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Original Research Article

# Drug Utilization Evaluation in Breast Cancer Patients in a Tertiary Cancer Hospital: A Descriptive Observational Study

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**Abstract:**

**Introduction:** Evaluating the prescribing patterns of anticancer and supportive care drugs in cancer breast patients is necessary for ensuring effectiveness and patient's quality of life. This study aims to evaluate the prescribing patterns in patients receiving chemotherapy.

**Methods:** A prospective observational study was conducted in the Department of Medical Oncology at Assam cancer care Hospital, Diphu center. The study was conducted from January 2021 to August 2023. Cancer breast patients who are on chemotherapy for ca breast along with supportive care medications were enrolled. Data were analyzed using descriptive statistics. Continuous data were expressed as mean ± standard deviation, and the nominal data were expressed as frequency and percentages.

**Results:** Among 37 patients, majority of patients were in the age group of 31-45 years. Only two were males and rest were females. Single regimen (57%) was the most commonly prescribed chemotherapy followed by multiple drug regimens (43%). Most common being 34encounters of Adriamycin with cyclophosphamide were seen followed by Epirubicin with cyclophosphamide and triple combination of docetaxel, cyclophosphamide with transtuzumab. The percentage of drugs prescribed from the National List Essential Medicine and the World Health Organization (WHO) model list was 74% and 70%, respectively.

**Conclusion:** Various anticancer drug prescription patterns are being used for treatment of patient with metastatic cancers. In this study, Adriamycin with cyclophosphamide was commonly used. Injudicious antibiotic prescribing was not observed. The percentage of drugs prescribed fromlist of essential drugs may be improved. Polypharmacy was not observed. Drug utilization review should be conducted periodically to minimize the untoward effects at least to some extent.

**Keywords:** Cancer breast, chemotherapy, prescribing patterns, World Health Organization.



## Introduction

Cancer is a group of disease, involving uncontrolled multiplication and spreading of abnormal forms of one's own body cells.[1] Mainly, there are two approaches for cancer treatment: local treatment approaches that include surgery and radiation and systemic treatment approaches that include development of drug-resistant cells to kill total tumor cells.[1] The chemotherapy-induced adverse effects may be uncomfortable; temporary or life-threatening adverse effects lead to reduction of doses of anticancer drugs, addition of supportive care drugs.[2] Chemotherapy is a treatment option for majority of cancers. In chemotherapy, drugs are used to destroy cancer cells. There are different types of chemotherapy that includes adjuvant chemotherapy, neoadjuvant chemotherapy, induction chemotherapy, consolidation therapy, maintenance therapy, and palliative chemotherapy. In olden days, cancers were treated with single drug; but, nowadays, combination of drugs are given to overcome the cancer cell heterogeneity and development of drug-resistant cells to kill total tumor cells.[1] Cancer supportive care involves the management of signs and symptoms or the management of chemotherapy-induced adverse effects.[3] This necessitates careful observation and evaluation of cancer chemotherapy, which in turn will help to optimize anticancer therapy with minimal toxicity and improved efficacy. While cardiovascular disease remains the leading cause of deaths world-wide, cancer has emerged as the

second most common cause of morbidity and mortality, especially in developing countries. In 2020, cancer incidence projections in India reflected higher rates among females than males. Geographically, the highest registrations for cancer cases were recorded in Chennai among women.

Breast cancer is the commonest malignancy among women globally. From being fourth in the list of most common cancers in India during the 1990s, it has now become the first. Breast cancers are clonal proliferations that arise from ductal or lobular breast cells with multiple genetic aberrations. This process is influenced by hormonal exposure, inherited susceptibility of genes, and environmental factors or their interplay [3]. The most common cancer in India is breast cancer (14% of the total cases) and it is one ofthe leading causes of cancer deaths (11.1% of the total cases) [4]. The treatment modalities for breast cancer are surgery, radiotherapy, and chemotherapy: selection of which depends on tumor size, number of lymph node involvement, and overall health of the patient [5].

Decision about optimal treatment pattern for breast cancer depends on trial data of efficacy and safety of chemo therapeutic agent, along with women's treatment preferences and socio-economic status [6].

While effectiveness and safety of breast cancer therapies are thoroughly studied in randomized clinical trials, only few data are available for the same in daily practice settings. Furthermore, some serious adverse drug reactions are only identified after cancer chemotherapy drugs have widely been used in clinical practice, which may be missed in clinical trial set-up [7]. Drug utilization research is defined as the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences, which provides very useful information regarding drug use pattern, rationality of drug usage, intervention to improve drug use, and quality control of drug use [8]. Systemic chemotherapy is being used extensively in breast cancer management, so it is important to know the utilization pattern of these agents in tertiary care hospitals. Prescribing pattern is an important tool in ascertaining the role of drugs. Prescription pattern is a process of analyzing the usage of drugs prescribed. Therefore, evaluating and monitoring the prescription patterns of anticancer drugs and supportive care drugs are necessary.

The World Health Organization (WHO) developed core prescribing indicators which are meant to measure the characteristics related to polypharmacy, antibiotic use, drugs prescribed from WHO model list of essential medicines, and the National List Essential Medicine (NLEM)[9].

## Methods

### Materials and Methods

The data was collected in regard to age, sex, stage of the disease, family history, any co-morbid condition etc. WHO core prescribing indicators will be used at the end of the study to know the amount of prescriptions with polypharmacy, percent of prescriptions with injectable, antibiotics and percent of drugs prescribed from Essential Drugs list.

This study was done at Assam cancer care Hospital, Diphu center. This study was done as a retrospective record based, cross sectional study among patients who have diagnosed for Ca Breast and treated for the same. The study was conducted from January 2021 to August 2023. Data was collected of all Ca Breast patients admitted during the period of study irrespective of age and sex. Data will be collected from medical records department and telephonic interview wherever required.

Diagnosed cases of Ca breast irrespective of age and sex were included in the study while cases with inadequate data were excluded. Data analysis was done by putting in the data in specially designed MS excel sheet and the output was analyzed using statistical software SPSS version 24.0. Ethical approval was taken prior to the study from institutional ethical committee, Diphu Medical College & Hospital

### Data Analysis

Prescribing patterns of chemotherapy were analyzed by collecting the details of drug usage including drug name, dose, indication, dosage form, and frequency, and duration, route of administration, chemotherapy cycles, and chemotherapy regimens and were recorded in the data collection form.

Similarly, prescribing pattern of supportive drugs used along with cancer chemotherapy was also recorded from the drug treatment chart and convened in the data collection form.

### Assessment of World Health Organization core drug prescribing indicators [10]

The following formulae were used for the assessment of the WHO core drug prescribing indicators:

The average number of cytotoxic drugs prescribed = Total number of cytotoxic drugs prescribed/total number of patients.

The average number of drugs prescribed = Total number of drugs prescribed/total number of patients.

- Percentage of drugs prescribed by generic name = (Number of drugs prescribed by generic name/total number of drugs prescribed) × 100.
- Percentage of encounters with injection prescribed = (Number of patients prescribed with injection/total number of patients) × 100.
- Percentage of encounters with a cytotoxic injection prescribed = (Number of patients prescribed with a cytotoxic injections/total number of patients) × 100.
- Percentage of encounters with antibiotic prescribed = (Number of patients prescribed with antibiotic/total number of patients) × 100.
- Percentage of drugs prescribed from NLEM = (Number of drugs prescribed from NLEM/total number of drugs prescribed) × 100.
- Percentage of drugs prescribed from WHO model list of essential medicines = (Number of drugs prescribed from WHO model list/total number of drugs prescribed) × 100.

**Results**

A total of 37 patients with breast cancer were enrolled in the study. Out of which, all the patients underwent multiple cycles of chemotherapy without any dropouts. A total of 274 encounters was there in our study population. In the age wise distribution, majority of patients were in 30-45 years (51%) followed by 45 to 60 years with 15 patients (40%) compared to the other age groups. The mean age of the study population was 49.86 ± 11.56 years. In gender wise distribution, majority of the patients were females (94.5%) when compared to males which is a well-known factor in case of cancer breast. Out of 37 patients, 18 patients had social habits, of which, majority of them were alcoholic (12.1%) followed by substance abuse (11.7%).

In our study 17 patients had some sort of co morbidities with hypertension being commonest followed by diabetes and was on treatment for that. In our study premenopausal cases were 15 and 20 were postmenopausal cases. Only two patients had family history of breast cancer in our study. Majority of the cancer patients was diagnosed with Stage IV (n=17), followed by Stage III (n=11).

In our study population of 37 patients, ER positive and PR positive were 20 patients each. Her2neu positive was seen in 11 cases. Triple positive was seen in 6 cases and triple negative in 8 cases.

**Table 1: General characteristics**

| | No Of Patients (N=37) |
|---|---|
| Gender | |
| Male | 2 |
| Female | 35 |
| Age Distribution | |
| <30 | 0 |
| 30-45 | 19 |
| 45-60 | 15 |
| 60-75 | 2 |
| >75 | 1 |
| Comorbidities | |
| Hypertension | 10 |
| Diabetes Mellitus | 7 |
| Asthma | 0 |
| CLD | 1 |
| IHD | 1 |
| Thyroid Disorder | 2 |
| CKD | 0 |
| No Comorbidities | 20 |
| Social Habits | |
| Smoking | 2 |
| Alcohol | 10 |
| Substance Abuse | 11 |
| Both Alcoholic and Smoker | 2 |
| Alcoholic, Smoker, And Substance Use | 2 |
| No Social Habits | 19 |
| Cancer Stages | |
| Stage I | 0 |

| | |
|---|---|
| Stage II | 9 |
| Stage III | 11 |
| Stage IV | 17 |
| Family History of CA Breast | |
| Present | 2 |
| Absent | 35 |

In our study population 8 encounters had palliative therapy,20 encounters had adjuvant therapy 10 was hormonal, 11 was NACT and 7 encounters was for maintainence therapy which sometimes had more than one cycle of encounter depending upon clinical presentation. In our study population few had adverse effects Peripheral neuropathy was seen in one patient, Hand and foot syndrome in four patients. Neutropenia in 5 patients and drug induced hepatitis in four patients. In spite of administration of antiemetic prophylactically one patient had the episode. Among a total of 274 encounters, Single regimen (57%) was the most commonly prescribed chemotherapy followed by multiple drug regimens (43%). Most common being 34 encounters of Adriamycin with cyclophosphamide were seen followed by epirubicin with cyclophosphamide and triple combination of docetaxel, cyclophosphamide with transtuzumab.

Among Single drug regimens most commonly used was Paclitaxel and tranztuzumab had maximum encounters followed by capcetabine. The most commonly prescribed chemotherapy regimens among different cancer types are described in Table 2.

**Table 2: Type of Chemotherapy regimens**

| **Chemotherapy Regimen** | |
|---|---|
| Docetaxel+Cyclophosphamide | 18 |
| Paclitaxel+Carboplatin | 7 |
| Gemcitabine + Carboplatin | 11 |
| Eribulin Mesylate | 8 |
| Epirubicin+Cyclophosphamide | 32 |
| Paclitaxel Only | 30 |
| Tamoxifen | 6 |
| Docataxel Only | 8 |
| Docetaxel+Cyclophosphamide+Tranztuzumab | 22 |
| Paclitaxel+Tranztuzumab | 20 |
| Tranztuzumab Only | 55 |
| Anastrazole | 8 |
| Capecitabine | 20 |
| Lapatinib | 2 |
| Adriamycin + Cyclophosphamide | 34 |
| Gemcitabine + Docetaxel | 1 |
| Gemcitabine | 1 |
| Trastuzumab + Letrozole | 3 |
| Capecitabine+Lapatinib | 2 |

Almost all patients received dexamethasone and the commonly prescribed antiemetic's were palonosetron (81.3%) followed by ondansetron (66.5%) Out of 274 encounters, only 3 were prescribed with antibiotics to treat infections. Similarly, almost all the patients had an encounter with ranitidine. Majority of the patients were prescribed with proton pump inhibitors with or without domperidone. Only few patients required analgesics with paracetamol being commonly used.

In this study, 168 among 274 encounters were prescribed with granulocyte-colony stimulating factors for prophylaxis and treatment of chemotherapy-induced myelosuppression. Antihistamines were prescribed for majority of the patients in all cycles of chemotherapy. The most commonly prescribed supportive care medications are depicted in Table 3.

**Table 3: Supportive care medicine**

| **Other Drugs** | **Number Of Patients Or Encounters** |
|---|---|
| Netupitan + Palonosertron/ Aprepetant/ Granisatron/ Ondensatron/ Fossaaprepitant | 203 |
| Dexamethasone | 189 |
| Ranitidine | 189 |

| | |
|---|---|
| Pheniramine | 161 |
| Domperidone | 106 |
| Ppi | 146 |
| Paracetamol | 116 |
| G-Csf | 168 |
| Lactulose | 81 |
| Olanzapine | 7 |
| Morphine | 4 |
| Zoledronic Acid | 4 |
| Pregabalin | 16 |
| Chlorhexidine M/W | 45 |
| Antibiotics | 3 |
| Acetaminophen + Tramadol | 9 |

As per the WHO core drug prescribing indicators, we calculated the percentages for 274 encounters over all cycles. The average number of drugs per prescription was 7.85%. The percentage of antibiotics prescribed was 1.05%. The percentage of drugs prescribed from the NLEM and theWHO model list of essential medicines was 74% and 70%, respectively.

Most importantly the number cytotoxic drugs prescribed was 1.193 per prescription among which 68.07% was injectable. The detailed WHO core drug prescribing indicators results are described in Table 4.

**Table 4: WHO core prescribing indicators**

| WHO core drug prescribing indicators | All cycles |
|---|---|
| Average number of cytotoxic drugs per prescription | 1.193 |
| Average number of drugs per prescription | 7.85 |
| Percentage of encounters with an antibiotic prescribed | 1.05 |
| Percentage of encounters with an cytotoxic injectable prescribed | 68.07 |
| Percentage of encounters with an injectable prescribed | 86.66 |
| Percentage of drugs prescribed from NLEM | 74 |
| Percentage of drugs prescribed from WHO model list of essential medicines | 70 |
| Percentage of drugs prescribed by generic name | 98 |

## Discussion

Alteration in chemotherapy regimen and supportive care medications is based on the variability of patients, demographic details, cancer types, and stages of cancer and depends on the expected toxicities, so it is necessary to evaluate the prescribing patterns of anticancer and supportive care drugs in breast cancer patients. This study was undertaken in 37 patients with 274 encounters.

In this study, most of the patients were in the age group of 30-45 years followed by 45 to 60 years; this was in correspondence with the study carried out by Catic et al. [11] where 48% of patients were in the age group of 45–60 years. However, contradictory findings were also observed in a study conducted by Onwusah and Korubo[12] where 19.6% patients were in the age group of 61–70 years. Out of 37 patients, except two all were femal as expected as our cases were breast cancer. Breast cancer in male is a rare malignancy with an estimated incidence rate of 0.5–1 % of all breast cancer cases.

In the present study, majority of the patients were in Stage IV of cancer followed by Stage III (26.5%). Ramalakshmi et al.[13] reported that majority of the cancer patients were in Stage III of cancer (68%) followed by Stage II (22%). The present study findings are in contradictory to above where most of the patients presented with Stage III of cancer.

In the present study, most common chemotherapy drug being 34 encounters of Adriamycin with cyclophosphamide was seen followed by epirubicin with cyclophosphamide and triple combination of docetaxel, cyclophosphamide with transtuzumab. Among Single drug regimens most commonly used was Paclitaxel and tranztuzumab had maximum encounters followed by capcetabine. A study conducted by Pentareddy et al. [14] reported that among the commonly prescribed double therapy, doxorubicin and cyclophosphamide (51.72%) was mostly prescribed in breast cancer followed by paclitaxel and carboplatin prescribed in esophagus (50%). This study was in contrast with the previous study where double regimen is commonly prescribed. Almost all patients received dexamethasone and the commonly prescribed antiemetic's were palonosetron (81.3%) followed by ondansetron (66.5%). which was in concurrence with the study conducted by Ramalakshmi et al.,[13] where the majority of patients received

dexamethasone and palonosetron (100%), respectively, followed by aprepitant (8%) and ondansetron (2%).

Out of 274 encounters, only 3 were prescribed with antibiotics to treat infections. Similarly, almost all the patients had an encounter with ranitidine. Majority of the patients were prescribed with proton pump inhibitors with or without domperidone. Ramalakshmi et al., [13] stated that all the patients received pantoprazole and sucralfate (100%) followed by laxatives (30%). Only few patients required analgesics with paracetamol being commonly used. These findings are similar with the study carried out by Ramalakshmi et al,[13] where paracetamol (62%) was mostly prescribed followed by aspirin (20%).

The average number of medications per prescription in the study was 7.85. A study conducted by Mugada et al. [15] reported that the average number of medications per prescription was 8.16 which is similar to the present study since it involves adjuvant therapies such as antiemetics, analgesics, and gastrointestinal agents for the prevention and management of expected adverse events.

In the present study, among all four cycles of chemotherapy, the percentage of antibiotics prescribed was 1.05%, and in the study conducted by Mugada et al.,[15] the percentage of antibiotics prescribed was 54.8% which is contrary to our study. It might be prescribed only for specific infections in our study.

The percentage of cytotoxic injections and percentage of other injections prescribed.

were 68.07% and 86.66% respectively. A study conducted by Mugada et al. [15] reported that the cytotoxic injections prescribed were 100% and the other injections were 75.5%, which is greater because the premedication given along with the cytotoxic drugs is prescribed in injectable form.

The percentage of drugs prescribed from the NLEM, and the WHO model list was 74% and 70%, respectively, which resembles the study conducted by Mugada et al.,[15] where the percentage of drugs prescribed from the WHO model list was 80.70% while the NLEM was contrary to the study since EDL was calculated. The percentage of the drugs prescribed was finite since drugs were given to a particular patient based on their risk– benefit ratio and for specific infections; so, there will be difference in percentage of drugs prescribed from the WHO and the NLEM.

## Conclusion

Various anticancer drug prescription patterns are being used for treatment of patient with metastatic cancers. In this study, Adriamycin with cyclophosphamide was commonly used. Injudicious antibiotic prescribing was not observed. The percentage of drugs prescribed from list of essential drugs may be improved. Polypharmacy was not observed. Drug utilization review should be conducted periodically to minimize the untoward effects at least to some extent.

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