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Original Article

Profile of Cytostatic Drug Use in Breast Cancer Patients (Mammae carcinoma) at Medan Hospital

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ABSTRACT

Breast cancer is the most common type of cancer in the world (2,261,419 cases) and in Indonesia (65,858 cases). This research aims to determine the class and type of cytostatic drugs most frequently used in breast cancer chemotherapy patients from January to March 2023 at RSUP Haji Adam Malik Medan. This study used a descriptive survey method with a saturated sample of 176 medical records. Data collection was done retrospectively by gathering information from the electronic medical records of the patients. The research results show that the characteristics of the patients are as follows: the majority were female, totalling 176 patients (100%). The most common age group was 45-54 years, with 111 patients (63.1%), and the prescription of cytostatic drugs was highest in March, with 80 patients (36.9%). In conclusion, the most commonly used class of cytostatic drugs was antibiotics, with 146 cases (32.88%), and the most commonly used type of cytostatic drug was Doxorubicin, with 114 cases (25.68%). This indicates that the use of antibiotics is a significant part of breast cancer treatment, and it is important to pay attention to the safety and regularity of drug use to prevent drug resistance and the severity of the disease.

Keywords: *Cytostatic Drugs, Chemotherapy, Breast Cancer*

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INTRODUCTION

The Minister of Health of the Republic of Indonesia has confirmed a transformation in the health sector and determined that six types of transformation will be carried out, one of which is the Referral Service Transformation. Referral Service Transformation will start with the three highest causes of death in Indonesia, one of which is cancer[1,2]. Cancer is a non-communicable disease characterized by the presence of abnormal cells or tissues that are malignant, grow quickly uncontrollably, and can spread to other parts of the patient's body. Cancer cells can attack and damage normal cells around them and affect the function of these tissues. Cancer can strike anyone, whether male or female, children or the elderly. Many types of cancer attack humans, but there are several types of cancer that often attack certain genders or age groups[3]. Of all the types of cancer that exist, breast cancer occupies the most cases of cancer in the world and also in Indonesia. According to the results of data from Global Burden of Cancer (Globocan), 6%) of a total of 396,914 new cases of cancer in Indonesia[4].

Breast cancer, also known as carcinoma mamae (Ca Mammae), is a type of cancer that

can affect anyone, both women and men. Breast cancer is still a big problem in Indonesia because 68.6% of women with breast cancer go to the doctor at stages IIIA, IIIB, and IIIC, while at an early stage, only 22.4 %[5].

Based on data from WHO, in 2020, 2.3 million women were diagnosed with breast cancer and 685 thousand deaths globally[6]. At the end of 2020, 7.8 million women had been diagnosed with breast cancer in the last five years, making it the most common cancer in the world. Based on data from RISKESDAS, the incidence of tumors/cancer in Indonesia shows an increase from 1.4 per 1000 population in 2013 to 1.79 per 1000 population in 2018. Meanwhile, the incidence of breast cancer in North Sumatra Province also shows an increase of 1.0 per 1000 population per person in 2013 and 1.55 per 1000 population in 2018[7]. There are several types of treatment management for breast cancer patients, one of which is chemotherapy. Chemotherapy is a type of treatment that uses cytostatic drugs with the main goal of destroying malignant tumor cells but also attacking healthy cells. Cytostatic drugs that are often used in chemotherapy are very diverse; some are generic, and some are branded. The type of cytotoxic drug used in chemotherapy depends on the type of cancer the patient is suffering from. In the study of Nuraini et al. 2022 at the Tangerang Regency General Hospital, the results of research that had been conducted on 22 medical record information for breast cancer patients undergoing chemotherapy in 2018 used a single treatment (9%) and a combination treatment (91%), with the results of the evaluation, namely the right drug (100%), the right time of administration (86%) and the right time interval (9%)[8,9]. Meanwhile, in Haryani's study at Fatmawati General Hospital in 2021, the research results obtained that the most used Cytostatic drug regimens were the CAF regimen in 8 patients (23.53%), followed by the Carboplatin and Paclitaxel combination drug regimen in 5 patients (14.71%) and the CEF regimen in 4 patients (11.77%). Drug therapy with the CAF regimen as the standard first-line was mostly used in 8 patients (23.53%) with appropriate doses and a deviation of 1-13% compared to the National Guidelines for Management of Breast Cancer. Regimen therapy that is not in accordance with the National Guidelines for Management of Breast Cancer that is most widely used is the combination of Carboplatin and Paclitaxel in 5 patients (14.71%) with appropriate doses and deviations ranging from 0-79% lower[10]. Acting as the National Oncology Referral Hospital, Haji Adam Malik General Hospital in Medan has opened an Integrated Oncology Service, which has been started since 2014. The CAF regimen was the predominant first-line drug therapy in 8 patients (23.53%), and the doses were generally appropriate with a deviation of 1-13% from the National Guidelines for Breast Cancer Management. The combination of Carboplatin and Paclitaxel was the most frequently used regimen that did not align with the National Guidelines for Breast Cancer Management, with 5 patients (14.71%) receiving appropriate doses but deviations ranging from 0-79% lower. Haji Adam Malik General Hospital in Medan, serving as the National Oncology Referral Hospital, initiated an Integrated Oncology Service in 2014.

Therefore, it is essential to understand the use of cytostatic drugs in cancer patients, particularly in breast cancer cases, at RS Adam Malik. This research is crucial because safe chemotherapy regimens for cancer treatment are of utmost importance. The study aims to identify the classes and types of cytostatic drugs most commonly used in breast cancer chemotherapy patients during the period from January to March 2023 at Haji Adam Malik General Hospital in Medan.

METHOD

This research has gone through the ethical clearence and was declared ethically appropriate with the number 01.1637/KEPK/ Poltekkes Kemenkes Medan. This study used a descriptive survey research type which was conducted at the medical records installation of Haji Adam Malik General Hospital Medan from April to May 2023. Using a saturated sample technique, the entire population prescribed the use of cytostatic drugs in breast cancer chemotherapy patients during the period January to March 2023 in Haji Adam Malik General Hospital in Medan was used as a sample. Data collection was carried out retrospectively by collecting data on the patient's electronic medical records[11] and then analyzed descriptively, which was then presented in the form of frequency distribution tables and pie charts.

RESULTS

Table 1. Characteristics of Patients by Age.

No.	Age (years)	N	%
1.	35-44	21	11,9
2.	45-54	111	63,1
3.	55-64	38	21,6
4.	>64	6	3,4
	Total	176	100

The characteristics of patients based on gender showed 176 patients (100%) were female. Based on Table 1, the characteristics of patients who have breast cancer are predominantly aged 45-54 years (63.1%).

Table 2. Cytostatic Drug Prescription Based on Month of Use

No.	Moon	N	%
1.	January	69	31,8
2.	February	68	31,3
3.	March	80	36,9
	Total	217	100

Table 2 shows the number of breast cancer chemotherapy patients at Haji Adam Malik General Hospital from January to March 2023. Based on the number of cytostatic drug prescriptions, data shows an increase in drug prescriptions in March of 5.6% compared to the previous month.

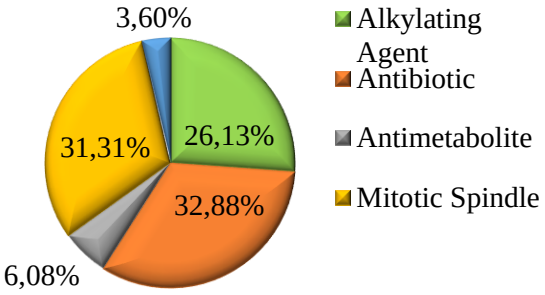

Figure 1. Profile of Cytostatic Drugs Based on Drug Classes

Figure 1 shows that Haji Adam Malik Hospital used five classes of cytostatic drugs to treat breast cancer chemotherapy patients from January to March 2023, namely Alkylating Agents totaling 116 (26.13%), Antibiotics totaling 146 (32.88%), Antimetabolites totaling 27 (6.08%), Mitotic Spindle totaling 139 (31.31%) and Monoclonal Antibodies totaling 16 (3.60%).

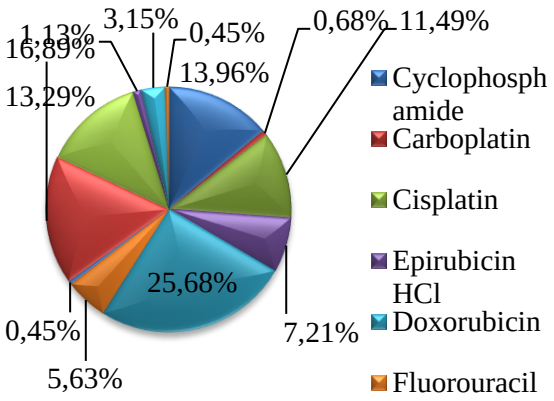

Figure 2. Cytostatic Drug Use Based on Drug Type

The types of cytostatic drugs used by breast cancer chemotherapy patients at Haji Adam Malik General Hospital from January to March 2023, there were 12 types of cytostatic drugs with the five most used, namely Doxorubicin 114 (25.68%), Paclitaxel 75 (16.89%), Cyclophosphamide 62 (13.96%), Docetaxel 59 (13.29%), and Cisplatin 51 (11.49%). A complete profile of the use of medicinal items can be seen in Figure 2 below.

DISCUSSION

Based on the research results obtained, it was shown that all breast cancer chemotherapy patients at Haji Adam Malik General Hospital from January to March 2023 were female. This is in line with research from Nuraini et al. (2022), who obtained research results with patient characteristics based on gender, namely the 100% female category, and in accordance with the theory, which states that women are at greater risk of developing breast cancer than men. One of the causes is the hormone factor that is owned by women, namely the hormones estrogen and progesterone[12,13].

Whereas in terms of age, the average age range is 45-54 years, which indicates that the age group with more cancer is >44 years. The main risk of cancer is increasing age because the functions of organs and cells in the body experience degeneration and long exposure to hormones with age, and breast cancer is more likely to occur in the productive age group and even the elderly. The occurrence of cancer at the age of > 44 years can be caused by long-term use of hormonal contraception, which exposes the body to too much of the

hormone estrogen and turns off the function of estrogen receptors, which will increase the risk of breast cancer[5,14].

There are two ways the hormone estrogen can cause cancer. The former causes breast tissue to undergo more cell division, or mitosis, by acting as a "mitogen." As a result of an increase in cell mitosis and the occurrence of errors in cell division (mutation), which results in cancer. Second, certain estrogen metabolism also acts as a carcinogen that damages DNA directly and causes the formation of cancer cells. This suggests that the hormone estrogen can increase the risk of developing breast cancer[15].

Figure 1 shows that in the treatment of breast cancer, Haji Adam Malik General Hospital uses the most cytostatic drug classes, namely antibiotics, with an amount of 146 or 32.88%. This is different from the research by Elisya et al., which obtained the results of the most widely used class of cytostatic drugs, namely Alkylating Agents because this study used samples of all types of cancer present at the researcher's location[16].

Anticancer antibiotics are one of the most important classes of antibiotics, which have a special inhibitory effect on cancer. *Anti-epithelial-mesenchymal-transition* (EMT) or inhibit the development and spread of cancer cells. In the process of surgical treatment of cancer, in some cases, the cancer cells have spread and entered the blood circulation; surgery can only remove cancer locally, not for cancer cells that have spread to the blood circulation. As a result, cancer surgery is often followed by systemic drug therapy with antibiotics to remove the cancer and minimize the risk of recurrence. However, during the use of antibiotics, bacteria become increasingly resistant to them, which causes antibiotic resistance. Antibiotic resistance can be intrinsic, meaning that the resistance of bacteria to naturally occurring antibiotics is obtained through a process of gene mutation or gene transfer. Therefore, it must be able to regulate the use of antibiotics to reduce bacterial resistance[17].

Whereas for the use of cytostatic drugs based on the type of drug, the most widely used was Doxorubicin, with an amount of 114 or 25.68%. This is in line with Prawira Pramudita's research (2018), which obtained research results that Doxorubicin was the most widely used antibiotic in Dr. Kariadi Semarang[18].

Doxorubicin is the most widely used type of cytostatic drug because it is one of the chemotherapeutic agents in first-line combination chemotherapy. For breast cancer, chemotherapy[19] has a strong cytotoxic effect. To date, Doxorubicin is the most widely used drug in standard chemotherapy regimens and is used to treat various types of cancer and hematology[13,10].

Doxorubicin is part of the anthracycline antibiotic group, which acts as a chemotherapeutic agent by inhibiting DNA and RNA synthesis. Doxorubicin, derived from the bacterium Streptomyces peucetius, has been used extensively as a chemotherapeutic agent since the 1960s. In addition to treating breast cancer, Doxorubicin can also be used to treat ovarian, bladder, and thyroid cancer, acute lymphoblastic leukemia, acute myeloblastic leukemia, Hodgkin's lymphoma, and small cell lung cancer[20].

The dose used for the treatment of breast cancer intravenously is 60 mg/m2 combined with Cyclophosphamide on the first day of every 21-day treatment cycle, for a total of 4 cycles[5,21]. Meanwhile, according to the U.S. Food and Drug Administration 2013, in combination therapy, the dose used is between the range of 40 to 75 mg/m2 given intravenously every 21 to 28 days[21,22]. The results of the study showed that all Doxorubicin uses doses between 57 and 138 mg; this shows that their use exceeds the literature dosage range.

The absorption of Doxorubicin is unstable in stomach acid, which causes the drug to experience little absorption. Therefore, it is administered intravenously, which has a faster absorption[17]. Doxorubicin is distributed into tissues, including the lungs, liver, heart, spleen, and kidney, with a distribution half-life of about 5 minutes and a terminal half-life of 20 to 48 hours. The binding rate of Doxorubicin and its main metabolite to plasma proteins is about 75%. Doxorubicin is detectable in breast milk after administration of 70 mg/m2 over 15 minutes by continuous intravenous infusion[19].

Doxorubicin is metabolized rapidly primarily in the liver by Aldo-keto reductase to the active Doxorubicin (adriamycin) and the inactive aglycones, conjugated sulfates, and glucuronides[5,21].

The plasma clearance rate of Doxorubicin ranges from 324 to 809 mL/min/m2 and is dominated by bile

metabolism and excretion. About 40% of the drug dose will be excreted in the feces within five days, and about 5-12% of the dose will be excreted in the urine with a terminal elimination half-life of 20-48 hours[22].

Doxorubicin's side effects can give your urine, tears, and sweat a reddish color. These effects may begin within the first hours after treatment and can last up to several days. Doxorubicin is also associated with significant cardiac toxicity, which limits long-term use of the drug. Chronic and advanced cardiac toxicity can also occur after administration of Doxorubicin and is the most serious and potentially lethal side effect associated with Doxorubicin therapy[20,22].

CONCLUSIONS

The conclusion from this study was that the most widely used class of cytostatic drugs were antibiotics, with 146 (32.88%), and the types of cytostatic drugs were Doxorubicin, with 114 (25.68%).

It is suggested that future researchers conduct research on the effectiveness and side effects of using cytostatic drugs in outpatient breast cancer patients undergoing chemotherapy at Haji Adam Malik General Hospital Medan.

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CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest in this research.

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