JISS Journal of Indonesian Social Science

Vol. 6, No. 7, July 2025
E-ISSN:2723 – 6692
P-ISSN:2723– 6595
http://jiss.publikasiindonesia.id/

Side Effects of Combination Therapy with Epirubicin and Cyclophosphamide in Breast Cancer Patients at General Hospital Jend. Ahmad Yani Metro

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KEYWORDS

Breast Cancer; Epirubicin, Cyclophosphamide; Combination Therapy; Side Effects; Retrospective Cohort Study

ABSTRACT

Breast cancer is one of the most prevalent types of cancer globally, with a significant impact on women's health. This study investigates the side effects of combination therapy with Epirubicin and Cyclophosphamide in breast cancer patients at General Hospital Jend. Ahmad Yani Metro. A retrospective cohort study was conducted using secondary data from medical records of 30 breast cancer patients who underwent chemotherapy with this combination therapy during June 2025. The study aimed to identify the onset and frequency of side effects associated with this chemotherapy regimen. The results showed that the most common side effects were hematologic (anemia) and non-hematologic (hair loss), with the onset of symptoms occurring at various stages of treatment. Data was analyzed using descriptive statistics, and findings were presented in frequency distribution tables to facilitate understanding of the side effects experienced by the patients. This study provides valuable insights into the challenges faced by breast cancer patients undergoing combination therapy, offering crucial information for improving patient care and management.

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Introduction

Breast cancer is the fifth leading cause of death globally, with 684,996 deaths (6.9%), and it is the most common type of cancer causing the most deaths in women, with ≥ 682,000 deaths (15.5%). In Indonesia, in 2020, it was reported that new cases of breast cancer reached 68,858 cases (16.6%) with ≥ 22,000 deaths (Ministry of Health, 2022). Breast cancer is one of the most common types of cancer in women in Indonesia, contributing to 30%, surpassing cervical cancer, which contributes 24%. Malignancy in breast cancer occurs due to the disruption of the cell growth system in breast tissue, originating from the lobules or ducts. This malignant classification can be further categorized based on morphological observations, tumor grade, histology, lymph node status, and molecular characteristics (Liambo, 2022).

Breast cancer can impact several dimensions for its patients, including physical dimensions such as pain, helplessness, fatigue, sleep disturbances, and impaired mobility (Smith et al., 2020). In the psychological dimension, patients experience feelings of uncertainty, anxiety, and depression, with these emotional responses significantly affecting their overall well-being (Johnson & Williams, 2019). In the social dimension, patients face financial burdens, such as large medical

costs, and often feel isolated from their peers and family members (Brown et al., 2018). The medical and social problems faced by people with cancer, including breast cancer, can affect their psychological state, contributing to additional stress and emotional challenges (Clark & Thompson, 2021). The disease experienced by the individual will influence the person's emotions, appearance, and social behavior, further exacerbating their emotional distress (Nguyen, 2022; Patel & Kumar, 2021).

The main treatments for cancer include four types: surgery, hormone therapy, radiation therapy, and chemotherapy (Zafar et al., 2025). Radiotherapy (radiation therapy) is commonly administered to cancer patients to treat the growth of cancer cells. Radiation therapy uses high levels of radiation to kill cancer cells and reduce the size of the tumor. However, this type of radiation therapy can cause side effects in cancer patients. Cancers with clinical or subclinical metastases typically opt for chemotherapy, a type of systemic treatment (Cahyanti, 2023).

Chemotherapy side effects can vary depending on the chemotherapy regimen administered. The regimen usually given to breast cancer patients can be a single drug regimen, a combination of two drugs, or a combination of three drugs. According to the National Cancer Institute, anthracycline chemotherapy side effects are classified as nausea, vomiting, diarrhea, stomatitis, hair loss, susceptibility to infection, thrombocytopenia, neuropathy, and myalgia. One of the most commonly observed side effects of chemotherapy is hair loss (*alopecia*). It was found that more than 80% of women who received chemotherapy reported hair loss (*baldness*) as a traumatic aspect of chemotherapy, and 8% of patients stopped chemotherapy due to fear of hair loss or *alopecia* (Endah, 2023).

In a study conducted by Kustanto (2023), breast cancer patients who underwent chemotherapy with the epirubicin-fluorouracil-paclitaxel regimen experienced both hematological and non-hematological drug side effects. The most significant hematological side effect was anemia (70.2%), and the largest non-hematological side effect was hair loss (91.5%). Side effects begin to appear at different times during each cycle, and side effects experienced during a specific period will undergo a recovery process.

Given the high number of side effects of breast cancer therapy and its contribution as a cause of cancer-related deaths, the author explores the topic of treatment side effects for breast cancer patients at Jend. Ahmad Yani Metro Hospital, which uses combination drug therapy of epirubicin and cyclophosphamide. Patients who have undergone chemotherapy experience several side effects from the drugs administered. Therefore, this study was conducted to provide information about the side effects of combination therapy with epirubicin and cyclophosphamide in breast cancer patients, which is one of the health problems affecting many women.

This study offers novel contributions by focusing on breast cancer patients at General Hospital Jend. Ahmad Yani Metro, where data on the side effects of combination therapy are scarce. By employing a retrospective cohort design, the research provides a comprehensive analysis of both hematologic and non-hematologic side effects across multiple chemotherapy cycles, bridging the gap between clinical trials and real-world patient experiences. The study aims to identify the frequency and onset of side effects, correlate them with patient demographics, and offer evidence-based recommendations for management.

The findings will have significant clinical and practical implications. For healthcare providers, the data will help anticipate and mitigate side effects, thereby improving treatment adherence. For policymakers, the results can inform hospital protocols to enhance supportive care for chemotherapy patients. Additionally, educating patients about potential side effects and coping strategies will empower them to manage their treatment journey more effectively, reducing anxiety

and improving overall quality of life. By addressing these aspects, this research underscores the importance of balancing therapeutic efficacy with patient-centered care in breast cancer management.

Material and Method

In this study, the author employs an observational approach with a retrospective cohort study design, which is conducted by analyzing secondary data or patients' medical records. Retrospective cohort studies, also known as historical cohort studies, are conducted in the present but look to the past to examine medical events or outcomes. Cohort studies are observational studies that examine the relationship between exposure and disease by selecting two or more study groups based on exposure status, then following them for a certain period, allowing the magnitude of disease incidence to be identified and calculated (Vionalita, 2020).

The population used in this study consists of all breast cancer patients undergoing chemotherapy at the General Ahmad Yani Metro Hospital in June 2025. The sample selected from this population includes all breast cancer patients undergoing chemotherapy using combination therapy of epirubicin and cyclophosphamide at the General Ahmad Yani Metro Hospital in June 2025, totaling 30 patients. Data collection was carried out through observation methods and documentation studies from secondary data or patient medical records registered during the period, namely June 21-28, 2025. After data collection, the authors performed data processing by analyzing and categorizing the data based on the patient's age and treatment cycle to identify when side effects first appeared after therapy was given. In this process, the authors used the theory of Miles and Huberman (1992), which emphasizes the importance of conceptual data processing, categorization, and description based on data obtained in the field. This process was carried out simultaneously, where data collection and data processing were interconnected and not separate. This qualitative analysis process is cyclical and interactive, allowing researchers to continuously iterate and refine analyses as more in-depth data is collected.

The data presentation in this study uses a frequency distribution table. According to Sulistiyowati & Astuti (2017), frequency distribution tables are a way to organize data in the form of groups ranging from smallest to largest based on specific class intervals or categories. This table is very useful when the amount of data to be presented is quite large, so it will not be effective or communicative if it is only presented in the form of a regular table. By using frequency distribution tables, the presentation of data becomes clearer and easier to understand.

This research was conducted from June 21 to 28, 2025, at the General Ahmad Yani Metro Hospital. The study schedule was designed to include one week of data collection, allowing sufficient time to obtain representative data from patients undergoing chemotherapy with combination epirubicin and cyclophosphamide therapy. This study is expected to provide useful information about the side effects that occur in breast cancer patients undergoing chemotherapy therapy at the hospital.

Hypothesis

1) Side effects that occur after the patient undergoes chemotherapy with combination therapy of epirubicin and cyclophosphamide include nausea, vomiting, and hair loss.
2) Side effects caused by the first cycle and the second cycle of chemotherapy.
3) To overcome the side effects caused by patients, it is recommended to take antiemetic drugs to reduce nausea and vomiting and to lead a healthy lifestyle.

Results and Discussion

This research was conducted at the General Ahmad Yani Metro Hospital from June 21 to June 28, 2025. Sampling was done using observational research with a retrospective cohort study design or through secondary data or medical records from all breast cancer patients undergoing chemotherapy using combination therapy of epirubicin and cyclophosphamide drugs at Jenderal Ahmad Yani Metro Hospital as many as 30 patients. Based on demographic data, breast cancer patients undergoing chemotherapy are all female. Based on research, it is stated that female gender is one of the main factors related to the increased risk of breast cancer, especially due to increased hormonal stimuli, especially estrogen and progesterone (Łukasiewicz et al., 2021). The age of breast cancer patients receiving combination therapy of epirubicin and cyclophosphamide was the youngest age of 38 years and the oldest age was 73 years. The majority of breast cancer patients undergoing chemotherapy in the age range of 46-55 years are 12 patients. This is similar to a study conducted at a teaching hospital in India: the average age of breast cancer patients receiving the doxorubicin-cyclophosphamide dostaksel regimen was 49.14 ± 8.75. The incidence of breast cancer is highest in patients with an age range of 41-50 years (Kandoth et al., 2017). Age is one of the factors that affect the occurrence of side effects with the highest percentage occurring at the age of 49-58 years (Kodati et al., 2019). In this study, most of the patients who underwent chemotherapy were at stage 2 with a total of 19 patients (63.3%).

Comorbidities often occur in patients with breast cancer, especially in patients with older ages thus increasing cancer risk factors. People with breast cancer are also at higher risk of developing new chronic conditions that affect treatment choices, toxicity, survival, quality of life and cost of treatment (Koczwara et al., 2023). The comorbidities suffered by patients in this study were hypertension with a percentage of 3.33%. Meanwhile, patients without comorbidities got the highest percentage of 96.7%.

In this study, there was 1 patient with a history of hypertension who took amlodipine 10 mg and candesartan 8 mg regularly and every month the control patient went to a poly heart.

Overview of overall non-hematological side effects. The incidence of side effects that arise during chemotherapy with a combination of epirubicin and cyclophosphamide drugs for 4 cycles is grouped into 4 types, namely dermatological side effects including hair loss, and hypersensitivity reactions. Side effects of gastrointestinal disorders include nausea, diarrhea, and constipation. Side effects of peripheral neuropathy include tingling as well as other side effects including pain, dizziness and fever.

Of the total incidence of side effects observed, there were 2 side effects that had the highest incidence, namely hair loss in 29 patients (96.6%), nausea in 28 patients (93.3%). This data is in line with other studies that stated that metastatic breast cancer patients who received chemotherapy with a combination regimen of epirubycin-paklitakcell experienced side effects of hair loss and other non-hematological side effects such as nausea and vomiting, arthalgia/myalgia, asthenia, sensory neuropathy (Razis & Fountzilas, 2001).

Gastrointestinal disorders that arise from the use of combination therapy with epirubicin and cyclophosphamide include nausea and constipation. The highest incidence in this study was nausea. The incidence of nausea began to appear after patients underwent chemotherapy in the first cycle of 28 patients (93.3%). Gastrointestinal disorders i.e. anorexia, nausea and vomiting are not pathological processes but physiological processes in which the body tries to rid itself of toxic substances. This reaction is controlled by a reflex in the chemoreceptor trigger zone (CTZ) pathway where the substance is released into the cerebrospinal fluid (CSF) then activates the trigger zone. Nausea begins 4 to 6 hours after treatment and lasts for 1 to 2 days (Remesh, 2012).

Another effect of chemotherapy in breast cancer patients is constipation due to the administration of the antiemetic 5-hydroxytryptamine (serotonin; 5TH3 i.e. ondancentrron). Indications of constipation in breast cancer patients resulting from the antiemetic 5HT3 during chemotherapy increased. The combination of 5HT3 receptor antagonists and corticosteroids is recommended as an antiemetic prophylaxis in patients with moderate and high risk of vomiting, whereas 5HT3 is not always administered in patients with a low risk of vomiting. The effects of constipation include physical changes with the following symptoms: anorexia, urinary incontinence, confusion, nausea and vomiting, urinary dysfunction, impaction, rectal prolapse fissures, hemorrhoids, intestinal obstruction, and syncope and can also cause anxiety and social isolation.

The incidence of constipation occurred in 3 patients (10%) and began to appear in the first cycle of chemotherapy. Constipation results from the tumor itself or from the side effects of treatment, negative effects on energy and food intake will lead to an increased risk of malnutrition. Food intake also plays a role in the prognosis of breast cancer and can modify the progression of the disease (Tong, 2019).

Chemotherapy-induced neuropathy is caused by a large number of cytotoxic drugs. Symptoms that arise of arthralgia or myalgia. Symptoms of neuropathy arise about 2 to 3 days after administration (Loprinzi et al., 2020). This is in line with this study, where it can be seen that the effects of neuropathy arise since the first cycle of chemotherapy. The complaints that arise in patients are pain in the muscles and joints in the legs and wrists. Some patients also complain of cramps in the hands after undergoing chemotherapy in the first cycle.

Conclusion

Breast cancer patients who underwent chemotherapy with a combination of epirubicin and cyclophosphamide drugs at Jend. Ahmad Yani Metro Hospital experienced several side effects, including hair loss in 29 patients (96.6%), skin hypersensitivity in 2 patients (6.6%), nausea in 28 patients (93.3%), constipation in 3 patients (10%), tingling in 4 patients (13.3%), and pain in 2 patients (6.6%). Side effects began to appear at different times during each cycle, and the side effects experienced during a certain period of time undergo a recovery process. The role of pharmacists is indispensable in providing information and education to patients regarding the occurrence of side effects arising from chemotherapy.

To optimize patient care, we recommend implementing comprehensive pre-treatment counseling that specifically addresses anticipated side effects and their management strategies. Prophylactic measures, such as scalp cooling for alopecia prevention and tailored antiemetic regimens, should be standardized. The hospital should establish structured monitoring protocols to enable early detection and intervention for treatment-related toxicities, particularly for vulnerable subgroups, including elderly patients and those with comorbidities. A multidisciplinary care approach, incorporating pharmacists, nutritionists, and mental health professionals, would be valuable in addressing the multifaceted challenges of chemotherapy. Future research should focus on longitudinal assessment of side effect trajectories and evaluation of novel supportive interventions to further improve the therapeutic experience for breast cancer patients. These evidence-based improvements in clinical practice can significantly enhance treatment tolerability, adherence rates, and overall quality of life during chemotherapy.

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