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ANALYSIS OF ADVERSE DRUG REACTIONS (ADRs) AND THEIR SEVERITY IN BREAST CANCER PATIENTS TREATED WITH THE DOCETAXEL-DOXORUBICIN REGIMEN

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ABSTRACT
The use of the docetaxel-doxorubicin regimen in breast cancer treatment has been associated with Adverse Drug Reactions (ADRs). This study aims to analyze the occurrence of ADRs and their severity in breast cancer patients undergoing therapy with the docetaxel-doxorubicin regimen at the hospital. The research design employed a quantitative cross-sectional approach, and purposive sampling was used as the sampling technique. Six primary Adverse Drug Reactions (ADRs) were identified among breast cancer patients undergoing chemotherapy with the docetaxel-doxorubicin regimen: nausea (21,32%), anemia (13,71%), peripheral neuropathy (7,45%), alopecia (23,01%), cardiac disorders (7,11%), and anorexia (9.81%). Breast cancer patients treated with the docetaxel doxorubicin regimen experienced various levels of ADR severity. Among the 591 adverse drug reaction (ADR) incidents recorded, the majority (55.6%) were classified as mild (severity level 1), with nausea reported as the most common side effect. At severity level 2 (moderate), alopecia was predominant, while at severity level 3 (severe), anemia was the most common reaction. There were no ADR incidents reported at severity levels 4 and 5.

Keywords: Adverse Drug Reactions (ADRs); docetaxel-doxorubicin; breast cancer.

1. INTRODUCTION

Breast cancer is one of the most common cancers affecting women worldwide and is a leading cause of cancer-related deaths (Wilkinson & Gathani, 2022). According to the World Health Organization (WHO), the number of breast cancer cases continues to rise annually, particularly in developing countries (Rahayuwati et al., 2020). The Global Burden of Cancer (GLOBOCAN) report from the International Agency for Research on Cancer (IARC) noted that in 2018, there were 18.1 million new cancer cases and 9.6 million cancer-related deaths worldwide. Breast cancer accounted for the highest incidence and mortality rate, with a global prevalence of 43.3%. The number of cancer cases globally is projected to increase, reaching 30.2 million by 2040 (Bray et al., 2018).

In Indonesia, the National Basic Health Research (Riskesdas) 2018 reported a rise in breast cancer prevalence to 1.79 per 1,000 population, up from 1.4 per 1,000 in 2013. This places Indonesia 23rd in Asia for breast cancer incidence. Specifically, the 2018 Riskesdas for Central Java estimated approximately 68,638 individuals affected by cancer. In Semarang City, breast cancer cases totaled 3,590, including 16 cases in men and 3,574 cases in women. This marked an increase from the previous year's 2,498 cases, with prevalence rising from 0.6% to 0.85% (Kemenkes, 2018). At Sultan Agung Islamic Hospital (RSI Sultan Agung), breast cancer

accounts for 40-50% of all cancer diagnoses. In 2022, more than 1,000 cases of breast cancer were recorded at the hospital (SIM RSI Sultan Agung, 2021).

Treatment for breast cancer typically involves a combination of surgery, radiation therapy, hormonal therapy, and chemotherapy (Wang & Wu, 2023). Chemotherapy regimens such as docetaxel and doxorubicin are standard treatments, showing effectiveness in enhancing tumor response and extending patient survival. However, these regimens carry significant risks of adverse drug reactions (ADRs) (Romero Lagunes & Pezo, 2021). Common ADRs among breast cancer patients receiving chemotherapy include nausea, vomiting, neutropenia, neuropathy, and cardiotoxicity. These reactions can severely affect the patients' quality of life and, in severe cases, may pose life-threatening risks. The severity of ADRs varies based on individual patient factors, drug dosage, and the body's response to therapy (BPOM RI, 2020).

Previous studies have highlighted the prevalence of ADRs in breast cancer chemotherapy. Basuki et al., (2020) found that chemotherapy caused nausea (92.7%), alopecia (82.9%), and anemia (80.49%) in most breast cancer patients, with common regimens including docetaxel, epirubicin, and carboplatin. Arisanti et al., (2020) identified Cyclophosphamide, Doxorubicin, and Fluorouracil as frequent regimens, causing nausea and vomiting in over 90% of cases. Assi et al., (2021) reported severe neuropathy associated with docetaxel, while Barcelos et al., (2019) noted serious side effects such as dyspnea and general pain. Doxorubicin was linked to neutropenia, nausea, and skin reactions, whereas Hager et al., (2024) highlighted the gastrointestinal, cardiac, and musculoskeletal side effects of docetaxel.

RSI Sultan Agung Semarang serves as a referral hospital for cancer treatment in Central Java. In 2022, the hospital managed 1,751 outpatients and 923 inpatients for breast cancer. Given the high incidence of breast cancer cases and reports of ADRs, a study analyzing ADRs and their severity among breast cancer patients undergoing docetaxel-doxorubicin chemotherapy is essential. A deeper understanding of the most common ADRs and their severity levels can aid in improving patient management, optimizing therapy, and mitigating the risk of severe complications. Furthermore, this information can guide healthcare professionals in designing more effective prevention and intervention strategies.

The novelty of this study lies in its specific focus on adverse drug reactions (ADRs) in breast cancer patients treated with the docetaxel-doxorubicin regimen at RSI Sultan Agung Semarang, a major referral hospital for cancer treatment in Central Java. Unlike previous studies that have analyzed ADRs in breast cancer patients across diverse healthcare settings, this research provides localized data that offer a more precise representation of ADR occurrences within the regional population. Additionally, while prior studies have primarily examined ADRs in various chemotherapy combinations, such as cyclophosphamide, doxorubicin, and fluorouracil or epirubicin and carboplatin, this study uniquely focuses on the docetaxel-doxorubicin regimen, a key treatment protocol at RSI Sultan Agung. Another critical aspect of novelty is the comprehensive evaluation of ADR severity, as most prior research has primarily reported prevalence without an in-depth severity classification. By analyzing the severity levels, this study provides essential insights for optimizing patient management strategies. The findings have significant implications for improving clinical practices, including enhanced ADR monitoring, risk stratification, and personalized treatment adjustments to mitigate the adverse effects of chemotherapy. This study aims to analyze the occurrence and severity of ADRs in breast cancer patients undergoing docetaxel-doxorubicin therapy at Sultan Agung Islamic Hospital. The findings are expected to contribute significantly to enhancing healthcare quality and improving breast cancer treatment management.

2. METHODS

This study employed a cross-sectional design with quantitative analysis and purposive sampling techniques. The research was conducted on breast cancer patients undergoing

chemotherapy with the Docetaxel-Doxorubicin regimen at Sultan Agung Islamic Hospital (RSI Sultan Agung) in Semarang. Data collection was carried out through patient medical records and questionnaires over one chemotherapy cycle for breast cancer patients treated with the Docetaxel-Doxorubicin regimen. The study was conducted over three months, from November 2023 to January 2024. Subjects of the study were breast cancer patients at RSI Sultan Agung who met the following inclusion criteria: [1] Female patients diagnosed with breast cancer aged >18 years, [2] Patients receiving the Docetaxel-Doxorubicin regimen, [2] Patients willing to participate in the study. All respondents meeting the inclusion criteria were included as samples.

Analysis of ADRs (Adverse Drug Reactions) was performed using the Naranjo Algorithm by answering 10 predefined questions and scoring based on the patient's condition. The total score for each ADR was calculated and categorized into four probability categories > 9: Highly Probable, 5–8: Probable, 1–4: Possible, 0: Doubtful. The occurrence of ADRs was then presented as percentages.

Severity analysis of ADRs was conducted using ADR severity forms derived from CTCAE (Common Terminology Criteria for Adverse Events) versions 5.0 and 3.0. These forms included patient identity, ADR categories, severity grading (from grade 1 to grade 5), and supporting laboratory data. Severity analysis was based on the assigned grading, with higher grades indicating more severe ADRs. Each ADR was then presented as a percentage.

Univariate analysis was performed to descriptively analyze the variables by calculating frequency distributions and proportions to characterize the study subjects. This analysis provided a descriptive overview of patient characteristics, ADR occurrences based on the Naranjo Algorithm, and ADR severity levels based on CTCAE. The results of the univariate analysis were presented as percentages. The research has received ethical clearance from the Health Research Ethics Commission (KEPK) of RSI Sultan Agung No. 120/KEPK-RSISA/VI/2024.

3. RESULTS AND DISCUSSION

The study was conducted from June 2024 to August 2024 on 136 breast cancer patients at Sultan Agung Islamic Hospital (RSI Sultan Agung) in Semarang, who underwent chemotherapy with the Docetaxel-Doxorubicin regimen.

3.1. Characteristics of Research Respondent

The respondents in this study (Table 1) were all women with breast cancer, which is consistent with the fact that 99% of breast cancer cases occur in women due to the influence of estrogen and progesterone hormones. The use of hormonal contraceptives containing estrogen and progesterone can increase the risk of breast cancer, especially with long-term use. Although rare, men can also develop breast cancer (Al-Shami et al., 2023). The risk increases with age, especially after 50 years, due to the increase in local estrogen. Local estrogen is believed to be responsible for the increased risk of breast cancer in postmenopausal women. Older age carries a higher risk than younger age, as the likelihood of developing breast cancer increases with age (Łukasiewicz et al., 2021). Most patients were under 50 years old (51.47%), and cancer is rarely found in individuals under 35 years of age. Breast cancer is often diagnosed at an advanced stage, with symptoms such as lumps, spread to other organs, and serious complications (Ketut et al., 2022). The majority of patients (79.41%) had no comorbidities, but 16.16% had hypertension, which is linked to cancer through mechanisms such as inflammation and oxidative stress. Hypertension and breast cancer are closely related and both become more common with age. They share similar pathophysiological mechanisms and risk factors, such as inflammation, oxidative stress, diabetes, obesity, smoking, physical inactivity, and sleep apnea. Cancer-related symptoms and treatments can also worsen hypertension by affecting the heart, blood vessels, and kidneys (Deswindra et al, 2018).

Table 1. Characteristics of breast cancer patients receiving the doxetacel-doxorubicin regimen at Sultan Agung Islamic Hospital Semarang (N=136)

Variables	Freq (%)
Gender	
Woman	136 (100%)
Age	
≤50	70 (51.47%)
> 50	66 (48.53%)
Cancer Stage	
Early stage (1 and 2)	20 (14.7%)
Advanced stage (3 and 4)	116 (85.3%)
Accompanying Diseases	
None	108 (79.41%)
Hypertension	22 (16.18%)
Diabetes	9 (6.62%)
Colesteamatom media	1 (0.74%)
Congested	1 (0.74%)
Chemotherapy Cycle	
≤3	46 (33.8%)
> 3	90 (66.1%)
Length of Hospitalization	
1 day	0 (0.00%)
2 days	129 (94.85%)
3 days	7 (5.15%)
4 days	0 (0.00%)
5 days	0 (0.00%)
Education	
None	3 (2.21%)
SD	16 (11.76%)
Junior High School	32 (23.53%)
Senior High School	48 (35.29%)
Diploma/College degree	23 (16.91%)
Bachelor degree	14 (10.29%)
Job status	
Housewives	47 (34.56%)
Private sector	31 (22.79%)
Self-employed	17 (12.50%)
None	16 (11.76%)
Farmer	9 (6.62%)
Civil servant	6 (4.41%)
Retired	5 (3.68%)
Laborer	4 (2.94%)
Etc	1 (0.74%)

The chemotherapy regimen of docetaxel-doxorubicin was administered on an inpatient basis, with an average of six cycles every three weeks (Hermawan, 2016). Most patients underwent more than three cycles (64%), but had not completed the therapy. The majority of patients had a normal BMI (58.82%), with a higher risk of cancer among those who are obese. Being overweight or obese increases the risk of breast cancer by 20%–60% compared to women with a normal weight (Arafah & Kiptiyah, 2020). The majority of patients had a high school education (35.29%) and were housewives (34.56%). This study emphasizes the importance of early detection and close monitoring during therapy to minimize the risk of complications.

3.2. Adverse Drug Reactions (ADRs) in Breast Cancer Patients with the Docetaxel-Doxorubicin Regimen at RSI Sultan Agung Semarang

In this study, a total of 591 ADRs were reported across 136 patients. Below is a detailed breakdown of the ADR events experienced by patients receiving the Docetaxel-Doxorubicin regimen at RSI Sultan Agung Semarang. Table 2 shows that there are 6 ADRs with the highest

incidence rates: nausea in 126 (21,32%) patients, anemia in 81 (13,71%) patients, peripheral neuropathy in 44 (7,45%) patients, alopecia in 136 (23,01%) patients, heart disorders in 42 (7,11%) patients, and anorexia in 58 (9.81%) patients. Side effects like alopecia and anemia are common in breast cancer patients undergoing chemotherapy because chemotherapy targets rapidly dividing cells, both cancerous and healthy. Alopecia occurs due to damage to the hair follicles, while anemia results from reduced red blood cell production in the bone marrow, leading to fatigue and weakness (Kang et al., 2019). Anorexia can occur as chemotherapy affects the digestive system and brain, causing taste changes or inducing nausea, which reduces appetite. Patients often feel fatigued or emotionally distressed, further worsening the loss of appetite (Gustini et al., 2019). Peripheral neuropathy happens when certain chemotherapy drugs, such as taxanes or platinum-based drugs, damage peripheral nerves that connect the brain and spinal cord to other parts of the body. This nerve damage leads to symptoms like tingling, numbness, and pain in the hands or feet (Zajaczkowską et al., 2019). Meanwhile, heart disorders occur when chemotherapy drugs like doxorubicin damage the heart muscle, leading to cardiotoxicity. This can result in reduced heart function and may even lead to heart failure, as the heart's ability to pump blood efficiently is impaired (Belger et al., 2024). The results of this study are consistent with previous research. Basuki et al. (2020) reported alopecia and anemia as the main ADRs of breast cancer chemotherapy. Arisanti et al., (2020) linked doxorubicin to nausea and vomiting, while Barcelos et al., (2019) mentioned that docetaxel frequently causes dyspnea, pain, and other general disorders, and doxorubicin triggers neutropenia and vasculitis. Hager et al., (2024) also associated docetaxel with ischemic colitis and the risk of heart failure.

Table 2. Overview of ADRs in patients receiving the docetaxel-doxorubicin regimen at RSI Sultan Agung Semarang

Adverse Drug Reactions	Freq (%) [n= 591]
Alopecia	136 (23.01%)
Nauseous	126 (21.32%)
Anemia	81 (13.71%)
Anorexia	58 (9.81%)
Peripheral Neuropathy	44 (7.45%)
Heart Disorders	42 (7.11%)
Blackened Skin	29 (4.91%)
Injection Site Reactions	27 (4.57%)
Vomit	16 (2.71%)
Black Nails	6 (1.02%)
Oral Mucositis	5 (0.85%)
Fever	5 (0.85%)
Itchy	4 (0.68%)
Diarrhea	2 (0.34%)
Extravasation	2 (0.34%)
Acites	2 (0.34%)
Leukopenia	2 (0.34%)
Constipation	1 (0.17%)
Thrombocytopenia	1 (0.17%)
Dry Skin	1 (0.17%)
Out of breath	1 (0.17%)

3.3. Causality of Adverse Drug Reactions (ADRs) in Breast Cancer Patients with the Doxetacel-Doxorubicin Regimen at RSI Sultan Agung Semarang

The causality assessment of ADRs was conducted using the Naranjo Algorithm. Below is the breakdown of the causality of ADRs based on Naranjo's categories.

Table 3.Incidence of ADRs and causality based on naranjo in breast cancer patients receiving the doxetacel-doxorubicin regimen at Sultan Agung Islamic Hospital Semarang

Adverse Drug Reactions (N=591)	Doxorubicin Causality Category				Docetaxel Causality Category			
	Possible	Probable	Highly Probable	Freq (%)	Possible	Probable	Highly Probable	Freq (%)
Alopecia	0	136	0	136 (23.01%)	0	136	0	136 (23.01%)
Nauseous	0	126	0	126 (21.32%)	0	126	0	126 (21.32%)
Anemia	0	81	0	81 (13.71%)	0	81	0	81 (13.71%)
Anorexia	19	39	0	58 (9.81%)	19	39	0	58 (9.81%)
Peripheral Neuropathy	-	-	-	-	4	40	0	44 (7.45%)
Peripheral Edema	-	-	-	-	2	0	0	2 (0.34%)
Heart Disorders	9	33	0	42 (7.11%)	-	-	-	-
Blackened Skin	0	29	0	29 (4.91%)	-	-	-	-
Injection Site Reactions	0	27	0	27 (4.57%)	0	27	0	27 (4.57%)
Vomit	0	16	0	16 (2.71%)	0	16	0	16 (2.71%)
Black Nails	1	5	0	6 (1.02%)	1	5	0	6 (1.02%)
Oral Mucositis	0	5	0	5 (0.85%)	0	5	0	5 (0.85%)
Fever	0	5	0	5 (0.85%)	0	5	0	5 (0.85%)
Itchy	4	0	0	4 (0.68%)	-	-	-	-
Diarrhea	0	2	0	2 (0.34%)	0	2	0	2 (0.34%)
Extravasation	0	2	0	2 (0.34%)	0	2	0	2 (0.34%)
Leukopenia	0	2	0	2 (0.34%)	0	2	0	2 (0.34%)
Constipation	1	0	0	1 (0.17%)	1	0	0	1 (0.17%)
Thrombocytopenia	0	1	0	1 (0.17%)	0	1	0	1 (0.17%)
Dry Skin	0	1	0	1 (0.17%)	-	-	-	-
Out of breath	0	1	0	1 (0.17%)	-	-	-	-
Total	34	511	0	545 (92,22%)	27	487	0	514 (86,97%)

3.4. Severity of Adverse Drug Reactions (ADRs) in breast cancer patients with Doxetacel-Doxorubicin regimen at RSI Sultan Agung Semarang.

Based on Table 3, the highest causality category for all ADRs occurring in patients due to the use of Doxorubicin is probable, with 511 occurrences. For the use of Docetaxel, the highest causality category for all ADRs is also probable, with 511 occurrences (86.4%). The next category is highly probable, with 487 occurrences (82.4%). The lowest causality category for all

ADRs is possible, occurring 34 times (5.7%) with Doxorubicin and 27 times (4.5%) with Docetaxel. This means that these ADRs may not necessarily occur in patients using the Docetaxel-Doxorubicin regimen. In the context of using Doxorubicin and Docetaxel in breast cancer patients, most adverse drug reactions (ADRs) fall into the *probable* category. This indicates that the reactions are most likely caused by the drugs, with appropriate timing and symptom improvement after the drug is discontinued. This aligns with various research findings. Doxorubicin, an anthracycline-class drug, is known to have toxic effects on several body tissues, particularly the bone marrow and heart. A study by Arrigoni et al., (2025) stated that Doxorubicin has a high toxicity profile and frequently causes side effects such as cardiotoxicity, anemia, and nausea, making it a drug with a high proportion of *probable* ADRs. Similarly, Docetaxel, a taxane-class agent, works by disrupting the cell division process and is commonly associated with side effects such as neutropenia, hypersensitivity reactions, and peripheral neuropathy. Research by Wijayanti et al., (2023) showed that the side effects of Docetaxel generally have a strong causal relationship, leading most of them to be classified as *probable*. On the other hand, the number of ADRs categorized as *possible* is relatively small, indicating that most adverse effects are very likely directly caused by the drugs themselves, rather than by other factors such as underlying disease or combination therapy. This underscores the importance of close monitoring of patients undergoing chemotherapy to manage side effect risks and maintain quality of life throughout treatment. In the context of chemotherapy, achieving the *definite* category is quite challenging because it requires strong evidence, such as the recurrence of a reaction after re-administration of the drug (*rechallenge*), which is often not performed due to patient safety concerns. Therefore, reactions that are very likely caused by Doxorubicin or Docetaxel are more realistically categorized as *probable*, even though the causal relationship is clinically convincing.

ADRs Severity Analysis is performed using the ADRs severity form sourced from CTCAE. Severity grading consists of grades 1 to 5: severity 1 (mild), severity 2 (moderate), severity 3 (severe), severity 4 (life-threatening/requires emergency treatment) and severity 5 (causing death). The following is an overview of the severity of ADRs. Based on the data (Table 4), breast cancer patients undergoing chemotherapy with Docetaxel Doxorubicin experienced ADRs with three levels of severity. Out of 591 reported ADR events, 329 (55.6%) events were classified as severity level 1, 245 (41.4%) events were classified as severity level 2, and 17 (2.8%) events were classified as severity level 3. There were no events reported at severity levels 4 and 5. At severity level 1 (mild), the most common ADR was nausea, experienced by 79 patients. At severity level 2 (moderate), alopecia was the most common ADR, affecting 96 patients. At severity level 3 (severe), anemia was the most common ADR, occurring in 6 patients. Nausea, hair loss, and anemia are common side effects of breast cancer chemotherapy. The severity of nausea is influenced by the drug dosage (Mustian, 2014), while hair loss occurs because the drug targets body cells, including hair roots (Citra Tri Wahyumi Faisel, 2022). Anemia frequently occurs, with the severity depending on the chemotherapy regimen, type of disease, age, and other risk factors (Listyawardhani et al., 2018).

Table 4. Severity of ADRs based on CTCAE

Adverse Drug Reactions	Severity Based on CTCAE					
	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Freq
Alopecia	40	96	0	0	0	136
Nauseous	79	47	0	0	0	126
Anemia	44	31	6	0	0	81
Anorexia	53	1	4	0	0	58
Peripheral Neuropathy	26	18	0	0	0	44
Heart Disorders	34	8	0	0	0	42
Blackened Skin	0	29	0	0	0	29

Injection Site Reactions	25	2	0	0	0	27
Vomit	10	6	0	0	0	16
Black Nails	6	0	0	0	0	6
Oral Mucositis	0	1	4	0	0	5
Fever	4	1	0	0	0	5
Itchy	3	1	0	0	0	4
Diarrhea	2	0	0	0	0	2
Extravasation	0	0	2	0	0	2
Peripheral Edema	0	2	0	0	0	2
Leukopenia	1	1	0	0	0	2
Constipation	1	0	0	0	0	1
Thrombocytopenia	0	0	1	0	0	1
Dry Skin	0	1	0	0	0	1
Out of breath	1	0	0	0	0	1
Total	329	245	17	0	0	591

The results of this study indicate that six Adverse Drug Reactions (ADRs) with the highest incidence among breast cancer patients undergoing chemotherapy with the Docetaxel-Doxorubicin regimen are nausea, anemia, peripheral neuropathy, alopecia, cardiac disorders, and anorexia. Alopecia is the most frequently occurring side effect (21.48%), followed by nausea (19.91%) and anemia (12.80%). These data suggest that ADRs in chemotherapy patients are more related to side effects affecting physical aspects of the patients, such as hair and the gastrointestinal system. Nausea, occurring in 19.91% of patients, is a well-known side effect of chemotherapy, especially with drugs like doxorubicin, which can irritate the gastrointestinal tract (Arisanti et al., 2020). Nausea typically occurs within 24 hours of chemotherapy and can last for weeks, disrupting the patient's comfort and quality of life. These findings are consistent with Basuki et al., (2020), which reported that nausea is one of the main ADRs experienced by breast cancer patients undergoing chemotherapy.

Anemia (12.80%) is also a common side effect in chemotherapy patients, caused by the drug's effect on the bone marrow, reducing red blood cell production. This can lead to fatigue, shortness of breath, and reduced immunity. Anemia in breast cancer patients undergoing chemotherapy can impact their ability to perform daily activities and decrease their quality of life. The severity of anemia is influenced by drug dosage, type of cancer, and other underlying health conditions (Listyawardhani et al., 2018).

Alopecia, occurring in 21.48% of patients, is a side effect that often has psychological impacts on patients, particularly women. Hair loss occurs because chemotherapy drugs like doxorubicin attack rapidly growing cells, including hair root cells. This aligns with Faisel (2022) study, which stated that hair loss is a very common side effect in chemotherapy patients, frequently affecting self-confidence and mental health.

Peripheral neuropathy (6.95%) and cardiac disorders (6.64%) are other side effects found in this study. Peripheral neuropathy is caused by nerve damage due to the toxic effects of chemotherapy, which can lead to sensations of tingling, numbness, or pain in the hands and feet. Cardiac disorders, associated with the use of docetaxel, can increase the risk of heart failure, as reported by Hager et al., (2024). While the percentage is lower, cardiac disorders are serious side effects that require special attention. Anorexia (9.16%), found in a portion of the patients, is also a common side effect of chemotherapy, caused by the drugs' effects on appetite and the digestive system. This condition can lead to weight loss and malnutrition, exacerbating the patient's condition during treatment (Ma et al., 2018).

Overall, the results of this study are consistent with previous research reporting nausea, anemia, alopecia, and cardiac disorders as major side effects of chemotherapy in breast cancer patients. It is essential to monitor and manage these ADRs effectively to improve patient comfort and quality of life during therapy. Proper and responsive management of these side

effects can help patients complete their treatment more effectively and minimize the negative impact of ADRs on their health.

Based on the results of this study, it can be seen that breast cancer patients undergoing chemotherapy with the Docetaxel-Doxorubicin regimen experience various Adverse Drug Reactions (ADRs) with three levels of severity. The highest incidence of ADRs occurred at severity level 1 (55.6%), indicating that most side effects experienced by patients were mild in nature. Nausea was the most common side effect at severity level 1, found in 79 patients. Nausea is one of the most common side effects of chemotherapy, influenced by drug dosage and chemotherapy agents that irritate the gastrointestinal system, as explained by Gour et al., (2023). While nausea is usually not life-threatening, its impact on patients' quality of life can be significant, as it can cause discomfort and disrupt daily activities.

At severity level 2, which occurred in 41.4% of ADR cases, the most frequently reported side effect was alopecia, which affected 96 patients. Alopecia, or hair loss, is a common side effect of chemotherapy because chemotherapy drugs not only target cancer cells but also healthy cells, including hair follicle cells (Faisel, 2022). While hair loss is not life-threatening, its impact on the psychological well-being of patients, especially women, is often quite profound. Alopecia can lead to emotional stress and a decrease in self-confidence, requiring special attention in cancer patient care (Aukerman & Jafferany, 2023).

Severity level 3 (moderate) was found in 2.8% of ADR cases, with anemia being the most frequent side effect, affecting 6 patients. Anemia, which commonly occurs in breast cancer patients undergoing chemotherapy, can significantly affect their quality of life. Anemia in chemotherapy patients is usually caused by a reduction in red blood cell count due to the drug's effect on the bone marrow (Listyawardhani et al., 2018). The severity of anemia is influenced by various factors, such as drug dosage, type of cancer, age of the patient, and other risk factors, which can lead to fatigue, shortness of breath, and decreased immunity (David & Maureen, 2019).

It is important to note that there were no ADRs with severity levels 4 and 5 in this study, indicating that although chemotherapy can cause serious side effects, the majority of patients experienced ADRs of mild to moderate severity. This may suggest the effectiveness of ADR management in the hospital or possibly because the majority of patients had relatively good clinical conditions during chemotherapy. Overall, this study provides a clear picture of the types and severity levels of ADRs in breast cancer patients undergoing chemotherapy with the Docetaxel-Doxorubicin regimen. Nausea, alopecia, and anemia were the most common side effects, and appropriate monitoring and management are necessary to minimize the negative impact of these ADRs on patients' quality of life. Successful ADR management can enhance patient comfort and help them complete their chemotherapy cycles more effectively (Salam & Abhinesh, 2024).

4. CONCLUSION

Based on the results of the study, there were six main Adverse Drug Reactions (ADRs) observed in breast cancer patients undergoing chemotherapy with the Docetaxel-Doxorubicin regimen: nausea (21.32%), anemia (13.71%), peripheral neuropathy (7.45%), alopecia (23.01%), cardiac disorders (7.11%), and anorexia (9.81%). Breast cancer patients undergoing chemotherapy with the Docetaxel-Doxorubicin regimen experienced varying degrees of ADR severity. Of the 591 ADR occurrences recorded, the majority (55.6%) were classified as severity level 1 (mild), with nausea being the most frequent side effect. At severity level 2 (moderate), alopecia was the dominant side effect, while at severity level 3, anemia was the most common. No ADRs were recorded at severity levels 4 and 5. This study highlights key clinical strategies to enhance the management of breast cancer patients receiving docetaxel-doxorubicin chemotherapy. Effective ADR monitoring, including antiemetics for nausea and psychological

support for alopecia, improves patient comfort. Proactive anemia management through hemoglobin monitoring and supplementation prevents complications, while pre-therapy cardiovascular assessments and neurotropic vitamins help mitigate neuropathy and cardiac toxicity. Nutritional counseling supports proper intake, and individualized dose adjustments for high-risk patients optimize treatment outcomes. These findings contribute to a more patient-centered approach in chemotherapy management.

5. ACKNOWLEDGMENT

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6. CONFLICT OF INTEREST

All Authors declared that there was no conflict of interest.

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