Jurnal Farmasi dan Ilmu Kefarmasian Indonesia
Pharmacy and Pharmaceutical Sciences Journal
Published by Faculty of Pharmacy Universitas Airlangga
OPEN ACCESS
E-ISSN 2580-8303
P-ISSN 2406-9388

Jurnal Farmasi dan Ilmu Kefarmasian Indonesia Vol. 11 No. 2 August 2024, 253-259
DOI: 10.20473/jfiki.v11i22024.253-259
Available online at https://e-journal.unair.ac.id/JFIKI/

Evaluation of Adverse Drug Reactions (ADRs) in Breast Cancer Patients Who Received Doxorubicin, Cyclophosphamide (AC) and Doxorubicin, Cyclophosphamide, Paclitaxel (AC-T) Chemotherapy at West Nusa Tenggara Provincial Hospital

Baiq Lenysia Puspita Anjani*, Rahma Nanda Muriani, Baiq Nurbaety, Baiq Leny Nopitasari
Program Studi Farmasi, Fakultas Ilmu Kesehatan, Universitas Muhammadiyah Mataram, Mataram, Indonesia

*Corresponding author: baiqlenysia@gmail.com
Orcid ID: 0009-0004-9014-184X

Submitted: 20 May 2024
Revised: 27 July 2024
Accepted: 30 August 2024

Abstract

Background*: Chemotherapy is commonly used to treat breast cancer (BC). Chemotherapy may cause ADRs in patients, affecting their physical and psychological wellbeing.* ***Objective:*** *To understand the adverse drug reaction (ADR) profile in patients with breast cancer who received AC-T and AC chemotherapy at the West Nusa Tenggara Provincial Hospital.* ***Methods:*** *This observational study used cross-sectional data collected from medical records and direct interviews with the patients between May and June. Probability categories were measured using the Naranjo algorithm questionnaire, causality categories were measured using a causality flowchart, and the severity level of ADRs was determined using the Common Terminology Criteria for Adverse Events (CTCAE) 5.0.* ***Results:*** *The probability results for the AC-T regimen were as follows: possible (10 %), probable (54.44 %), and definite (35.56 %). whereas The AC regimen showed categories of possible (6.67%), probable (63.33%), and definite (30%). The causality results for the AC-T regimen were categorized as unlikely (1.11%), possible (12.22%), probable (25.56%), or certain (61.11%), whereas those for the AC regimen were categorized as possible (6.67%), probable (43.33%), or certain (50%). The most common ADRs were alopecia and nausea, with the highest probability in the probable category for AC-T (54.44%) and AC (63.33%), respectively.* ***Conclusion:*** *Respondents who received the AC-T regimen experienced more severe ADRs in terms of hematologic disorders (anemia, leukopenia, and thrombocytopenia) and symptoms of nausea, pain, and fever than those who received the AC regimen.*

Keywords*: chemotherapy, breast cancer, adverse drug reactions (ADRs), probability, common terminology criteria for adverse events (CTCAE)*

How to cite this article:
Anjani, B. L. P., Muriani, R. N., Nurbaety, B. & Nopitasari, B. L. (2024). Evaluation of Adverse Drug Reactions (ADRs) in Breast Cancer Patients Who Received Doxorubicin, Cyclophosphamide (AC) and Doxorubicin, Cyclophosphamide, Paclitaxel (AC-T) Chemotherapy at West Nusa Tenggara Provincial Hospital. *Jurnal Farmasi dan Ilmu Kefarmasian Indonesia*, 11(2), 253-259. http://doi.org/10.20473/jfiki.v11i22024.253-259

P-ISSN: 2406-9388
E-ISSN: 2580-8303

INTRODUCTION

Breast cancer (carcinoma mammae) is the abnormal growth of cells in the breast caused by oncogenes, leading to their transformation into cancerous cells (Syamsuddin et al., 2020). According to Global Burden of Cancer (GLOBOCAN) data from the International Agency for Research on Cancer (IARC) in 2018, there was an increase of 18.1 million cases globally, with 9.6 million deaths worldwide, accounting for the highest percentage of deaths at 43.3% (Bray et al., 2018). The Basic Health Research of Indonesia in 2018 showed an increase in the prevalence of breast cancer to 1.79 per 1000 population, up from 1.4 per 1000 2013. Indonesia ranks 23rd in terms of the number of breast cancer cases in Asia. Based on the results of Basic Health Research in West Nusa Tenggara (2018), breast cancer cases increased from 0.6% to 0.85% (Pangribowo, 2019).

Chemotherapy involves treatment with cytostatic drugs that actively target the growing and dividing cells (Piepoli et al., 2016). Advancements in pharmaceutical technology and various anticancer drug discoveries have increased optimism in addressing cancer malignancy. However, chemotherapy treatment has both physical and psychological side effects (Hidayatullah, 2015).

The World Health Organization (WHO) defines ADRs as unfavorable and unintended responses to a drug occurring at doses typically used in humans for the prevention, diagnosis, disease therapy, or modification of physiological functions (Balai Pengawasan Obat dan Makanan Republik Indonesia, 2020). ADRs and differences in hematological profiles before and after chemotherapy in patients with breast cancer breast cancer patients at Yogyakarta City Hospital showed that nausea was the most common manifestation (Basuki et al., 2020). The most commonly received chemotherapy regimens for patients with breast cancer at West Nusa Tenggara Provincial Hospital are AC-T and AC, which potentially lead to different manifestations of ADRs. The objective of this study was to understand the ADR profile in patients with breast cancer receiving AC-T and AC chemotherapy at the West Nusa Tenggara Provincial Hospital.

MATERIALS AND METHODS

Method

This observational study was conducted using cross-sectional data collected from medical records and direct interviews with patients in June 2023. The study population included all patients diagnosed with breast cancer between May and June 2023 at the West Nusa Tenggara Provincial Hospital, who received chemotherapy. Non-probability sampling using a convenience sampling/quota sampling methodology was employed. The inclusion criteria for this study were patients who received combination therapy with AC-T and AC combination therapy. The exclusion criteria were Patients who received radiotherapy or surgery and those who were unwilling to participate were excluded.

Following data collection, a descriptive analysis was performed on general patient profiles by presenting data based on age, occupation, comorbidities, chemotherapy cycles, and breast cancer stages. Probability categories were measured using the Naranjo algorithm questionnaire, causality categories were measured using a causality flowchart, and the severity level of ADRs was determined using the Common Terminology Criteria for Adverse Events (CTCAE) 5.0. This research was approved with Reference Number 00.9/18/0386/RSUDP/2023 and ethically cleared with Approval Number 00.9.1/08/KEP/2023.

RESULTS AND DISCUSSION

The study sample consisted of 120 patients, with 90 patients receiving the AC-T chemotherapy regimen and 30 patients receiving the AC chemotherapy regimen. As shown in Table 1, the breast cancer patients were in the age range of 46-55 years old, with 43 patients (47.78%) received AC-T chemotherapy, and 13 patients (43.33%) received AC chemotherapy. Table 1 indicates that older age at the onset of menopause poses a greater risk of breast cancer than a younger age at menopause. Elevated estrogen levels in women can delay menopause, thus increasing the risk of breast cancer (Wahyuni, 2021).

Table 2 shows that the majority of patients diagnosed with breast cancer were homemakers, with 55 patients (61.11%) receiving AC-T chemotherapy and 19 patients (63.33%) receiving AC chemotherapy. Research indicates that working women have a higher proportion of breast examinations than do non-working women. The primary factor is the lack of self-breast examination (SBE) due to the lack of knowledge and interaction among non-working women compared to their working counterparts (Wongkar et al., 2022).

Tables 3 and 4 show the probability and causality of ADRs observed in each chemotherapy cycle. Respondents who received AC-T chemotherapy were mainly in the probable (54.44%) or certain (61.11%) categories. Respondents to AC chemotherapy regimens were predominantly in the probable (63.33%) or certain (50%) categories. Respondents who received chemotherapy with either AC-T or AC regimens. A higher chemotherapy frequency correlated with a higher

P-ISSN: 2406-9388
E-ISSN: 2580-8303

Naranjo score, indicating an increased ADR category level. This aligns with the theory that as the frequency of chemotherapy increases, more cancer cells undergo damage and death. Similarly, healthy cells in the body also experience damage, and after a few periods, typically one– three weeks, these cells recover but undergo significant damage, leading to a decline in function and overall body resilience. This treatment was continued along with subsequent chemotherapy (Hilli, 2017).

The occurrence of adverse drug reactions varies in each cycle, and is attributed to chemotherapy reactions affecting each patient differently and in diverse ways (Khairani et al., 2019). According to a previous research, ADRs occurring in patients undergoing chemotherapy do not show significant differences in each cycle (Prieto-Callejero et al., 2020). In Table 3 and 4, it can be observed that the most common causality category experienced by patients is the "certain" category (highly associated with drug use), with 55 patients (61.11%) receiving AC-T chemotherapy and 15 patients (50%) in the AC chemotherapy group. The degree of certainty, "certain" and "probable" (likely associated with the drug), indicates a relatively high value for the causality link between the drug and the occurring side effects. These values suggest the sequential occurrence of reactions with chemotherapy administration.

Side effects were aligned with the known profile of the suspected drug. This is assured by the cessation of chemotherapy, which is a three-week interval between administrations. Meanwhile, for the degree of certainty and "possible" (not yet certain association with the drug), as mentioned, other possibilities exist, such as other ailments suffered by the patient or due to other therapies (Sukandar et al., 2014).

Table 1. Respondent characteristics based on age

Age (years)	Number of AC-T Respondent		Number of AC Respondent	
	(n)	(%)	(n)	(%)
17 - 25	0	0	1	3.33%
26 - 35	1	1.11%	1	3.33%
36 - 45	27	30%	9	30%
46 - 55	43	47.78%	13	43.33%
56 - 65	16	17.78%	6	20%
≥65	3	3.33%	0	0
Total	**90**	**100%**	**30**	**100%**

Table 2. Respondents' characteristics based on occupation

Occupation	Number of AC-T Respondents		Number of AC Respondents	
	(n)	(%)	(n)	(%)
Housewife	55	61.11%	19	63.33
Farmer	11	12.22%	5	16.67%
Entrepreneur	11	12.22%	3	10%
Farm laborer	5	5.56%	0	0
Civil servant	5	5.56%	0	0
Teacher	3	3.33%	2	6.67%
Student	0	0	1	3.33%
Total	**90**	**100%**	**30**	**100%**

Table 3. Probability and causality of ADRs based on chemotherapy cycle of respondents who received AC-T

Chemotherapy Cycle	Number of Respondents	Probability			Causality			
		Possible	Probable	Definite	Unlikely	Possible	Probable	Certain
1	21 (23.33%)	8 (38.10%)	13 (61.90%)	0	0	11 (52.38%)	10 (47.62%)	
2	15 (16.67%)	1 (6.67%)	13 (86.67%)	1 (6.67%)	1 (6.67%)	0	8 (53.33%)	6 (40%)
3	18 (20%)	0	9 (50%)	9 (50%)	0	0	3 (16.67%)	15 (83.33%)
4	14 (15.56%)	0	5 (35.71%)	9 (64.29%)	0	0	1 (7.14%)	13 (92.86%)
5	9 (10%)	0	5 (55.56%)	4 (44.44%)	0	0		9 (100%)
6	13	0	4	9	0	0	1	12

P-ISSN: 2406-9388
E-ISSN: 2580-8303

	(14.44%)		(30.77%)	(69.23%)			(7.69%)	(92.31%)
Total	**90 (100%)**	**9 (10%)**	**49 (54.44%)**	**32 (35.56%)**	**1 (1.11%)**	**11 (12.22%)**	**23 (25.56%)**	**55 (61.11%)**

Table 4. Probability and causality of ADRs based on chemotherapy cycle of respondents who received AC

Chemotherapy Cycle	Number of Respondents	Probability				Causality		
		Possible	Probable	Definite	Unlikely	Possible	Probable	Certain
1	3 (10%)	2 (66.67%)	1 (33.33%)	0	0	2 (66.67%)	1 (33.33%)	0
2	1 (3.33%)	0	1 (100%)	0	0	0	1 (100%)	0
3	6 (20%)	0	6 (100%)	0	0	0	4 (66.67%)	2 (33.33%)
4	6 (20%)	0	4 (66.67%)	2 (33.33%)	0	0	2 (33.33%)	4 (66.67%)
5	8 (26.67%)	0	5 (62.50%)	3 (37.50%)	0	0	3 (37.50%)	5 (62.50%)
6	6 (20%)	0	3 (50%)	3 (50%)	0	0	2 (33.33%)	4 (66.67%)
Total	**30 (100%)**	**2 (6.67%)**	**19 (63.33%)**	**9 (30%)**	**0**	**2 (6.67%)**	**13 (43.33%)**	**15 (50%)**

Table 5. Probability and causality based on stage respondent received AC-T

Stage	Number of Respondents	Probability				Causality		
		Possible	Probable	Definite	Unlikely	Possible	Probable	Certain
1	20 (22.22%)	4 (20%)	11 (55%)	5 (25%)	0	4 (20%)	7 (35%)	9 (45%)
2	42 (46.67%)	3 (7.14%)	24 (57.14%)	15 (35.71%)	0	6 (14.29%)	10 (23.81%)	26 (61.90%)
3	27 (30%)	2 (7.41%)	13 (48.15%)	12 (44.44%)	1 (3.70%)	1 (3.70%)	5 (18.52%)	20 (74.07%)
4	1 (1.11%)	0	1 (100%)	0	0	0	1 (100%)	0
Total	**90 (100%)**	**9 (10%)**	**49 (54.44%)**	**32 (35.56%)**	**1 (1.11%)**	**11 (12.22%)**	**23 (25.56%)**	**55 (61.11%)**

Table 6. Probability and Causality Based on Stage Respondent Received AC

Stage	Number of Respondents	Probability				Causality		
		Possible	Probable	Definite	Unlikely	Possible	Probable	Certain
1	4 (13.33%)	1 (25%)	3 (75%)	0	0	1 (25%)	3 (75%)	0
2	18 (60%)	1 (5.56%)	11 (61.11%)	6 (33.33%)	0	1 (5.56%)	7 (38.89%)	10 (55.56%)
3	8 (26.67%)	0	6 (75%)	2 (25%)	0	0	3 (37.50%)	5 (62.50%)
Total	**30 (100%)**	**2 (6.67%)**	**20 (66.67%)**	**8 (26.67%)**	**0**	**2 (6.67%)**	**13 (43.33%)**	**15 (50%)**

Table 7. ADRs Based on CTCAE 5.0

ADRs Experienced	Level CTCAE							
	AC-T				AC			
	Number of Respondents	1	2	3	Number of Respondents	1	2	3
Nausea	**84 (93.33%)**	26 (30.95%)	58 (69.05%)	0	**28 (93.33%)**	6 (78.57%)	22 (21.43%)	0
Vomiting	**38**	38	0	0	**12**	12	0	0

	(42.22%)	(100%)			**(40%)**	(100%)		
Alopecia	**86**	22	64	0	**29**	3	26	0
	(95.56%)	(25.58%)	(74.42%)		**(96.67%)**	(10.34%)	(89.66%)	
Diarrhea	**45**	45	0	0	**13**	13	0	0
	(50%)	(100%)			**(43.33%)**	(100%)		
Constipation	**28**	28	0	0	**7**	7	0	0
	(31.11%)	(100%)			**(23.33)**	(100%)		
Pain	**62**	34	24	4	**22**	11	10	1
	(68.89%)	(54.84%)	(38.71%)	(6.45%)	**(73.33%)**	(50%)	(45.45%)	(4.55%)
Mouth sores	**42**	33	9	0	**13**	9	4	0
	(46.67%)	(78.57%)	(21.43%)		**(43.33%)**	(69.23%)	(30.77%)	
Fever	**32**	31	1	0	**9**	9	0	0
	(35.56%)	(96.88%)	(3.13%)		**(30%)**	(100%)		
Nail discoloration	**12**	12	0	0	**4**	4	0	0
	(13.33%)	(100%)			**(13.33%)**	(100%)		
Anemia	**12**	11	1	0	**3**	3	0	0
	(13.33)	(91.67%)	(8.33%)		**(10%)**	(100%)		
Leukopenia	**11**	7	3	0	**4**	3	1	0
	(12.22%)	(63.64%)	(36.36%)		**(13.33%)**	(75%)	(25%)	
Thrombocytopenia	**3**	2	0	1	**0**	0	0	0
	(3.33%)	(66.67%)		(33.33%)				

The results in Tables 5 and 6 show that the majority of respondents were at stage 2 of breast cancer, both for those receiving AC-T chemotherapy (46.67%) and AC chemotherapy (60%). Chemotherapy is one of the factors that influences success. Patients with lower disease stages have a lower risk of breast cancer recurrence, thus achieving better outcomes with chemotherapy (Wicaksono, 2022). These results indicate that the Naranjo score (which determines the category of ADRs) does not affect cancer staging. This aligns with Belachew et al.'s (2016) research, which indicates a significant influence of age and number of chemotherapy agents on the severity of ADRs, whereas the risk factor of cancer stage does not have a substantial impact on the severity level of ADRs.

CTCAE is a descriptive terminology used to determine the scale of assessment (severity) for reporting adverse events. Grade refers to the severity of adverse events. The CTCAE displays grades 1 through 5, with unique clinical descriptions of the severity of each adverse event. Grade 1, "mild," indicated asymptomatic or mild symptoms, clinical or diagnostic, observation only, and intervention was not indicated. Grade, 2 "moderate," indicated as minimal, and local or noninvasive intervention was indicated. Grade 3 was "severe" or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated a disability. With a grade of 4, life-threatening consequences and urgent interventions were indicated. Grade 5 deaths are related to adverse events (Cancer Institute 2017).

Table 7 shows the patients with breast cancer, including those with nausea, vomiting, alopecia, diarrhea, constipation, pain, mouth sores, fever, nail discoloration, and hematologic disorders (anemia, leukopenia, and thrombocytopenia). According to CTCAE 5.0, the majority of patients experienced ADRs of grades 1 and 2, with the most minor occurrences in grade 3, whereas no patients experienced reactions in grades 4 or 5.

The occurrence of drug reactions based on the Common Terminology Criteria for Adverse Events (CTCAE) (Table 7) revealed that in grade 1 (mild) ADRs, the most commonly experienced was diarrhea, with an increase of <4 stools per day. On average, patients experienced diarrhea approximately 3-5 times per day. These results contrast with those of a study conducted by Van Rossum et al. (2018), who compared toxicity reactions between AC and AC-T chemotherapy regimens, which showed a higher level of anemia and a lower incidence of diarrhea. However, in this study, there was a lower level of anemia and a higher incidence of diarrhea.

The highest grade 2 (moderate) ADRs was associated with alopecia and nausea. Alopecia presented with hair loss of 50% normal for that individual, which was readily apparent to others, whereas nausea was characterized by decreased oral intake without significant weight loss. These results align with those of a study conducted by (Kim et al. 2019), who evaluated the safety of the AC regimen in breast cancer patients, and showed that the most common side effects included nausea, alopecia, general muscle weakness, myalgia, mucositis, anorexia, dyspepsia, and diarrhea.

The most frequently experienced grade 3 ADRs were categorized as severe and limited self-care ADRs. These results align with those of a study by Kang et al. (2021) that evaluated the safety of cyclophosphamide in

anthracycline and taxane-based neoadjuvant chemotherapy in breast cancer patients, indicating that the addition of cyclophosphamide may increase the risk of thrombocytopenia, sensory/motor neuropathy, and nausea/vomiting.

Respondents who received the AC-T chemotherapy regimen experienced more severe grade of ADRs in terms of hematologic disorders, such as anemia (grade 2, 8.33%), leukopenia (36.6%), and thrombocytopenia (grade 3, 33.33%), as well as symptoms of nausea (grade 2, 69.05%), pain (grade 3, 6.45%), and fever (grade 2, 3.13%), compared to respondents who received the AC chemotherapy regimen. However, for ADR grades related to alopecia (grade 2, 89.66%) and mouth sores (grade 2, 30.77%), the respondents who received the AC chemotherapy regimen experienced slightly more severe symptoms than those who received the AC-T regimen.

Chemotherapy-related ADRs affect the quality of life of patients with breast cancer. Quality of life is one of the factors that determine the effectiveness of a chemotherapy regimen. (Oh et al., 2021; Ratna et al., 2021). Hematologic disorder ADRs are one of the most common issues resulting from chemotherapy regimens used in breast cancer treatment. Managing hematologic disorders leads to high treatment costs and increases the economic burden on the patients and their families. The severity of these ADRs is a significant factor in selecting an optimal chemotherapy regimen for patients (Yuniarti et al., 2021). The use of additional medications may also be necessary to manage chemotherapy-induced ADRs. This increases the need for other medications that can pose a risk for drug interactions. Therefore, selecting a chemotherapy regimen with the lowest risk of ADRs is crucial for preventing potential drug interactions (Effendi and Anggun, 2019).

A limitation of this study was that the numbers of respondents who received AC-T and AC chemotherapy regimens were not equal, making comparisons between the two somewhat challenging. This is because the AC-T regimen is more commonly used than the AC regimen at West Nusa Tenggara Provincial Hospital. Future studies are expected to further examine the relationship between ADRs and quality of life, with ADRs potentially serving as determinants of the effectiveness of chemotherapy regimens in breast cancer treatment.

CONCLUSION

Respondents who received the AC-T regimen experienced more severe ADRs in terms of hematologic disorders (anemia, leukopenia, and thrombocytopenia) as well as symptoms of nausea, pain, and fever compared to respondents who received the AC regimen. However, for ADR grades related to symptoms of alopecia and mouth sores, respondents on the AC regimen experienced slightly more severe symptoms than those on the AC-T regimen.

AUTHOR CONTRIBUTIONS

Conceptualization, B.L.P., R.N.M.; Methodology, B.L.P., R.N.M.; Software, B.L.P., R.N.M.; Validation, B.L.P., R.N.M.; Formal Analysis, B.L.P., R.N.M.; Investigation, B.L.P., R.N.M.; Resources, B.L.P., R.N.M.; Data Curration; B.L.P., R.N.M.; Writing - Original Draft, B.L.P., R.N.M.; Writing - Review & Editing, B.N., B.L.N.; Visualization, B.N., B.L.N.; Supervision, B.L.P., R.N.M.; Project Administration, B.L.P., R.N.M.; Funding acquisition, B.L.P., R.N.M.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

REFERENCES

Balai Pengawasan Obat dan Makanan Republik Indonesia. (2020), *Modul Farmakovigilans Dasar*, *Project for Ensuring Drug and Food Safety. Jakarta*, Project for Ensuring Drug and Food Safety :BPOM, Jakarta.

Basuki, A.R., Perwitasari, D.A. and Hardiyanto, H. (2020), "Adverse Drug Reactions (ADRS) Antikanker pada Pasien Ca Mammae yang Menjalani Kemoterapi di RSUD Kota Yogyakarta", *Jurnal Health Sains*, Vol. 1 No. 6, pp. 349–359.

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R.L., Torre, L.A. and Jemal, A. (2018), "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries", *CA: A Cancer Journal for Clinicians*, Wiley Online Library, Vol. 68 No. 6, pp. 394–424.

Effendi, J.A.J. and Anggun, N. (2019), "Studi Efek Samping Penggunaan Obat Kemoterapi Pasien Kanker Payudara (Carcinoma Mammae) di RSUD Kraton Pekalongan", *Pena Medika Jurnal Kesehatan*, Vol. 9 No. 2, pp. 48–54.

Hidayatullah, M.T. (2015), *Profil Adverse Drug Reactions Cisplatin Regimen Kemoterapi Pada Pasien Kanker Servik Di RSUD Prof. Dr. Margono Soekardjo Purwokerto*, Universitas Muhammadiyah Purwokerto, Purwokerto.

Hilli, Y.W. (2017), "Hubungan Karakteristik dan Frekuensi Kemoterapi dengan Tingkat Gangguan Fisik (Alopesia, Nausea dan Vomit) pada Pasien Kanker yang Menjalani Kemoterapi di Ruangan Mutis RSUD Prof. Dr. WZ Johannes Kupang", *CHMK Nursing Scientific Journal*, Vol. 1 No. 2.

Kang, Y.-K., Si, Y.-R., An, G.-Y. and Yuan, P. (2021), "Efficacy and safety of cyclophosphamide in anthracycline-and taxane-based neoadjuvant chemotherapy in breast cancer: a meta-analysis", *Gland Surgery*, Vol. 10 No. 1, p. 252.

Khairani, S., Keban, S.A., and Afrianty, M. (2019), "Evaluation of drug side effects chemotherapy on quality of life (QOL) breast cancer patients at hospital x in Jakarta", *Jurnal Ilmu Kefarmasian Indonesia*, Vol. 17 No. 1, pp. 9–13.

Kim, G.M., Kim, J.H., Kim, J.H., Cho, Y.U., Kim, S. Il, Park, S., Park, H.S., *et al.* (2019), "A phase II study to evaluate the safety and efficacy of pegteograstim in Korean breast cancer patients receiving dose-dense doxorubicin/cyclophosphamide", *Cancer Research and Treatment: Official Journal of Korean Cancer Association*Vol. 51 No. 2, pp. 812–818.

National Cancer Institute. (2017), Common Terminology Criteria for Adverse Events (CTCAE) Common Terminology Criteria for Adverse Events (CTCAE) v5.0.

Oh, H.-J.S., Menéndez, Á.F., Santos, V.S., Martínez, Á.R., Ribeiro, F.F., Vilanova-Trillo, L., Figueiras, M.C., *et al.* (2021), "Evaluating health related quality of life in outpatients receiving anticancer treatment: results from an observational, cross-sectional study", *Health and Quality of Life Outcomes*, Vol. 19 No. 1, pp. 1–8.

Pangribowo, S. (2019), "Beban Kanker di Indonesia", *Pusat Data Dan Informasi Kesehatan Kementerian Kesehatan RI*, pp. 1–16.

Piepoli, M.F., Hoes, A.W., Agewall, S., Albus, C., Brotons, C., Catapano, A.L., Cooney, M.-T., *et al.* (2016), "2016 European Guidelines on cardiovascular disease prevention in clinical practice", *Kardiologia Polska (Polish Heart Journal)*, Vol. 74 No. 9, pp. 821–936.

Prieto-Callejero, B., Rivera, F., Fagundo-Rivera, J., Romero, A., Romero-Martín, M., Gómez-Salgado, J. and Ruiz-Frutos, C. (2020), "Relationship between chemotherapy-induced adverse reactions and health-related quality of life in patients with breast cancer", *Medicine*, Vol. 99 No. 33.

Ratna, R., Supadmi, W. and Yuniarti, E. (2021), "Kualitas Hidup Pasien Kanker Rawat Jalan yang Menjalani Kemoterapi di RSUD Kota Yogyakarta", *Majalah Farmaseutik*, Vol. 17 No. 2, pp. 278–286.

Sukandar, E.Y., Hartini, S. and Rizkita, P. (2014), "Evaluasi Reaksi Obat Merugikan pada Pasien Kemoterapi Kanker Payudara di Salah Satu Rumah Sakit di Bandung (Evaluation of Adverse Effects in Patient with Breast Cancer Chemotherapy at A Hospital in Bandung)", *Jurnal Ilmu Kefarmasian Indonesia*, Vol. 12 No. 2, pp. 183–192.

Syamsuddin, S., Tahir, M.Y. and Plasay, M. (2020), "Hubungan Efek Samping Kemoterapi Dengan Kualitas Hidup Pasien Kanker Payudara di Rumah Sakit Ibnu Sina Makasar", *J. Keperawatan*.

Wahyuni, R.S. (2021), "Hubungan Pengetahuan dan Tindakan Terhadap Deteksi Dini Kanker Payudara Pada Remaja Putri di SMAN 10 Pekanbaru", *Jurnal Kesehatan Medika Udayana*, Vol. 7 No. 02, pp. 104–113.

Wicaksono, A.W. (2022), *Analisis Adverse Drug Reactions (Adrs) Dan Penanganannya Pada Pasien Kanker Payudara Dengan Regimen Paclitaxel-Epirubicindi RSUD Dr. Moewardi Surakarta*, Universitas Muhammadiyah Surakarta, Surakarta.

Wongkar, R., Angka, R.N. and Angeline, R. (2022), "Karakteristik Pasien Kanker Stadium 4 yang Mendapatkan Perawatan Paliatif di Rumah Sakit X", *Jurnal Kedokteran Meditek*, Vol. 28 No. 2, pp. 126–132.

Yuniarti, E., Supadmi, W., Wahyuni, F.A. and Ratna, R. (2021), "Kualitas Hidup Pasien Kanker yang Menjalani Kemoterapi di Rumah Sakit Yogyakarta", *Prosiding University Research Colloquium*, pp. 594–606.