Prescription Patterns of Anticancer Drugs for Breast Cancer in Oncology Unit at a Tertiary Hospital in Oman: A Retrospective Observational Study

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Abstract:

Cancer is a large group of diseases that can begin in practically any organ or tissue of the body and spread to other organs. The latter process is called metastasizing, a leading cause of cancer death. Breast cancer is common cancer in women worldwide. Multiple factors are related to an increased risk of breast cancer, like family history, obesity, processed foods intake, and physical inactivity.

This retrospective cross-sectional study was designed to assess the prescription pattern of anticancer drugs in breast cancer patients in the oncology unit at Sultan Qaboos University Hospital (SQUH). Female patients aged ≥ 18 years diagnosed with breast cancer as the first occurring primary cancer type and received at least one treatment, who were admitted from January 2018 to December 2020 at SQUH constituted the sample.

A total of 191 patients were included in this study. Most patients received an average of 4.73 anticancer drugs. The most commonly prescribed medication was Anthracycline, Cyclophosphamide, and Docetaxel (AC-D) regimen, used in 33.5% of patients. Cyclophosphamide was the most commonly prescribed drug, followed by Doxorubicin and Docetaxel. The total drug expenditure on anticancer therapy in the whole course of therapies was approximately 1.655 million Omani Riyals (OR). Targeted therapy represented three-quarters of the total spending (75%), Whereas Chemotherapy and Hormonal therapy represented one-quarter, 20% and 5%, respectively.

Our study's prescription pattern of anticancer drugs is comparable with previous studies conducted in different countries. Different drug prescription guidelines from one setting to another may contribute to the differences between our study and previous studies. Our findings show how analyzing drug prescription patterns can help institutions manage inventory and use healthcare resources more efficiently.

Keywords:

Anticancer drugs, Breast cancer management, Prescription pattern

Introduction:

Cancer is a group of diseases that can start in almost any organ or tissue of the body and then spread to other organs when aberrant cells proliferate uncontrollably and invade regions and organs adjacent to them. The invasion of aberrant cells into surrounding areas is also called metastasis, a major cause of cancer death. Malignant tumors or neoplasms are other terms used to describe cancer. With 9.6 million fatalities from cancer in 2018, or one in every six deaths, cancer is the second leading cause of death globally [1]. The most common cancer among women globally is breast cancer, and studies have shown that its incidence increases significantly with age [1]. Breast cancer was the fifth most prevalent cause of cancer-related death in women in 2018, accounting for 627,000 fatalities, according to the World Health Organization's International Agency for Research on Cancer (WHO) [2].

In Oman, breast cancer accounts for 32% of all cancer cases among women [3] and is the second leading cause of death in the nation [4]. From 53 reported cases in 1996 to 104 reported cases in 2008, the incidence of breast cancer has grown and is an increasing trend. [5]. Muscat had the highest number of breast cancer cases in 2008 (45/per 100,000), as per the National Cancer Registry of Oman. A breast cancer diagnosis occurs in one out of every five Omani women during their lifetime, with a typical incidence rate of 15.6 cases per 100,000 people [6]. Cancer incidence among Omani females has steadily increased from 58 in 1999 to 147 in 2011 [4].

A higher risk of breast cancer is associated with factors such as family history, obesity, processed food consumption, and physical inactivity, as well as having fewer children, an earlier age at menarche, and a shorter duration of breastfeeding [7-8]. Immunohistochemistry can be used to determine cancer cells' stage and prognosis. The Nottingham prognostic index (NPI) is a commonly used scoring system for breast cancer. NPI accounts for histopathological factors such as tumor size and grade, as well as lymph node spread; it is helpful in detecting the aggressiveness of the cancer as well as monitor its progress and spread. The NPI scoring system takes into account the differentiation, or resemblance, of the cancer cells compared to normal tissue. The scoring system is as follows [9]:

• Grade I - Well differentiated (3-5 points)

• Grade II - Moderately differentiated (6-7 points)

• Grade III - Poorly differentiated (9- points)

Breast cancer progression is impacted heavily by the homeostatic imbalance of hormones such as estrogen and progesterone. Breast cancer cells predominantly express the receptors for those hormones. Human epidermal growth factor receptor 2 (HER2) receptors are also found in many cancer cells. The nature of these receptors determines the success of hormone-targeted therapy. However, a small fraction of breast cancer cells expressing no receptor are triple-negative cancers [10].

Management of breast cancer patients has advanced significantly in recent years, which has significantly benefitted patient care and quality of life. Today, many approaches can be made to treat breast cancer, such as surgery, radiation therapy, chemotherapy, hormonal therapy, and recently targeted therapy [11]. Anticancer treatments have been shown to enhance patients' prognoses, but they are also known to cause toxicity; as a result, it is crucial to use them responsibly. Rational drugs use can be defined as receiving medications at the lowest possible cost, with appropriate dosage regimens given for the indication [11]. On the other hand, irrational drug use can have negative consequences such as ineffective treatment, unnecessary drug prescriptions, the emergency of drug resistance and unfavorable side effects, and an increased financial burden on the hospitals and the patients.

A prescribing pattern is a potential tool for confirming the role of drugs in society. In addition, it significantly helps in healthcare budget-making. Prescribing pattern is a method of analysis of the prescription use of drugs [12]. There is limited evidence in Oman on the anticancer drugs' prescription patterns for breast cancer patients and their clinical outcome. This study will allow us to observe the prescribing patterns and give us insight on the early indicators of irrational drug use, providing intervention tools to improve drug use and realizing continuous treatment quality improvement.

Methods:

Study design

This study is retrospective cross-sectional study. It was conducted on patients admitted at SQUH from January 2018 to December 2020. Female patients diagnosed with breast cancer were identified from the SQUH (TrackCare®) hospital information system (HIS).

Study population

The participants in this study were females under the age of 18 who had been diagnosed with breast cancer as their primary cancer type and had undergone at least one treatment. Patients with breast cancer who were female and under 18 years old were not included.

Data collection

Patient information was extracted from the TrackCare system. Extracted data included the demographic information (age, height, weight, body mass index, menopausal status, pregnancy), patient's comorbidities (HTN, DM, CKD), side of diagnosis with breast cancer, metastatic status, breast cancer stage, breast cancer grade, the hormonal status of the patients, chemotherapeutic regimens, number of drugs, therapies patients received (radiotherapy, surgery, chemotherapy, hormonal therapy, targeted therapy) chemotherapeutic medications (drugs, doses, route of administration, frequency, and cost of treatment), settings of treatments (Neoadjuvant/Adjuvant) outcome of treatment.

Ethical consideration

Ethical approval was obtained by the Medical & Research Ethics Committee (MREC) at the College of Medicine and Health Sciences (CoMHS), Sultan Qaboos University, Muscat, Oman, on 25th July 2021 (MREC #2509).

Statistical analysis

For systematic data sampling and analysis, an excel spreadsheet and the Statistical Package for the Social Sciences program (SPSS, version 26) were employed. The demographic features of the patients, the therapeutic variables, the clinical variables, the research results, and other variables were conveyed using descriptive statistics (i.e., means and frequencies). The total drug spending was calculated as a sum of all drugs prescribed during the study period. The analyzed data were described using the graphical representation tools of the SPSS program, such as bar chart, pie chart, and cross-tabulation, to present the categorized and uncategorized variables.

Results:

Demographics and clinical characteristics:

The records of 321 patients were reviewed in the TrackCare database. Of those, 191 patients met our inclusion criteria. Those that refused any therapy, were diagnosed with another type of cancer, or underwent any therapy in another country were excluded. The patients were between the age range of 26 and 92 years. The majority of patients, 61 (31.9%), were aged between 41 and 50 years, followed by 42 (22%), were aged between 31 and 40 years, and 40 (20.9%) were aged between 51 and 60, as shown in Table 1.

Table 1: Age distribution of breast cancer

Age Groups	Frequency	Percentage
21-30	3	1.6 %
31-40	42	22 %
41-50	61	31.9 %
51-60	40	20.9 %
61-70	24	12.6 %
71-80	12	6.3 %
81-90	8	4.2 %
91-100	1	0.5 %
Total	191	100 %

The patient's demographics and clinical features are displayed in Table 2. The mean age was 51.3 years (± 13.35), mean height was 154.64 cm (±6.99), mean weight was 69.82 kg (± 18.31), mean BMI was 29.15 kg\m2 (±7.46), and mean Ki67 marker was 46.82 (± 26.5). Menopausal status of the patients was found as follows 56.5% (n=108) of patients were in the pre-menopausal stage followed by 39.8% (n=76) in the post-menopausal stage, 3.7% (n=7) in the peri-menopausal stage. 11%(n=21) of patients were pregnant when they were diagnosed with breast cancer. Our findings showed that 18.8% (n=36) of the patients were hypertensive, 16.8% (n=32) were diabetic, and 2.6% (n=5) had chronic kidney disease.

Table 2: Patients' demographics and clinical characteristics

Demographic Factor		Mean ± SD (Range) or No. %
Age (mean, SD)		51.3 years (± 13.35)
Height (mean, SD)		154.64 cm (±6.99)
Weight (mean, SD)		69.82 kg (± 18.31)
BMI (mean, SD)		29.15 kg\m2 (±7.46)
Ki67 marker (mean, SD)		46.82 (± 26.5)
Menopausal status	Pre	56.5% (n=108)
	Peri	3.7% (n=7)
	Post	39.8% (n=76)

Pregnancy	11% (n=21)
Hypertension	18.8% (n=36)
Diabetes	16.8% (n=32)
Chronic kidney disease	2.6% (n=5)

Figure *1* shows that most of the patients had breast cancer in grade 2 (n = 84, 59.57%), followed by grade 3 (n = 53, 37.59%) and grade 1 (n = 4, 2.84%).While, Table *3* describe Breast cancer stage, most common stage patients had is stage IIB (n = 44, 23%), followed by stage IV (n = 43, 22.5%) and stage IIA (n = 27, 14.1%).

Figure 1: Breast cancer grade
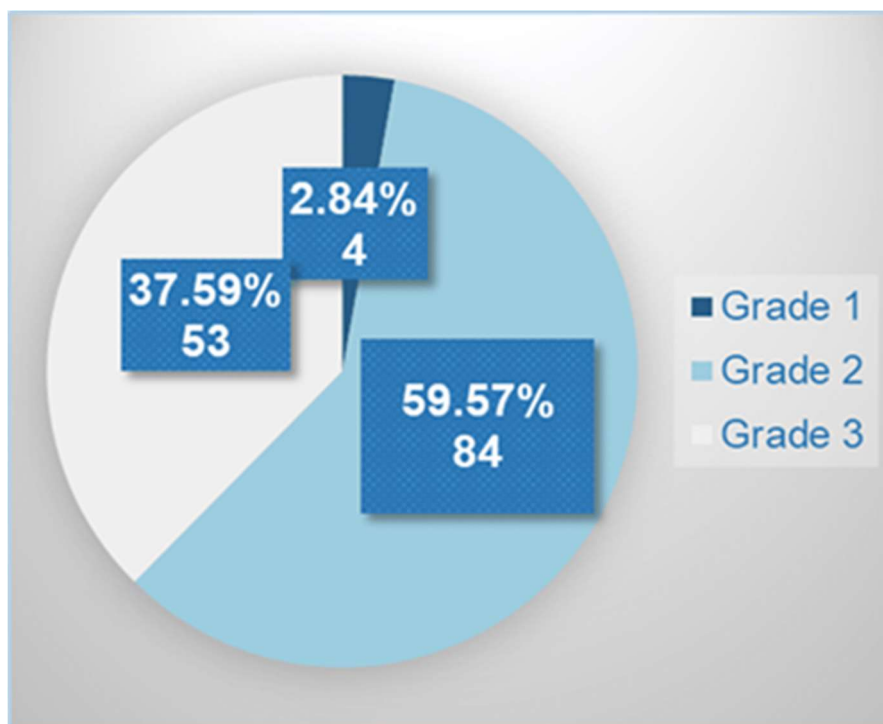
Table 3: Breast cancer stage

Breast cancer stage	Frequency	Percentage
Stage I A	11	5.8%
Stage I B	3	1.6%
Stage II A	27	14.1%
Stage II B	44	23%
Stage III A	24	12.6%
Stage III B	13	6.8%
Stage III C	23	12%
Stage IV	43	22.5%
Not available	3	1.6%
Total	191	100%

The majority (n = 96, 50.3%) of the patients had cancer in the left breast, followed by the right breast (n = 87, 45.5%), and only (n = 8, 4.1%) patients had cancer in both breasts as shown in figure *2*. Looking at the metastatic status, (n = 39, 20.4%) patients had de novo metastatic breast cancer as shown in figure *3*.

Figure 2: Side of diagnosis with breast cancer
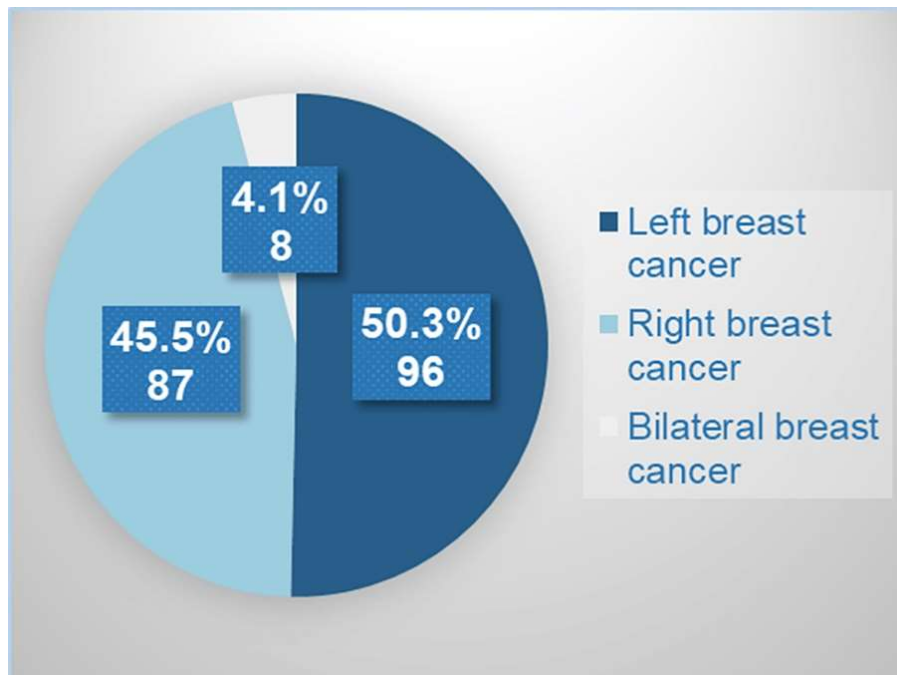
Figure 3: Metastatic status
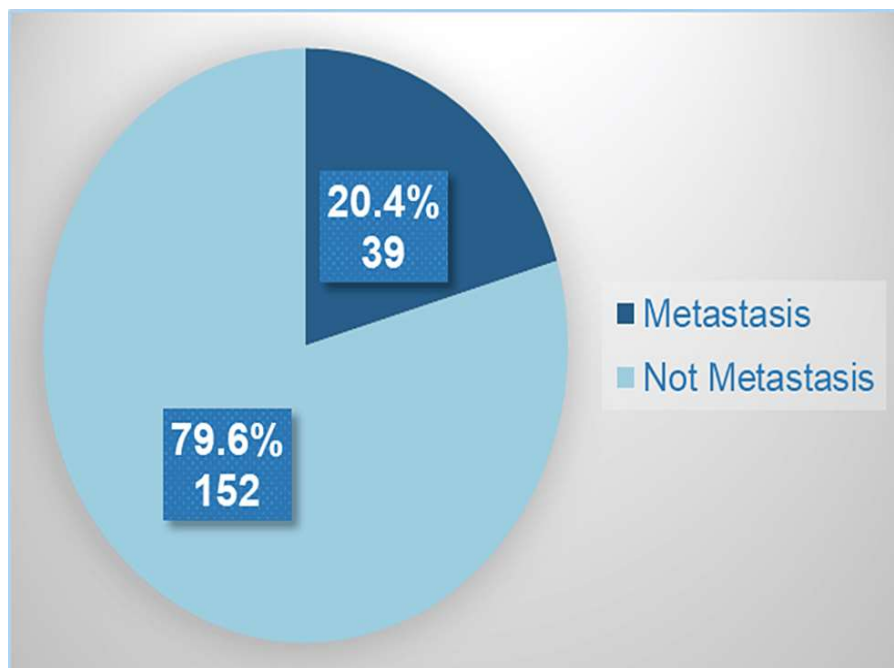
Hormonal status in terms of the presence of hormonal receptors is reported in Figure 4. Most patients (n=127, 66.5%) were found to have estrogen receptors (ERs) followed by progesterone receptors (PRs) (n=112, 58.95%). Both estrogen and progesterone receptor positive breast tumor lesion was found in 108 cases (56.54%). 66 (34.74%) patients were found to be HER2 neu receptor positive. Triple negative was in 35 cases (18.32%), and estrogen, progesterone, and HER2 neu receptor were present in 29 cases (15.18%).

Figure 4: Hormonal status of the patients, Estrogen receptor (ER), progesterone receptor (PR), and HER-2 overexpression status in the study population.
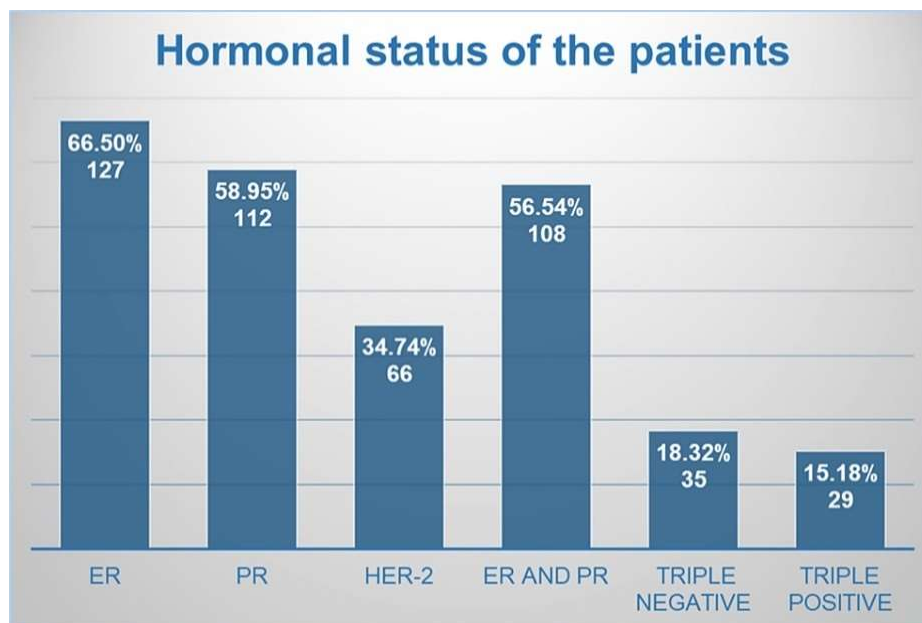
Treatments and therapies:

The average number of anticancer drugs received per patient was 4.73 (±1.78). Majority of patients (84.8% n=162) underwent surgery operation, and (83.2% n=159) of patients underwent Radiotherapy. Settings of treatments were found with almost equal prescribed frequency i.e., 50.3% (n=96) and 49.7% (n=95) of patients were in the neoadjuvant setting and adjuvant setting respectively. The most common therapy prescribed was chemotherapy (89.5% n=171) followed by hormonal therapy (71.2% n=136) and targeted therapy (43.5% n=83) (Table 4).

Table 4: Treatments and therapies

Treatment type	Number and percentage of patients utilizing the treatment
Radiotherapy	83.2% (n=159)
Surgery	84.8% (n=162)
Chemotherapy	89.5% (n=171)
Hormonal therapy	71.2% (n=136)

Targeted therapy		43.5% (n=83)
Number of drugs (mean, SD)		4.73 (±1.78)
Setting of treatments	Neoadjuvant	50.3% (n=96)
	Adjuvant	49.7% (n=95)

The most commonly prescribed regimen, which was used in 33.5%(n=64) of patients, was a combination of anthracycline, Cyclophosphamide and Docetaxel (AC-D) followed by anthracycline, Cyclophosphamide and Paclitaxel (AC-P) 12.6% (n=24), anthracycline, Cyclophosphamide, Docetaxel, Trastuzumab and Paclitaxel (AC-DHP) 12.6% (n=24), anthracycline, Cyclophosphamide, Docetaxel and Trastuzumab (AC-DH) 7.8% (n=15), Fluorouracil, Epirubicin, Cyclophosphamide and Docetaxel (FEC-D) 2.6% (n=5) (Figure 5).

Figure 5: Various anticancer regimens used in breast cancer patients. A, anthracycline; C, Cyclophosphamide; D, Docetaxel; P, Paclitaxel; H, Trastuzumab; F, Fluorouracil; E, Epirubicin
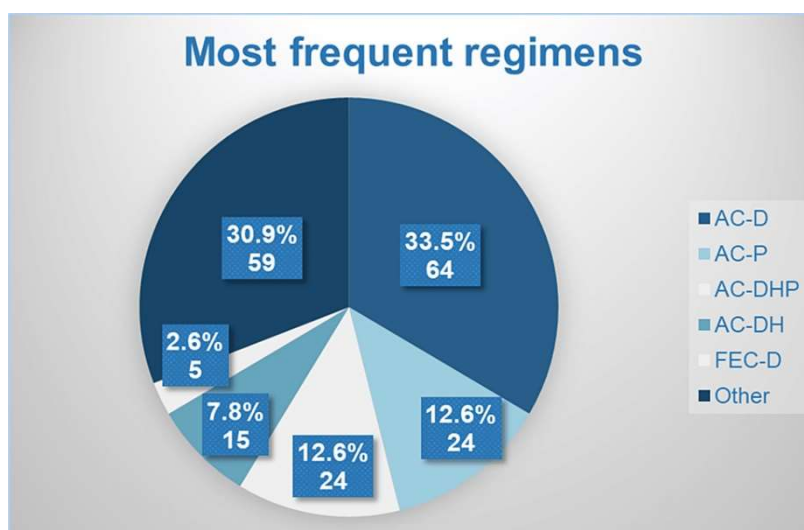
Breast cancer treatment outcomes according to recist criteria were recorded, and the results are shown in Figure 6. A total of 14.1%(n=27) of the included patients showed complete response, 19.9% (n=38) showed partial response, 9.9% (n=19) showed stable disease, 18.3% (n=35) showed progressive disease.

Figure 6: Breast cancer treatment outcomes according to Recist Criteria CR, Complete Response; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease; NA, not available
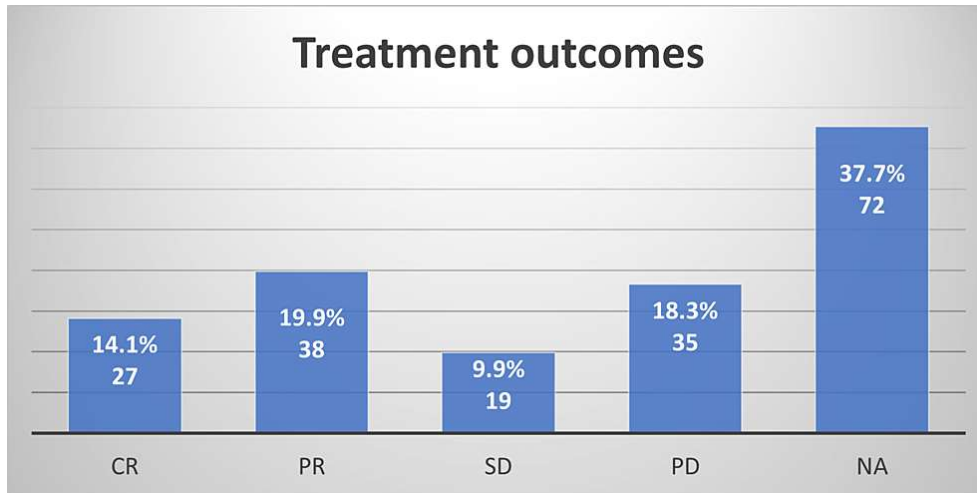
Drug Expenditure:

Our study indicates that the drug expenditure on anticancer therapy in whole course of therapies was approximately 1.655 million Omani Riyals. Cyclophosphamide was the most commonly used drug in Chemotherapy and all therapies, with 78.5% of the patients receiving Cyclophosphamide followed by Doxorubicin (72.3%) and Docetaxel (68.6%). Tamoxifen and Trastuzumab were the most prescribed drugs in hormonal and targeted therapies, respectively. Targeted therapy costed the most (75.5%), followed by chemotherapy (19.6%) and hormonal therapy (4.9%). (Figure 7)

Figure 7: Anticancer medication spending by group (total spending 1655377.95 OR \ Average spending 8666.9 OR per/ patient)
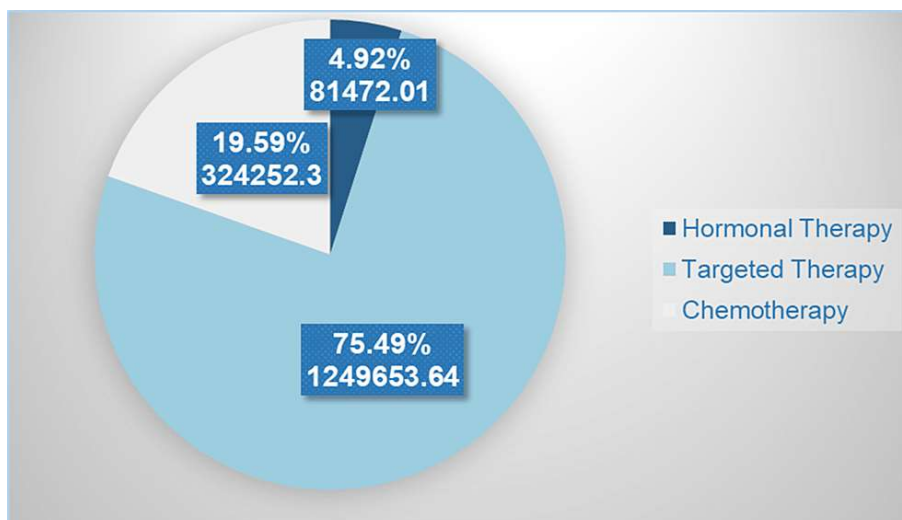
Discussion:

Breast cancer is a significant cause of mortalities and accounts for a significant portion of healthcare expenditure [13]. Age is directly correlated with the incidence of breast cancer. [14]. In this study, the average age of the sample was 51.3 years, which is higher than what was reported in other similar studies [15, 16]. The majority of the participants had stage 2 or stage 3 breast cancer, indicating a late diagnosis. Progesterone receptor (PR) and estrogen receptor (ER) positivity was found in 59% and 67% of the patients, respectively, while 35% of the patients had an overexpression of HER-2. In comparison to a similar study from Saudi Arabia, the PR and ER were positive among 67% and 80% of patients. Furthermore, HER-2 was overexpressed in 31% of the patients in that study [17]. The treatment of breast cancer patients requires an extensive utilization of medications and resources. Irrational drug prescription is widespread in healthcare systems, resulting in an increase in costs of treatment as well as poor patient outcomes. WHO encourages drug prescription studies in all healthcare systems to assess and ensure rational drug use [18].

The average number of anticancer drugs prescribed per patient in the current study was 4.73, which was more than the three-medication average in the study from Saudi Arabia. [17]. Our study's most frequently used regimen was AC-D, which differs from a study conducted in India, which was the AC regimen [19]. Chemotherapy was the most frequently utilized treatment regimen in our study, with the most popular anticancer medications being cyclophosphamide (78.5%), doxorubicin (72.3%), and docetaxel (68.6%). Various studies showed varying patterns of anticancer drug prescribing. Docetaxel, followed by Cyclophosphamide, 5-Fluorouracil, and Epirubicin, has been reported in a study from Saudi Arabia as the most prescribed anticancer drugs [17]. Cisplatin, followed by 5-fluorouracil, have been reported as the most utilized anticancer drugs in two studies [15, 16]. Another study showed that carboplatin followed by paclitaxel was the most prescribed regimen [20]. The user management guidelines, cancer stage, and patient status are all factors contributing to the variation in drug prescriptions among the different studies.

The increased prevalence of cancer is linked to an increase in overall healthcare costs. Cancer patients in Omani public hospitals are treated for free by the Omani government. Thus, expenditure analysis is in high demand to ensure that the budget is used effectively. The expenditure on anticancer drugs in the whole course of therapies on patients admitted from January 2018 to December 2020 was approximately 1.655 million Omani Riyals. Targeted therapy accounted for 75% of overall spending in this study, compared to earlier studies where the cost distribution among other anticancer medications was more variable [18]. Trastuzumab had the highest drug cost, where it alone accounted for 41.7% of the total cost. Chemotherapy and Hormonal therapy represented one-quarter of 20% and 5%, respectively. That is different from previous studies [21]. There may be discrepancies between local and global cost distribution of international medications depending on the population, product accessibility, availability of biosimilars and generics, and clinical guidelines [21].

Drug prescription pattern review and cost distribution analysis for anticancer drugs are essential among healthcare professionals as it highlights the importance of assessing optimal drug use with cost-effectiveness. This study provided breast cancer patients' demographic data, most commonly prescribed anticancer drugs and regimens, and estimated total drug expenditure on anticancer therapies.

Some limitations we encountered while conducting this study included the small sample size and missing data from the electronic records. Moreover, this was a retrospective study conducted in a single center so the generalizability of this study to other institutes may be affected.

Conclusion:

To conclude, AC-D was the most common regimen received by breast cancer patients in this study. The most common drug prescribed is Cyclophosphamide, followed by Doxorubicin and Docetaxel. Approximately 1.655 million Omani Riyals was spent on anticancer therapy. Our study's prescription pattern of anticancer drugs is comparable with previous studies conducted in different countries. We discovered many similarities and differences when we compared our findings to previous studies. Different drug prescription guidelines from one setting to another may contribute to the differences between our study and previous studies.

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