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Characteristics of Chemotherapy Treatments for Breast Cancer Patients at Bhayangkara Tk.1 Pudsdokkes Polri Hospital, Jakarta

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ABSTRACT

Sackground: Breast cancer is a malignant breast tumor that develops in the ductal or lobular epithelium and usually attacks women. Chemotherapy is a cornerstone of breast cancer treatment, particularly for patients with advanced disease or those who are not candidates for surgery or radiation therapy. This research aims to observe the use of chemotherapy drugs for breast cancer patients in terms of chemotherapy regimens and cycles at Bhayangkara Tk.1 Pudsdokkes Polri Hospital.

Methods: This study employs descriptive quantitative approaches. Data were gathered retrospectively from medical records of breast cancer patients receiving chemotherapy at Bhayangkara Tk.1 Pudsdokkes Polri Hospital Jakarta from July to December 2021.

Results: From 110 patients, 86 (78.18%) patients used the CAF regimen, 18 (16.36%) patients used the AC regimen, and 3 (2.73%) patients used the TAC regimen, while the regimen that did not comply with the guidelines was 2 (1.82%) patients using the combination of paclitaxel and epirubicin, 1 patient utilizing the combination of paclitaxel and doxorubicin. Forty-six (41.82%) patients with the CAF regimen had completed six cycles of chemotherapy with intervals of 3 weeks or 21 days, while only 5 patients (3.63%) completed four cycles of the AC regimen at 3-week or 21-day intervals. At the time of data collection, 11 patients, and 1 patient utilizing the AC regimen. This was because 59 patients had not yet finished the chemotherapy cycle, specifically in the advanced stage.

Conclusions: The CAF regimen was the most commonly used chemotherapy regimen, followed by the AC and TAC regimens. This finding aligns with current clinical guidelines for breast cancer treatment. A significant number of patients had not yet completed their chemotherapy cycles, particularly those with advanced-stage breast cancer. This highlights the challenges associated with treating advanced disease and the need for more effective and less toxic treatment options.

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INTRODUCTION

⁵reast cancer is one of the most prevalent cancers in women worldwide. According to the World Health Organization (WHO), 2.3 million women and 685,000 fatalities occurred globally in 2020. Bbhayreast cancer develops in women of all ages after puberty. The day's incidents later became more serious [1]. Breast cancer has the highest rate of new cases, with 2,261,419 (11.7%). Southeast Asia had the highest rate of new cases, with 158,939 (4.46%). Out of 396,914 cases, new breast cancer cases comprised the majority in Indonesia, accounting for 65,858 patients (16.6%). More than 80% of patients in Indonesia have complicated medical needs [2].

Breast cancer is a tumor that mainly develops from the epithelial cells that line the organs and breast tissue and grows uncontrollably in one or both breasts. Allover or partial breast swelling, orange-peel-like skin dimpling, aching breasts or nipples, inverted nipples that turn inward, red, dry, peeling or thicker skin on the nipple, and discharge from the nipple on the outside are common symptoms—swollen lymph nodes under the arms or close to the collarbone and breast milk [3]. Depending on the type of tumor and the severity of the disease, treatment for breast cancer may involve a variety of pharmacological therapies, including systemic chemotherapy, endocrine therapy, or HER2-targeted therapy. The presence of lymph nodes, estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status are indicators of early-stage breast cancer [4].

Chemotherapy is the process of using medications to kill or halt cancer cell growth. Drugs used in systemic chemotherapy enter the bloodstream, circulate throughout the body, and specifically target cancer cells that divide quickly in organs and tissues. Chemotherapy that is administered locally targets the malignancy. Cancer patients frequently get neoadjuvant, adjuvant, and palliative chemotherapy [5]. Chemotherapy is given in stages, often over 6 to 8 cycles rather than straight away, hoping the side effects will be tolerable. According to research by Irawati & Sardjan [6], the chemotherapy drugs most often prescribed for breast cancer are cyclophosphamide, docetaxel, and paclitaxel. The most common drug combination is cyclophosphamidedocetaxel (TdC) and paclitaxel-carboplatin (TpCar).

Based on the description above, the researcher wants to observe the characteristics of breast cancer patients undergoing chemotherapy regarding age, gender, occupation, highest level of education, and stage of cancer, and to describe the use of chemotherapy drugs for breast cancer patients at Bhayangkara Tk.1 Pudsdokkes Polri Hospital Jakarta from July until December 2021.

METHODS

This was a descriptive quantitative study, which focused on observing and numerically analyzing the characteristics of breast cancer patients undergoing chemotherapy without experimental interventions. Data were collected retrospectively from the Medical Records Installation at the hospital between July and December 2021. Purposive sampling was employed in this study to selectively choose participants based on specific criteria, ensuring targeted and relevant sample for the research on the research on the selectively.

The sample population in this study consisted of 134 medical records who were diagnosed with breast cancer between July and December 202. It Bhayangkara Tk.1 Pudsdokkes Polri Hospital Jakarta. Breast cancer patients who met the inclusion criteria and underwent chemotherapy, as determined by the Slovin formula calculation, established the sample size for this study as 110 cancer patients. The patient's inclusion criteria were individuals with breast cancer who were receiving Indonesian National Health Insurance (BPJS Kesehatan) chemotherapy and had positive ER and PR status, ranging in age from 10 to over 60. HER-2-positive breast cancer patient's medical records and those with incomplete medical records fell within the exclusion criteria for this study.

Secondary variables encompassing patient demographics, disease stage, chemotherapy details, and cycles were collected and subjected to descriptive analysis using the Microsoft Excel application. The study's findings were subsequently presented in tabular form, offering insights into the characteristics of the breast cancer patient population under investigation.

RESULTS

Table 1 shows the demographic profile of breast cancer patients at Bhayangkara Tk.1 Pudsdokkes Polri Hospital. Fifty-nine (53.64%) patients were aged 45–59 years, 18 (16.36%) patients were over 60 years old, while 33 (30%) patients were aged 20-44 years. All 110 patients (100%) were female. Among the patients, 89 (80.91%) were housewives, 15 (13.64%) were private employees, 6 (5.45%) were State Civil Apparatus members, and none (0%) were TNI/POLRI members. In terms of education, 59 (53.64%) patients had completed high school, 14 (12.73%) patients had completed a bachelor's degree, 13 (11.82%) patients had completed junior high school, 12 (10.91%) patients had completed elementary school, 7 (6.36%) patients had not attended school, and 5 (4.54%) patients had completed an associate degree. Regarding the stage of cancer, 90 (78.18%) patients were in stage III, 15 (13.63%) patients were in stage IV, 5 (4.55%) patients were in stage II, and none (0%) were in stage I.

The chemotherapy program for breast cancer patients at Bhayangkara Tk.1 Pudsdokkes Polri Hospital follows the vational Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology 2022 and the Ministry of Health 2018 guidelines, as indicated in the research results presented in **Table 2**. Eighty-six 1.8.18%) patients utilized the CAF regimen, 18 (16.36%) patients opted for an AC regimen, and 3 (2.73%) patients underwent a TAC regimen. Regimens not following the guidelines were observed in 1 (1.82%) patients, who received a combination of paclitaxel and epirubicin, 1 (0.91%) patient using a combination of paclitaxel and doxorubicin, and no patients (0%) for the CMF, CEF, and AC-T regimens.

Table 3 presents the research findings on the chemotherapy cycles administered to preast cancer patients at Bhayangkara Tk.1 Pudsdokkes Polri Hospital. Twelve (10.91%) patients underwent cycle 1, 13 (11.82%) patients underwent cycle 3. Additionally, 23 (20.91%) patients completed cycle 4, 4 (3.63%) patients completed cycle 5, and 46 (41.82%) patients completed cycle 6.

Table 1. Patient characteristics

Characteristics	n	%
Age		
10–19	0	0
20–44	33	30
45–59	59	53.64
> 60	18	16.36
Gender		
Female	110	100
Male	0	0
Occupation		
Housewife	89	80.91
Private employees	15	13.64
Civil Servants	6	5.45
Police/TNI members	0	0
Education		
Not at school	11	6.36
Elementary school	12	10.91
Junior High school	13	11.82
Senior High school	59	53.64
Diploma III	5	4.54
Bachelor degree	14	12.73
Stages of Cancer		
I	0	0
II	5	4.55
III	90	81.82
IV	15	13.63

TNI, The Indonesian National Armed Forces

DISCUSSION

Women enter adulthood or their reproductive years typically between the ages of 20 and 44. Research findings indicate that breast cancer occurs 30% of the time during this period. Since this age range falls within a woman's reproductive window, chemical contraception, which increases the risk of breast cancer, might be a contributing factor. Although the risk decreases after discontinuation, women who use oral contraceptives have a slightly higher risk of breast cancer compared to those who never use them [7]. Family history may also play a role; women with one first-degree relative with the disease are 1.75 times more likely to develop breast cancer due to genetic abnormalities in the BRCA1 and BRCA2 breast cancer genes [8].

Ages between 45 and 59 years are pre-elderly; research results show that the incidence of breast cancer is 53.64%, while for those over 60 years or elderly, it is 16.36%. According to the study, patient characteristics Table 2. Chemotherapy characteristics based on regimen

Regimen	n	%
In accordance with the NCCN 2022 guidelines		
CAF	86	78.18
AC	18	16.36
TAC	3	2.73
CMF	0	0
CEF	0	0
AC-T	0	0
Not in accordance with NCCN 2022 guidelines		
PE	2	1.82
PD	1	0.91

CCN, National Comprehensive Cancer Network ¹⁴AF, Cyclophosphamide + Adriamycin (Doxorubicin) + 5-Fluorouracil; AC, Adriamycin (Doxorubicin) + Cyclophosphamide; TAC, Taxane (Docetaxel) + Adriamycin (Ovorubicin); CMF, Cyclophospamide + Methotrexat (Fluorouracil; CEF, Cyclophosphamide + Epirubicin + 5-Fluorouracil AC-T, Adriamycin (Doxorubicin) + Cyclophosphamide + Taxane PE, Paclitaxel + Epirubicin PD, Paclitaxel + Doxorubicin

Table 3. Chemotherapy characteristics based on cycles

Cycle	n	%	Regimen
1	12	10.91	CAF, AC
2	13	11.82	CAF, AC, PE
3	12	10.91	CAF, AC
4	23	20.91	CAF, AC, TAC
5	4	3.63	CAF
6	46	41.82	CAF, PE, PD

NCCN, National Comprehensive Cancer Network

CAF, Cyclophosphamide + Adriamycin (Doxorubicin) + 5-Fluorouracil;

AC, Adriamycin (Doxorubicin) + Cyclophosphamide;

TAC, Taxane (Docetaxel) + Adriamycin (Doxorubicin);

CMF, Cyclophospamide + Methotrexat + 5-Fluorouracil;

CEF, Cyclophosphamide + Epirubicin + 5-Fluorouracil

AC-T, Adriamycin (Doxorubicin) + Cyclophosphamide + Taxane

PE, Paclitaxel + Epirubicin

PD, Paclitaxel + Doxorubicin

were based on age in 28 samples, and the majority were 46-55 years old, namely 11 patients (39.29%) [9]. A possible influencing factor is postmenopausal obesity, which tends to develo cancer. Women with a greater body mass index (BMI) were associated with more aggressive tumor biologic features, including higher lymph node metastasis and larger size. Increased body fat can increase inflammatory conditions and affect circulating hormone levels, increasing pro-carcinogenic activity [10]. 80% of breast cancer patients are over 50 years old. Breast cancer in the elderly is not specific to breast cancer, but accumulation in a large cell cycle and exposure to carcinogens can increase carcinogenesis. Postmenopausal physical activity factors may be associated with a reduced risk of breast cancer, which may prevent cancer and reduce the effects of endogenous sex hormones, alter immune system responses, or alter levels of insulinlike growth factor-1 [10].

According to the study, women comprise 100% of the population. This may be due to the estrogen hormone's ability to increase breast cancer risk in women, particularly during menstruation, pregnancy, and breastfeeding, as well as the presence of numerous estrogen receptors that can promote the growth of breast tissue and bind to cancerous cells, accelerating the development of tumors and cell growth [11]. Lifestyle factors may also increase the risk of breast cancer such as consuming fatty foods and the impact of diet and alcoholic drinks. Rich foods can cause reversible epigenetic changes, leading to oncogenesis. An essential diet can inhibit metabolic processes and signaling pathways, increase blood lipid levels, stimulate inflammation and vascular endothelial dysfunction, and increase abdominal obesity, body weight, and insulin resistance. Alcohol affects the estrogen pathway by activating aromatase and the menstrual cycle by reducing cycle changes and frequency length [12].

According to research by Nuraini et al. [13] the characteristics of patients based on gender were 22 samples, namely male (0%) and female patients (100%) and the lowest gender percentage was male at 0%. A factor that may raise the risk of breast cancer is increased hormone levels. While women's breast cells are susceptible to hormones (mainly estrogen and progesterone) and their balance is upset, men have low estrogen levels. Strong links exist between circulating estrogens and androgens and a higher risk of breast cancer [7].

In accordance with research by Arisanti et al. [9], the characteristics of patients based on work from 28 samples. Homemakers are in first place at 60.71%, and patients in the working category have a health value. The research results show that the highest percentage of work is that of housewives at 80.91% (89 samples) and these are better than patients who are not working is related to guality of life (HRQoL). This most likely occurs because anxiety levels at work can change. After all, interacting with coworkers and others while working helps lower anxiety levels. In contrast, 60% of homemakers are more likely to experience anxiety because they are more concerned with caring for their family and have more time for modest social activities [14,15]. According to the research findings, none of them worked as TNI/ Police officers. Employment status and income or money can be related and influence therapy. Work affects activity and rest levels, affecting a person's degree of stress [16]. Because it lowers hormonal circulation, regular exercise or physical activity can slow the growth process and prevent breast cancer [17].

The study's findings show that 53.64 % of patients with a high school diploma work as housewives and follow the same daily routines, likely leading to sadness and raising the risk of breast cancer. Maintaining a home is a never-ending, exhausting job that can lead to melancholy and perhaps increase the risk of breast cancer [18]. By this study, where the majority of respondents had a high school education (36.4%), there may be no relationship between education and depression or stress because not all patients with low education have low knowledge. The research's findings show that the diploma III degree has the lowest educational percentage (4.54%). This possibility arises because education level influences quality of life (P = 0.05), and high education raises awareness of treatment compliance, resulting in better management of side effects and symptoms [18].

This study shows the highest percentage was stage III (81.82%), in accordance with research conducted by Narisuari & Manuaba [19] that the majority of patients who came for examination were already stage III (64.06%). This possibility occurred because of delays in patient treatment which can be seen from the patient's stage when initially diagnosed. The little information that is known may be one of the reasons why the disease cannot be treated early because no effort is made to find information about breast cancer for fear of the possibility of it happening to her [20-21]. Patients may experience significant psychological strain due to the staging terminology since women with advanced breast cancer may need more treatments than those with earlier stages of the disease, adding to their physical and mental stress [22]. The socioeconomic position and stage of the disease are strongly correlated with the quality of life for women with breast cancer [23].

On the other hand, stage II breast cancer accounts for the lowest percentage of cases (4.55%). This is probably because more people are becoming aware of breast cancer and its early detection methods, such as self- and clinical breast exams [24]. According to the histology, adjuvant chemotherapy can be administered at an early/operable stage (stages I and II) if the tumor is a grade III. Triple Negative Breast Cancer (TNBC), Ki67 is getting more muscular, young age, lymphatic and vascular embolism, or lymph gland more than 3 [2].

The research findings showed that the NCCN 2022 guidelines' CAF chemotherapy regimen was used in 78.18% of cases. Based on Arisanti's [9] research, 28 (100%) patients received the CAF chemotherapy regimen. First-line chemotherapy, the CAF regimen consists of six cycles spaced by three weeks or 21 days [2]. A high likelihood of employing a CAF chemotherapy regimen results from the superiority of doxorubicin + 5-fluorouracil

and cyclophosphamide (CAF) over methotrexate + 5-fluorouracil and cyclophosphamide (CMF) as adjuvant chemotherapy (given after surgery) [25].

The chemotherapy drug cyclophosphamide belongs to the class of alkylating agents whose action is to produce labile alkyl groups that inhibit deoxyribonucleic acid (DNA) replication and transcription [26]. Doxorubicin and epirubicin, two chemotherapy medicines that are members of the anthracycline class, work by forming a compound with DNA and topoisomerase II that causes cell death and prevents the synthesis of DNA and ribonucleic acid (RNA), respectively. Docetaxel and paclitaxel, two chemotherapy medicines in the taxane family, work by stabilizing the fibrous spindle microtubules (which aid in chromosome division and prevent cell division and function) [27]. Because 5-fluorouracil (5-FU) binds to DNA, it inhibits thymidylate synthase (TS), which is necessary for DNA synthesis. This prevents DNA synthesis and repair and alters the nucleotide sequence. The annual likelihood of recurrence was further reduced by 12% when the anthracycline regimen was compared to the CMF regimen (P = 0.006). An additional 11% reduced the yearly mortality event in the anthracycline-containing regimen (P = 0.02). Anthracycline-containing regimens are suggested for individuals with node positivity since a full-dose CAF chemotherapy program is necessary. However, a fourcycle AC treatment produced overall survival and disease-free survival rates comparable to CMF chemotherapy. With a considerable improvement in disease-free survival (DFS) and a marginal improvement in overall survival (OS), the TAC chemotherapy regimen outperformed the CAF regimen in treating axillary lymph node-positive breast cancer [28-30].

The chemotherapy regimen that did not comply with the guidelines in this study was a combination of taxane drugs (paclitaxel) with epirubicin and paclitaxel with doxorubicin. The combination of doxorubicin with paclitaxel is often associated with cardiotoxicity and neurotoxicity. Paclitaxel can increase the regulation of matrix metalloproteinase-3 (MMP3), which is vital in inflammation and damage after nerve injury. At the same time, doxorubicin cardiotoxicity affects oxidative stress arough direct cell damage, induction of apoptosis, and activation of nuclear kappa B (NF-kB), which stimulates production. And nurtures the release of inflammatory mediators [31]. First-line treatment for patients with metastatic breast cancer consists of six cycles of paclitaxel coupled with epirubicin, with a median disease-free survival (DFS) of 9.2 months and a response rate of 42% [32]. The fact that a clinician uses a different guideline regimen than the NCCN, such as the European Society for Medical Oncology (ESMO) Clinical Practice Guideline, a guideline for metastatic breast cancer, does not always suggest that the chemotherapy regimen is incorrect. Axanes and

anthracyclines should be considered, particularly in patients who have not received these medications or those with a DFI 12 months after utilizing these treatments. If they are accessible, protein-bound paclitaxel or liposomal anthracyclines may be used as a second challenge. If a subsequent anthracycline challenge is intended, cardiac monitoring and consideration for lifetime cumulative dose limitations should be taken [33].

According to the research findings, six cycles, or 41.82% of the total, had the most significant proportion. Compliance with treatment for breast cancer patients receiving chemotherapy, such as the desire to recover, carry out daily tasks as before, fight for the family, and pursue unfulfilled aspirations, is a potential influencing factor [34]. According to Juwita et al. [35], 50% of patients underwent the sixth cycle, and the quality of life values in each cycle demonstrated significant differences in each scale (P < 0.05). This possibility is related to patient complaints about treatment in each process, particularly nausea and vomiting, dyspnea, and financial issues. In addition, patients with advanced breast cancer receiving the first chemotherapy cycle may have anxiety due to the adverse effects, making them reluctant to undergo treatment [35]. Factors for non-compliance in breast cancer patients undergoing chemotherapy include the remote location of the hospital, low costs, side effects of chemotherapy drugs, and others [16].

Based on the results of the study, 46 patients completed six cycles of chemotherapy with intervals of 3 weeks or 21 days, consisting of regimens according to the guidelines. Forty-four patients used the CAF regimen and one patien Used the TAC regimen, while the regimen that did not comply with the guidelines was one patient using paclitaxel + epirubicin and one atient using paclitaxel + doxorubicin. Five patients Completed four cycles of the AC regimen at 3-week or 21-day intervals. Based on the research results, 59 patients still had not completed the chemotherapy cycle due to limited research time, so at the time of data collection, 12 patients (10.91%) had just undergone cycle one chemotherapy using the CAF regimen, 11 patients and one patient using the AC regimen. At advanced stages (stages III and IV), this possibility occurs due to the patient's ignorance or delay in realizing the presence of breast cancer [13]. Cycle _ patients using the CAF regimen are planned to underge x cycles of chemotherapy with intervals of 3 weeks or 21 days. Patients with the AC regimen are scheduled to undergo four ycles of chemotherapy with intervals of 3 weeks or 21 days. Meanwhile, 47 other patients are still in the stage of completing the complete cycle; 13 patients have just undergone the 2nd cycle with the CAF, AC, and paclitaxel + epirubicin regimen, 12 patients have undergon the 3rd cycle with the CAF and AC regimen, 18 patients have undergone the 4th cycle with the CAF and AC

regimen. TAC and four patients underwent cycle 5 with the CAF regimen. Patients with the TAC regimen are planned to undergo six chemotherapy cycles with intervals of 3 weeks or 21 days, as are patients with the paclitaxel + epirubicin regimen. The limitation of this research is that the research time is too short, so further research is needed over a more extended period until all breast cancer patients have completed the chemotherapy cycle to determine the level of compliance of breast cancer chemotherapy patients.

The CAF regimen was the most commonly used chemotherapy regimen, followed by the AC and TAC regimens. This finding aligns with current clinical guidelines for breast cancer treatment. A significant number of patients had not yet completed their chemotherapy cycles, particularly those with advancedstage breast cancer. This highlights the challenges associated with treating advanced disease and the need for more effective and less toxic treatment options.

BECLARATIONS

Competing interest

The authors declare no competing interest in this study.

Ethics approval

The study was conducted following the guidelines and regulations set forth by the hospital ethical committee, with the reference number KET/EC.01/I/Lit 6.1/2023/ RS.BHAY.TK.I.

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