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Pattern and Appropriateness of Antiemetic Drug Utilization in Breast Cancer Patients at Sultan Agung Islamic Hospital, Semarang, Indonesia

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ABSTRACT: Chemotherapy-induced nausea and vomiting (CINV) are common adverse effects experienced by patients undergoing chemotherapy. Antiemetic therapy is a key strategy for the prevention and management of CINV; therefore, appropriate antiemetic use is essential. This study aimed to determine the patterns of chemotherapy and antiemetic utilization and to evaluate the appropriateness of antiemetic therapy based on the emetogenic risk of chemotherapy agents and antiemetic dosing standards in breast cancer patients at Sultan Agung Islamic Hospital, Semarang, Indonesia, in accordance with the National Comprehensive Cancer Network (NCCN) Guidelines 2024. The study was conducted observationally using a cross-sectional design with retrospective data collection from patients' medical records. A total of 84 breast cancer patients were included through purposive sampling, according to predefined inclusion and exclusion criteria. The most frequently used chemotherapy regimen was paclitaxel–cisplatin (26%). Antiemetics were administered both prophylactically and post-chemotherapy, with ondansetron combined with dexamethasone as the most commonly used regimen (99.4%), along with ranitidine and diphenhydramine as adjunctive therapy. Evaluation of antiemetic appropriateness showed that 98.8% of patients did not receive antiemetic therapy consistent with the emetogenic risk of the chemotherapy agents, particularly among those receiving high-emetogenic-risk regimens. In addition, dose evaluation revealed inappropriate dexamethasone dosing, primarily due to underdosing and non-standard dosing frequency compared with the NCCN Guidelines 2024. Overall, antiemetic use was largely inconsistent with NCCN Guidelines 2024 recommendations, potentially compromising optimal CINV prevention in highly emetogenic chemotherapy.

Keywords: Antiemetic; Breast Cancer; CINV; Chemotherapy; Emetogenic Risk

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INTRODUCTION

Breast cancer is a malignancy that occurs in the breast tissue. Breast cancer is a global health problem because the number of cases continues to increase and contributes significantly to mortality rates (Hero, 2021). In Indonesia, GLOBOCAN (2022) estimated approximately 49,939 breast cancer cases, accounting for about 19.3% of the total 259,192 cancer cases, with 22,598 deaths (9.3%). At the regional level, the Semarang City Health Office reported 3,590 cases of breast cancer, consisting of 16 cases in males and 3,574 cases in females. These figures indicate an increase compared with the previous year, which recorded 2,498 cases (Dinkes, 2019).

Chemotherapy is a form of systemic therapy that uses cytotoxic drugs. In clinical practice, chemotherapy is classified into adjuvant, neoadjuvant, and palliative therapy. (Arisanti et al., 2020; Tarigan et al., 2024). National guidelines recommend several first-line chemotherapy regimens for breast cancer, including CMF (cyclophosphamide, methotrexate, and fluorouracil), CEF (cyclophosphamide, epirubicin, and fluorouracil), and CAF (cyclophosphamide, doxorubicin, and fluorouracil) (Kemenkes RI, 2018). Despite its effectiveness, chemotherapy is often associated with various adverse effects. One of the most common adverse effects of chemotherapy is chemotherapy-induced nausea and vomiting (CINV). Chemotherapy drugs are classified into four emetogenic risk levels: minimal, low, moderate, and high risk. CINV can significantly impair patients' quality of life and reduce treatment adherence. The risk of nausea and vomiting is related to the emetogenic potential of chemotherapy agents, which is influenced by the type and dose of drugs, the route of administration, and the number of agents used in combination therapy (Putra, 2024; Amelia et al., 2023; Ariyani et al., 2022).

Khairani et al. (2019) reported that the majority of patients undergoing chemotherapy experienced CINV, with nausea occurring in 67.5% of cases and vomiting in 60%. Similar findings were reported by Juwita et al. (2019), who found that nausea and vomiting were the most frequently reported adverse effects, with incidence rates of 68% and 28.82%, respectively. However, studies evaluating the patterns of chemotherapy and antiemetic use and their appropriateness based on emetogenic risk using current guidelines are still limited, particularly in local healthcare settings. Therefore, assessing antiemetic drug utilization and its concordance with current guideline recommendations is crucial to identify potential gaps in supportive care and inform quality improvement strategies.

Antiemetic therapy plays a crucial role in the prevention and management of CINV. Antiemetic therapy can be administered either prophylactically or as post-chemotherapy therapy (Rimawan, 2021). To guide clinical practice, several international guidelines, including those issued by the National Comprehensive Cancer Network (NCCN), provide recommendations for antiemetic use based on the emetogenic risk of chemotherapy agents. Adherence to these guidelines is essential to ensure optimal prevention of CINV and improve patient outcomes.

Sultan Agung Islamic Hospital, Semarang, is a tertiary healthcare facility that provides treatment for cancer patients, including those with breast cancer. Based on medical record data from 2024, a total of 7,251 breast cancer cases were recorded at this hospital. Sultan Agung Islamic Hospital lacks clinical guidelines for selecting antiemetics during chemotherapy, and no evaluation of their use has ever been conducted. This study aimed to determine the patterns of chemotherapy and antiemetic therapy used in breast cancer patients at Sultan Agung Islamic Hospital, Semarang, in 2024, and to evaluate the appropriateness of antiemetic use based on the emetogenic risk of chemotherapy agents according to the National Comprehensive Cancer Network (NCCN) Guidelines 2024.

METHODS

Research Design

This study used an observational, cross-sectional design. Data were obtained retrospectively from patient medical records and analyzed descriptively. The results are presented in the form of distribution tables accompanied by descriptive explanations.

Population, Sample, and Sampling Technique

The study population consists of 501 inpatients diagnosed with breast cancer at Sultan Agung Islamic Hospital, Semarang, in 2024. A sample is selected from patients who meet the predefined inclusion and exclusion criteria. The minimum sample size is calculated using Slovin's formula with a correction factor of 0.1, resulting in a sample size of 84. Non-probability sampling, specifically purposive sampling, is used to select patients based on predefined criteria (Sugiyono, 2015). This approach is chosen because not all patients in the population meet the study criteria. Inclusion criteria are patients diagnosed with breast cancer who receive chemotherapy and prophylactic or post-chemotherapy antiemetic therapy. Exclusion criteria are patients who have died, patients with metastatic breast cancer or comorbidities, and medical records that are incomplete or unreadable.

Data Analyze

All data are analyzed descriptively. Patient characteristics (gender, age, cancer diagnosis), chemotherapy profile (regimen and emetogenic risk level), and antiemetic therapy profile (type and timing) are analyzed descriptively and presented in distribution tables. The evaluation of antiemetic use focuses on the appropriateness of dose and type according to the emetogenic risk of chemotherapy agents based on the National Comprehensive Cancer Network (NCCN) Guidelines 2024.

RESULT AND DISCUSSION

Patient Characteristics

Patient characteristics include gender, age, and cancer diagnosis. As shown in Table 1, breast cancer occurs predominantly in females. The higher incidence in females is associated with long-term exposure to the hormones estrogen and progesterone, which play a role in the development of female reproductive organs (Hasnita et al., 2019). These hormones can stimulate cancer cell growth through their respective receptors, which are classified as estrogen receptor-positive (ER+) or estrogen receptor-negative (ER-), and progesterone receptor-positive (PR+) or progesterone receptor-negative (PR-) (Dewi, 2011). This finding is consistent with the study conducted by Meilani et al. (2025) at Grandmed Hospital, Lubuk Pakam, in 2023, which reported that breast cancer occurs more frequently in women due to the dominant effect of estrogen.

The age distribution shows that most patients are in the 45-59 years age group, followed by those aged 60 years or older. Guidelines issued by the Indonesian Ministry of Health (2018) state that women aged over 50 years have a higher risk of developing breast cancer. Firdaus & Susilowati (2023) also reported that increasing age is a risk factor for breast cancer due to long-term exposure to estrogen and prolonged exposure to other factors that are required to induce carcinogenesis, such as lifestyle patterns.

Table 1. Characteristics of patients

Characteristics	Frequency (n)	Percentage (%)
Gender		
Male	-	-
Female	84	100
Age (In years)		
10-19	0	0
20-44	17	20.24
45-59	44	52.38
>60	23	27.38
Diagnose		
Molecular Type		
Carcinoma Invasive Ductal	51	61
Carcinoma Invasive Lobular	13	15
Mixed Carcinoma Invasive Ductal & Lobular	4	5
Carcinoma Invasive No. Special Type	11	13
Unknown	5	6
Grade		
1 (Low grade)	16	19
2 (Intermediate grade)	22	26
3 (High grade)	41	49
Unknown	5	6

Invasive ductal carcinoma mammae (IDCM) is the most predominant histopathological type of breast cancer. This cancer originates from the epithelial cells lining the milk ducts and invades the ductal wall, spreading into the surrounding breast tissue (American Cancer Society, 2021). Els (2021) reports that IDCM accounts for approximately 75% of all breast cancer cases, supporting the predominance of this histopathological type. While grade 3 is the most frequently observed histopathological grade, the high proportion of grade 3 tumors indicates that many patients present with poorly differentiated and more aggressive cancer, which may influence treatment decisions and supportive care requirements (Oktaprianti et al., 2024). Patient characteristics may modify the individual risk of CINV, thereby influencing the intensity of antiemetic prophylaxis required beyond the intrinsic emetogenic potential of the chemotherapy regimen.

Drug Utilization Profile of Chemotherapy and Antiemetic Agents

In clinical practice, chemotherapy is classified into adjuvant, neoadjuvant, and palliative chemotherapy. Adjuvant chemotherapy is administered after surgery and/or radiotherapy to eliminate residual cancer cells and reduce the risk of recurrence. Neoadjuvant chemotherapy is given prior to surgery to reduce tumor size and improve surgical outcomes. Meanwhile, palliative chemotherapy is not intended to achieve a cure, but rather to control symptoms, slow disease progression, and improve patients' quality of life (Mufrizal & Nashirah, 2022; Shinta & Surarso, 2016). The distribution of drug utilization is presented in Table 2.

Table 2. Drug Utilization Profile of Chemotherapy and Antiemetic Agents.

Drug Utilization		Frequency (n)	Percentage (%)
Chemotherapy Regimens	**Emetogenic Risk**		
Paclitaxel + Epirubicin	High	7	8
Paclitaxel + Doxorubicin	High	14	17
Cyclophosphamide + Epirubicin + 5-FU	High	1	1
Cyclophosphamide + Epirubicin	High	2	2
Cisplatin + Paclitaxel	High	22	26
Docetaxel + Doxorubicin	High	5	6
Cyclophosphamide + Doxorubicin	High	6	7
Paclitaxel + Carboplatin	High	12	14
Carboplatin + Docetaxel	High	11	13
Cisplatin + 5-FU	High	1	1
Paclitaxel + Cyclophosphamide	Moderate	1	1
Cisplatin + Docetaxel	High	1	1
Docetaxel	Low	1	1
Antiemetic Regimens	**Timing of Administration**		
Dexamethasone + Ondansetron	Prophylaxis	83	98.81
Dexamethasone + Ondansetron + Metoclopramide	Prophylaxis	1	1.19
Dexamethasone + Ondansetron None	Post-Chemotherapy	83	98.81
	Post-Chemotherapy	1	1.19
Other supportive agent			
Ranitidine	Prophylaxis+ Post-	84	100
Diphenhydramine	Chemotherapy	84	100

Combination chemotherapy is generally more effective than single-agent therapy due to its ability to reduce drug resistance, enhance cytotoxicity, and improve efficacy against heterogeneous tumor cells (Rusdi et al., 2023). In the present study, the paclitaxel-cisplatin combination was the most frequently used chemotherapy regimen among breast cancer patients at Sultan Agung Islamic Hospital, Semarang. Although this regimen is not classified as a first-line therapy for breast cancer, it may be considered an alternative option in specific clinical situations. Elserafi et al. (2018) reported that the paclitaxel-cisplatin combination is effective in the management of breast cancer, particularly in metastatic cases; however, it is associated with a higher toxicity compared to other chemotherapy regimens.

According to the National Comprehensive Cancer Network (NCCN) Guidelines 2024, chemotherapy agents are classified into four levels of emetogenic risk: high emetogenic risk (HEC - Highly Emetogenic Chemotherapy), moderate emetogenic risk (MEC - Moderately Emetogenic Chemotherapy), low emetogenic risk (LEC – Low Emetogenic Chemotherapy), and minimal emetogenic risk. Hesketh (1999) proposed a principle for determining the emetogenic risk of combination chemotherapy, in which the agent with the highest emetogenic potential in the regimen defines the overall emetogenic risk. This principle supports rational antiemetic prophylaxis by minimizing undertreatment in high-risk regimens, and avoiding overtreatment in low-risk regimens. Hesketh initially proposed

classifying chemotherapy emetogenicity, which has since been refined and standardized into four risk categories in contemporary international guidelines, including the NCCN Antiemesis Guidelines 2024. As shown in Table 2, most patients received chemotherapy regimens with high emetogenic risk; therefore, accurate risk classification is essential as the basis for appropriate antiemetic selection to prevent chemotherapy-induced nausea and vomiting (CINV).

Antiemetic prophylaxis is administered to prevent chemotherapy-related nausea and vomiting, while post-chemotherapy antiemetic therapy aims to prevent delayed symptoms. Antiemetics may be given via intravenous (IV) or oral (PO) routes, both demonstrating comparable efficacy when doses are adjusted for bioavailability (Rimawan, 2021; Sartika et al., 2023). Rahmadi et al. (2020) reported that administration of antiemetic prophylaxis 15-30 minutes prior to chemotherapy reduces the incidence of CINV, particularly in patients receiving highly emetogenic chemotherapy agents.

The combination of ondansetron and dexamethasone dominated the antiemetic prophylaxis profile in this study. Ondansetron acts as a selective 5-hydroxytryptamine type 3 (5-HT3) receptor antagonist. At the same time, dexamethasone enhances antiemetic efficacy by modulating inflammatory mediators and central nervous system pathways, thereby contributing synergistically to improved control of CINV (Katzung et al., 2012). This pattern is consistent with current clinical practice, in which 5-HT3 receptor antagonist–based regimens, particularly in combination with corticosteroids, are commonly used for patients receiving moderately to highly emetogenic chemotherapy (NCCN, 2024).

In addition, metoclopramide, a dopamine receptor antagonist recommended for low emetogenic risk chemotherapy, was used in a single patient (NCCN, 2024). Supportive medications such as ranitidine and diphenhydramine were also administered as adjunctive therapy to manage gastrointestinal discomfort and hypersensitivity reactions during chemotherapy (Hasdin et al., 2022; Giovani et al., 2020).

Evaluation of Antiemetic Appropriateness Based on the Emetogenic Risk of Chemotherapy Agents

Based on the antiemetic prophylaxis profile described above, further evaluation is required to assess whether the administered antiemetic regimens are appropriate for the emetogenic risk of the chemotherapy agents used. Therefore, an evaluation of antiemetic use was conducted by comparing the type of antiemetics administered with the recommendations of the National Comprehensive Cancer Network (NCCN) Guidelines 2024, stratified by chemotherapy emetogenic risk. This evaluation aims to determine the rationality of antiemetic selection and identify potential under- or over-treatment in the prevention of chemotherapy-induced nausea and vomiting (CINV). The distribution of antiemetic appropriateness based on the emetogenic risk of chemotherapy agents is presented in Table 3.

As presented in Table 3, the majority of patients in this study received a chemotherapy regimen classified as having a high emetogenic risk. However, most of these patients did not receive antiemetic regimens that were fully consistent with NCCN recommendations for high-risk chemotherapy. The recommended use of NK1 RA in high-risk chemotherapy is based on its ability to block substance P-mediated signalling in the central nervous system, which plays a key role in both the acute and delayed phases of CINV. Similarly, olanzapine is recommended due to its broad receptor antagonism, including dopamine (D2), serotonin (5-HT2 and 5-HT3), and histamine receptors, making it effective in

Table 3. Distribution of Antiemetic Appropriateness Based on the Emetogenic Risk of Chemotherapy Agents According to NCCN Guidelines 2024.

Emetogenic Risk	Antiemetics Administered	Guidelines Recommendation	Frequency (n)	Appropriate		Inappropriate	
				n	%	n	%
High	Corticosteroid + 5-HT3 RA	Olanzapine + NK1 RA + 5-HT3 RA + Corticosteroid	82	0	0	82	97.6
Moderate	Corticosteroid + 5-HT3 RA	5-HT3 RA + Corticosteroid	1	1	1.2	0	0
Low*	Corticosteroid + 5-HT3 RA	Corticosteroid or Metoclopramide or Prochlorperazine or 5-HT3 RA	1	0	0	1	1.2
Minimal	No Antiemetic Required		0	0	0	0	0
	TOTAL		**84**	**1**	**1.2**	**83**	**98.8**

*Note: Antiemetic recommended for low emetogenic risk chemotherapy is monotherapy.

controlling both nausea and vomiting across multiple phases of CINV (Chelkeba et al., 2017; Kurniawati et al., 2025).

In this study, antiemetic prophylaxis for high emetogenic risk chemotherapy was predominantly limited to the combination of a 5-HT3 RA and a corticosteroid. Although this combination is effective for moderate emetogenic risk chemotherapy, the absence of NK1 RA and/or olanzapine in high-risk regimens likely contributed to the high proportion of inappropriate antiemetic use observed. This practice may result in suboptimal control of CINV, particularly delayed nausea and vomiting, which is less responsive to 5-HT3 RA alone (Katzung et al., 2012).

For moderate emetogenic risk chemotherapy, most patients received antiemetic regimens that were consistent with NCCN recommendations. In contrast, one patient receiving low-emetogenic-risk chemotherapy was administered combination antiemetic therapy, which exceeded guidelines recommendations. This overtreatment may increase the risk of unnecessary adverse effects and healthcare costs without providing additional clinical benefit.

The observed non-adherence to guideline-recommended antiemetic regimens may be influenced by several factors, including limited availability of NK1 RA and olanzapine, prescribing practices guided by institutional protocols, cost considerations, or a lack of routine emetogenic risk stratification in clinical practice (Sun et al., 2021). These findings highlight the need for improved implementation of guideline-based antiemetic strategies to optimize CINV prevention and enhance the quality of supportive care in breast cancer patients.

Evaluation of the Appropriateness of Antiemetic Dosage According to Guidelines

The determination of appropriate antiemetic dosing is crucial, as it affects the effectiveness of preventing chemotherapy-induced nausea and vomiting (CINV) and

reduces the risk of adverse effects resulting from inappropriate dosing. The distribution of antiemetic dosage compliance with standard guidelines is presented in Table 4.

Table 4. Distribution of Antiemetic Dosage Compliance with Standard Guidelines.

Drug Name	Administered Dose[a]	Standard Dose[b]	Frequency (n)	Appropriate		Inappropriate	
				n	%	n	%
Ondansetron	8 mg IV	8-24 mg PO/IV	84	84	49.7	0	0
Dexamethasone	5 mg IV	8-12 mg PO/IV	84	0	0	84	49.7
Metoclopramide	10 mg PO	10-20 mg PO/IV	1	1	0.6	0	0
TOTAL			**169**	**85**	**50.3**	**84**	**49.7**

a. Dose administered to patients based on medical record data.
b. Refers to the National Comprehensive Cancer Network (NCCN) Guidelines 2024.

Overall, a higher proportion of patients received antiemetic doses consistent with standard guidelines than those who received inappropriate doses. However, further improvement in the rational use of antiemetics is still required, particularly in dose adjustment and regimen optimisation for patients receiving moderate- to high-emetogenic chemotherapy. Dose inappropriateness was mainly observed in dexamethasone use. According to the NCCN Guidelines 2024, the recommended dexamethasone dose is 12 mg for moderate- and high-emetogenic chemotherapy and 8–12 mg for low-emetogenic chemotherapy. In contrast, all patients in this study received dexamethasone at a uniform dose of 5 mg twice daily, whereas the guidelines recommend once-daily administration, as with ondansetron.

In clinical practice, increasing the frequency of antiemetic administration is often intended to enhance the prevention of chemotherapy-induced adverse effects, particularly in patients with a history of severe CINV. Based on chemotherapy adverse effect monitoring records, no adverse effects were documented during routine monitoring. This suggests that increased dosing frequency may be clinically effective in preventing CINV. Nevertheless, despite its clinical acceptability, this practice does not fully comply with the NCCN Guidelines 2024 recommendations.

These findings are consistent with previous studies in Indonesia reporting inappropriate antiemetic dosing in breast cancer patients undergoing chemotherapy, particularly dexamethasone underdosing. Azizah (2017) reported that only 29.53% of patients received dexamethasone doses consistent with MASC/ESMO Guidelines, while ondansetron dosing was generally compliant. This indicates that dexamethasone underdosing remains a common issue despite the use of appropriate antiemetic combinations.

Several limitations of this study should be acknowledged. This study did not include patient follow-up; therefore, the effectiveness of antiemetic regimens that were not fully consistent with guidelines recommendations could not be evaluated. In addition, the retrospective use of medical record data limited the assessment of clinical outcomes, as the effectiveness of the administered antiemetics could not be directly determined. Consequently, further prospective studies are needed to evaluate the clinical effectiveness

of antiemetic therapy. Importantly, non-adherence to guidelines recommendations does not necessarily indicate that the antiemetic therapy was clinically ineffective.

CONCLUSION

Most breast cancer patients received chemotherapy with high emetogenic risk, predominantly the paclitaxel-cisplatin regimen, with antiemetic prophylaxis mainly consisting of a 5-HT3 RA combined with a corticosteroid. However, antiemetic prophylaxis was largely inconsistent with the NCCN Guidelines 2024, particularly among patients receiving high-emetogenic-risk regimens. In addition, evaluation of antiemetic dosing revealed inappropriate dexamethasone dosing, characterized by underdosing and non-standard dosing frequency. These findings highlight the need for improved adherence to guideline-based antiemetic utilization, including appropriate dose selection and dosing frequency, to optimize CINV prevention.

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AUTHOR CONTRIBUTION

ATS: collected the data or investigation; performed data analysis; drafted the manuscript
SS: conceived and designed the study; review & editing of the manuscript

ETHICS APPROVAL

This study received ethical approval from the Health Research Ethics Committee of Sultan Agung Islamic Hospital, Semarang with number of 185/KEPK-RSISA/VIII/2025

CONFLICT OF INTEREST

"None to declare"

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