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# ASSESSMENT OF DRUG RELATED PROBLEMS IN THE MANAGEMENT OF BREAST CANCER

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## Abstract

**Introduction:** Breast cancer is the leading cause of cancer death among women worldwide. Globally cancer is one of the top ten leading causes of death. It is estimated that 7.4million people died of cancer in 2004(international Scholar research,2015). The rising global incidence of malignant diseases such as breast cancer is an issue of serious concern because is one of the leading causes of death among women globally It is a descriptive Cross sectional assessment of patient with breast cancer that have undergone management in oncology unit Jos university Teaching Hospital from May to June 2021. The data obtained using questionnaires on drug related problem associated with chemotherapy used in the management of Breast cancer patient in oncology unit, the most prevalent Drug related problem in the study was Adverse drug reaction which occurred in 80% of the population. The Adverse drug reactions detected were nausea and vomiting, alopecia, anaemia and nail changes which were also recorded in our study (Itchipruchyabun,2008). In this study, Hair loss occurred in 30% of the patients, nausea and vomiting occurred in (25%) patients of which most of the patients needed aprepitant when they took highly emetic chemotherapy. But unavailability of medication is one major problem in our case. The factor having the strong association with incidence of Drug related problem was Presence of Co-morbidity ($p=0.017$), reason for missed dose($p=0.03$), number of medication ($p=0.02$) and stage of breast cancer($p=0.04$) which have a P-value $<0.05$ which indicates that there is strong association/ statistical significant between them and drug related problem.

## 1.0 INTRODUCTION

Breast cancer is the leading cause of cancer death among women worldwide. Globally cancer is one of the top ten leading causes of death. It is estimated that 7.4million people died of cancer in 2004(international Scholar research,2015). The rising global incidence of malignant diseases such as breast cancer is an issue of serious concern because is one of the leading causes of death among women globally. According to American cancer society(ACS), Breast cancer is malignant neoplasm of the breast arising from the epithelial lining of the lobule, ducts and nipple. It is a disease in which normal cells grows out of control in the breast tissue. **It is important to note that most breast lumps are benign and not Cancerous.** Nonmalignant breast lumps are abnormal growths, but they do not spread outside the breast and not life threatening, however some have been found to increase a woman's risk of developing Breast cancer (ACS,2018).

Breast cancer arises from cells in the breast that have grown abnormally and multiplied to form a lump or tumour. The earliest stage of breast cancer is non-invasive disease (Stage 0), which is contained within the ducts or lobules of the breast and has not spread into the healthy breast tissue (also called in situ carcinoma). Invasive breast cancer has spread beyond the ducts or lobules into healthy breast tissue, or beyond the breast to lymph nodes or distant organs (Stages I IV) (Balogun, O. D 2015).

Breast cancer is the most common cause of cancer-related deaths in women and occurs most frequently in postmenopausal women over the age of 50. Breast cancer also occurs in men but is very rare, making up around 1% of all breast cancer cases. The treatment of breast cancer depends on how far advanced the cancer is (Stage 0 to IV) and what type of cancer is present (ESMO,2017).

The increase in number of available drugs and drug users as well as more complex drug regimens lead to more side effects and drug interactions, and complicate follow-up. Drug related problems (DRPs), which includes adverse drug reactions (ADRs), unnecessary drug therapy, inappropriate choice of drugs, and untreated conditions, has been reported in up to 25% of hospitalized patients. Drug related problems can lead to substantial morbidity and mortality.

Drug toxicity is also a major limitation in providing healthcare to patients at a global level. It affects the patient's recovery as well as the economy of healthcare (Rahmawati, 2019)

A drug-related problem (DRP) is defined as an event involving drug therapy that has a potential to interfere with the desired health outcomes. Alternatively, a drug therapy problem is any detrimental event experienced by a patient which impedes attainment of the desired goals of treatment. In the absence of appropriate intervention, medication problems have considerable negative impact on the health of the patients (Cipolle R,2016).

In systemic cancer therapy, drug regimens are administered following established protocols which have been carefully evaluated in clinical trials. The more complex drug therapy is the higher the risk of experiencing Drug related problems such as adverse effects, interactions, medication errors, and non-adherence. The use of anticancer drugs often results in the use of other agents to reduce or prevent side-effects of the anticancer treatment, thereby increasing the interaction potential. Furthermore, cancer itself increases the need for more medications. Cytotoxic agents have a narrow therapeutic window and a complex pharmacologic profile. In oncology patients, pharmacokinetic parameters can be altered by the disease itself or due to malnutrition, reduced levels of serum-binding proteins, edema, or hepatic and/or renal dysfunction. Patients with cancer are therefore more at risk for drug interactions (DRP) (Koh Y,2015).



Drug Related Problems (DRPs) in cancer chemotherapy can have severe consequences originating from the high toxicity and narrow therapeutic range of anticancer drugs. A study done showed that Drug related Problem were common with cancer. The risk factors associated with drug related problems are present with comorbid patient, number of medications and length of hospital stay. cancer patients are one of the groups who are most at risk of developing Drug related problems. The objectives of the study is to investigate the type drug related problem in breast cancer management and to assess the risk factors associated with drug related problem in breast cancer patients.

## 1.2 METHODOLOGY

### 1.2.1 STUDY DESIGN, AREA, PERIOD AND POPULATION

It is a descriptive Cross sectional assessment of patient with breast cancer that have undergone management in oncology unit Jos university Teaching Hospital from May to June 2021. The

study population are patients with breast cancer, who were managed of breast cancer in oncology unit Jos university Teaching Hospital within the study period.

### 1.2.2 SAMPLING METHOD

A Convenient sample of the number of Patient diagnosed of breast cancer and were being managed of breast cancer in the oncology unit Jos university teaching hospital within the study period was used as sample size. This was due to the limited number of patients available for the study.

### 1.2.3 DATA COLLECTION

In the study data was collected from patient using a questioner and a Profoma in which some information was gotten. The questioner and Profoma was developed by the researcher according to the research objectives in oncology unit Jos university teaching Hospital.



### 1.2.4 ETHICAL CONSIDERATION

Ethical clearance was sought for from the JUTH ethical committee and approvals was gotten from the Oncology unit, with ethical clearance number JUTH/DCS/IREC/127/XXXI/2503 and all data collect was strictly handled confidentially.

### 1.2.5 DATA ANALYSIS:

Data collected was analysed using the statistical package of social sciences (SPSS), version 24.0. Frequency distribution of the data, statistical tests of significance will be carried out.

## 1.3 RESULTS & DISCUSSION

### 1.3.1 RESULTS

A total of 20 patients were included in the study, of which majority of the patient (20%) were within the age range 46-50 years. 50% of the patients were married and majority of the patient 35% were civil servant. All the patients were female.

The most prevalent type of cancer was Breast cancer type 1 (95%), about 75% of the patient were diagnosed of breast cancer about 1-3 years ago. About 65% of the patients were placed on two cytotoxics. 45% of the patient have missed their doses for the reason that 15% was due to unavailability of the medication whereas 30% was due to the cost of the medication.

55% of the patients believed that the medication was always available whereas 45% said they were not always available. The major side effects observed by the patient was Hair loss (30%) followed by Nausea and headache (25%). The most common stage of breast cancer were Stage 1 and stage 2 both having 40% followed by stage 3. The common co-morbid disease recorded was Hypertension (35%).

Altogether, 32 drug therapy problem were identified in 20 patients. The most prevalent Drug related problem was Adverse drug reaction/ side effects (80%) followed by Unavailability of drugs (50%), Drug-drug interaction (30%), among the adverse drug reaction Hair loss (30%) was the most prevalent followed by Nausea and vomiting (25%). And unnecessary drug therapy (10%).

The following variables were tested for their association with drug related problem, age, Marital status, Occupation, number of medications, reason for missed dose, stage of breast cancer and presence of co-morbidity. Presence of Co-morbidity (p=0.017), reason for missed dose(p=0.03) Number of medication (p=0.02) and stage of breast cancer(p=0.04) were positively and significantly associated with drug related problem.



**Table 1: Socio-Demographic Data N=20**

| VARIABLE | ATTRIBUTES | FREQUENCY | PERCENTAGE(%) |
|---|---|---|---|
| **Age (In Years)** | | | |
| | 20-25 | 3 | 15 |
| | 26-30 | 2 | 10 |
| | 31-35 | 2 | 10 |
| | 36-40 | 3 | 15 |
| | 41-45 | 2 | 10 |
| | 46-55 | 4 | 20 |

| | | | |
|---|---|---|---|
| | 55-60 | 2 | 10 |
| | 61-65 | 1 | 5 |
| | >65 | 1 | 5 |
| **Marital Status** | | | |
| | Single | 5 | 25 |
| | Married | 10 | 50 |
| | Divorced | 5 | 25 |
| **Occupation** | | | |
| | Student | 3 | 15 |
| | Housewife | 6 | 30 |
| | Business women | 3 | 15 |
| | Civil servant | 7 | 35 |
| | Retiree | 1 | 5 |



**Table 2: Medical History N=20**

| VARIABLE | ATTRIBUTES | FREQUENCY | PERCENT(%) |
|---|---|---|---|
| **Diagnosis** | | | |
| | Breast cancer type 1 | 19 | 95 |
| | Breast cancer type 2 | 1 | 5 |
| **Length Of Diagnosis** | | | |
| | <1 year | 4 | 20 |
| | 1-3 years | 15 | 75 |
| | 4-6 years | 1 | 5 |
| **Number Of Medication** | | | |

| | | | |
|---|---|---|---|
| | 2 | 13 | 65 |
| | 3 | 7 | 35 |
| **Number of missed dose** | | **9** | **45** |
| | 1 | 3 | 15 |
| | 2 | 5 | 25 |
| | 3 | 1 | 5 |
| **Reason for missed dose** | | | |
| | Unavailability of drugs | 3 | 15 |
| | Cost of medication | 6 | 30 |
| **How can you assess the cost of medication** | | | |
| | Costly | 20 | 100 |
| **Do you often keep to clinic appointment?** | | | |
| | Yes | 17 | 85 |
| | No | 3 | 15 |
| **How available is the medication Prescribed?** | | | |
| | Always available | 11 | 55 |
| | Not available | 9 | 45 |
| **Side effects** | | | |
| | Anemia | 1 | 5 |
| | Nausea/ headache | 5 | 25 |

| | | | |
|---|---|---|---|
| | Hair loss | 6 | 30 |
| | Nail changes | 4 | 20 |
| **Stage of Breast cancer** | | | |
| | Stage 1 | 8 | 40 |
| | Stage 2 | 8 | 40 |
| | Stage 3 | 4 | 20 |
| **Comorbidity** | | | |
| | Hypertension | 7 | 35 |
| | Ulcer | 2 | 10 |
| | Diabetes | 1 | 5 |



**Table 3: Premedication N=20**

| PRE-MEDICATION | FREQUENCY | PERCENTAGE(%) |
|---|---|---|
| **Dexamethasone** | 20 | 100 |
| **Omeprazole** | 20 | 100 |
| **Ondasentrone** | 14 | 70 |
| **Granisetrone** | 7 | 35 |
| **Furosemide** | 5 | 25 |
| **Hydrocortisone** | 3 | 15 |
| **Promethazine** | 3 | 15 |
| **Metoclopramide** | 1 | 5 |
| **Normal saline** | 18 | 90 |

The table shows the premedication given to patients before the chemotherapy

**Table 4: Chemotherapy Regimen N=20**

| Chemotherapy Regimen | Number of patient (%) |
|---|---|
| **Dacarbazine + Cisplatin + Camustine** | 1(5) |
| **Oxaliplatin + Gemcitabine** | 1(5) |
| **Paclitaxel + Doxorubicin(Adraimycin) + Cyclophosphomide** | 2(10) |
| **5-Fluoracil + Paclitaxel + Carboplatin** | 2(10) |
| **Doxorubicin + Cyclophosphomide** | 1(5) |
| **Docetaxel + Gemcitabin** | 2(10) |
| **Paclitaxel + Carboplatin** | 2(10) |
| **Docetaxel + Carboplatin** | 1(5) |
| **Epirubicin + Cyclophosphomide + 5- Fluoracil** | 1(5) |
| **Doxcetaxel + Cisplatin** | 1(5) |
| **Vincristine + Doxorubicin(Adraimycin) + Cyclophosphomide** | 1(5) |
| **5-Fluoracil + Doxorubicin** | 1(5) |
| **Epirubicin + Cyclophosphomide** | 2(10) |
| **Gemcitabin + Carboplatin** | 2(10) |



The table shows the different chemotherapy initiated to patients

**Table 5: Classification of Drug-related problems in cancer in-patients JUTH N=20**

| Classification of Drug related problem | Number of occurrence(%) |
|---|---|
| Unavailability of drugs | 10(50) |
| Adverse drug reaction/Side effects | **16(80)** |
| **Anemia** | 1(5) |
| **Nausea and Vomiting** | 5(25) |
| **Hair loss** | 6(30) |
| **Nail changes** | 4(20) |
| Drug-drug interaction | 6(30) |
| Unnecessary drug therapy | 2(10) |

**Note:**Total does not add up to 100% as some patients had >1 reported Drug related problem

**Table 6: Factors associated with Drug related problemN=20**

| Variables | Attributes | DRP | | P-value ($X^2$) |
|---|---|---|---|---|
| | | **Yes (%)** | **No(%)** | |
| Age in years | 20-25 | 3(15) | 0(0) | 0.252(10.19) |
| | 26-30 | 2(10) | 0(0) | |
| | 31-35 | 1(5) | 1(5) | |
| | 36-40 | 3(15) | 0(0) | |
| | 41-45 | 2(10) | 0(0) | |
| | 46-50 | 3(15) | 1(5) | |
| | 55-60 | 2(10) | 0(0) | |
| | 61-65 | 1(5) | 0(0) | |
| | >70 | 0(0) | 1(5) | |
| Marital status | Single | 5(25) | 0(0) | 0.555(1.97) |
| | Married | 8(40) | 2(10) | |
| | Divorced | 4(20) | 1(5) | |
| Occupation | Student | 5(25) | 1(5) | 0.688(2.260) |
| | Housewife | 3(15) | 0(0) | |
| | Business women | 3(15) | 0(0) | |
| | Civil servant | 5(25) | 2(0) | |
| | Retiree | 1(5) | 0(0) | |
| Number of medication | 2 | 10(50) | 3(15) | 0.168(0.02) |
| | 3 | 7(35) | 0(0) | |
| Reason for missed dose | Unavailability of drugs | 3(15) | 0(0) | 0.03(19.2) |
| | Cost of medication | 5(26) | 1(5) | |

| | | | | |
|---|---|---|---|---|
| Stage of breast cancer | Stage 1 | 6(30) | 2(10) | 0.04(13.7) |
| | Stage 2 | 7(35) | 1(5) | |
| | Stage 3 | 4(20) | 0(0) | |
| Comorbidity | Hypertension | 6(30) | 1(5) | 0.017(14.05) |
| | Ulcer | 2(10) | 0(0) | |
| | Diabetes | 0(0) | 1(5) | |

### 1.3.2 DISCUSSION

Drug-related morbidities are a significant healthcare problem, and great proportions are preventable. Increasingly, there have been numerous reports of the incidence, prevalence, and preventability of medication error-related deaths, drug-related hospital admissions, and adverse drug events in the inpatient and outpatient setting (Singh,2011).

Altogether 32 drug related problem were identified in 20 patients which was much lower as compared with the prospective study done in Netherland that showed 952 Drug related problems in 546 patients (Bain,2006).

But a higher number of drug related problem was detected in this study when compared with another retrospective study done in Portugal that detected 27 Drug related Problem in 56 patients although it focused mainly on intervened drug related problem (avoidable) which do not account for unavoidable drug related problems like adverse drug reaction (Cavaco,2012). This variation indicates that as such comparisons are hampered by different settings, measurement methods and classification systems. In breast cancer chemotherapy adverse drug reaction are strongly connected to the treatment itself. Because of the fact that most cytotoxic agents cannot distinguish between normal and neoplastic cells, most adverse drug reactions seem to be unavoidable. They are often accepted not only by patients but also by health care providers. The most prevalent Drug related problem in the study was Adverse drug reaction which occurred in 80% of the population. The study done in Florida among elderly patients found an actual or potential Adverse drug reaction in 56.3% of the study participants (Bain,2006).

Similarly, a study done in Thailand showed that Adverse drug reaction was the most common Drug related problems which was seen in 44 of 68 breast cancer patients (64.70%) both in inpatient and outpatient setting. The Adverse drug reactions detected were nausea and vomiting,

alopecia, anaemia and nail changes which were also recorded in our study (Itchipruchyabun,2008). Another study done in Portugal where the team of oncology pharmacists monitored 56 patients between showed that interventions related to adverse effects such as emesis protocol optimization and other supportive treatment accounted for about 11.6%. This indicates the presence of Adverse drug reaction as a drug related problem but the percentage is low compared to this study and it could possibly be due to the study sample differences and this study recorded all Adverse drug reactions not the interventions made to Adverse drug reaction (Cavaco,2012). In this study, Hair loss occurred in 30% of the patients, nausea and vomiting occurred in (25%) patients of which most of the patients needed aprepitant when they took highly emetic chemotherapy. But unavailability of medication is one major problem in our case. The second more prevalent Drug related problem in this study was unavailability of drugs that occurred in 50% of the participants. Unavailability of drug was also the second more prevalent Drug related problem in the Thailand study which occurred in 52% of the study population, (BCCA,2011).

If the drug chart is written as “premedication” then the nurse will encounter a problem in administering appropriate chemotherapy, since the chemotherapy drugs need a different kind of premedication according to the regimen selected, some may be mild emetic or highly emetic or some might need prophylaxis for infusion reaction like in paclitaxel. Unnecessary drug therapy is one of DRPs which occurs when there is duplication of therapy (multiple drug products are being used for a condition that requires single drug therapy), contraindication or when the drug is given in the absence of a medical condition (or when not it is needed). In this study, duplication of the antiemetic’s was found. Antiemetic’s were given while they were not important in the low and moderately emetic chemotherapy regimens. The factor having the strong association with incidence of Drug related problem was Presence of Co-morbidity ($p=0.017$), reason for missed dose($p=0.03$), number of medication ($p=0.02$) and stage of breast cancer($p=0.04$) which have a P-value $<0.05$ which indicates that there is strong association/ statistical significant between them and drug related problem. This was found realistic because most of the patient are placed on more than one medication of which patients adherence to that might be quite very low as to match with the treatment pattern. This is also in line with a study carried out in Florida which shows that there is strong association with Number of medication and drug related problem.

## 1.4 CONCLUSION

The study showed that Drug related problems were common at JUTH Oncology clinic which include Adverse drug reaction, unavailability of drugs, drug-drug interaction and unnecessary drug therapy. The risk factors associated with drug related problems were the presence of comorbidity, number of medications, reasons for missed dose and stage of breast cancer. Our findings indicated that cancer patients are one of the groups who are most at risk of developing drug related problems. This calls for interventions which could include involvement of a pharmacist in management of breast cancer patient to detect and intervene drug related problem to ensure a better therapeutic outcome.

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**1.6 CONFLICT OF INTEREST:** All authors declare no any conflict of interest

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