 Data analysis

The collected data were then analyzed descriptively for univariate data such as demographic, disease, and therapy characteristics. A normality test using the Kolmogorov-Smirnov test resulted in  $p=0.000$ , or the data were not normally distributed. Therefore, the comparison of CINV data based on blood groups used the Kruskal-Wallis test.

#### 2.5 Ethical considerations

The ethics committee of Universitas Jenderal Achmad Yani Yogyakarta approved this research with registry number: Skep/056/KEPK/VII/2020. The respondents also filled out and signed the informed consent forms, and this study did not discriminate against the samples. The researchers destroyed the hard file data (CINV diaries and demographic and disease form sheets) four months after the analysis to ensure they were correctly used.

### 3. Results

#### 3.1 Demographic characteristics of the participants

The study ascertained the demographic characteristics of the cancer patients as presented in Table 1. The mean age of the participants was 54.4 years (SD=11.32 years). The patients in both hospitals were mostly female (85.8%), married (88.6%), with a senior high school education background (32.9%), income below the minimum wage (68.6%), and A blood type group (34.3%).

**Table 1.** Demographic characteristics of the participants (n=70)

Characteristics	f	%	Mean	SD
Age (year)			54.4	11.32
Gender				
Male	10	14.3		
Female	60	85.8		
Marriage Status				
Widow/Widower	8	11.4		
Married	62	88.6		
Education Background				
Elementary School	19	27.1		
Junior High School	12	17.1		
Senior High School	23	32.9		
University	16	22.9		
Income				
Below RMW*	48	68.6		
Above RMW	22	31.4		
Blood Group				
A	24	34.3		
B	19	27.1		
O	22	31.4		
AB	5	7.1		

Note. \*RMW=Regional Minimum Wage

#### 3.2 Characteristics of the diseases and treatments

Concerning the patient disease and treatments (Table 2), most patients had breast cancer (71.4%), were in stage IV (50%), received chemotherapy (94.3%), were not in metastatic condition (75.7%), and had not experienced previous gastrointestinal (GIT) issues (85.7%). The patients in this study received chemotherapy with moderate (31.4%) and high (35.7%)

emetogenic agents. The patients had been diagnosed with cancer for at least three months, and the longest had been diagnosed for 84 months. As for the duration of chemotherapy, the patients had undergone chemotherapy for at least three months and, at most, for 18 months.

**Table 2.** Characteristics of the diseases and treatments (n=70)

Characteristics	f	%	Min	Max
Primary cancer				
Breast	50	71.4		
Lung	11	15.7		
Lymphoma	3	4.3		
Bladder	3	4.3		
Colorectal	3	4.3		
Stage of cancer				
II	10	14.3		
III	25	35.7		
IV	35	50		
Therapy type				
Chemotherapy	66	94.3		
Chemoradiation	4	5.7		
Metastasis				
No	53	75.7		
Yes	17	24.3		
GIT irritation history				
No	60	85.7		
Yes	10	14.3		
Emetogenic agent*				
Minimal	7	10		
Low	16	22.9		
Moderate	22	31.4		
High	25	35.7		
Length of diagnosis (months)			3.00	84.00
Length of chemotherapy (months)			3.00	18.00

Note. \*The emetogenicity of the chemotherapy drugs table (Celio, 2022; Gupta et al., 2021).

### 3.3 Characteristics of CINV and its frequency among blood group

Table 3 shows that most patients (68.6%) experienced CINV, with 64.6% experiencing delayed CINV (31/48 samples). CINV mainly occurred 3 and 4 days after chemotherapy (22.15%), and as many as 52.9% of patients stated that their CINV was in the moderate category.

**Table 3.** CINV characteristics among cancer patients (n=70)

CINV characteristics	f	%
CINV		
No	22	31.4
Yes	48	68.6
CINV Type (n=48)		
Acute	17	35.4
Delayed	31	64.6
CINV daily occurrence		
Day 1	17	10.76
Day 2	26	16.46
Day 3	35	22.15
Day 4	35	22.15
Day 5	23	14.56
Day 6	12	7.59
Day 7	10	6.33
CINV Severity		
Mild	22	31.4
Moderate	37	52.9
Severe	10	14.3
Very Severe	1	1.4

The total frequency of CINV from day one to seven among the patients was calculated and compared based on blood group (Table 4). The results indicated that there was no significant difference in the mean rank of CINV frequency based on blood types in chemotherapy patients ( $p=0.068$ ). The results showed a significant difference in the mean rank of CINV frequency in cancer patients on the fourth day after chemotherapy ( $p=0.020$ ). The A blood type patients experienced the highest frequency of CINV (mean=44.21) on day four.

**Table 4.** CINV frequencies comparison based on blood group (n=70)

Blood Group	CINV frequency		
	f	mean rank	p
Total CINV in 7 days			
A	24	42.02	0.068*
B	19	27.66	
O	22	32.86	
AB	5	45.60	
CINV Day 1			
A	24	33.23	0.127*
B	19	34.76	
O	22	35.18	
AB	5	50.60	
CINV Day 2			
A	24	37.90	0.428*
B	19	31.92	
O	22	33.89	
AB	5	44.70	
CINV Day 3			
A	24	42.90	0.077*
B	19	28.95	
O	22	32.23	
AB	5	39.30	
CINV Day 4			
A	24	44.21	0.020*
B	19	26.95	
O	22	32.30	
AB	5	40.30	
CINV Day 5			
A	24	42.48	0.055*
B	19	28.92	
O	22	32.89	
AB	5	38.50	
CINV Day 6			
A	24	38.13	0.495*
B	19	33.45	
O	22	35.77	
AB	5	29.50	
CINV Day 7			
A	24	38.31	0.365*
B	19	32.68	
O	22	35.89	
AB	5	31.00	

Note. \*Kruskal-Wallis Test

#### 4. Discussion

This study aimed to compare CINV frequencies based on blood types in cancer patients. As many as 70 cancer patients who participated in this study were monitored to see the incidence and frequency of nausea and vomiting that occurred due to chemotherapy (CINV) from the end of the chemotherapy (day 1) and then each day up to the seventh day after the chemotherapy. The results showed no significant difference between CINV frequency in cancer patients with blood types A, B, O, and AB who received chemotherapy in general. This is somewhat different from the

results of Habibi et al. (2016) but with a different setting, namely the comparison of radiotherapy-induced nausea and vomiting (RINV) in cancer patients. In their study, A blood type is the blood group that is most at risk of developing RINV compared to other blood groups (Habibi et al., 2016). Their statement supports the statement of Elahimanesh et al. (2013), who stated that A blood type is the blood group which is most sensitive to radiotherapy. The association between Rhesus antigen and the time of maximum severity of RINV may indicate that Rhesus antigen affects the time of maximum severity of RINV (Habibi et al., 2016). The relationship between the ABO blood group and CINV has not been specifically studied yet. However, it must be noted that there is a relation between the ABO blood group and cardiovascular diseases such as ischemic heart diseases (Parente et al., 2020) and cancers (Zhang et al., 2014) such as gastric cancer (Mao et al., 2019), and breast cancer (Meo et al., 2017).

CINV in this study was defined as nausea and/or vomiting that occurred at least once during the administering of chemotherapy (considered to be the first day) up to the sixth day after chemotherapy (considered day 7). About 20 to 30 percent of patients experienced nausea and vomiting secondary to the administration of cytostatic drugs (Shinta & Surarso, 2016). The results showed a higher result since the incidence of CINV in cancer patients in this study was 68.6%. The results regarding CINV incidence in this research supported a previous study that stated that the risk of nausea and vomiting in chemotherapy patients was thought to be between 70 and 80 percent, and the same proportion of patients would suffer the symptom if they had not had enough antiemetic medication (Al Qadire, 2018; Lavdaniti & Tsitsis, 2014). Most patients in this study experienced delayed-type CINV, and the others experienced acute-type CINV. Acute CINV occurs within 1–2 hours of chemotherapy administration and can last up to 24 hours, while delayed CINV presents more than 24 hours and up to 7 days after the chemotherapy is administered (Hayashi et al., 2021; Rapoport, 2017). This result is in line with a study that stated that with antiemetic prophylaxis, acute nausea occurs in up to 35% and acute vomiting occurs in approximately 13% of chemotherapy patients (Escobar et al., 2015; Gupta et al., 2021), while the incidence of delayed nausea and vomiting among patients after antiemetic prophylaxis is 20–50% (Escobar et al., 2015; Gupta et al., 2021). The CINV experienced by the patients in this study reached a peak on the third and fourth days, with the patient's perception of their CINV being moderate.

Although there was no significant difference between the frequency of CINV in general based on blood types, there was a significant difference in the frequency of CINV based on blood types that occurred on the fourth day after chemotherapy. The results showed that A blood type had a high mean frequency of CINV that increased after the first day and peaked on the third and fourth days compared to other blood types. The result that showed A blood type has a higher incidence of CINV is similar to a previous study related to the ABO blood group and RINV conducted by Habibi et al. (2016) and a study in 2010 in pregnancy setting by Phan (2010). They stated that A blood type has a higher incidence of nausea and vomiting than the other blood types in the setting. In addition, based on the mean rank increase of CINV, there was a possibility that A blood type was associated with a high incidence of delayed-type CINV. Delayed CINV is predominantly driven by a central pathway involving the neurotransmitter/neuromodulator substance P and usually occurs on the second day after chemotherapy until the fifth to seventh day (Hayashi et al., 2021; Rapoport, 2017). The cause of the high rate of delayed CINV in the A blood group in this study is unknown. However, the high rate of delayed CINV in the entire sample in this study could relate to the emetogenic agents given to the patient. Delayed CINV is more problematic than acute CINV in patients receiving moderate or high emetogenic agents. Based on a study in Rapoport (2017), adult patients who received chemotherapy for the first time and received highly emetogenic chemotherapy (HEC) and moderate emetogenic chemotherapy (MEC) agents experienced delayed nausea and vomiting in 50 and 60% for HEC and 58 and 28% for MEC. Meanwhile, those with acute CINV had 12 and 33% for HEC and 13 and 37% for MEC (Rapoport, 2017).

In addition, the AB blood group had the highest mean frequency of CINV on the first day and then decreased until the sixth day, after which it did not increase on the seventh day. So, it also can be concluded that there is a possibility that blood type AB is associated with acute-type CINV in cancer patients receiving chemotherapy. Acute CINV occurs within the first 24 hours after chemotherapy, and it is largely mediated by 5-HT<sub>3</sub> receptors in the intestine that interact with serotonin, which is induced by the generated free radicals after the administration of



chemotherapy and projected to the area postrema and nucleus tractus solitarius (NTS), stimulating the vomiting reflex (Rapoport, 2017). The high rate of acute CINV in AB blood type patients in this study is supported by a previous study in a different setting, which found that post-adenotonsillectomy patients with AB and B blood groups experienced a significantly higher incidence of postoperative nausea and vomiting (PONV) than the A and O blood groups did within 24 hours (Shen et al., 2022). Higher PONV in postoperative patients could be caused by higher preoperative anxiety. A study found preoperative anxiety differences between ABO blood types, and it was found that the AB group displayed a high preoperative anxiety level (Xu et al., 2019). A high level of preoperative anxiety has been reported as one of the risk factors resulting in postoperative nausea and vomiting (PONV) because it decreases the pH of the stomach content while increasing its volume (Alipour et al., 2021; Xu et al., 2019). This study did not discuss surgery on the patients; however, it did not rule out the possibility of anxiety experienced by patients ahead of the chemotherapy procedure, which can be a factor in increasing the incidence of acute CINV.

The most common primary cancer suffered by the patients in this study was breast cancer, and they were in stage IV. This result is in line with worldwide observations that show breast cancer is a prevalent tumor in women, as it accounts for 22% of all cancers in women (Jannat et al., 2022). Breast cancer causes a burden in terms of prevention, diagnosis, and treatment regardless of a nation's economic situation. Breast cancer has high incidence and fatality rates in developed nations like the U.S. Even while mortality rates are rising, developing nations still have low incidence rates, suggesting that these nations lack the resources for preventive screening for early detection and proper treatment (Francies et al., 2020). Yogyakarta province has the highest prevalence of cancer in Indonesia (Hutajulu et al., 2022; Ministry of Health Republic of Indonesia, 2019). After more than 30 years of breast cancer history in this country, the pattern is still the same that most breast cancer patients have sought medical attention when their diseases were already advanced (stage III or IV) (Gautama, 2022).

This study showed that most patients were in a high stage of cancer (stage III and IV), experienced no metastatic condition, and received chemotherapy as their definitive therapy. In high-stage cancer, whether it has metastasized or not, chemotherapy is one of the modalities of treatment that is given either in the form of definitive or adjuvant therapies. Chemotherapy is a cancer treatment that uses substances or medications that can destroy cancer cells. It is a treatment that may be administered locally or systemically (Shinta & Surarso, 2016). It can be successful depending on the type of cancer and how advanced it is. Chemotherapy can cure cancers by destroying cancer cells to the point that doctors can no longer detect them in the patient's body, and they will not grow back. Chemotherapy can also control cancer by keeping it from spreading, slowing its growth, destroying cancer cells that have spread to other body parts, or easing its symptoms. Chemotherapy is also called palliative care when it shrinks tumors that cause pain or pressure (National Cancer Institute, 2018).

Aside from CINV, chemotherapy has also been shown to interfere with the digestive tract, causing diarrhea and constipation as one of its side effects (Escalante et al., 2017). The patients in this study had no previous history of gastrointestinal irritation, and the rest had gastrointestinal irritation after chemotherapy. Nausea and vomiting are also side effects of chemotherapy on the gastrointestinal tract due to high doses of the treatment's agents with high emetogenic agents. Patients receiving chemotherapy experience different degrees of nausea and vomiting depending on the emetogenic potential of the anti-cancer drugs given and the patient's individual characteristics (Navari & Rapoport, 2016; Rapoport, 2017; Sekine et al., 2013). In this study, 31.4% of the patients received moderate emetogenic agents, and 35.7% received high emetogenic agents in their chemotherapy regimen. Chemotherapeutic drugs' inherent emetogenicity, or relative propensity to induce emesis, varies widely. The treatment is divided into four groups, which are highly emetogenic chemotherapy (HEC; affecting >90% of patients), moderately emetogenic chemotherapy (MEC; 30–90% of patients), low emetogenic chemotherapy (LEC; 10–30% of patients), and minimally emetogenic chemotherapy (<10% of patients). While multi-target antiemetic regimens are advised for both emetogenicity categories of HEC and MEC drugs, which both cause CINV during the acute and delayed phases, LEC agents only cause acute CINV, and single-agent prophylaxis prior to chemotherapy administration is advised (Celio, 2022).

## 5. Implication and limitation

The description of CINV in cancer patients based on blood type can be used as additional information in the nursing management of CINV, where it should be noted that cancer patients with blood type A are more at risk of developing delayed CINV, which has a higher incidence than with other blood types. One limitation of this study is the small number of subjects (less than what is calculated to be the minimum sample size) and the diversity of primary cancer types being studied. The other limitations were confounding factors such as the history of gastrointestinal irritation, chemotherapy dosages, chemotherapy emetogenicity, and the type of therapy given, all of which were not controlled.

## 6. Conclusion

In general, there was no difference in the incidence of CINV based on the blood group; however, based on the onset of CINV, there was a significantly higher incidence in the A blood type group compared to the other blood groups on the fourth day after chemotherapy. Therefore, in terms of clinical practice, the researchers suggest that management or other complementary therapies need to be provided to cancer patients undergoing chemotherapy aside from additional antiemetic drugs they receive in hospitals. Management of CINV can be more focused on patients with the delayed type of CINV because its incidence is higher. Furthermore, A more extensive and homogeneous study is needed in order to increase the understanding of CINV's etiology by controlling for several factors such as a larger sample, uniformity of cancer cases, emetogenic therapy, and what prophylactic antiemetic regimens are given in order to prove further explore the correlation between blood group and CINV. Further research may also be needed to determine the mechanism of nausea and vomiting based on blood type and whether a relationship between CINV and blood type is demonstrated.

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## Author contribution

DKR and MN have a mutually supportive role in making this research publication. The design and conception of the study were contributions from all authors. DKR and MN prepared the material, and they also collected the data. DKR wrote the final draft of the manuscript as well as the analysis.

## Conflict of interest

The researcher states that there is no conflict of interest in this study.

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ORIGINAL RESEARCH

# Glossophobia: A Cross-Sectional Assessment of Public Speaking Anxiety among Saudi Nursing Students



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## Abstract

**Background:** Public speaking anxiety or glossophobia is common among college students, especially those studying in their non-primary language. Effective public speaking is considered an essential skill for nursing students to grasp as their future roles require it as patient advocates. Little is known about the effects of glossophobia amongst Arab students studying nursing in a second language (English).

**Purpose:** This study aimed to examine glossophobia and its association with English oral presentations among Saudi nursing students in three academic levels.

**Methods:** A correlational comparative study with a cross-sectional approach was conducted on a total of 209 baccalaureate level nursing students at a governmental, Saudi university. Convenience sampling was used with a comparison between three levels of student cohorts (second, third and fourth) of a single academic year. The data were collected using an online self-reported questionnaire consisting of three sections: a sociodemographic questionnaire, the Foreign Language Classroom Anxiety Scale (FLCAS), and the Personal Report of Public Speaking Anxiety (PRPSA). Data were analyzed using descriptive statistics, a one-way ANOVA, and Pearson correlation tests.

**Results:** Nursing students had moderate anxiety on the FLCAS and PRPSA scales in all three academic years. There was a significant, moderate, and positive relationship between the two scales ( $r=0.450$ ,  $p<0.01$ ).

**Conclusions:** Glossophobia among nursing students needs to be addressed. This study highlights a gap in current training where there is insufficient support, meaning that levels of anxiety remains unchanged across the trajectory of a nursing training program. Future research should explore culturally tailored strategies to decrease nursing students' anxiety while building their confidence and self-esteem.

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## 1. Introduction

Glossophobia, also known as public speaking anxiety, is classified by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as a social anxiety disorder (American Psychiatric Association, 2013) commonly experienced by students, specifically those studying in their non-primary language. Students with glossophobia could experience difficulty in verbally articulating their thoughts and ideas consequently, limiting their ability to advance academically (Dincer et al., 2022). Glossophobia is relatively common among nursing students with most studies reporting moderate levels (El-Nagar et al., 2022; Khan et al., 2015; Perveen et al., 2018). According to a cross-sectional study of 288 students from all academic years at four medical colleges, it was found that glossophobia was at its lowest among final-year students as they exhibited the least anxiety levels (Khan et al., 2015). This change in prevalence between the first- and final-year students may be due to effective teaching strategies and/or experience development over time, as it is expected that students in the final year would have gained maturity and increased their level of knowledge and confidence (Aljohani et al., 2021).

Glossophobia tends to present itself as changes seen in cognitive, behavioral, emotional, and physiological states (Dincer et al., 2022). Such changes include palpitations, flushed skin, avoiding eye contact with others and rapid breathing, making it difficult for students to present and/or communicate effectively with others. In a recent study investigating the prevalence of public speaking anxiety among undergraduate students, it was reported that students expressed public speaking anxiety much more frequently than the fear of death (Perveen et al., 2018). The main external factors that contribute to glossophobia among students are the audience's size and composition, the marks or grades awarded for public speaking, the venue, grades obtained in previous public speaking assignments, the speaker's emotional state, and the time of the day (Ibrahim et al., 2022). Whereas the internal factors include nervousness, incorrect core beliefs of learners, fear of a large audience, anxious personality types, fear that the other presentations are better, lack of presentation skills, poor preparation, low confidence levels, forgetting words, and lack of confidence in one's physical appearance, and overall negative learning experiences (Al-Hnifat et al., 2020; Ibrahim et al., 2022).

Another important factor impacting glossophobia among students is language. Many studies support that speaking in English in the classroom causes discomfort for students whose first language is not English (Dellah et al., 2020; Miskam & Saidalvi, 2019), hence indicating a significant relationship between speaking anxiety levels and students' English proficiency (Dellah et al., 2020; Lin et al. 2020; Miskam & Saidalvi, 2019). Studying in a foreign language is a unique experience because students are obliged to communicate in a language they have not mastered (Aliyu et al., 2019). Therefore, teachers should be made aware of the main causes of anxiety regarding public speaking among students and that language learning, specifically oral output, might be stressful for some students (Al-Hnifat et al., 2020). While these results could explain the reasons for glossophobia, consideration is needed for nurses studying in languages other than their first language. This is because Saudi Arabia has a distinct culture that may affect how students with different language proficiencies behave during a presentation. Further studies are needed to determine nursing-specific contributors to glossophobia within an Arab context as Arab nurses are likely to have unique challenges that may affect their presentation skills and abilities.

Consistent with the 2030 vision of Saudi Arabia (Al-Dossary, 2018), which focuses on improving nurses' roles, the current research study measured and compared anxiety levels among nursing students from the first to fourth years to help develop nurses' self-confidence—a personality trait that nurses should develop during their academic training. This includes the ability to present information, which is a core competency of the profession as they must interact with patients from different cultures and communicate with different healthcare teams. The theoretical model by Ansari (2015) was applied to the current study, which links the theoretical construct of second or foreign language speaking anxiety to everyday classroom practice. The model considers communication apprehension (CA), fear of unpleasant evaluations, and test anxiety (TA)—the three elements of foreign language anxiety in this study.

While a limited body of qualitative research has demonstrated the presence of glossophobia in Saudi Arabia among college level students (Al-Hnifat et al., 2020), the researchers were unable to identify any quantitative literature specifically exploring changes over the course of a nursing program. While this issue has been explored in a number of different countries and cultural contexts, current research exploring glossophobia among nursing students in Saudi Arabia is still lacking. This represents a gap in the literature as previous research has shown that even where nursing students within Saudi report the same stressors as in other countries, the context for why they are experiencing them, and the supportive solutions required differ based on unique cultural contexts (Aljohani et al., 2021). Thus, the objective of the current study was to identify and compare the glossophobia level regarding giving presentations in English among three academic years of nursing students to understand whether there is a change across the trajectory of a nursing training program.

## **2. Methods**

### *2.1 Research design*

A descriptive cross-sectional research design was used. This design is appropriate to the study's aim as the study compared glossophobia levels among nursing students regarding presentations in English language among three different cohorts within a single academic year (Polit & Beck, 2021).

## 2.2 Setting and samples

The participants of the current study comprised a convenience sample of 209 nursing students. They were included in the study if they were willing to participate, their first language was Arabic, and they were studying full-time in the second to fourth year of a bachelor's degree of nursing science program at a governmental university in Saudi Arabia during the 2021 academic year. They were excluded from the study if they had studied at an international high school, as international schools in Saudi Arabia follow an all-English language-based curriculum. Therefore, to avoid it being a confounding variable, students from such schools were excluded. Furthermore, nursing students who were on academic leave were also excluded from this study. The overall number of nursing students was 453, including 185 second-year, 150 third-year, and 118 fourth-year students. For this study, 71 second-year, 70 third-year, and 68 fourth-year students were recruited (almost 50% of each academic year). According to the Raosoft program, the required sample size given a 5% significance level was 209 nursing students (Raosoft, 2004).

## 2.3 Measurement and data collection

A socio-demographic questionnaire and two psychometric instruments were used to collect the required data. Cronbach's  $\alpha$  values were used to assess the instruments' internal consistency and reliability;  $\alpha > 0.70$  denoted acceptable consistency. Convergent validity was tested by assessing the correlation of each item with the overall scale.

### 2.3.1 Socio-demographic characteristics of study participants

This questionnaire assessed the characteristics of the study participants. It assessed age, academic year, semester, gender, whether the respondents lived with family or friends, whether they attended a government or international high school, family income, parents' occupation, and the number of siblings.

### 2.3.2 Foreign Language Classroom Anxiety Scale

The Foreign Language Classroom Anxiety Scale (FLCAS), developed by Horwitz (1986), was used to measure language anxiety among students. The original instrument comprised 33 items, but was modified for this study with the original author's permission. Some questions were omitted as inapplicable for this sample (items 8, 10, 11, 19, 21, 23, 25, 28, 29, 30, 32, and 33), leaving 21 items. However, the method of score indications and calculations remained the same. According to Horwitz (1986), items are rated on a five-point Likert scale, with response options of *strongly agree*, *agree*, *neither agree nor disagree*, *disagree*, and *strongly disagree*. Accordingly, each item is assigned a score ranging from five to one, with five indicating strong agreement (more anxiety) and one indicating strong disagreement (less anxiety). The scoring is reversed for negatively phrased items (items 2, 5, 11, 15, and 17). Possible scores on the current, modified version of the FLCAS ranged from 21 to 105. Summing up the scores from all the 33 items indicated that the higher the score, the higher the foreign language anxiety level. Additionally, scores were classified as a cut off score of the anxiety level as follows: 21–48 = mild anxiety; 49–77 = moderate anxiety; 78–105 = high anxiety. The instrument is subcategorized into three distinct forms of performance anxiety: CA, which describes the fear and the shyness to speak or listen to a foreigner language (items 1, 4, 8, 13, 15, and 18); TA, which is the construct that involves the anxiety of must having the essential skills to communicate the foreigner language, such as being to attentive (items 3, 5, 6, 9, 14, 16, 17, and 19); and fear of negative evaluation, which articulates how comfortable are the student and the teacher in their communication to equip the student to positively receive the evaluation (items 2, 7, 10, 12, and 21). Cronbach's  $\alpha$  for this study was acceptable ( $\alpha = 0.74$ ).

### 2.3.3 Personal Report of Public Speaking Anxiety

The Personal Report of Public Speaking Anxiety (PRPSA) was developed by McCroskey (2013) as a 34-item instrument. It was modified for this study by removing items 21, 28, 32, and 33 because of repetition, forming a 30-item instrument. The PRPSA measures fear of public speaking, which centers on public speaking anxiety. For example, "While preparing for giving a speech, I feel tense and nervous" and "I get anxious when I think about a speech coming up." Each item is rated on a scale comprising *strongly disagree* (1 point), *disagree* (2 points), *neutral* (3 points), *agree* (4 points), and *strongly agree* (5 points). Scores are classified as follows: 30–69 =



mild; 70–110 = moderate; 111–150 = high. Its reliability in this study was confirmed (Cronbach's  $\alpha=0.76$ ).

The FLCAS and PRPSA are valid tools and were examined carefully by a panel of three academic experts from nursing mental health in order to ensure the content's validity and relevance. The panel's remarks and suggestions as some items related to FLCAS were omitted because it was not related to objective of the research.

In the main study, data were collected online using structured questionnaires, which included the socio-demographic, FLCAS and PRPSA. After obtaining the necessary ethical approval to conduct the study and permission to use the instruments from the copyright holders, the questionnaires were distributed using an online survey tool. The participants were approached via social media platforms such as WhatsApp, Twitter, and Facebook. The participants were asked to distribute the link to increase the number of study participants. The participants were informed about the inclusion criteria at the beginning of the survey to ensure that they met the required criteria.

#### 2.4 Data analysis

SPSS version 23.0 was used to analyze the data. The data were described using frequencies, percentages, means, and standard deviations. A one-way ANOVA was used to assess the differences in anxiety levels across academic years. Pearson correlations were used to test the relationship between FLCAS and PRPSA scores. A *p*-value of less than 0.05 was considered statistically significant.

#### 2.5 Ethical considerations

The Nursing Research and Ethics Committee of King Abdulaziz University approved the study (NREC Serial No: Ref No 2B.48). All information and test results acquired from the study participants were considered confidential. To protect privacy, each study participant's data were anonymized by assigning a code. Detailed information about the study was presented on the first page of the online survey tool. Hence, participants had the opportunity to read the information provided and decide whether to engage in the study before they started filling out the survey. Informed consent was implied by the participants' completion and submission of the survey.

### 3. Results

#### 3.1 Demographic information

As shown in Table 1, of the 209 nursing students at the faculty of nursing who participated in this study, 89% were women and 11% were men. Further, 63.2% were aged 19–21 years, and 87.2% attended government schools. Each academic year (second, third, and fourth) accounted for approximately one-third of the study population. Most participants lived with their families (94.7%), and more than half had two to four siblings.

**Table 1.** Frequencies and percentages of study participants' socio-demographic information (n= 209)

Socio-demographic information	Frequency	Percentage
Gender		
Female	186	89.0
Male	23	11.0
Age		
19–21	132	63.2
22–26	77	36.8
School attended		
Government schools	183	87.6
International schools	3	1.4
Private schools	23	11.0
Academic year		
Second year	71	34.0
Third year	70	33.5
Fourth year	68	32.5

**Table 1.** Continued

Socio-demographic information	Frequency	Percentage
Living situation		
Family	198	94.7
Relatives or friends	5	2.4
University student housing	1	0.5
Alone	5	2.4
Number of siblings		
None	9	4.3
2-4	116	55.5
More than 5	84	40.2

### 3.2 Level and differences of foreign language anxiety among academic years

Table 2 shows the mean score and standard deviation of study participants' responses to the FLCAS. The total mean scores for second-, third-, and fourth-year students were moderate — 63.18(9.30), 62.53(8.60), and 60.60(9.31), respectively. An F-test indicated that the differences among years were nonsignificant ( $F=1.51$ ,  $p=0.22$ ). For the mean differences in FLCAS scores among academic years, one-way ANOVA was used. The differences in mean scores across academic years were nonsignificant ( $p>0.05$ )—all academic years had the same anxiety level.

**Table 2.** Mean scores and standard deviations of FLCAS responses

Category	Second year (n=71)	Third year (n=70)	Fourth year (n=68)	F/ p-value
	Mean(SD)	Mean(SD)	Mean(SD)	
Communication apprehension (CA)	2.99(0.51)	2.99(0.52)	2.92(0.57)	0.42/0.66
Test anxiety (TA)	2.93(0.44)	2.90(0.44)	2.78(0.46)	1.94/0.15
Fear of negative appraisal (FNA)	3.23(0.53)	3.11(0.50)	3.07(0.51)	1.71/0.18
Foreign Language Classroom Anxiety Scale (FLCAS)	63.18±9.30 Moderate	62.53(8.60) Moderate	60.60(9.31) Moderate	1.51/0.22

#### 3.2.1 Communication apprehension

CA was measured by five items. The total mean scores for second- and third-year students were the highest (2.99(0.51) and 2.99(0.52), respectively), followed by that of the fourth-year students (2.92(0.57)). However, an F-test indicated that the differences among years were not significant ( $F = 0.42$ ,  $p = 0.66$ ) (Table 2).

#### 3.2.2 Test anxiety

TA was measured by 11 items. The total mean score for the second year was the highest (2.93(0.44)), followed by that for the third (2.90(0.44)) and the fourth (2.78(0.46)). However, an F-test indicated that the differences were nonsignificant ( $F = 1.94$ ,  $p = 0.15$ ) (Table 2).

#### 3.2.3 Fear of negative appraisal

Fear of negative appraisal (FNA) was measured by five items. The total mean score for the second year was the highest (3.23(0.53)), followed by that for the third (3.11(0.50)) and the fourth (3.07(0.51)). However, an F-test indicated that the differences were nonsignificant ( $F=1.71$ ,  $p=0.18$ ) (Table 2).

### 3.3 Public speaking anxiety among academic years

Table 3 shows public speaking anxiety scores as measured by 30 items. The total mean score for the second year was the highest (97.56(12.35); moderate level), followed by the third (97.47(10.48); moderate level) and the fourth (95.28(10.31); moderate level). An F-test indicated that the differences were not significant among academic years ( $F=0.93$ ,  $p=0.39$ ).

**Table 3.** Mean scores and standard deviations of responses to the PRPSA

PRPSA	Second year (n= 71)	Third year (n=70)	Fourth year (n=68)	F/ p value
	Mean(SD)	Mean(SD)	Mean(SD)	
Personal Report of Public Speaking Anxiety (PRPSA)	97.56(12.35) Moderate	97.47(10.48) Moderate	95.28(10.31) Moderate	0.93/0.39

Note. Items marked with “(R)” are reverse-coded. The mean scores associated with each item and presented in this table are after reverse-coding. These scores should be considered to suggest the anxiety level, not the level of agreement with the item as stated.

### 3.4 Relationship between FLCAS and PRPSA scores

As shown in Table 4, Pearson correlations were used to assess the relationship between FLCAS and PRPSA scores. There was a significant, moderate, and positive relationship between FLCAS and PRPSA scores ( $r=0.450$ ,  $p<0.01$ ). Moreover, TA scores were most strongly related to PRPSA scores ( $r=0.489$ ,  $p<0.01$ ), followed by CA scores ( $r=0.399$ ,  $p<0.01$ ). However, FNA scores were not related to PRPSA scores ( $r=0.133$ ,  $p>0.05$ ).

**Table 4.** Pearson correlations between FLCAS and PRPSA scores

Variable / dimensions	CA	TA	FNA	FLCAS	PRPSA
CA	1				
TA	0.631**	1			
FNA	0.471**	0.491**	1		
FLCAS	0.807**	0.903**	0.746**	1	
PRPSA	0.399**	0.489**	0.133	0.450**	1

\*\*Denotes that the correlation was significant at the 0.01 level (2-tailed).

FLCAS, Foreign Language Classroom Anxiety Scale; PRPSA, Personal Report of Public Speaking Anxiety

## 4. Discussion

This study aimed to examine glossophobia and its association with English oral presentations among Saudi nursing students in three academic levels. Critical finding from the analysis is that public speaking anxiety (PRPSA) increases with greater exposure or engagement with foreign languages (FLCAS), as there was a significant, moderate, and positive relationship between FLCAS and PRPSA scores ( $r=0.450$ ,  $p<0.01$ ). The observation contributes to the consensus that foreign language is a critical determinant of foreign language performance. Zhang (2019) observed that familiarity or proficiency with a foreign language could predict an individual's self-perception, belief, and behavioral performance on its application, including reading, writing, speaking, and listening. Hence, impediments to foreign language proficiency could undermine a person's relative achievement of expected performance. According to Teimouri et al. (2019), the above inference implicates the negatively connotated second language anxiety as it significantly impedes learning and second language performance outcomes, including speaking anxiety, which is the present study's focus. Chou (2018) argues that foreign language anxiety affects an individual's input (taking in new information), processing (incorporating new information or retrieving schemata), and output (verbal production) abilities, making it challenging for them to construct accurate, complex, and fluent communication, which are the essential pillars of successfully speaking a foreign language. Thus, increasing foreign language anxiety will increase susceptibility to public speaking anxiety, a direct relationship corroborated by the present research findings.

From the correlation between PRPSA, and FLCAS subcategories, the findings suggest that there is a significant positive association between public speaking anxiety and TA and CA. TA refers to an individual's affective and emotional feelings about foreign language tests, while CA refers to the fear experienced when delivering or preparing a speech to an audience (Nemati et al., 2020; Zhang, 2019). The two predictors are considered key to developing an appropriate learning climate, suggesting the significance of developing foreign language competence and

proficiency through learning and development. It is an especially critical observation, particularly since the research findings indicate a relative reduction in anxiety levels as students' progress through the levels. Notably, most fourth years recorded the lowest anxiety levels in public speaking and moderate foreign language classroom anxiety. Although the latter may not tell much, the findings suggest an inverse relationship between the high anxiety standards of lower-level and higher-level classes in support of discussions suggesting that age or greater experience with a foreign language can help reduce anxiety. It could result from improved teaching methods, accumulated knowledge, or maturity, potentially contributing to the overall capacity and competence to public speak, thus reducing susceptibility to anxiety (Gaibani & Elmenfi, 2016; Sadighi & Dastpak, 2017).

Although knowledge creation is part of developing appropriate vocabulary and confidence in communicating using a foreign language, some evidence suggests that it is not a prerequisite since its impact is not a significant factor determinant. First, greater experience may contribute to increased complexity in the foreign language, leading to higher reluctance and lower commitment to learning, thus contributing to a higher incidence of foreign language anxiety, as observed by Dewaele et al. (2018). Alternatively, knowledge and learning may not be a sufficient predictor of student foreign language outcomes as anxiety is prone to internal and external factors within and outside the control of the individual (Ibrahim et al., 2022). The latter is perhaps more in tune with the findings owing to the lack of differentiation between the participants from different class levels, suggesting the lack of difference between the knowledge and experience achieved as one passes through the various foreign language learning levels (i.e., second, third, and fourth year, or even age). Nevertheless, some authors have rationalized that knowledge of a foreign language should be a prerequisite from which other capabilities and capacities around the use of the foreign language can be developed. According to Byram & Wagner (2018), foreign language knowledge and learning are core to competence development and proficiency, as it provides a basis from which students can critically reflect and understand their respective positions and identities relative to the foreign language, influencing their ability to adjust, accommodate, and commit to learning, ultimately influencing their public speaking capabilities in the foreign language (Byram & Wagner, 2018)

Also worth noting is that the study is representative of a predominantly female student profile, which skews the insights to suggest that foreign language anxiety may greatly affect females more than males. Nonetheless, the research presents mixed findings on the difference between male and female students. Some, like Jiang and Dewaele (2019), find that females more predisposed to worry about foreign languages than males. In other research, Dewaele and Alfawzan (2018) find that females enjoy foreign language classes more than males, which makes them more eager and have greater fun with the language, suggesting a lower potential to experience foreign language-related impediments, including public speaking. Nevertheless, the sample is overly representative of the female demographic, potentially presenting a biased perspective on the relationship between male and female variation of English oral presentations. It is an issue that future studies on the topic should consider when attempting to replicate findings.

## **5. Implications and limitations**

Despite the challenges identified, the research findings offer valuable insight into potential solutions that could enhance nurse competence and capacity development in public speaking. First, knowledge and exposure to the language may play a significant role in reducing glossophobia, as evidenced by the general reduction in anxiety scores as nursing students progress through their academic years. However, the most significant variables are CA and TA, which implicates the curriculum and pedagogical approach to learning. First, it would be appropriate to consider practice-based learning for nursing students in university, where students are provided opportunities to practice their learning to improve their competence and capability to public speak (Logue, 2017). The recommendation should be accompanied by supporting measures like a general review of the curriculum and discourse and person-centered learning initiatives to identify individual strengths, weaknesses, and specific learning needs regarding second language learning. These could enhance the ability to develop nurse competence around their contextual circumstances and conditions, ultimately influencing their public speaking and

subsequent contribution to person-centered care in the field, irrespective of the patient's cultural or linguistic orientation.

Despite the relative success of the study in achieving the general research objective, it is worth noting that the results and findings may be skewed, given the demographic imbalance (i.e., more males than females). Hence, there is a possibility that the findings may not be generalizable to a wider population, especially one that comprises more males than females. There is the possibility of self-report bias, particularly because of the contextual circumstance of the competence being assessed and respondents providing socially desirable responses or exaggerating their responses to create a favorable impression on the researcher (Caputo, 2017). Further, convenience sampling may not have been the best sampling strategy considering that readiness and willingness to participate somewhat subverts the attribute being assessed, as participation does require some level of confidence from the participant, meaning that the results generated a pre-emptive finding.

## 6. Conclusion

Glossophobia among nursing students needs to be addressed. This study highlights a gap in current training where there is insufficient support meaning that levels of anxiety remain unchanged across the trajectory of a nursing training program. Future research should explore culturally tailored strategies to decrease nursing students' anxiety while building their confidence and self-esteem. For future similar studies, it would be worth exploring the gender-based differences to understand whether there needs to be a varied approach to helping students with foreign language anxiety and the contextual circumstances or conditions that would significantly impact proficiency and confidence in communicating using a foreign language.

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## Author contribution

Conceptualization, Deena Raiany, Reem Barayan, AlBatool Bin Sallman, Raghad Maghrabi, Nahed Morsy and, Hala Elsayes; methodology, Nahed Morsy, and Hala Elsayes; formal analysis, Deena Raiany, Reem Barayan, AlBatool Bin Sallman, and Raghad Maghrabi; investigation, Nahed Morsy and, Hala Elsayes; writing—original draft preparation, Deena Raiany, Reem Barayan, AlBatool Bin Sallman, and Raghad Maghrabi; writing—review and editing, Alaa Mahsoon, and Loujain Sharif; supervision, Nahed Morsy and, Hala Elsayes and; project administration, Alaa Mahsoon, and Loujain Sharif.

## Conflict of interest

There is no conflict of interest to declare.

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ORIGINAL RESEARCH

# Factors Influencing the Quality of Life in Thai Cancer Patients Receiving Chemotherapy during COVID-19 Pandemic



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## Abstract

**Background:** The Coronavirus disease (COVID-19) pandemic has physical and mental impacts on cancer patients receiving chemotherapy and this can lead to a decline in their quality of life (QoL). Little is currently known about the factors that affect QoL among cancer patients in Thailand during the COVID-19 pandemic.

**Purpose:** This study aimed to examine the factors influencing the QoL of cancer patients receiving chemotherapy during the COVID-19 pandemic.

**Methods:** This descriptive cross-sectional study was conducted among 102 cancer patients undergoing chemotherapy recruited using a simple random sampling technique. Four instruments were used; 1) Demographic and clinical characteristics questionnaires; 2) the Thai Hospital Anxiety and Depression Scale (Thai HADS); 3) the Revised Thai version of the Multidimensional Scale of Perceived Social Support (r-Thai MSPSS); and 4) the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQC-30, Thai version). Descriptive statistics and multiple linear regression were used for data analysis.

**Results:** According to the findings, the study demonstrated that depression had a statistically significant negative influence on QoL, physical functioning, and emotional functioning (B=-2.196,  $p=0.001$ ; B=-2.630,  $p<0.001$ ; B=-1.605,  $p=0.009$ , respectively). Similarly, anxiety exhibited a negative influence on emotional functioning, cognitive functioning, and social functioning (B= -2.593,  $p<0.001$ ; B=-1.508,  $p=0.037$ ). However, social support did not significantly influence QoL.

**Conclusion:** The study underscores the negative impact of depression and anxiety on QoL, emphasizing the importance of addressing psychological well-being. While social support's influence on QoL was not significant in this context, the research highlights the factors affecting cancer patients' well-being during challenging times. These insights could inform interventions to enhance QoL and patient care.

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## 1. Introduction

Since the coronavirus disease 2019 (COVID-19) outbreak began in December 2019, it has impacted daily life and medical care. The impact of the pandemic has led to the government implementation of lockdowns, social distancing, and inefficiencies in healthcare systems, causing interruptions in cancer screening during the first months of the pandemic (Waterhouse et al., 2020).

The postponement or cancellation of patient appointments and screening tests will result in fewer newly screened cancer cases and a delay in starting treatments. Approximately 40-50% reduction in new cancer diagnoses across various cancer types was reported compared to previous years (Boettcher et al., 2020). In Thailand, the data found that approximately 16.1% of those diagnosed with cancer delayed treatments, including chemotherapy, surgery, and tissue biopsy. This delay was attributed to patients' anxiety regarding the COVID-19 pandemic. The postponement of treatment extended by approximately 1.6 to 2 months, leading to disease progression in around 22.7% of cases (Sukhokanjanachusak, 2021). As a result of these postponements, cancer patients are at an increased risk of developing severe illnesses following infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Grivas et al., 2021). Notably, cancer patients undergoing chemotherapy within two weeks of admission have



faced the highest risk of disease severity and mortality if they contract COVID-19 during the pandemic (Tian et al., 2020). Unfortunately, these patients might also be at a high risk of death from COVID-19 compared to non-cancer patients (Sharafeldin et al., 2021; Tian et al., 2020).

Furthermore, the disruption in accessing medical care resulting from the pandemic has emerged as an impact of psychological distress. Some cancer patients had to postpone chemotherapy appointments and follow-up visits because of the disrupted healthcare systems (Nnaji & Moodley, 2021). This situation could lead to emotional disorders, including anxiety, depression, and loneliness (Brooks et al., 2020). Additionally, the impact of the disease and its treatments cause patients to experience stress and anxiety. Some patients may have feelings of depression when faced with cancer prognosis and its treatment (Dehghan et al., 2020). Recent studies suggest that the prevalence of depression and anxiety among cancer patients worldwide could be higher than among non-cancer patients (Miaskowski et al., 2020; Obispo-Portero et al., 2022; Qian et al., 2020; Salari et al., 2020; Wang et al., 2020). When compounded with emerging illnesses like COVID-19, cancer patients may experience high levels of depression and anxiety (Adzrago et al., 2022).

Social distancing amid a pandemic also leads to mental health disorders, along with the erosion of motivation and self-esteem (Park et al., 2020). Cancer patients may have distanced themselves from their family members and friends due to the risk of contracting COVID-19 infection (Bergerot et al., 2022). This circumstance might have resulted in a decrease in social support from family members and healthcare providers, as Qian et al. (2020) stated, potentially leading to reduced provision of social support and poorer clinical outcomes in these patients (Davis et al., 2021). According to Brooks et al. (2020), cancer patients must adhere to social distancing, which could result in emotional disorders including anxiety, depression, and loneliness. Fortune et al. (2023) also found that the impact on families was a significant predictor of anxiety. Consequently, these factors might affect the QoL of cancer patients (Hofman et al., 2021).

In the literature review, it was found that many factors might affect the QoL in cancer patients. These factors include support from family, friends, and others (Lee & Jeong, 2019; Raz et al., 2016;), and depression-anxiety (Bužgová et al., 2015; Fujisawa et al., 2016; Li et al., 2016). A systematic review of 22 studies demonstrated that social support enhances QoL, particularly on emotional and physical dimensions (Hofman et al., 2021). According to Fujisawa et al. (2016), it was found that patients with depression have experienced lower QoL. Additionally, anxiety has impacted adverse effects on various QoL dimensions (Bužgová et al., 2015).

Amidst the COVID-19 pandemic, numerous studies conducted by Obispo-Portero et al. (2022) and Adzrago et al. (2022) demonstrated a significant increase in anxiety and other psychiatric issues when compared to pre-pandemic levels. Adzrago et al. (2022) specifically identified a heightened likelihood of individuals experiencing mild to severe symptoms of anxiety and depression during the pandemic compared to before. According to Ayubi et al. (2021) and Momenimovahed et al. (2021), cancer patients are experiencing a noteworthy increase in overall depression and anxiety rates. This trend highlights the mental health challenges posed by the pandemic.

During the pandemic in Thailand, cancer patients with weakened immune systems and a high risk of infection have been encouraged to stay home to prevent getting infected with COVID-19. Consequently, cancer patients amidst the pandemic might lack the opportunity to receive treatment or may have to postpone treatments. These situations can cause increased stress and anxiety, which can further worsen QoL. Additionally, the lack of social support from family, friends, and peers due to social distancing can compound the emotional strain and intensify the adverse effects on QoL. Cancer patients may face critical dilemmas that significantly affect their overall QoL due to complicated situations, which could lead to unfavorable therapeutic outcomes. (Ciazynska et al., 2020; Brooks et al., 2020; Heidary et al., 2023).

According to the literature review, limited studies have examined the factors influencing QoL among cancer patients receiving chemotherapy in Thailand during the COVID-19 pandemic. As the literature review indicates, the researcher is particularly interested in studying factors such as anxiety, depression, and social support. Consequently, this study was conducted to investigate the factors influencing the quality of life of cancer patients receiving chemotherapy during the COVID-19 pandemic. The results of this study can contribute to evidence-based practice for providing care to cancer patients in the post COVID-19 period.

## 2. Methods

### 2.1 Research design

This study used a cross-sectional design to investigate the levels of anxiety, depression, social support, and quality of life, and the factors influencing the QoL among cancer patients receiving chemotherapy during the COVID-19 pandemic at a university hospital in Bangkok, Thailand.

### 2.2 Setting and samples

Data were collected during February-May 2022 at a university hospital in Bangkok, Thailand. The participants were chosen by simple random sampling according to the following criteria: (1) age older than 18, diagnosis with Stage 1- 4 cancer; (2) receiving chemotherapy, and (3) having a smartphone and being able to use Android or IOS well. The exclusion criteria were patients with brain metastasis and limitations on smartphone usage.

The sample size was calculated with the G\*Power 3.1.9.4 program by setting the effect size at 0.26 based on a previous study (Jeppesen et al., 2021), with power of the test equal to 0.90, significance level at 0.05 and a size of 82 cases. The sample size was increased to 102 participants to account for a possible 20% loss to follow-up.

### 2.3 Measurement and data collection

Data collection was conducted by the principal researcher and two research assistants, all of whom were affiliated with the chemotherapy ward. The data collection process involved the utilization of online questionnaires administered through Google Forms. Prior to seeking informed consent from participants, the researchers provided detailed explanations regarding the study's objectives, potential benefits, and any associated risks. Participants were also informed of their right to decline participation or withdraw from the study at any time. To ensure consistency, the research team thoroughly briefed the research assistants about the data collection procedures and methods before commencing the data collection process.

The research instrumentation consisted of 4 instruments, including demographic and clinical characteristic questionnaires; the Thai Hospital Anxiety and Depression Scale (Thai HADS); the Revised-Thai version of the Multi-dimensional Scale of Perceived Social Support (r-T-MSPSS); and the EORTC-QLQ-C 30 (version 3) with details as follows.

#### 2.3.1 Demographic and clinical characteristic questionnaires

Demographic and clinical characteristic questionnaires collected data on gender, age, education level, marital status, economic condition, working status, household, cancer diagnosis, and stage of the disease. Moreover, the researcher collected data from medical records, including the type and stage of cancer, and the time of the latest chemotherapy.

#### 2.3.2 The Thai hospital anxiety and depression scale (Thai HADS)

The Thai HADS was translated from the English version of Zigmond and Snaith by Nilchaikowit and colleagues (Nilchaikovit et al., 1996). The instrument contains 14 items, seven for anxiety assessment and seven for depression assessment. The items were rated on 4-point Likert scales (0-3), with 0 indicating the lowest level of agreement and a 3 indicating the highest level of agreement. For each subscale of anxiety and depression, a score of 8-10 indicated a borderline anxiety or depression while a score of  $\geq 11$  was suggestive of clinical anxiety or depression. This instrument was tested in 30 cancer patients before collecting data. Cronbach's alpha reliability coefficient of anxiety and depression for this study were 0.86 (anxiety) and 0.81 (depression), respectively. Additionally, the sensitivity values for the anxiety and depression subscales of the Thai HADS were reported as 100% and 85.71% respectively. The specificity values were 86.0% for anxiety and 91.3% for depression (Nilchaikovit et al., 1996).

#### 2.3.3 The revised Thai version of the multi-dimensional scale of perceived social support (r-T-MSPSS)

The r-TMSPSS measures perceptions of multidimensional social support from significant others, family, and friends. Containing 12 questions, the questionnaire was translated into Thai and revised by Wongpakaran et al. (2018). The items were rated on 7-point rating scales, one of which referred to strongly disagree and seven to strongly agree. The total scores ranged from 12-

84 points. For score interpretation, the mean scoring scale ranged from 1 to 2.9, which indicated low support; a score of 3 to 5 indicated moderate support; a score of 5.1 to 7 indicated high support. This instrument was tested in 30 cancer patients before collecting data. In this study, Cronbach's alpha reliability coefficient of the r-TMSPSS was 0.91. The validity test showed a positive correlation with the r-T-MSPSS and the Rosenberg Self-Esteem Scale (RSES) ( $r=0.44$ ,  $p<0.001$ ), and a negative correlation with r-T-MSPSS and TDI ( $r=-0.31$ ,  $p<0.001$ ) (Wongpakaran & Wongpakaran, 2012).

#### 2.3.4 The European organization for research and treatment of cancer quality of life questionnaire-core 30 (EORTC-QLQ-C 30)

The EORTC-QLQ-C 30 version 3 is a standardized cancer-specific 30-item instrument (Aaronson et al., 1993) to measure QoL in cancer patients. Translated into Thai (Silpakit et al., 2006), the instrument contains 30 items that include five functional scales (cognitive, emotional, physical, role, and social functioning), a global health status/QoL scale, eight symptom scales, and a scale on financial difficulties. Each item was rated on a four-point Likert scale according to the symptom scale (not at all, slightly, high, and highest). The scores ranged from 0 to 100. A higher score on the functional scale and the global health status QoL represents good functioning, while a higher score on the symptom scale represents poor functioning. This instrument was tested in 30 cancer patients before collecting data. The Cronbach's alpha reliability coefficient of the EORTC-QLQ-C 30 (Version 3) was 0.93. The validity test revealed that all item-scale correlation coefficients exceeded 0.40, confirming satisfactory item convergent validity.

#### 2.4 Data analysis

Descriptive statistics were used for demographics and clinical characteristics. Quality of life, anxiety, and depression were expressed as means and standard deviations. The collected data were tested for normality using the Shapiro-Wilk test ( $p>0.05$ ). The results indicated that the data did not follow a normal distribution ( $p=0.04$  for anxiety,  $p<0.01$  for depression,  $p=0.02$  for social support, and  $p<0.01$  for QoL). As a result, Spearman's rank correlation coefficient was computed to assess the relationships between the factors (anxiety, depression, and social support) and the domains of QoL. To investigate factors influencing individual domains of quality of life, a multiple linear regression analysis was employed. Separate multivariable linear regression models were used for each domain, resulting in a total of six models. All statistical analyses were performed by IBM SPSS Statistics for Windows Version 28.0 (IBM Corp., Armonk, NY, USA). The significance level of the statistical analysis was set at 0.05.

#### 2.5 Ethical considerations

This study obtained approval from the Research Ethics Review Board of the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, under approval number 275/64E, dated 21 January 2022. The researchers requested informed consent from participants and clearly described the purposes, research benefits, and risks that might occur with the participants. The researchers also clarified the freedom to refuse or consent to participate in this research project and the ability to withdraw from participating at any time.

### 3. Results

#### 3.1 Demographic and clinical characteristics

Table 1 shows that the average age was 54.60 (13.08), with 62.7% below the age of 60, and 66.7% were women. About 31.4% had primary education, and 60.8% were married, had sufficient income for expenses (64.7%), and were employed (43.1%). One-third of the participants lived with their spouses and children (30.4%). Most were diagnosed with breast cancer (26.5%). Lastly, more than half of the participants (53.9%) were diagnosed with Stage 3 cancer.

#### 3.2 Anxiety, depression, social support, and QoL of cancer patients receiving chemotherapy

Table 2 indicates that most participants reported that they did not experience anxiety and depression. Regarding social support, most of the participants reported perceiving high levels of support from their families. In terms of quality of life, the functional scales showed that the role

functioning score achieved the highest value, indicating good functioning. Conversely, within the symptom scales, the fatigue dimension obtained the highest score, indicating poor functioning.

**Table 1.** Demographic and clinical characteristics of cancer patients receiving chemotherapy (n=102)

Characteristics	f	(%)
Age (years), Mean(SD)	54.60(13.08)	
<60	64	(62.7)
≥60	38	(37.3)
Gender		
Male	34	(33.3)
Female	68	(66.7)
Education Level		
Primary	32	(31.4)
Secondary	27	(26.4)
Diploma	10	(9.8)
Undergraduate	26	(25.5)
Postgraduate	7	(6.9)
Marital status		
Married/Living Together	62	(60.8)
Single	21	(20.6)
Widowed/Divorced/Separated	19	(18.6)
Income		
Sufficient for Expenses	66	(64.7)
Sufficient with Savings	19	(18.6)
Insufficient for Expenses	17	(16.7)
Occupational Status		
Employed	44	(43.2)
Unemployed	39	(38.2)
Retired	19	(18.6)
Household		
Living with Spouse	30	(29.4)
Living with Spouse and Descendants	31	(30.4)
Living with Descendants/Parents	26	(25.5)
Living Alone	15	(14.7)
Cancer Diagnosis		
Breast Cancer	27	(26.5)
Endometrium/Cervical	18	(17.6)
Colorectal Cancer	17	(16.7)
Head Neck Cancer	15	(14.7)
Lung Cancer	13	(12.8)
Liver Cancer	3	(2.9)
Other Cancer	9	(8.8)
Cancer Stage		
1	3	(2.9)
2	4	(3.9)
3	55	(54.0)
4	40	(39.2)

**Table 2.** Anxiety, depression, social support, and quality of life of cancer patients (n=102)

Quality of Life (EORTC-QLQ-C 30)	Mean(SD)	f	(%)
Anxiety, Mean(SD)	6.80(3.79)		
No Anxiety		62	(60.8)
Borderline Anxiety		20	(19.6)
Clinical Anxiety		20	(19.6)
Depression, Mean(SD)	5.25(3.66)		
No Depression		67	(65.7)
Borderline Depression		27	(26.5)
Clinical Depression		8	(7.8)

**Table 2.** Continued

Quality of Life (EORTC-QLQ-C 30)	Mean(SD)	f	(%)
Social Support, Mean(SD)	5.97(0.80)		
Significant Others	6.13(0.93)		
Family	6.26(0.85)		
Friends	5.53(1.06)		
Global Health/QoL Mean(SD)	70.34(19.96)		
<i>Functional Scales Mean(SD)</i>			
Physical Functioning	75.88(19.25)		
Role Functioning	76.31(22.91)		
Emotional Functioning	74.26(16.42)		
Cognitive Functioning	75.98(18.99)		
Social Functioning	70.42(19.61)		
<i>Symptom Scales Mean(SD)</i>			
Fatigue	40.74(19.49)		
Nausea and Vomiting	19.77(21.59)		
Pain	29.08(21.71)		
Dyspnea	23.20(22.39)		
Insomnia	32.68(24.81)		
Appetite Loss	32.68(25.68)		
Constipation	26.14(25.53)		
Diarrhea	8.82(16.20)		
Financial Difficulties	31.70(27.50)		

### 3.3 Correlations among factors related to QoL

According to the findings (Table 3), anxiety and depression had a negative correlation with Global health/QoL with statistical significance ( $p < 0.05$ ). Both anxiety and depression also had a negative correlation with physical functioning; emotional functioning; cognitive functioning; and social functioning with statistical significance.

**Table 3.** Correlation analysis for factors related to quality of life (n=102)

Factors	$\rho$	95%CI	p-value
Global Health/QoL			
Anxiety	-0.39	(-0.55, -0.21)	<0.001*
Depression	-0.48	(-0.62, -0.31)	<0.001*
Perceived Social Support	-0.04	(-0.24, 0.16)	0.672
Physical Functioning			
Anxiety	-0.21	(-0.39, -0.01)	0.035*
Depression	-0.36	(-0.52, -0.17)	<0.001*
Perceived Social Support	-0.07	(-0.27, 0.13)	0.496
Role Functioning			
Anxiety	-0.19	(-0.37, 0.01)	0.061
Depression	-0.29	(-0.46, -0.09)	0.003*
Perceived Social Support	-0.04	(-0.24, 0.16)	0.673
Emotional Functioning			
Anxiety	-0.76	(-0.84, -0.67)	<0.001*
Depression	-0.70	(-0.79, -0.59)	<0.001*
Perceived Social Support	0.15	(-0.06, 0.34)	0.142
Cognitive Functioning			
Anxiety	-0.39	(-0.55, -0.21)	<0.001*
Depression	-0.28	(-0.45, -0.09)	0.004*
Perceived Social Support	0.06	(-0.14, 0.26)	0.559
Social Functioning			
Anxiety	-0.32	(-0.49, -0.12)	0.001*
Depression	-0.27	(-0.45, -0.08)	0.005*
Perceived Social Support	0.02	(-0.18, 0.22)	0.864

Notes:  $\rho$ : Spearman's correlation coefficient; (CI) confidence interval; \* Significant at  $p$ -value <0.05

### 3.4 Factors influencing QoL in cancer patients receiving chemotherapy

As shown in Table 4, the results indicate that depression exhibited a significant negative influence on Global health/QoL. Additionally, depression demonstrated a statistically significant negative impact on physical functioning. Both anxiety and depression were found to affect emotional functioning significantly. Similarly, anxiety exhibited a negative influence on cognitive functioning and social functioning with statistical significance.

**Table 4.** Multiple linear regression analysis for the factors related to the quality of life

Factors	B	SE(B)	$\beta$	t	p-value
Global Health/QoL <sup>a</sup>					
Anxiety	-1.049	0.641	-0.198	-1.637	0.105
Depression	-2.196	0.662	-0.401	-3.318	0.001*
Perceived Social Support	-4.252	2.556	-0.143	-1.664	0.099
Physical Functioning <sup>b</sup>					
Anxiety	0.554	0.667	0.109	0.831	0.408
Depression	-2.630	0.689	-0.501	-3.819	<0.001*
Perceived Social Support	-2.908	2.660	-0.102	-1.093	0.277
Role Functioning <sup>c</sup>					
Anxiety	0.585	0.839	0.096	0.697	0.487
Depression	-2.277	0.867	-0.364	-2.628	0.010
Perceived Social Support	-2.790	3.347	-0.082	-0.834	0.406
Emotional Functioning <sup>d</sup>					
Anxiety	-2.593	0.384	-0.600	-6.753	<0.001*
Depression	-1.065	0.397	-0.239	-2.684	0.009*
Perceived Social Support	0.175	1.532	0.007	0.114	0.909
Cognitive Functioning <sup>e</sup>					
Anxiety	-1.944	0.664	-0.385	-2.927	0.004*
Depression	-0.277	0.686	-0.053	-0.404	0.687
Perceived Social Support	-0.329	2.650	-0.012	-0.124	0.902
Social Functioning <sup>f</sup>					
Anxiety	-1.508	0.714	-0.289	-2.111	0.037*
Depression	-0.327	0.738	-0.061	-0.443	0.659
Perceived Social Support	-1.059	2.850	-0.036	-0.372	0.711

Notes: B: Regression coefficient, SE(B): Standard error of B,  $\beta$ : Standardized regression coefficient

<sup>a</sup>F = 14.235 (p-value < 0.001), R-squared = 0.306, Adjusted R-squared = 0.284; <sup>b</sup>F = 7.208 (p-value < 0.001), R-squared = 0.182, Adjusted R-squared = 0.157; <sup>c</sup>F = 3.236 (p-value = 0.026), R-squared = 0.091 Adjusted R-squared = 0.063; <sup>d</sup>F = 53.635 (p-value < 0.001), R-squared = 0.624, Adjusted R-squared = 0.612; <sup>e</sup>F = 7.020 (p-value < 0.001), R-squared = 0.178, Adjusted R-squared = 0.153; <sup>f</sup>F = 3.968 (p-value = 0.010), R-squared = 0.109, Adjusted R-squared = 0.082. \* Significant at p-value < 0.05

## 4. Discussion

The aim of this study was to investigate the factors influence the QoL among cancer patients receiving chemotherapy during the COVID-19 pandemic. The results showed a low prevalence of anxiety and depression, which is consistent with the research conducted by Aminisani et al. (2017) among colorectal cancer survivors. However, the scores differed from a study in Ethiopia (Wondie et al., 2020), which reported higher mean scores for anxiety and depression. This difference could possibly be attributed to the fact that the cancer patients in the recent study had high social support from family members, healthcare providers, and friends, as indicated by the elevated perceived social support scores.

Concerning perceived social support among cancer patients, the results indicated varying levels of perceived social support as follows: family, significant others, and friends, with findings consistent with previous studies. The study by Zhang et al. (2020) on Chinese patients diagnosed with oral cancer reported high perceived social support in cancer patients, as did studies involving patients referring to Sayed Al-Shohada Hospital, Iran (Naseri & Taleghani, 2012). Similarly, the study of Faghani et al. (2014) in cancer survivors in Iran found that participants perceived substantial social support from family, significant others, and friends. Additionally, a study with Thai women recovering from breast cancer treatment also reported a high level of social support (Sumdaengrit & Limthongkul, 2014). Aligning with these findings, a study conducted in Indonesia (Sinaga et al., 2022) found that factors involving support for older people had a high score in the social domain due to the majority of older people living with a spouse or family. This living

arrangement allows older individuals to receive attention and spend time with family, reducing feelings of loneliness. These findings collectively suggest that prior research consistently generated elevated levels of perceived social support, wherein family support frequently involves emotions such as concern, love, attachment, and sympathy. These emotions contribute to enhancing patients' mental stability and fostering a sense of security. The strong emphasis on mutual assistance within Thai society, whether provided by family, significant others like healthcare providers, friends, or community members, is likely a contributing factor to the highlighted high levels of social support observed in this study.

In terms of QoL results from this study, the mean of global QoL was found to be similar to those of Danish patients with cancer who were studied by Jeppesen et al. (2021) during the COVID-19 pandemic. This similarity might be attributed to the participants' characteristics, such as mostly living with a spouse and being diagnosed with breast cancer. Consequently, both studies suggest a parallel trend in QoL scores among breast cancer patients. However, contrasting results emerged from a study conducted by Ciężyńska et al. (2020) in Poland. The outcomes of this Polish study revealed that the global health/QoL and other dimensions of QoL for Polish cancer patients were comparatively lower than the QoL observed among Thai cancer patients in our study. This variation could potentially be attributed to the fact that data collection took place in March and April 2020, a time when the impact of COVID-19 was particularly severe in Poland. In alignment with the study in Vietnam, it was discovered that the average QoL was relatively reduced. This decline was due to the lack of vaccination coverage in Vietnam, which led to the central quarantine, social distancing, and lockdowns. These factors could contribute to the fear of COVID-19 and distress, ultimately impacting QoL. (Nguyen et al., 2022).

Nevertheless, in the symptom scales, the scores exhibited a similarity. This similarity may potentially find its origin in a shared characteristic among patients who were in stages 3 and 4 of cancer progression and undergoing chemotherapy. Patients in advanced stages of cancer often experience similar symptoms, which can lead to the manifestation of consistent symptoms across different populations of cancer patients.

For the factors predicting QoL, anxiety, and depression negatively influenced emotional functioning, and depression negatively influenced the Global health/QoL as well, possibly due to the hardships and stresses experienced by the patients. Patients reported stress, and anxiety, from being quarantined at home and being concerned about infection. This is in line with a study by Brooks et al. (2020) which also found that patients who were placed under home quarantine had a higher risk of developing anxiety and depression. It was demonstrated that the cause of anxiety and depression increased because the patients worried about becoming infected with COVID-19. These results are consistent with a study by Aminisani et al. (2017) which revealed that depression and anxiety negatively influenced QoL and survival rates in colorectal cancer patients. In addition, a study by Ramasubbu et al. (2021) illustrated that depression also harmed QoL among colorectal cancer patients in Japan. A study in Vietnam also stated that depression had a similar impact on QoL in lung cancer patients (Khue et al., 2019) confirmed that depression was very highly correlated and able to predict QoL. Interestingly, social support could not predict QoL which was different from previous studies (Hofman et al., 2021; Khue et al., 2019; Li et al., 2016). This can be explained in that majority of the participants might have had the same level of social support scores that could not predict the QoL as the previous studies.

## **5. Implications and limitations**

The findings of this study are important for enhancing the QoL for cancer patients. Understanding related factors that impact the QoL among these patients is crucial. This understanding can guide professional nurses and healthcare teams in offering screenings for anxiety and depression, as well as implementing intervention programs customized to manage these psychological aspects. The overarching aim is to elevate the quality of life for cancer patients undergoing chemotherapy.

This study has limitations. The data for this study were collected from a single hospital in Bangkok, which may not be representative of all regions in Thailand. Therefore, the study's findings are not generalizable to the entire population. Future research could conduct the study in collaboration with multiple hospitals across different regions of Thailand. This would provide a more diverse and comprehensive dataset that better represents the entire population.

## 6. Conclusion

The finding concluded that depression had negative influence on global health/QoL, physical, emotional, cognitive, and social functioning. Anxiety similarly contributed to negative effects on emotional, cognitive, and social functioning. These findings emphasize the need for comprehensive psychological support to alleviate anxiety and depression among cancer patients, as well as interventions targeting functional domains to enhance overall quality of life. For future research, subsequent studies could explore the effectiveness of psychological interventions in alleviating anxiety and depression among cancer patients. For long-term research, examining how consistent emotional support influences diverse aspects of patients' lives, as well as investigating the relationship between mental well-being and treatment outcomes, could provide a more comprehensive perspective.

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## Author contribution

All authors (SJ, AV) contributed significantly throughout the development of the manuscript, including its conception, design, data analysis, writing, and revision.

## Conflict of interest

There is no conflict of interest in this study.

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ORIGINAL RESEARCH

# Contextual Factors, Health History, and Daily Living Activities for Ovarian Cancer Risks: A Case-Control Study in Indonesia



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## Abstract

**Background:** Women are encouraged to aware for risk factors that may aid in the early detection of ovarian cancer before symptoms and sign appear. However, limited studies evaluated the broad aspects of the risk factors for ovarian cancer, particularly in Indonesia. For a more thorough analysis of ovarian cancer risk factors, more variables and a research approach that can make it easier to uncover risk factors of ovarian cancer are necessary. Detecting factors associated with ovarian cancer could serve as the foundation for developing an early warning model.

**Purpose:** The aim of this study was to analyze contextual factors, reproductive health history, and Activity Daily Living (ADLs) associated with ovarian cancer risks.

**Methods:** This retrospective case-control study included 408 women with a 1:1 balanced composition: 204 women diagnosed with ovarian cancer and 204 without. The study was conducted at the Cancer Referral Hospital in West Java Province, Indonesia, from April to November 2020. The instrument was developed based on previous studies and hospital medical/nursing records. The data were analyzed using the Chi-square test and the logistic regression test. The sensitivity and specificity were examined using the Receiver Operating Characteristic (ROC).

**Results:** The variables significantly associated with an increased risk of developing ovarian cancer were advanced age ( $\geq 45$  years) with an odds ratio (OR) of 19.76, low education (OR: 225.00), obesity (OR: 6.04), prior surgery (OR: 51.06), parity (OR: 110.38), and poor sleep quality (OR: 15.75). These factors were found to have the strongest associations with ovarian cancer development.

**Conclusion:** The present study has identified risk factors that have a statistically significant association with the occurrence of ovarian cancer. Healthcare practitioners have the potential to employ this information as foundational data for future research in the development of a self-detection tool for assessing the risk of ovarian cancer.

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## 1. Introduction

Globally, ovarian cancer is the fifth leading cause of morbidity and mortality in women (Arora et al., 2023). In Indonesia, ovarian cancer is the third leading cause of death in women after breast and cervical cancer (Ministry of Health Republic of Indonesia [MOHRI], 2019). It is estimated that, by 2040, the cancer mortality rate will have increased significantly (National Cancer Institute, 2020). Individual women, families, communities, health workers, and the government are all concerned about ovarian cancer's high morbidity and mortality rates. This cancer is known as a silent killer because it does not present a typical symptom (Kemppainen et al., 2019; Mahoney & Pierce, 2022; Mathieu et al., 2018). Most patients present at health services with an advanced stadium, which increases the risk of death (Mathieu et al., 2018; Momenimovahed & Salehiniya, 2019). The annual incidence of ovarian cancer ranges from 9 to 15 per 100.000 women, with an average mortality rate of 5.4 to 11.6 deaths per 100.000 women (Mathieu et al., 2018). Almost 300.000 new cases were reported in 2018, placing Indonesia at number 22 among the top 25 countries with the highest ovarian cancer rates, with an incidence rate of 9.7 (Arora et al., 2023).

A comprehensive approach that includes early self-detection by identifying risk factors, screening in health services, early diagnosis, and treatment programs could help prevent diagnosis delays.

Ovarian cancer is divided into five histological subtypes, each with its own set of risk factors, cell origin, molecular composition, clinical features, and treatment options (Matulonis et al., 2016). Since early detection of ovarian cancer is difficult, one strategy to pursue is prevention by understanding the risk factors (Jauhari et al., 2016). According to research conducted in several countries, hormonal, lifestyle, women in postmenopausal ages were contributed factors to the formation of ovarian cancer (Koskela-Niska et al., 2013; Schöler et al., 2013; Umakanthan et al., 2019). The research in Indonesia found that menarche, parity, contraceptive use, family history, infertility treatment, age, occupation, menopause, body mass index (BMI) are risk factors for ovarian cancer (Agusweni et al., 2020; Arania & Windarti, 2015; Jauhari et al., 2016; Kamajaya et al., 2021; Latief et al., 2023; Wulandari et al., 2019). Unfortunately, these studies only calculate the frequency of occurrence and demographic characteristics without analyzing which factors increase or decrease ovarian cancer risks. In addition, several studies on ovarian cancer risk factors have only been conducted in cross-sectional form (Nababan et al., 2021). Previous research found risk variables that can be divided into three categories: contextual factors, health history, and health behavior. However, more variables and a research methodology that can aid the finding of risk factors that influence ovarian cancer occurrence are required for a more thorough and detailed investigation of ovarian cancer risk factors. This study aimed to investigate the association between contextual factors, reproductive health history, ADLs, and ovarian cancer risks. Identifying risk variables for ovarian cancer can be the foundation for developing an early-warning ovarian cancer model.

## **2. Methods**

### *2.1 Research design*

The quantitative analytic observation with a retrospective case-control study approach was used in this study. This study compares two groups of respondents, that focuses on comparing two groups of women: those with cancer (cases group) and non-cancer (controls group) to look at factors associated with ovarian cancer.

### *2.2 Setting and samples*

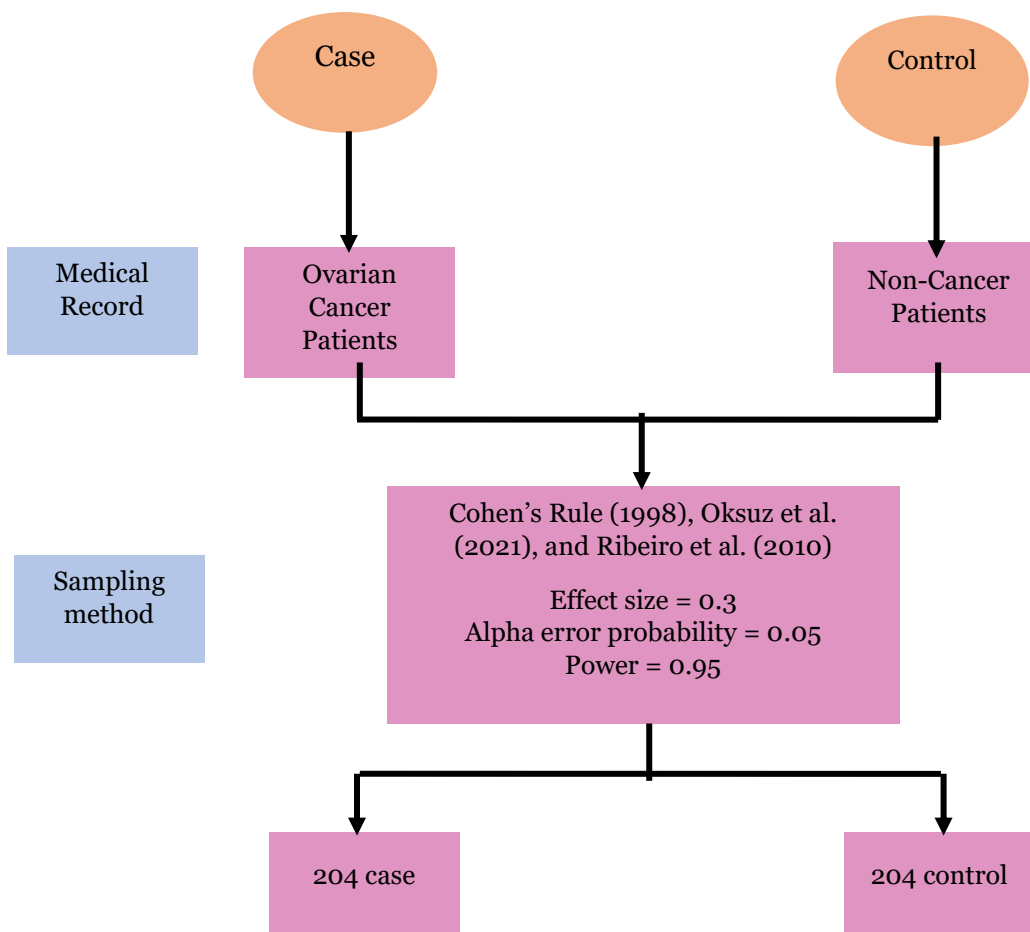
The samples were selected using a consecutive sample technique. The unpaired categorical comparative analytic formula was used to calculate the sample size. The case inclusion criteria were patients diagnosed with ovarian cancer, a treatment history, or being hospitalized at a referral hospital in West Java, Indonesia. The population in the control group had to be free of ovarian cancer, and not hospitalized in the cancer ward. Both groups were adult women, and their health data information was captured in the medical record. G-Power analysis was used to calculate the sample determination, with alpha error probability 0.05, effect size 0.3, and power 0.95. The Cohen's rule (1988) and studies by Ribeiro et al. (2010) and Oksuz et al. (2021) were used to calculate the effect size. According to the computation, the minimum sample size for each group was 191, with an additional 5% sample added to prevent respondents from dropping out. As a result, 408 samples were taken from 204 individuals in the case group and 204 participants in the control group. The study was conducted from April to November 2020. The samples' recruitment explained in the Figure 1.

### *2.3 Measurement and data collection*

The dependent variable in this study was the incidence of ovarian cancer. The selection of independent variables was informed by prior research on the examination of risk factors associated with ovarian cancer globally (Huusom et al., 2006; Kempainen et al., 2019; Matulonis et al., 2016; Momenimovahed & Salehiniya, 2019); these studies contained valid variables. The contextual factors (demographic data, medical and health history, and activity daily living), medical history, and daily activities were investigated as independent variables. The contextual factors were categorized and adjusted with the Indonesian formal category, especially in demographic data: age, education level, occupation, and economic level (MOHRI, 2019; Public Relations West Java Regional Government Agency, 2020; The Central Statistics Bureau of Indonesia, 2020). Variables of medical and health history included menstrual history, marriage status, reproductive health, illness, family health, family planning, and gynecological health (Bell,

2013; Lowdermilk et al., 2013; Matahari et al., 2018; National Population and Family Planning Agency, 2018; Saryono, 2009). Daily activity factors included nutrition status, elimination pattern, sleep patterns, and exercise. Nutritional status factors include BMI, dietary patterns, food portions, amount of drink, caffeine consumption, and smoking (MOHRI, 2018a, 2018c; 2018d). Basic Health Research and the Cohort of the Ministry of Health of the Republic of Indonesia were used to create the questionnaire used in this study (MOHRI, 2018b). The detail of variables described in the results section (Table 1). The instrument's validity was assessed through a two-stage process. Initially, the assessment of content validity was conducted through a comparative analysis of the instrument's contents with prior research. Subsequently, the establishment of construct validity was achieved by consulting with two distinct groups of nursing professionals: basic nursing experts and women's health nurse specialists (Bolarinwa, 2015; Cresswell, 2013).

The administrator at the national referral hospital in West Java provinces collected data from the medical record in the case group, which was subsequently forwarded to the research team. The data for the control group were obtained online by sharing survey formulations on WhatsApp, which were linked to the Google Form from April to November 2020. It took them roughly 15-20 minutes to complete the survey formula. Following the collection of data, the nurse proceeded to undertake the editing phase, wherein the information obtained from the medical records of the hospital was cross-referenced to ensure the accuracy of the data provided by the participants. All members of the study team were taught in the COVID-19 transmission prevention procedure, research objectives, data collection method, how to fill out the survey format through Google Forms, and paying attention to the general health state of participants while collecting data.



**Figure 1.** The flowchart of samples' recruitment

#### 2.4 Data analysis

The SPSS version 25 was utilized by the researchers to examine the research data. The information was entered into a spreadsheet and analyzed using the Chi-square test and logistic regression. Chi-square analysis was performed to analyze the link between each variable and the

risk of ovarian cancer, while logistic regression was utilized to determine which variable was the most influential (Umami et al., 2021). In this investigation, the  $p$ -value for all statistical tests was less than 0.05, with a 95% confidence level for the adjusted odds ratio (AOR). The multivariate logistic regression findings found the estimated coefficient and divided it by the standard error to find the least number, which was then rounded off. The scoring accuracy was validated using ROC, which was utilized to examine sensitivity and specificity (Nahm, 2022).

### 2.5 Ethical considerations

This study received ethical approval from the Health Research Ethics Committee of Universitas Padjadjaran, Indonesia, number: LB.02.01/X.B.5/180/202. The research ethics principles applied in this study were respect for human dignity, privacy and confidentiality, and justice. In applying these ethic principles, this study had no risk of causing physic or mental harm to the subjects. Respondents might leave the research at any time and with no consequences to their health treatment. The data of the respondents were kept private by the researchers.

## 3. Results

The results are presented in four parts: first, a table of the relationship between respondent characteristics, medical history, and ADLs on ovarian cancer incidence, and second, the results of logistic regression analysis, the estimated  $\beta$  coefficient, and third, the ROC findings.

### 3.1 Relationship of respondent characteristics, health history, and ADLs with ovarian cancer

Table 1 shows the findings of risk factors associated with ovarian cancer ( $p < 0.05$ ). The risk factors were age  $> 45$  years, low level of education, and unemployed. Several additional risk factors related to reproductive history were menarche age (15 years), menstrual cycle (less than or more than the standard time,) dysmenorrhea, marriage age 20 years, number of pregnancies, history of pregnancy problems, breastfeeding history, fertility treatment, non-hormonal contraception and contraception problems. Then, risk factors related to health history included family history of cancer, surgeries, and history of disease complication. Lastly ADLs risk factors were coffee drinking, exercise, food, drinking practices, smoking, sleep, defecation and urination patterns.

**Table 1.** The association of respondent characteristics, health history, and ADLs with ovarian cancer (n=408)

Variable	Ovarian Cancer (n=204) f (%)	Normal (n=204) f (%)	p-value	Crude OR (95% CI)
<b>Demography</b>				
Age (years)				
>45	103 (50.5)	3 (1.5)	<0.001*	68.33 (21.15 – 220.72)
12-45 (ref)	101 (49.5)	201 (98.5)		
Education				
Junior High School or less	166 (81.4)	7 (3.4)	<0.001*	122.94 (5.49 – 282.55)
Senior High School or more (ref)	38 (18.6)	197 (96.6)		
Occupation				
Jobless	149 (73.0)	97 (47.5)	<0.001*	2.99 (1.98 – 4.52)
Workers (ref)	55 (27.0)	107 (52.5)		
<b>Menstrual History</b>				
Menarche				
≥15 years	58 (28.4)	35 (17.2)	0.007*	1.92 (1.19 – 3.08)
<15 years (ref)	146 (71.6)	169 (82.8)		
Length of Menstruation				
≤14 days	204 (100.0)	204 (100.0)	-	
>14 days (ref)	0 (0.0)	0 (0.0)		
Menstrual Cycle				
<21 days	0 (0.0)	54 (26.5)	<0.001*	167.97 (10.22 – 2726.81)
21-35 days (ref)	204 (100.0)	133 (65.2)		
>35 days	0 (0.0)	17 (8.3)	0.006*	53.61 (3.20 – 899.14)

Table 1. Continued

Variable	Ovarian Cancer (n=204)	Normal (n=204)	p-value	Crude OR (95% CI)
	f (%)	f (%)		
<b>Menstrual symptoms</b>				
Yes	53 (26.0)	122 (59.8)	<0.001*	0.24 (0.16 – 0.36)
No (ref)	151 (74.0)	82 (40.2)		
<b>Type of menstrual symptoms</b>				
Dysmenorrhea	52 (98.1)	84 (68.9)	<0.001*	23.52 (3.14 – 176.53)
Others (ref)	1 (1.9)	38 (31.1)		
<b>Marriage History</b>				
<b>Marriage status</b>				
Married	180 (88.2)	128 (62.7)	<0.001*	4.45 (2.67 – 7.43)
Single (ref)	24 (11.8)	76 (37.3)		
<b>Age of Marriage</b>				
<20 years	67 (37.2)	12 (9.4)	<0.001*	5.73 (2.94 – 11.17)
≥20 years (ref)	113 (62.8)	116 (90.6)		
<b>Reproductive Health History</b>				
<b>Pregnant History</b>				
None (ref)	19 (9.3)	88 (43.2)	<0.001*	5,28 (2.71 – 10.29)
Once	41 (20.1)	36 (17.6)		
More than two	144 (70.6)	80 (39.2)		
<b>Pregnancy and Delivery health problems</b>				
Yes	51 (27.6)	33 (28.4)	0.868	0,96 (0.57 – 1,60)
No (ref)	134 (72.4)	83 (71.6)		
<b>Type of Pregnancy and Delivery health problems</b>				
Bleeding/PROM/Eclampsia	47 (25.4)	2 (1,7)	<0.001*	14,56 (3.44 – 61.52)
Other problems	5 (2.2)	31 (26.7)		
None/normal (ref)	134 (72.4)	83 (71.6)		
<b>Breastfeeding experience</b>				
Yes	185 (90.7)	103 (50.5)	<0.001*	9,55 (5.53 – 16.49)
No (ref)	19 (9.3)	101 (49.5)		
<b>Infertile History</b>				
Yes	6 (2.9)	12 (5.9)	0,148	0,49 (0.18 – 1.32)
No (ref)	198 (97.1)	192 (94.1)		
<b>Infertile Therapy</b>				
Yes	0 (0.0)	10 (4,9)	0.033*	0.05 (0.003 – 0.78)
No (ref)	204 (100.0)	194 (95.1)		
<b>Illness History</b>				
<b>History of disease complication</b>				
Yes	136 (66.7)	27 (13.2)	<0.001*	13.11 (7.96 – 21.59)
No (ref)	68 (33.3)	177 (86.8)		
<b>Type of health complications</b>				
Surgery	126 (92.6)	7 (25.9)	<0.001*	46.85 (20.83 – 105.41)
Other complications	10 (4.9)	20 (9.8)		
No complication (ref)	68 (33.3)	177 (86.8)	0.523	1.30 (0.58 – 2.92)
<b>Family health history</b>				
<b>Family history with cancer</b>				
Yes	3 (1.5)	18 (8.8)	0.001*	0.15 (0.05 – 0.53)
No (ref)	201 (98.5)	186 (91.2)		
<b>History of Family Planning</b>				
<b>Type of Contraception</b>				
None (ref)	154 (75.5)	128 (62.7)	0.379	0,78 (0.45 – 1.35)
Hormonal Contraception	30 (14.7)	32 (15.7)		
Non-Hormonal Contraception	20 (9.8)	44 (21.6)		
<b>Contraception problems</b>				
Yes	36 (72.0)	26 (34.2)	<0.001*	4.95 (2.27 – 10.77)
No (ref)	14 (28.0)	50 (65.8)		



Table 1. Continued

Variable	Ovarian Cancer (n=204) f (%)	Normal (n=204) f (%)	p-value	Crude OR (95% CI)
<b>Type of problems</b>				
Irregular periods	24 (48.0)	13 (17.1)	<0.001*	6.59 (2.69 – 16.19)
Other problems	12 (24.0)	13 (17.1)	0.017*	3.30 (1.23 – 8.81)
None (ref)	14 (28.0)	50 (65.8)		
<b>Gynecological Health History</b>				
<b>History of Gynecological Problems</b>				
Yes	204 (100.0)	20 (9.8)	<0.001*	3681 (221 – 61295)
No (ref)	0 (0.0)	184 (90.2)		
<b>Type of Gynecology problems</b>				
Cancer in reproductive system	204 (100.0)	0 (0.0)	<0.001*	18405 (356 – 950247)
Others (ref)	0 (0.0)	22 (100.0)		
<b>Nutrition status</b>				
<b>BMI</b>				
Overweight/Obese (>25,0)	143 (70.1)	66 (32.4)	<0.001*	4.90 (3.22 – 7.46)
Normal (18,5-25,0) (ref)	61 (29.9)	138 (67.6)		
<b>Dietary pattern</b>				
≤3 times/day	204 (100.0)	199 (97.5)	0.061	11.28 (0,62 – 205,27)
>3 times/day (ref)	0 (0.0)	5 (2.5)		
<b>Food Portion</b>				
≤1 Portion	204 (100.0)	185 (90.7)	0.009*	42.99 (2.58 – 717.14)
>1 Portion (ref)	0 (0.0)	19 (9.3)		
<b>Amount of drink</b>				
<8 glasses	108 (52.9)	124 (60.8)	0.110	0.73 (0.49 – 1.08)
≥8 glasses (ref)	96 (47.1)	80 (39.2)		
<b>Caffein consumption</b>				
Yes	5 (2.5)	88 (43.1)	<0.001*	0.03 (0.01 – 0.08)
No (ref)	199 (97.5)	116 (56.9)		
<b>Smoking</b>				
Yes	1 (0.5)	3 (1.5)	0.623	0.33 (0.03 – 3.20)
No (ref)	203 (99.5)	201 (98.5)		
<b>Elimination pattern</b>				
<b>Defecation pattern</b>				
1-4 times/day	204 (100.0)	179 (87.7)	0.005*	58.10 (3.51 – 961.30)
>4 times/day (ref)	0 (0.0)	25 (12.3)		
<b>Characteristic of feses</b>				
Solid	202 (99.0)	200 (98.1)	0.685	2.02 (0.37 – 11.15)
Liquid/blood (ref)	2 (1.0)	4 (1.9)		
<b>Urination Pattern</b>				
<b>Urinate pattern</b>				
<3 times/day	0 (0.0)	8 (3.9)	0.049*	0.06 (0.003 – 0.99)
≥3 times/day (ref)	204 (100.0)	196 (96.1)		1
<b>Colour</b>				
Clear	200 (98.0)	196 (96.1)	0.241	2.04 (0.61 – 6.89)
Yellow pale (ref)	4 (2.0)	8 (3.9)		
<b>Sleep pattern and Exercise</b>				
<b>Length of take a nap</b>				
≤3 hours	204 (100.0)	204 (100.0)	-	
>3 hours	0 (0.0)	0 (0.0)		
<b>Length of night sleep</b>				
≤7 hours	162 (79.4)	79 (38.7)	<0.001*	6.10 (3.93 – 9.49)
>7 hours (ref)	42 (20.6)	125 (61.3)		
<b>Exercise</b>				
Yes	26 (12.7)	100 (49.0)	<0.001*	0.15 (0.09 – 0.25)
No (ref)	178 (87.3)	104 (51.0)		
<b>Income status</b>				
< country's standard	129 (63.2)	131 (64.2)	0.837	0.96 (0.64 – 1.44)
≥ country's standard (ref)	75 (36.8)	73 (35.8)		

Note. Chi-square test, \*Statistically significant ( $p < 0.05$ )

### 3.2 Multivariate analysis of the most relating risk factors of ovarian cancer

The logistic regression test was used to perform a multivariate analysis. Table 2 shows the final model, which identifies the factors most associated with ovarian cancer and increasing the risk of ovarian cancer, such as age >45 years, junior high school education or below, the number of pregnancies, history of surgery, overweight/obesity, and  $\leq 7$  hours of sleep duration. According to the AOR results, education has the highest level of risk, with an AOR of 225 (95% CI: 34.22–1479.52), meaning that a low education (junior high school and below) increases the risk of ovarian cancer by 225 times, followed by the number of pregnancies (AOR: 110.38), history of surgery (OR: 51.06), age > 45 years (AOR: 19.76), duration of sleep  $\leq 7$  hours (AOR: 15.75), and overweight/obese (AOR: 6.04). The results also reveal factors associated with lowering cancer risks, such as menstrual complaints, marriage history, family history of cancer, and coffee consumption. A family history of cancer was the factor with the highest risk reduction, with an AOR of 0.01 (95% CI: 0.00–0.21), meaning that a family history of cancer could reduce the risk of ovarian cancer by 99%, followed by a history of marriage, coffee consumption, and menstrual complaints.

**Table 2.** Results of multivariate analysis (n=408)

Variable	P-value	Adjusted OR	95% CI	
			Lower	Upper
Age >45 years	0.010*	19.76	2.03	192.55
Education (Junior High School and less)	<0.001*	225.00	34.22	1,479.52
Menstrual problem Symptoms	0.006*	0.19	0.06	0.63
Marriage History	0.045*	0.02	0.00	0.92
Pregnancy number				
No history		1		
One time	0.022*	110.38	1.98	6,167.87
More than $\geq 2$	0.110	27.29	0.47	1,575.24
History of disease complications				
No history		1		
Surgery	<0.001*	51.06	8.58	304.01
Other complication	0.472	0.49	0.07	3.45
Family history with cancer	0.003*	0.01	0.00	0.21
BMI Overweight/Obese	0.003*	6.04	1.87	19.51
Caffein consumption	<0.001*	0.04	0.01	0.19
Length of night sleep $\leq 7$ Jam	<0.001*	15.75	4.30	57.64

Note. *Logistic regression*

\* Statistically significant ( $p < 0.05$ )

### 3.3 Results of the Receiver Operating Characteristic (ROC) test

The ROC test was used to verify the scoring accuracy. In Table 3, the area under the ROC curve (AUC) value was 0.988 (95% CI 0.973–0.996), meaning that the risk factor scoring model was very accurate in predicting the incidence of ovarian cancer.

**Table 3.** Scoring validation using the ROC test (n=408)

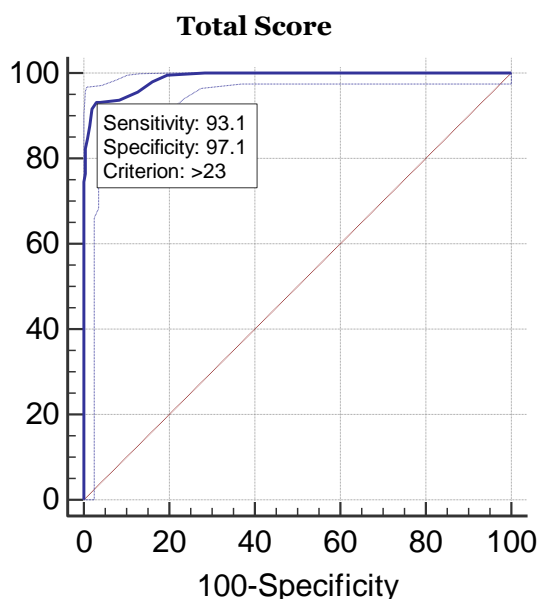
Variables	AUC (95%CI)	p-value
Scoring Model	0.988 (0.973 – 0.996)	<0.001
Cut-off poin	>23	
Sensitivity	93.1%	
Specificity	97.1%	

Note. *ROC test*, AUC = Area Under the Curve

\* Statistically significant ( $p < 0.05$ )

The ROC analysis revealed that the cutoff score was >23, with a sensitivity of 93.1%, a specificity of 97.1%, and a sensitivity and specificity of >80%, meaning that a cutoff score of >23

had good accuracy in predicting ovarian cancer incidence. If a woman's total score is  $>23$ , she has a high risk of ovarian cancer (Figure 2).



**Figure 2.** ROC curve predicted score on the incidence of ovarian cancer

#### 4. Discussion

This study analyzed contextual factors, reproductive health history, and ADLs associated with ovarian cancer risks. The results showed that various contextual factors, medical history, and ADLs were significantly associated with the risk of ovarian cancer. These included being over 45, having a low education level, and being unemployed. Other factors were related to menstrual and reproductive history including menarche more than 15 years, menstrual cycles less than 21 days, menstruation problems, marital status, age of marriage, parity, bleeding and other issues during childbirth, breastfeeding, and fertility treatment. Next medical history factors included history of complications of certain diseases, history of surgery, family history of cancer, and history of non-hormonal contraception. Finally ADLs risk factors were eating less than three times, consuming coffee, defecating one to four times a day, urinating less than three times, and sleep duration less than seven hours at night. It can be seen that the risk factor variables in this study are more numerous dan more complex than previous studies. Previous research in Indonesia only analyzed between one and three factor variables; none examined as many as this study that analyzed ten factor variables (Purwoko, 2018; Widodo et al., 2019).

This study also identifies the same associated factors and several different factors from previous study. Previous study has shown that there is a significant relationship between age, occupation (Crane et al., 2014; Dixon-Suen et al., 2019), number of pregnancies, oral contraceptives, menarche, obesity, nutritional patterns, exercise, smoking, family history, surgical history, and ovarian cancer (Aarestrup et al., 2019; Bhatti et al., 2013; Bodelon et al., 2013; Jiang et al., 2014; La Vecchia, 2017; Tworoger & Huang, 2016). There is no significant relationship between alcohol consumption and the incidence of ovarian cancer (La Vecchia, 2017). Obesity is associated with ovarian cancer, but not the specific types of food consumed (Crane et al., 2014). In line with previous studies, this study's results and the factors that were found to be significant give new insight into studies that examine a more diverse range of factors associated with ovarian cancer especially from Indonesian participant's culture, such as less alcohol consumption in Indonesian women (13.2%) (Our World in Data, 2016), adolescent's marriage before 15 years old (0.5%) (UNICEF, 2018), and high rate in smoking (World Health Organization, 2020). Multi-center research and various cultures needs to be carried out that would describe and identify more specific ovarian cancer risk factors, then the cancer prevention and control program approaches, especially for ovarian cancer, will develop with more specific, effective and efficient.

The multivariate test determined the factors most associated with ovarian cancer, as well as the characteristics of the relationship that increases or reduces the risk of ovarian cancer based on the bivariate analysis. The multivariate test was conducted in two stages of modeling, with the final model revealing that age >45 years, junior high school education and below, number of pregnancies, history of surgery, overweight/obese, and  $\leq 7$  hours of sleep duration all increased the risk of ovarian cancer. Meanwhile, menstrual problems, a history of marriage, a family history of cancer, and coffee consumption all reduce the risk of ovarian cancer. The contextual factors that increased risk of ovarian cancer in this study were age and low education. Previous research has found that older age is a risk factor for ovarian cancer in women over the age of 65 (Mohammadian et al., 2017). Moreover, low education can increase risk factor of ovarian cancer (Alberg et al., 2016). Age and education were common risks for various health problems, including ovarian cancer. However, if a screening tool is developed for self-early warning of ovarian cancer, this cancer can be managed appropriately and optimally. This risk factor analysis study can be fundamental data for developing tools for self-early signs of ovarian cancer.

The health history variables identified that obesity and surgery history as factors that increased risk ovarian cancer. Obesity has been found as predominantly impacting the hormonal, inflammatory, and metabolic channels in the context of health history, notably gynecological cancers (Staley et al., 2020). Next, surgery is still the most successful method of treating cancer; nonetheless, roughly one-third of patients will experience a systemic or local recurrence of the disease, surgery treating cancer is a double-edged sword because, as has been well discussed for more than a century, it can sometimes encourage the growth of certain cancers. Based on anticipated population cancer rates, a retrospective cohort analysis of 13,488 women who underwent augmentation mammoplasty and were monitored for 12 years found a 21% increase in total cancer risk. There was a considerable and more than doubled incidence of leukemia, brain cancer, and stomach cancer among implant patients (Goldstein & Mascitelli, 2011). This study focuses on ovarian cancer, which is a different type of cancer from previous studies, however illustrates that the same thing might happen to ovarian cancer.

Daily activity, particularly sleep duration, and its association to cancer risk are still hotly debated topics. Sleep is crucial for both physical and mental health. The findings of Chen et al's study found that neither short nor long sleep duration were significantly associated with cancer risk. Surprisingly, the subgroup analysis revealed that in Asian people, inadequate sleep duration was associated with an increased risk of cancer (Chen et al., 2018). Sleep duration is important for women's health, especially in Indonesia, women have big roles in taking care of their family, so they are at risk of experiencing sleep deprivation for a long time. More study needed to assess in detail the sleep pattern of Indonesian women.

This study found that family history, menstrual history, and coffee consumption as factor that reduce the risk of ovarian cancer. Previous study found that family history is a significant risk factor for several common diseases, including diabetes, coronary heart disease, stroke, and malignancies of the breast, ovary, and colon (Acheson et al., 2010). The findings of this study differ from Acheson et al.'s study; this could be due to the fact that almost all of the respondents in this study did not have a family history of cancer (c: 98.5%, nc: 91.2%), which could have influenced the results of statistical tests. Unlike consuming tea, which has been proven to significantly prevent women from ovarian cancer (Zhan et al., 2017), there is minimal literature analyzing this risk factor in relation to coffee that reduces the risk of cancer. More research on the effect of coffee consumption on ovarian cancer is needed because drinking coffee habit is currently popular among men and women both developed and developing countries. We performed the ROC test to determine whether the results were genuine or not after identifying the most relevant factors. The AUC value of 0.988 indicates that this result had a good accuracy to predict the risk factor of ovarian cancer (Hajian-Tilaki, 2013). The ROC test enhanced the risk factor associated with ovarian cancer that was noted from the AUC value (95 CI, 0.973-0.996). Although the findings of this study indicate that the risk factors for ovarian cancer are valid, further investigation using a qualitative approach is required to supplement and reinforce the quantitative findings of this study.

## **5. Implications and limitations**

As health service providers, nurses play a role in preventing disease, improving health, and making innovations in health services, including women's health. The results of this study can be

an initial step toward developing an independent early detection instrument for women at high risk of ovarian cancer, which could become an independent early warning system for women, allowing them to take preventive actions as soon as risk factors are found, protecting them from the advanced stages of cancer.

This study was only conducted at a cancer referral hospital in West Java, where particular ethnicities may predominate, it has an impact on the identified risk factors for ovarian cancer. Another limitation is that medical records, which are the main source of data in this study, are still in paper-based form, thus patient data may not be adequately identifiable.

## 6. Conclusion

The ovarian cancer is influenced by various risk factors, including contextual factors, medical history, and activities of daily living (ADLs). These factors can either reinforce or inhibit the chance of developing ovarian cancer. The findings of this study have contributed to the existing knowledge on the factors associated with ovarian cancer. However, it is evident that further investigation is necessary to conduct a more comprehensive analysis of the data and gather additional qualitative information. This can be achieved by employing alternative research methodologies or by including a larger and more diverse sample of participants. In addition, healthcare practitioners have the potential to employ this information as foundational data for future research in the development of a self-detection tool for assessing the risk of ovarian cancer.

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## Author contribution

RW: conceptualization (lead), methodology (lead), writing-original draft (lead), data collection (lead) review (lead) and editing (lead); WN: conceptualization (supporting), data collection (lead), data analysis (lead), and writing-developed draft (supporting); KN: review (lead), discussion (equal) and writing-developed draft (supporting); TP: review (equal), discussion (equal) and writing-developed draft (supporting) editing (lead)

## Conflict of interest

There were no conflicts of interest in this publication.

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