

Prescription of Antineoplastic Agents in Management of Breast Cancer Patients at Teaching Hospital in North-Central Nigeria

F. E. Williams^{*1}, S. O. Agodirin², S. I. Bello¹, N. O. Bello¹, H. K. Jimoh¹

¹Department of Clinical Pharmacy and Pharmacy Practice, University of Ilorin, Ilorin, Nigeria

²Department of Surgery, University of Ilorin, Ilorin, Nigeria

*Corresponding author: E-mail address: williams.fe@unilorin.edu.ng Telephone: +2348033354532

Abstract

The therapeutic management and prognosis of breast cancer (BCa) has undergone a significant reformation using antineoplastic agents. Despite their use at the study site, dearth of information on their prescription has attracted concerns. Hence, this research was conducted to assess the prescription of antineoplastic agents in management of BCa patients at a teaching hospital in North-Central Nigeria. It was conducted at the oncology clinic of a teaching hospital, Nigeria. It involved the interview of 60 eligible BCa patients using structured questionnaire and data extraction from patients' medical folders. Statistical Package for Social Sciences version 20 was used for quantitative data entry and analyses. Ethical approval was obtained from relevant Ethical Review Committee. Patients' consents were obtained before inclusion into the study. The study showed that 93.3% of the study participants were married, 50% had primary education and the modal age class was 31 – 40 years. The modal class for duration of illness since diagnosis was 1 – 5 years. More than three-fifth of the study participants (63.3%) were on cancer chemotherapy, the highest cancer chemotherapy cycle was 7 while the highest proportion of the study participants (15%) had 6 cycles of cancer chemotherapy. Cancer chemotherapy combination regimen included Doxorubicin+Cyclophosphamide+5-Fluorouracil, Doxorubicin + Cyclophosphamide, Doxorubicin+Cyclophosphamide+Docetaxel. Tamoxifen was the most prescribed antineoplastic agent (66.7%) either as neoadjuvant or adjuvant, followed by Cyclophosphamide (41.7%). Antineoplastic agents administered were in line with recommendations for the management of BCa. However, the high number of cancer chemotherapy cycles calls for intervention.

Keywords: Breast Cancer, Antineoplastic Agents, Cancer Chemotherapy, Teaching Hospital, Nigeria

INTRODUCTION

The burden of breast cancer (BCa) in developing countries is enormous¹. Breast Cancer is the most common neoplasm and it is the second primary cause of cancer-related deaths in women globally as well as in Nigeria^{2, 3}. According to World Health Organization 627,000 women died from breast cancer in 2018⁴. This is approximately 15% of all cancer deaths among women. While breast cancer rates are higher among women in more developed regions, rates are increasing in nearly every region globally⁴. Almost 50% of breast cancer cases and 58% of deaths occur in less developed countries⁵. In developing countries, it is the leading

cause of death among women with 324,000 deaths which represented 14.3% of all deaths⁶. In Nigeria, Agbo *et al.* reported that the prevalence rate in Sokoto was 10.4% in 2011⁷. Generally, there is increasing incidence of breast cancer⁸. The precise causes of breast cancer are not clear⁹. However, cancer has been associated with mutation to a cell's DNA which could be due to genetic or environmental factors¹⁰. In most cases a combination of both genetic and environmental factors could cause cancer¹⁰. Risk factors that could increase the chances of having cancer include: age, race/ethnicity, breast density, gender, menstrual and reproductive history, birth control pills, certain genomic changes,

excess alcohol consumption, family history, genetic factors, obesity and weight gain, poor diet, combined hormonal replacement therapy, radiation to the chest and lack of physical activity, breast cellular changes/breast lesions, exposure to diethylstilbesterol (DES), exposure to estrogen, height, bone mineral density, night shift work, smoking tobacco, breastfeeding history, pregnancy history and exposure to environmental pollutants such as polycyclic aromatic hydrocarbons (PAHs) and polychlorinated biphenyls (PCBs) dioxins and organic solvents that increase the susceptibility to carcinogenesis¹⁰⁻¹². Most breast cancers develop either in the lobules or in the ducts¹².

Breast cancer management involves the combination of surgery, radiotherapy and pharmacotherapy^{13,14}. This gold standard for cancer treatment has led to an increase in patient survival¹⁴. Pharmacotherapy in breast cancer treatment involves systemic therapy (ST)¹². ST is treatment that travels through the bloodstream. It affects and treats almost all parts of the body. It includes chemotherapy, hormone therapy, and targeted therapy¹². Examples of antineoplastic medicines approved for the management of breast cancer include: Tamoxifen, Paclitaxel, Docetaxel, Doxorubicin, Cyclophosphamide, Methotrexate, 5-Fluorouracil, Vinca Alkaloids (Vincristine, Vinblastine), Gemcitabine, and Epirubicin¹⁵. The chemotherapy combination regimens include Doxorubicin+Cyclophosphamide (AC), Doxorubicin + Cyclophosphamide + Paclitaxel (AC-T), Cyclophosphamide +Doxorubicin+Fluorouracil (CAF), Cyclophosphamide + Methotrexate +Fluorouracil (CMF), Fluorouracil+ Epirubicin + Cyclophosphamide (FEC), Docetaxel+Doxorubicin+Cyclophosphamide (TAC)¹⁵.

Previous study on prescription pattern of antineoplastic agents in patients with breast cancer showed that Cyclophosphamide was the most

prescribed (77.14 %). This was followed by Doxorubicin (68.57 %) and 5-fluorouracil (44.29 %)¹⁶. Gafitinib was the least prescribed (1.43 %)¹⁶. In addition, the most prescribed chemotherapy combination regimen was cyclophosphamide + 5-fluorouracil + doxorubicin (40.9 %).¹⁶ In another study, Cyclophosphamide (20 %) was the most prescribed antineoplastic agent, but it was followed by docetaxel (13 %), doxorubicin (12 %) and 5-fluorouracil (12 %)¹⁷. Carboplatin was the least prescribed¹⁷. An earlier study in Chandigarh, India showed that Fluorouracil + Doxorubicin + Cyclophosphamide chemotherapy combination regimen was the most prescribed (41.58 %) while paclitaxel alone (22.7 %) was next¹⁸. Additionally, a study in Hyderabad showed that Doxorubicin+ Cyclophosphamide + Paclitaxel (AC-T) was the most prescribed (51.72 %) while Paclitaxel+ Carboplatin (18.96 %) was the next¹⁹. Despite the use of antineoplastic agents in the management of breast cancer patients in North-Central Nigeria, dearth of information on prescription of antineoplastic agents has attracted concerns. This study thus examined prescription of antineoplastic agents in the management of breast cancer patients at a teaching hospital in North-Central Nigeria.

MATERIAL AND METHODS

Study Location

The study was conducted at a teaching hospital in North-Central Nigeria. The teaching hospital belongs to the second generation of Teaching Hospitals which were established by law on the 2nd of May 1980²⁰. The hospital has 21 clinical departments that render specialist care in Obstetrics and Gynaecology, Surgery, Family Medicine, Paediatrics, Anaesthesia, Pain and Palliative Care, Pharmacy, Urology, Behavioural Science, Physiotherapy, Radiology, Ophthalmology and otorhinolaryngology²⁰. It serves as a

referral center for other primary and secondary health care facilities. It is also a training facility for undergraduate and postgraduate programs in Medicine, Pharmacy and allied courses.

Study Population

The study population was female breast cancer patients who attend the oncology clinic of a teaching hospital in North-Central Nigeria.

Study Design

The study was a cross-sectional, single-center research. There was a pilot study over one week. The study involved the interview of breast cancer patients using piloted structured questionnaire and data extraction from breast cancer patients' medical folders using designed data extraction forms.

Inclusion Criteria

The inclusion criteria were:

Female ambulatory breast cancer patients who were on antineoplastic agents.

Female breast cancer patients above 18 years who consented to participate in the study.

Exclusion Criteria

The Exclusion Criteria were:

Breast Cancer female patients who were on antineoplastic agents and on hospital admission.

Breast Cancer patients who were mentally incapacitated.

Sample Size Determination and Sampling

Representative sample size was determined based on Fisher's formula¹⁹ at 95 % confidence level and 5 % margin of error. With regards to this study, the

prevalence of breast cancer (10.4 %) reported by Agbo *et al.*⁷ was used as the proportion of target population estimated to have a particular characteristic. The obtained minimum sample size was 59 but approximated to 60. Thus, 60 copies of questionnaire were administered. Eligible breast cancer patients were consecutively sampled at the oncology clinic until the sample size was attained.

Study Instrument and Administration

Structured questionnaire was administered to breast cancer patients. The interview was conducted in English Language. However, Yoruba was used for patients who could not communicate in English Language. Also, the interviewed patient's medical folders were obtained and relevant data were extracted.

Data Analyses

The filled questionnaires were sorted and coded for easy reference. The Statistical Package for Social Sciences (SPSS) version 20 was used for data entry and analysis. Frequency distributions of quantitative variables were generated.

Ethical Issues

RESULTS AND DISCUSSION

A total of 60 breast cancer patients participated in the study with a mean age of 46.5 years (± 14.5) and modal age class of 31- 40 years. Majority (93.3 %) of the participants were married. Half (50 %) of the participants had primary education (Table 1).

Additionally, more than half (55 %) of the study participants' spouses had primary education and more than three-fifth (63.3 %) of the study participants were Muslims. None of the participant smoked cigarette or consumed alcohol (Table 2).

Ethical approval was obtained from the Ethics and Research Committee of University of Ilorin Teaching Hospital (ERC PAN/2018/07/1812). Relevant cooperation and assistance of the head of department was sought and obtained. Voluntary informed consents (signatures/finger print) were obtained from the patients before inclusion in to the study. Confidentiality of the data and

information obtained was ensured. All research ethics such as anonymity and x

Regarding the duration of illness since diagnosis (DISD), three-fifth of the study participants had modal duration of illness since diagnosis (DISD) of 1-5 years. On the other hand, only 5% of the study participants had duration of illness since diagnosis (DISD) of 6-10 years (Table 3).

Table 1: Socio-demographic characteristics of study participants

Variables	Frequency (%)
Age in Years (n=60)	
<20	2 (3.3)
21-30	6 (10)
31-40	17 (28.3)
41-50	10 (16.7)
51-60	13 (21.7)
61-70	9 (15)
>70	3 (5)
Marrital Status (n=60)	
Single	4 (6.7)
Married	56 (93.3)
Educational Status (n=60)	
Primary Education	30 (50)
SSCE/GCE	6 (10)
Diploma	5 (8.4)
B.Sc.	17 (28.3)
Masters	2(3.3)

Table 2: Further socio-demographic characteristics of study participants

Variables	Frequency (%)
Husband's educational status (n=60)	
Primary Education	33 (55)
SSCE/GCE	2 (3.3)
Diploma	6 (10)
B.Sc.	7 (11.7)
Masters	10 (16.7)
Ph.D.	2 (3.3)
Religion (n=60)	
Islam	38 (63.3)
Christianity	22 (36.7)
Traditional	0 (0)
Smoking of Cigarette (n=60)	
Yes	0 (0)
No	60 (100)
Alcohol consumption (n=60)	
Yes	0 (0)
No	60 (100)

Table 3: Duration of illness since diagnosis of breast cancer in study participants

Duration of illness since diagnosis (n=60)	Frequency (%)
≤ 1 Year	21(35)
1-5 Years	36 (60)
6-10 Years	3 (5)

The mean age of the study participants (46.5 years) is not in line with reports of Center for Disease Control and Prevention²² which stated that on average, women over 60 are more likely to be diagnosed with breast cancer and only about 10 – 15 percent of breast cancers occur in women younger than 45 years. The difference may be due to the variation in median age of diagnosis which varies with race and ethnicity²³. Black women tend to be diagnosed at younger age than white women²³.

Also, the findings of this study that majority (93.3 %) of the participants are married is not surprising. This is due to marital status having a significant correlation with health seeking behaviour²⁴. In the study, about half of the participants had primary education. This contrasts with a previous study by Zimmerman *et al.*²⁵ According to Zimmerman *et al.*, education endows

people with the means to become “effective” individuals, who gain control of their health by developing a healthy lifestyle, thus mediating the association between education and health. This contrast could be due to the location of the study and the specific nature of the disease under consideration in this study. Majority of the patients who participated in the study had modal duration of illness since diagnosis of 1-5 years. This corroborates with previous qualitative research in women with breast cancer, which has demonstrated that statistics on the outlook for a certain type and stage of breast cancer is often given as 5-year survival rate²⁶.

Regarding the use of cancer chemotherapy, more than three-fifth of the study participants had received cancer chemotherapy (Table 4). The highest number of cycles received by the study participants was 7 (Table 4).

Table 4: Use of Cancer Chemotherapy

Variables	Frequency (%)
Use of cancer chemotherapy (n=60)	
YES	38 (63.3)
NO	22 (36.7)
Number of cycles of cancer chemotherapy (n=38)	
1	6 (10)
2	7(11.7)
3	5 (8.3)
4	5 (8.3)
5	4 (6.7)
6	9 (15)
7	2 (3.3)

However, the number of chemotherapy cycle with the highest proportion of patients (15%) was 6. This finding correlates with the reports made by breast

cancer care²⁷ that chemotherapy is tailored to the individual situation. Therefore, individualization of chemotherapy cycle is

facilitated by the type and stage of breast cancer in a particular patient.

The chemotherapy combination regimen prescribed for the study participants are

shown in Table 5. The most prescribed chemotherapeutic regimen in this study was (Doxorubicin or Epirubicin) + Alkylating agent (Cyclophosphamide) + Taxane (Docetaxel or Paclitaxel).

Table 5: Chemotherapy combination regimen used by the study participants

S/N	Chemotherapeutic Regimen (n=38)	Frequency (%)
1.	Anthracycline (Doxorubicin or Epirubicin) + Alkylating agent (Cyclophosphamide)	11 (28.95)
2.	Anthracycline (Doxorubicin or Epirubicin) + Alkylating agent (Cyclophosphamide) + Taxane (Docetaxel or Paclitaxel).	13 (34.21)
3.	Anthracycline (Doxorubicin or Epirubicin) + Alkylating agent (Cyclophosphamide) + Pyrimidine analog (5-Fluorouracil).	3 (7.89)
4.	Anthracycline (Doxorubicin or Epirubicin) + Taxane (Docetaxel or Paclitaxel).	5 (13.16)
5.	Anthracycline (Doxorubicin or Epirubicin) + Taxane (Docetaxel or Paclitaxel) + Capecitabine.	5 (13.16)
6.	Anthracycline (Doxorubicin or Epirubicin) + Alkylating agent (Cyclophosphamide) + Taxane (Docetaxel or Paclitaxel) + Pyrimidine analog (5-Fluorouracil).	1 (2.63)

The prescribed chemotherapy combination regimens in this study are in line with the recommendations of American Cancer Society¹² that combination of chemotherapeutic agents is effective in the management of breast cancer especially as adjuvant and neoadjuvant treatment which results in optimum therapeutic effects. Also, the combination of chemotherapeutic agents prescribed to breast cancer patients in this study site is in line with the recommendations of National Cancer Institute¹⁵ for breast cancer management. However, the most prescribed chemotherapy combination regimen in this study: anthracycline (Doxorubicin or Epirubicin)+Alkylating agent (Cyclophosphamide) + Taxane (Docetaxel or Paclitaxel) is not in line with the findings of earlier studies in which Doxorubicin (anthracycline) + Cyclophosphamide (alkylating agent) + 5-Fluorouracil (Pyrimidine analog)¹⁶; and Fluorouracil + Doxorubicin + Cyclophosphamide¹⁸ combination

regimens were the most prescribed. The individualization of chemotherapy of breast cancer based on patients' medical conditions may be responsible for this contrast.

The antineoplastic agents prescribed for the breast cancer patients are as shown in Figure 1. Of the 10 antineoplastic agents prescribed to the study participants, Tamoxifen 40 (66.7 %) was the most prescribed agent. Of the 40 patients, 30 (75 %) received Tamoxifen as neoadjuvant while 10 (25 %) received it as adjuvant. The next most prescribed antineoplastic agent was Cyclophosphamide which was received by 41.7 % of the study participants. This is in contrast with the findings in earlier studies in which cyclophosphamide was the most prescribed, 20 % in a tertiary care hospital¹⁷ and 77.14 % in another tertiary care teaching hospital¹⁶. The contrast may be due to individualization of chemotherapy based on patients' medical conditions.

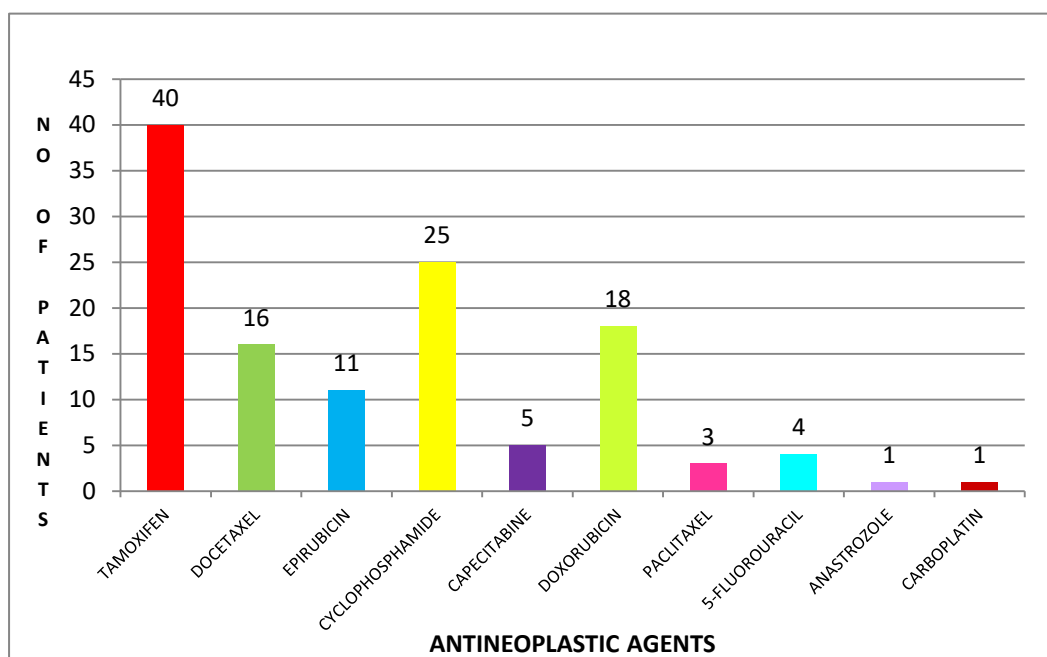


Figure 1: Antineoplastic agents prescribed for the study participants

CONCLUSIONS

The antineoplastic agents administered were in line with recommended antineoplastic agents for the management of breast cancer. The most prescribed antineoplastic agent was Tamoxifen while the most prescribed chemotherapy combination regimen was Anthracycline (Doxorubicin or Epirubicin)+Alkylating agent (Cyclophosphamide) + Taxane (Docetaxel or Paclitaxel).

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CONFLICT OF INTEREST: NONE

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