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**Original Article**

# Pattern Of Chemotherapeutic Practice And Their Adverse Effects In Breast Carcinoma Patients Attending Two Public Tertiary Care Hospitals In Dhaka City

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**Abstract**

**Background:** Cancer is a group of diseases with creation of abnormal cells which can invade adjoining parts of the body and spread to other organs. Breast cancer topped the list of the women affected with various types of cancers in Bangladesh. It alone accounts for 25% of all cancer cases and 15% of all cancer deaths among females. The present study was done to evaluate the pattern of drug management, their adverse effects and socio demographic characteristics of the patients of breast carcinoma admitted and getting chemotherapy in two tertiary hospitals of Bangladesh.

**Materials and Methods:** It was a cross sectional observational study carried out from January to December 2015 at DMCH & NICRH. During this period, 102 patients were studied in purposive sampling technique by using a set of pre-tested structured questionnaire. Data analysis was done using SPSS version 21.

**Result:** Most of the patients were in 4$^{th}$ decade (34.9%), came from low (59.6%) or middle (39.4 %) income family, were married (89.9 %), had one child (40.19 %). The mean duration of treatment for cancer was found 9.35±5.17 months. Cyclophosphamide (57.8%) and Doxorubicin (55.9%) were the most frequently prescribed drugs. Other drugs frequently used were Paclitaxel, 5 fluorouracil, Cisplatin and Gemcitabine. Nausea, vomiting, loss of hair, loss of appetite, mucositis, diarrhea and constipation were caused by any chemotherapeutic agents used whereas myelosuppression, cough, dyspnoea, hypersensitivity, amenorrhea , anemia, hyper-pigmentation, dizziness, neuropathy, metallic taste , increased risk of infection, bone pain, and allergy were evident for specific chemotherapeutic agents.

**Conclusions:** Cyclophosphamide and Doxorubicin were more common chemotherapeutic agents used in breast cancer in Bangladesh. Difference in ranking of severity of adverse effects were dependant on demographic pattern, drug used and doses of the drugs.

**Key words:** Breast carcinoma, Chemotherapeutic agents, Adverse effects of chemotherapy.

## Introduction

Cancer is one of the major causes of morbidity and mortality among the non communicable diseases. It is the sixth cause of mortality in Bangladesh and 60% of cancer patients die within five years of diagnosis.[1] Different studies showed that there are more than 1200,000 cancer patients in the Bangladesh, 200,000 cases are added to the number and the disease causes death to some 150,000 people every year.[2] Breast Cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females in the world, with an estimated 1.7 million cases and 521,900 deaths in 2012.[3] Rates are generally high in Northern America, Australia/New Zealand, and Northern and Western Europe; intermediate in Central and Eastern Europe, Latin America, and the Caribbean; and low in most of Africa and Asia. International variation in breast cancer incidence rates reflects differences in the availability of early detection as well as risk factors.[4] Risk factors for breast cancer include reproductive and hormonal factors such as a long menstrual history, recent use of oral contraceptives, and nulliparity. Potentially modifiable risk factors include weight gain after age 18 years, being overweight or obese (for postmenopausal breast cancer), use of menopausal hormone therapy (combined estrogen and progestin), physical inactivity, and alcohol

consumption.[4] Breast carcinoma once diagnosed, becomes a challenge for the surgeons and oncologists. The treatment options depend on type of cancer, stage, drugs availability, sensitivity to the drug and also to the socioeconomic condition. Surgery and radiation therapy, along with adjuvant hormone or chemotherapy when indicated, are now considered primary treatment for breast cancer. Surgical therapy may consist of lumpectomy or total mastectomy. Radiation therapy may follow surgery in an effort to eradicate residual disease and reducing recurrence rates. Hormone therapy and chemotherapy are the 2 main interventions for treating metastatic breast cancer. In Bangladesh several combinations of chemotherapy used to treat these types of cancer as neo-adjuvant or adjuvant therapy with or without radiation by individualization of patients.[5] Common chemotherapeutic drugs used to treat breast carcinoma in Bangladesh include Cyclophosphamide, Doxorubicin, 5-fluorouracil, Paclitaxel, Docetaxel, Gemcitabine, Carboplatin, Methotrexate and Cisplatin. Trustuzumab, Epirubicin, Tmoxifen, Pertuzumab, Anastrozole, Exemestane, Goserelin, Eribulin, Everolimus, Capcitabin, Navelbine, Ixabepilon, Bevacizumab, Fulvestrant, Abraxane, Letrozole are also included in chemotherapy protocol for breast cancer. Two selective estrogen receptor modulators (SERMs), Tamoxifen and Raloxifene are approved for reduction of breast cancer risk in high-risk women.[6] Adjustment of dosage of chemotherapy can be difficult, if the does is too low, it will be ineffective against the tumor, whereas, at excessive does, the side-effects will be intolerable to the patient[5]. Traditional chemotherapy agents are cytotoxic and they have potential immediate or late adverse effects; which causes potential fatality. Some newer anticancer drugs are not indiscriminately cytotoxic, but rather target proteins that are abnormally expressed in cancer cells and that are essential for their growth. Such treatments are often used alongside traditional chemotherapeutic agents in antineoplastic treatment regimens. Common side effects of chemotherapy are fatigue, nausea and vomiting, hair loss, increased risk of infection, anemia, bruising and bleeding, mouth sores, loss of appetite, changes in skin and nails, problem with memory and concentration, sleep problem, diarrhea, constipation, depression etc.[7] The result of this pharmacokinetic variability among patients is due to age ,immunological state, genetic, environmental factor and idiosyncrasy. So that many patients do not receive the right does to achieve optimal treatment effectiveness with minimized toxic effects.[6]

In Bangladesh traditional rather than newer anticancer drugs are mostly used. Therefore this study is designed to assess the pattern of use of chemotherapeutic agents along with their adverse effects to treat breast cancer in Bangladesh. This study might give the policy makers, a guidance for the best and effective management of breast carcinoma with minimum adverse effects.

## Materials And Method

A cross sectional observational study was carried out among the patients diagnosed as breast carcinoma and getting chemotherapy. The period of study was January to December 2015. Data was collected from DMCH and NICRH. The study population was consisted of 102 patients. The subjects were recruited by purposive sampling technique. Sample was selected depending on inclusion and exclusion criteria. Pregnant, severely ill and patients with other concomitant illness were excluded from the study. Data were collected by a face to face interview by using a set of pretested structured questionnaire. The prescriptions of the patients were reviewed. Data analysis was done using SPSS version 21. Data were presented by tables and graphs. Results were expressed as mean ± SD or number (percentage) as appropriate.

## Results

The mean age (yrs) was 43.17±8.42 of the 102 subjects. 53(52.0%) of the patients came from low and 47(46.0 %) from middle income group. Married patients were 91(89.2%).Number of children were one or two in 41 (40.19 %) and 39 (38.23 %) of patients. 8(7.84 % ) women were nulliparous. The mean duration of treatment for cancer was found 9.35±5.17 months.Patients were treated by different combinations of chemotherapeutic agents mostly (36.27 %) with Cyclophosphamide and Doxorubicine. 59(57.8%) patients received Cyclophosphamide followed by Doxorubicin57(55.9%), Paclitaxel (25.5%), 5-Flurouracil 22(21.6%), Gemcitabine 13(12.7%), Docetaxel 6(5.9 %), and Carboplatin 3(2.9 %). Patients received any chemotherapeutic agents were commonly suffered from nausea, vomiting, loss of hair, Ioss of appetite, mucositis, diarrhoea and constipation. Whereasnephrotoxicity, myelosuppression, hypersensitivity, alopecia were evident with Cisplatin. Hyperpigmentation, dizziness, neuropathy, constipation and metallic test were experienced by patients who received 5-fluorouracil. For Doxorubicin increased risk of infections, bone pain, hyperpigmentation, amenorrhea, anemia, diarrhea and allergy were common. Paclitaxel caused neuropathy, hyperpigmentation, flushing, burning of limbs, anemia, constipation, muscle and joint pain, numbness of hands and skin rash. Peripheral neuropathy and bone pain were caused by Carboplatin. Docetaxel specially causes cough, dyspnea,skin rashes. Gemcitabine shows fewer and some common side effects.

**Table I: Base line characteristics of study population**

| Variables | Values |
|---|---|
| Number of patients | 102 |
| Age (years) | 43.17±8.42 |
| Socio economic status - Low / Middle | 53 (52% ) / 47 (46 % ) |
| Married/ Widow, Separated/ Divorce | 91(89.2%) /11(10.8% ) |
| Number of children – One/Two | 41 ( 40.19 %)/ 39 (38.23) % |
| Duration of treatment (months) | 9.35±5.17 |
| Total no of drug prescribed | 2.11±1.09 |

Results were expressed as mean ± SD and numbers as appropriate

**Table II: Different combinations of chemotherapeutics prescribed to patients**

| Combination of Drugs | No of Subjects |
|---|---|
| Cyclophosphamide + Doxorubicine | 37 (36.27%) |
| Paclitaxel | 18 (17.64%) |
| Doxorubicine+5-Fluorouracil+Cyclophosphamide | 15 (14.7%) |
| Gemcitabine + Cisplatin | 07 (6.86%) |
| Gemcitabine | 05(4.9%) |
| Paclitaxel+Cisplatin | 04(3.92%) |
| Docetaxel + Cyclophosphamide + 5-Fluorouracil | 04(3.92%) |
| Cisplatin | 03(2.94%) |
| Doxorubicine + Cyclophosphamide + Docetaxel | 02(1.96%) |
| 5-Fluorouracil+ Cisplatin | 02(1.96%) |
| Doxorubicine + Paclitaxel | 02(1.96%) |
| Paclitaxel + Carboplatin | 02(1.96%) |
| Gemcitabine + Carboplatin + Doxorubicine | 01(0.98%) |
| 5-Fluorouracil + Cyclophosphamide | 01(0.98%) |
| Paclitaxel + 5-Fluorouracil | 01(0.98%) |
| Paclitaxel + Gemcitabine | 01(0.98%) |

Results were expressed as percentage and numbers as appropriate

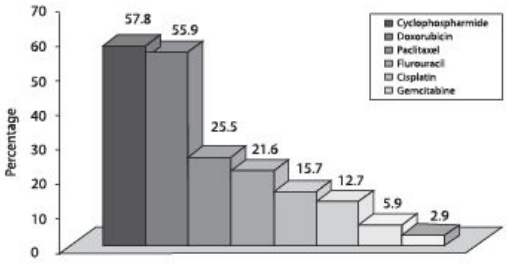


**Figure 1: Percent distribution of subjects prescribed with different chemotherapeutics.**

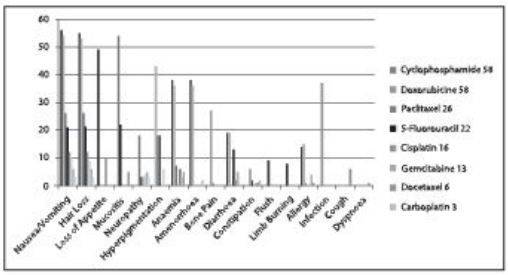


**Figure 2: Bar diagram shows adverse effects of study patients**

## Discussion

In developing countries breast cancer cases in younger women (ages 15-49) now make up 44.1 % of the overall number of cases.[8] In another study it was observed that maximum number of 21 patients were in age group 31-45 followed by age group of 46- 60.[9] In this present study it was observed that, majority 44 (43.1%) patients were in 4th decade; mean age was found 43.17±8.42 years. Similar findings were observed by other studies.[2,10,11] The overall risk accumulation is combined with the tendency for cellular repair mechanisms to be highly effective in a person at the age of 30-45.[11] which is comparable with the current study. Majority of the patients had low socio economic condition (52%). Most of the patients were married (89.2%). Similarly, another studies found married patients 80.0%.[9,10,11] Hormonetherapy and chemotherapy are the 2 main interventions for treating metastat ic breast cancer. In this study it was seen that majority of the patients received Cyclophosphamide(57.8%) followed by Doxorubicin (55.9%), Paclitaxel (25.5%), 5-Fluorouracil (21.6%) and Gemcitabine (12.7%). In another study it was reported that Paclitaxel (25%) was the most common antineoplastic agent used. Cyclophosphamide 18.0%, Cisplatin 11.0%, Vincristine 9.0% were also frequently used. Etoposide, Vinblastine and Carboplatin in 7.0%, 5-Fluorouracil and Adriamycin in 6.0%, Dactinomycin and Docetaxel each were used in 2.0% of patients. Paclitaxel is mostly used in the treatment of several types of cancer, either alone or in combination because of its effectiveness in wide range of tumors.[9] Cisplatin was most common drug which caused adverse drug reactions in 13 patients.[10] Cyclophosphamide was second most common drug, which caused adverse drug reactions in 11 patients. After receiving 5-fluorouracil (5-FU) and Paclitaxel five and four patients developed

adverse drug reactions respectively. Most common ADRs experienced were nausea & vomiting (85.45%), loss of appetite 72.72%, mucositis 65.45%, pain 63.63%, loss of breath 40.0%, constipation 52.72% and polyneuropathy 58.18% observed by another study[9]. In a study10 it was documented that most common adverse drug reaction was nausea and vomiting (16 patients). Neutropenia was the second most common finding (in 12 patients). Other adverse drug reactions were less common. Anemia (in 4 patients), skin rash and hepatotoxicity each in three patients, acute renal failure and severe diarrhea each in two patients, acute stomatitis, tingling, numbness and rare finding like cerebellar ataxia each was experienced by one patient. Cisplatin was responsible for 29.0% of the total ADRs. The ADRs associated with the use of Cisplatin are nausea, vomiting, myelosuppression, peripheral neuropathy, ototoxicity and nephrotoxicity[10,12,13] Elderly patients are at higher risk of myelosuppression, nephrotoxicity and neurotoxicity due to Cisplatin. Cyclophosphamide, 5-fluorouracil, Paclitaxel and Adriamycin were found to be other important drugs to cause ADRs. Cisplatin and these four drugs were very commonly used for the treatment of cancer. They resulted in development of maximum number of ADRs in our study. In another study[14] it was reported that gastrointestinal symptoms were the most frequently encountered toxicities. Except for 3 patients (6%), nausea and vomiting was in general mild or moderate, stomatitis was noted in 16 patients (31%), mild to moderate diarrhea was seen in 10 patients (20%), twenty patients (38%) developed peripheral neurotoxicity including 1 patient who experienced severe symptoms. Alopecia occurred in 37 patients with complete hair loss in 18 (35%). Gemcitabine associated increases of liver enzymes were noted in 16 patients (31%) including one severe reaction, and drug-related fever was observed in 10 patients (19%), which is comparable with the current study.[14]

**Conclusion**

This study was undertaken to determine the pattern of drug management and their adverse effects in patients of breast carcinoma getting chemotherapy and attending in two tertiary hospitals in Bangladesh. Patients were mostly in 4th decade, came from Low/middle income family and married having treatment for more than 9 months. Cyclophosphamide and Doxorubicin were more common chemotherapeutic agents used. Differences in ranking of severity of side-effects were evident when patient groups were divided by age, sex, marital status , domestic situation, diagnosis, used chemotherapeutic agents , and response .The study population was selected from two hospitals in Dhaka city, conducted at a short period of time with a small sample size so the results of the study may not reflect the exact picture of the whole country. However, treatment delays, deviations from standard dosing by body surface area or other parameters, use of ancillary medications (such as hematopoietic growth factors and bisphosphonates) were not evaluated .These questions are key priorities for future research.

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