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The Relationship Between Anxiety and Events Chemotherapy-Induced Nausea Vomiting (CINV) Breast Cancer Patients with Chemotherapy in Jember, East Java, Indonesia

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ABSTRACT

In Indonesia and worldwide, breast cancer accounts for the greatest number of cancer patients. Chemotherapy is the treatment used to treat breast cancer patients; however, it might cause One of the psychological adverse effects that chemotherapy usually causes for individuals with breast cancer is anxiety. Chemotherapy-Induced Nausea Vomiting (CINV) is the most common physical adverse effect experienced by breast cancer patients receiving chemotherapy. This cross-sectional study employs certain research approaches. Patients receiving chemotherapy for breast cancer at the RSD Dr. Soebandi Jember and Baladhika Husada Jember Hospital made up the study's population. This research was conducted for one month, and the number of samples used in this research was 120. Anxiety measurement uses a questionnaire Hamilton Anxiety Rating Scale (HAM-A) to measure levels of anxiety, and the Multinational Association of Supportive Care in Cancer (MASCC) Antiemesis Tool (MAT) to measure Chemotherapy Induces Nausea and Vomiting (CINV). Data analysis with a paired sample t test using the IBM SPSS v.25 for Windows programme. The results of the Pearson correlation test between anxiety and CINV in breast cancer patients undergoing chemotherapy showed a significance value of 0.00 or <0.05, which means there is a correlation between anxiety and CINV experienced by respondents. The higher the level of anxiety, the more CINV complaints the patient will experience. Vice versa, the lower the level of anxiety, the CINV experienced by the patient will be minimal.

Keyword: Anxiety, Chemotherapy-Induced Nausea Vomiting (CINV), Breast Cancer, Chemotherapy

ABSTRAK

Kanker payudara merupakan salah satu kanker dengan jumlah penderita terbanyak di Indonesia dan dunia. Kemoterapi yang banyak dilakukan untuk pengobatan pada pasien kanker payudara. Kemoterapi ini memiliki efek samping berupa gejala fisik maupun psikologis bagi pasien. Kecemasan merupakan salah satu efek samping psikologis yang banyak dialami dan diderita oleh pasien kanker payudara dengan kemoterapi. Efek samping secara fisik yang yang banyak di alami oleh pasien kanker payudara dengan kemoterapi adalah Chemotherapy Induced Nausea Vomiting (CINV). Metode penelitian yang digunakan dalam penelitian ini ada cross-sectional study. Populasi dalam penelitian ini adalah pasien kanker payudara dengan kemoterapi di klinik kemoterapi RSD dr. Soebandi Jember dan Rumkit Tk. III Baladhika Husada Jember. Metode pengambilan sampel yang dipakai yaitu simple random sampling dimana didapatkan jumlah sampel yaitu 120 responden. Hasil uji korelasi Pearson antara kecemasan dengan CINV pada pasien kanker payudara dengan kemoterapi didapatkan nilai signifikasi 0,00 atau < 0,05 yang artinya ada korelasi antara kecemasan dengan CINV yang dialami responden. Semakin tinggi tingkat kecemasan, maka akan diikuti dengan banyaknya keluhan CINV yang dialami pasien. Begitupun sebaliknya, semakin kecil tingkat kecemasan, maka CINV yang dialami pasien akan semakin minimal.

Kata Kunci: *Kecemasan, CINV, Kanker Payudara, Kemoterapi*

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Introduction:

According to WCRF, cancer ranks as the second leading cause of death worldwide (wcrf, 2024). As on the Ministry of Health's data for 2022, Indonesia has an eighth-place cancer prevalence rate in Southeast Asia, with 136 individuals affected per 100,000 inhabitants. Breast cancer is the world's largest number of sufferers patient cancer in the world and Indonesia. The Global Cancer Observatory states that 17% of cancer cases are breast cancer. Breast cancer globally in 2020 has a mortality rate of around 7%. In Indonesia, the breast cancer death rate reaches 10% of all people with cancer (Ministry of Health, 2019). Breast cancer occurs due to the uncontrolled growth of cells in breast tissue (Rangkuti et al., 2023).

Breast cancer occurs in breast cells and tissue, and the breast is a cell growth that cannot be controlled and invades surrounding healthy cells (Indah et al., 2021; Rastini et al., 2019). So, it is concluded that breast cancer is an abnormal growth in breast cells or tissue that is uncontrolled and eventually invades healthy surrounding tissue.

One method of treatment for breast cancer is chemotherapy. Chemotherapy has several types: adjuvant, neoadjuvant, and concurrent (Yao et al., 2016). Additionally, chemotherapy can be used in conjunction with immunotherapy, radiation, and other cancer treatments (Yu et al., 2019). In breast cancer, chemotherapy treatment options are widely used either alone or in combination with other therapies in cancer patients (Schirrmacher, 2019). This is because access to chemotherapy is more accessible, and existing services are spread across many hospitals in Indonesia (Leung et al., 2020).

Chemotherapy is frequently used to treat individuals with breast cancer but has a number of negative effects (Abotaleb et al., 2018). The patient may have psychological or physical problems as a result of these side effects (Wykes et al., 2017). A physical side effect of chemotherapy is anxiety. Anxiety is one of the psychological side effects that frequently occurs in breast cancer patients with chemotherapy (Lestari & Budiyarti, 2020). Anxiety that suffered by breast cancer patients with chemotherapy will affect the patient's physical condition when undergoing chemotherapy.

Chemotherapy-Induced Nausea Vomiting (CINV) is a common physical side effect experienced by breast cancer patients receiving chemotherapy (Salihah et al., 2016). Patients with breast cancer who are receiving adjuvant or neoadjuvant chemotherapy report experiencing mild, moderate, or severe nausea and vomiting (Son et al., 2024). The kind of chemotherapy medication taken, along with factors including age, gender, and past medical history, all affect how severe CINV is (Ain et al., 2019). Anxiety is thought to influence the severity of CINV experienced by patients.

A preliminary study of 30 patients conducted at Dr. Soebandi Hospital in Jember indicated that all breast cancer patients with chemotherapy suffered from CINV. Rapid CINV was experienced by 18% of patients, and slow CINV was experienced by 82% of chemotherapy-treated breast cancer patients endure worry, despite varying degrees of nausea and vomiting. The degree of anxiety experienced by patients varies, from mild, moderate, severe to even panic, especially in those undergoing chemotherapy for the first time. Because of the foregoing, the author is interested in learning the extent of the association between anxiety and the incidence of CINV in patients with breast cancer receiving chemotherapy.

Methods:

There are research methods used in this research cross-sectional study, where the author analyzes variable data collected at a certain point across a predetermined sample. Patients receiving chemotherapy for breast cancer at the RSD Dr. Soebandi Jember and III Baladhika Husada Jember Hospital comprised the study's population. Data analysis with a paired sample t test using the IBM SPSS v.25 for Windows programme. This research obtained evidence of ethical worthiness with number No. 5107/UN10.F17.10.4/TU/2023 from the Health

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Research Ethics Committee, Faculty of Health Sciences, Brawijaya University.

Simple random sampling is the sampling technique utilized, in which every member of the population has an equal chance of being selected and samples are drawn at random from the population without regard to the population's strata. The researcher's goals for this study were a minimum sample size of and either a sample confidence value of 95% or an error rate of 5% (Swarjana, 2022).This research was conducted for one month, and the number of samples used in this research was 120. Anxiety measurement uses a questionnaire Hamilton Anxiety Rating Scale (HAM-A) to measure levels of anxiety, and the Multinational Association of Supportive Care in Cancer (MASCC) Antiemesis Tool (MAT) to measure Chemotherapy Induces Nausea and Vomiting (CINV). The validity and reliability test of the questionnaire was carried out by researchers on cancer patients undergoing chemotherapy at the chemotherapy clinic at RSD Dr. Soebandi Jember, with the test results being reliable and valid.

Results:

The results of research on respondents on respondent characteristics data, the data obtained are as follows:

Table 1. Characteristics of respondents

Category		Presents
Gender	Woman	100 %
Domicile	Jember	67 %
	Outside Jember	33 %
Chemotherapy	Adjuvant	48 %
	Neoadjuvant	52 %
Diagnosis	Ca Mammae Dextra	47 %
	Ca Mammae Sinistra	53 %
Education	No School	12,5 %
	Elementary School	40 %
	High School	20 %
	Senior High School	20%
	College	7,5 %

According to the statistics on respondent characteristics provided above, it can be observed that the majority of individuals diagnosed with breast cancer are of the female gender. The bulk of responders reside in Jember, with one-third coming from other locations. Adjuvant chemotherapy was administered to 48% of the respondents in the overall sample, while neoadjuvant chemotherapy was given to the remaining 52%. The most common diagnosis was left breast cancer, namely 53% of the total sample, with the highest level of education being elementary school graduates, namely 40% of the total sample.

Table 2. Average Anxiety Among CINV Respondents

	Average	SD	CI 95%
Anxiety	22,3	4,73	11-33
CINV	17,8	3,11	10-25

From Table 2, the average anxiety value felt by respondents is 22.3, or moderate anxiety, with a standard deviation of anxiety of 4.73; the highest value is 33, and the lowest is 11. The average CINV value experienced by respondents is 17. 8 with a standard deviation of 3.11; the highest value is 25, and the lowest value is 10.

Table 3. Pearson Correlation Test

	Test Results
Pearson Correlation	0,000
Significance	0,447

From Table 3, it can be seen that the significance value between anxiety and CINV is 0.00 or <0.05. which means there is a correlation between anxiety and CINV experienced by respondents. The Pearson correlation value obtained was 0.447, which contained a moderate correlation between anxiety and CINV experienced by respondents. The Pearson correlation value is positive, meaning that anxiety positively correlates with CINV.

Discussion:

Anxiety in breast cancer patients undergoing chemotherapy often occurs (Handa et al., 2020; Chirico et al., 2020). The anxiety that occurs can differ between one individual and another, influenced by the physical and psychological conditions concerned (Dwi Windarwati, 2020). The recurring anxiety experienced by breast cancer patients during chemotherapy is strongly linked to the trauma resulting from prior post-chemotherapy issues (Chen et al., 2019). For the purpose of facilitating treatment decisions and patient complaints, a preliminary assessment of the potential anxiety levels experienced by breast cancer patients receiving chemotherapy is required.

Most chemotherapy patients have nausea and vomiting (Tageja & Groninger, 2016). Chemotherapy-induced nausea and vomiting, or CINV, might happen right away following chemotherapy or a few days later (Mu & Dwi Windarwati, 2023; Naito et al., 2020). This is due to the fact that most chemotherapy regimens prescribed to patients contain drugs with moderate emetogenic qualities, like cyclophosphamide and anthracyclines (Dupuis et al., 2020). The combination of these two regimens results in higher emetogenic properties (Inui, 2017; Schilling et al., 2022). Therefore, the majority of respondents will feel nauseous at the same time after chemotherapy.

From the research results, it was found that there was a relationship between anxiety and CINV experienced by patients with a moderate level of relationship strength, where the higher the level of anxiety felt by the respondent, the more CINV complaints they experienced. Vice versa, the lower the level of anxiety felt, the CINV experienced by the respondent will be minimal. This illustrates the strong connection between anxiety and CINV that occurs in respondents. The anxiety experienced by breast cancer patients when undergoing chemotherapy will have an impact on the physical complaints that the patient may feel. Mosa et al., (2020) said that anxiety is a risk factor that increases CINV complaints in breast cancer patients who are undergoing treatment. Carnio et al., (2018) stated that mild, moderate and severe anxiety also influences the severity of CINV felt by the patient.

Stress is a predisposing factor for anxiety. Patients with anxiety have abnormal basal plasma cortisol levels; hypercortisolemia only occurs in patients with severe levels of anxiety. Stress that causes anxiety can trigger the release of corticotropin releasing factor (CRF) by corticotropin releasing hormone (CRH) in the brain. CRH is a preproprotein coded for producing adult neuropeptide hormones. Autosomal recessive hypothalamic cortitotropin deficiency has fatal consequences in the metabolic system, namely hypoglycemia (Sukhareva, 2021; Deussing & Chen, 2018), therefore anxiety will result in physical complaints if not controlled properly.

Acute nausea and vomiting refers to symptoms that appear within the first 24 hours of chemotherapy drug administration; delayed nausea and vomiting, on the other hand, is defined as symptoms that appear longer than 24 hours following chemotherapy drug administration. It is believed that substance P in neurotransmitters plays a key role in delayed nausea and vomiting. Antagonists of the NK1 receptor have the ability to inhibit substance P's effect, which helps to prevent delayed nausea and vomiting. Other factors in the form of metabolic waste from chemotherapy, damage to the intestine and gastro mucosa, or chemotherapy induced by cytokine release also determine the incidence of delayed nausea and vomiting (Gibson et al., 2016). It is necessary to administer antiemetics during chemotherapy to minimize the effects of nausea and vomiting that may occur.

Hypersecretion of glucocorticoids is observed in patients with severe anxiety because of increased CRH synthesis in the central amygdaloid nucleus and defective regulation of hypothalamic pituitary adrenocortical (HPA) activity in the hippocampus. Cerebrospinal fluid (CSF) is higher in people with significant anxiety who have hypercortisolemia. The enhanced emotionality, anxiety, and neurovegetative instability linked to serious depression are

brought on by CRH in the central amygdaloid nucleus. Furthermore, the hypothalamic paraventricular nucleus (PVN) is directly and indirectly connected to the bed nucleus of the stria terminalis (BNST) by the central amygdaloid nucleus, which stimulates the HPA axis (Sukhareva, 2021; Vasconcelos et al., 2020).

The origin of anxiety disorders is a change in the relative contributions of the hippocampus and the central amygdaloid nucleus, which first act on the HPA axis and then, finally, on the nucleus accumbens in the frontal cortex, a part of the brain that regulates affective states. Amygdaloid output changes are also thought to affect autonomic outflow, which, in conjunction with elevated glucocorticoid secretion, may exacerbate immunological, metabolic, and physiological disorders frequently observed in anxiety patients. Additionally, autonomic outflow may lead to better CINV outcomes for patients undergoing chemotherapy for breast cancer (Sukhareva, 2021; Vasconcelos et al., 2020). Therefore, it is important to teach anxiety management and post-chemotherapy complaint management to patients to reduce existing complaints that may arise after chemotherapy.

The limitations of this research are that there were several patients who were undergoing chemotherapy who refused to become research respondents, thereby prolonging the research time, but the researchers guaranteed that these limitations did not affect the results of the study. Recommendations for this research are that there needs to be research with a larger sample size involving more hospitals so that it can represent the existing community. It is also necessary to conduct research on patients with different types of cancer, not only patients with breast cancer.

Conclusions:

The majority of cancer patients worldwide, including in Indonesia, are suffering from breast cancer. Chemotherapy is the treatment of choice for people with breast cancer, however it has an adverse effect on the patient's physical and psychological symptoms. One of the psychological adverse effects that chemotherapy patients with breast cancer often experience is anxiety. Chemotherapy-induced Nausea Vomiting (CINV) is the most common physical adverse effect experienced by breast cancer patients receiving chemotherapy. The results of the Pearson correlation test indicated a significant relationship between respondents' experiences of CINV and anxiety in breast cancer patients receiving chemotherapy. The getting worse the level of anxiety, the more CINV complaints the patient will experience. Vice versa, the less the level of anxiety, the CINV suffered by the patient will be minimal. The authors are grateful to MASCC for permission to use the questionnaire for this study. The authors are appreciative of the doctors, nurses and administrators from the Chemotherapy Clinic at Dr. Soebandi Jember and Chemotherapy Room at Baladhika Husada Hospital, Jember, for assistance with this study, as well as the participants who have agreed to take part in this study. Thanks to the Republic of Indonesia Ministry of Health for the research funding.

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