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Anticancer Drugs Utilisation for Cancer Chemotherapy in a Nigerian Health Care Facility

Aminu A. Biambo,[1*] Maxwell O. Adibe,[2] Usman M. Aliyu,[3] Aliyu Samaila, [1] Nuruddeen Usman,[1] Nafiu Abdullahi[1] and Chinwe V. Ukwe[2]

Aminu A. Biambo,[1*] Maxwell O. Adibe,[2] Usman M. Aliyu,[3] Aliyu Samaila,[1] Nuruddeen Usman,[1] Nafiu Abdullahi[1] and Chinwe V. Ukwe[2]

[1]Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University Sokoto, Nigeria
[2]Department of Clinical Pharmacy and Pharmacy Management, Faculty of Pharmaceutical Sciences, University of Nigeria, Nsukka, Nigeria
[3]Department of Radiotherapy and Oncology, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria

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* *Corresponding Author:*
biambo.aminu@udusok.edu.ng
https://orcid.org/0000-0001-5008-5602
+2348065268340

ABSTRACT

Background: Evaluating drug utilisation in disease conditions like cancer is important to assess the past, keep track of the present and improve future practices. The objective of this study was to evaluate the utilisation of anticancer drugs used for cancer chemotherapy in Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria.

Methods: This study used a retrospective cross-sectional design. Using systematic random sampling, prescriptions of anticancer drugs documented within five years (2014–2018) in the facility were reviewed. The data were analysed using descriptive statistics; mean, standard deviation and frequency.

Results: The most common cancer types in the facility were nasopharyngeal (n=99, 20%), breast (n=95, 19.2%) and cervical (n=69, 13.9%) cancers. There were 955 prescriptions containing 2,490 anticancer drugs translating to 2.6 drugs per encounter. The most utilised chemotherapeutic agents were cisplatin (n=418, 16.8%), doxorubicin (n=397, 15.9%), cyclophosphamide (n=311, 12.5%), fluorouracil (n=275, 11.0%) and paclitaxel (n=268, 10.8%). Doxorubicin+Cyclophosphamide+Paclitaxel (n=85, 8.9%) and Cisplatin+Fluorouracil+Paclitaxel (n=44, 4.6%) were the most common combinations. The mean prescribed daily doses (PDDs) per patient for the three most prescribed chemotherapeutic agents – cisplatin, doxorubicin and cyclophosphamide were 65.6±18.9mg, 64.7±17.4mg and 754.8±226.9mg respectively. The average cost of chemotherapeutic agents per prescription was 26,275.8NGN (68.8USD) (as at 13/08/2020).

Conclusion: The most utilised anticancer drugs in the facility were cisplatin, doxorubicin, cyclophosphamide, fluorouracil and paclitaxel. The average cost of chemotherapeutic agents per prescription was 26,275.8NGN (68.8USD) as at august 2020.These findings should be used by clinicians and policy makers to keep track of anticancer drug utilisation in the facility.

1. Introduction

Cancer is a disease of high public health importance due to its high morbidity and mortality.[1] According to the 2018 global cancer statistics, cancer incidence, death and 5-year prevalence were estimated to be 18.1, 9.6 and 43.8 million cases respectively.[2] In Nigeria, the 2018 cancer statistics show that the country's cancer incidence, death and 5-year prevalence were estimated to be 115,950, 70,327 and 211,052 cases respectively.[2]

Chemotherapy is a widely used treatment option for cancer globally.[3,4] However, recommendations and guidelines guiding its use frequently change, based on the outcomes of many studies. This is because new evidence regarding the benefits of different chemotherapeutic agents, and the frequent approval of new drugs, doses, dosage forms, etc., frequently becomes available which makes cancer treatment modalities very dynamic.

Drug utilisation research keeps track of the pattern, indicators and outcomes of drug use.[5] This research is

important especially in cancer given the dynamic nature of managing the disease. Outcomes of studies like this can improve future practice by providing more evidence for improving prescribing practices.

Unfortunately, a large gap exists in drug utilisation research among cancer patients, especially in developing countries like Nigeria. This is because most of the studies were conducted outside Nigeria. Yet, treatment guidelines developed based on evidence from those studies are also used in developing countries, despite a wide socioeconomic and genetic differences.

The few anticancer drug utilisation or prescription pattern studies conducted in Nigerian are deficient mostly in the dept or width of the study. For example, some studies only reported the classes of anticancer drugs utilised instead of individual drugs. Also, many other studies reviewed the utilisation of only one or two cancer cases instead of reviewing all the cancer cases, which would have provided a better picture of anticancer drug utilisation in the facility.[6,8]

These gap justifies the need for anticancer drug utilisation studies like this, especially in developing countries like Nigeria. This will help in the understanding of the consistency of prescribing practices with existing guidelines, add to the existing information about anticancer drug utilisation in developing countries, provide a basis for tracking the outcomes of the use of such drugs, and provide a basis for evidence-based decision making and possibly reviewing existing guidelines. In this study, anticancer drug utilisation for cancer chemotherapy in a Nigerian tertiary health care facility was evaluated.

2. Methods

2.1 Design and Setting

This study used a retrospective cross-sectional design. Prescriptions of chemotherapeutic agents documented within five years (2014–2018) in the facility were reviewed. The study was conducted at Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto. The hospital is a 720 beds capacity tertiary health care facility located at Sokoto state, north-western Nigeria. The Radiotherapy and Oncology unit of the hospital provides oncology care to patients within the state and other north-western states of the country, especially the neighbouring Kebbi, Zamfara and Katsina states. It also serves as a referral centre from all over the country and the neighbouring Niger republic.

2.2 Study Population and Eligibility Criteria

The study population was all cancer patients managed in the hospital within the study period. Only adult patients, 18-years or older that were prescribed at least one chemotherapeutic agent for neoadjuvant or adjuvant chemotherapy were considered eligible for the study. All case files with less than three prescriptions were excluded. Only prescriptions with chemotherapeutic agents were sampled.

2.3 Sample Size

As at the time of this study, there were 1,150 records of cancer patients in the hospital. Using Raosoft® sample size calculator at 5% error margin and 99% confidence level, a minimum of 421 records of patients are required to represent the population.[9]

2.4 Data Collection

In the hospital, out of the record of 1,150 cancer case files, 1,027 were available, from which 989 met the eligibility criteria. From the eligible files, systematic random sampling technique was used to select records and chemotherapy prescriptions of the patients. Every other file was sampled leading to a total of 495 sampled files. From each of the folder, the patient's sociodemographic and clinical characteristics were collected in a structured data collection form. Similarly, every third prescription (from the available ones) in each of the folders was recorded in the data collection form. A total of 955 prescriptions were recorded and analysed.

2.5 Data Analysis

The data collected were analysed using SPSS version 25 (IBM Corporation, Armonk, NY). The demographic and clinical characteristics, as well as the utilisation of anticancer drugs and its indicators, were analysed using descriptive statistics; mean, standard deviation and frequency. The difference in the frequency distribution of the chemotherapeutic agents used in the facility was analysed using chi-square test at $p<0.05$.

Because anticancer drugs have no defined daily dose (DDD),[10] the utilisation of anticancer drugs in the facility was further expressed and compared in the form of mean prescribed daily doses (PDDs) per patient and dosage units (DUs) per patient per day.

The DUs were calculated as the PDD (mg) divided by the minimum marketed dose (MMD) (mg) of the drug. Drugs are marketed in different dosage strengths per unit, the smallest dosage strength is considered one DU.[8]

The following MMDs were used: Actinomycin (0.5 mg), Bleomycin (15 IU), Capecitabine (150 mg), Carboplatin (150), Cisplatin (50 mg), Cyclophosphamide (500 mg), Dacarbazine (200 mg), Docetaxel (80 mg), Doxorubicin (50 mg), Epirubicin (50 mg), Etoposide (100 mg), Fluorouracil (500 mg), Gemcitabine (200 mg), Ifosfamide (500 mg), Methotrexate (25 mg), Mitomycin (5 mg), Oxaliplatin (100 mg), Paclitaxel (100 mg), Vinblastine (10 mg), Vincristine (1 mg).[11,12]

The price of chemotherapeutic agents in each prescription

was estimated using the Nigerian National Health Insurance Scheme (NHIS) price list. The International Medical Products Price Guide was used to obtain the prices that were not available in the NHIS list. The price of each drug was accordingly adjusted for the current exchange and inflation rates.[11,12]

2.6 Ethical Consideration

The ethical approval for this study was sought and granted by the Health Research and Ethics Committee of Usmanu Danfodiyo University Teaching Hospital, Sokoto (UDUTH/HREC/2018/No.733). The anonymity of the patients and the confidentiality of their records were maintained.

3. Results

The result of this study shows that more than half of the patients' folders evaluated belongs to female patients (n = 258, 52.1%) . Their average age was 46.3 ± 15.3 years as shown in Table 1. Nasopharyngeal (n = 99, 20%), breast (n = 95, 19.2%) and cervical (n = 69, 13.9%) cancers were the most frequently encountered cases. The average duration of the illness was 4.07 ± 1.44 years. Most of the patients (n = 381, 77.0%) were new on chemotherapy (Table 2).

The overall most utilised chemotherapeutic agents were cisplatin (n = 418, 16.8%), doxorubicin (n = 397, 15.9%), cyclophosphamide (n = 311, 12.5%), fluorouracil (n = 275, 11.0%), paclitaxel (n = 268, 10.8%), and vincristine (n = 149, 6.0%). These account for 73% of all the chemotherapeutic agents utilised in the facility. Chi-square test ($\chi^2_{(19)} = 2{,}676.5, p<0.001$) shows a significant diffierence between the distribution of the chemotherapeutic agents utilised in the facility (Table 3).

The chemotherapeutic agents utilised by the three most common cancer types were cisplatin (n = 140, 33.7%%), fluorouracil (n = 102, 24.6%) and paclitaxel (n = 81, 19.5%) for nasopharyngeal cancer; doxorubicin (n = 138, 26.5%), cyclophosphamide (n = 135, 25.9%) and paclitaxel (n = 109, 20.9%) for breast cancer; and cisplatin (n = 59, 41.3%), fluorouracil (n = 45, 31.5%) and carboplatin (n = 21, 14.7%) for cervical cancer.

The combinations of chemotherapeutic agents used for managing different cancer types include Doxorubicin + Cyclophosphamide + Paclitaxel (N = 955, n = 85, 8.9%) followed by Cisplatin + Fluorouracil + Paclitaxel (N = 955, n = 44, 4.6%) respectively used for the management of breast and nasopharyngeal cancers were the most commonly used combinations in the facility (Table 4).

The prescribed daily doses (PDDs) per patient for all the encountered chemotherapeutic agents that were used for managing different cancer types are presented in Table 5. The overall PPDs for the three most prescribed chemotherapeutic agents – cisplatin, doxorubicin and cyclophosphamide were 65.6±18.9 mg, 64.7±17.4 mg and 754.8±226.9 mg respectively.

The dosage units (DUs) for the chemotherapeutic agents used in the facility were compared (Figure 1). The DUs for most of the drugs like bleomycin, cisplatin, cyclophosphamide, docetaxel, doxorubicin, etc were observed to be ≤ 2. Only a few of the drugs like capecitabine, dacarbazine, etoposide mitomycin and vinblastine had a high DUs that is up to 8.0.

The prescribing indicator for all the cancer types is shown in Table 6. The overall prescribing indicators were the average number of anticancer per encounter (2.6), prescriptions by generic (82.9%), encounters with antibiotics (60.4%), injections (98.8%), prescriptions from essential drug list (100%) and the average cost of chemotherapeutic agents per prescription (26,275.8 NGN, 68.8 USD as at 13/08/2020).

Table 1: Sociodemographic Characteristics of the Patients, N = 495

Variables	Frequency (%)
Gender	
Female	258 (52.1)
Male	237 (47.9)
Total	*495 (100.0)*
Highest level of education	
Islamic Education	297 (60.0)
Post-Secondary School	104 (21.0)
None	54 (10.9)
Secondary School	30 (6.1)
Primary School	10 (2.0)
Total	*495 (100.0)*
Occupation	
Unemployed	203 (41.0)
Self-employed	143 (28.9)
Employee	74 (15.0)
Student	59 (11.9)
Retired	16 (3.2)
Total	*495 (100.0)*
Marital status	
Currently Married	376 (76.0)
Single	79 (15.9)
Widowed	25 (5.1)
Separated	15 (3.0)
Total	*495 (100.0)*
Smoking status	
Non-Smoker	465 (93.9)
Current Smoker	30 (6.1)
Total	*495 (100.0)*

Table 2: Cancer Types: Distribution, Duration of Illness and History of Chemotherapy, N = 495

			History of Chemotherapy	
			New on Chemotherapy	*Previously on Chemotherapy*
			[n (%)]	*[n (%)]*
Nasopharyngeal Cancer	99 (20.0)	4.06 ± 1.39	76 (76.8)	23 (23.2)
Breast Cancer	95 (19.2)	4.04 ± 1.71	65 (68.4)	30 (31.6)
Cervical Cancer	69 (13.9)	4.51 ± 1.52	57 (82.6)	12 (17.4)
Hand and Foot Cancer	45 (9.1)	4.25 ± 1.26	36 (80.0)	9 (20.0)
Anorectal Cancer	30 (6.1)	3.43 ± 1.22	30 (100.0)	0 (0.0)
Oropharyngeal Cancer	20 (4.0)	4.60 ± 1.27	10 (50.0)	10 (50.0)
Eye Cancer	17 (3.4)	3.56 ± 0.73	13 (76.5)	4 (23.5)
Others (e.g. Bone, ear, GIT, ovarian, virginal, parotid)	120 (24.3)	3.90 ± 1.37	95 (79.2)	25 (20.8)
Overall	*495 (100.0)*	*4.07 ± 1.44*	*381 (77.0)*	*114 (23.0)*

Table 3: Frequency of Chemotherapeutic Agents Used by Cancer Type, N = 2,490

		Cancer Type by Anatomical Location								
		Breast – n (%)	*Cervical – n (%)*	*Nasopharyngeal – n (%)*	*Anorectal – n (%)*	*Hand & Foot – n (%)*	*Oropharyngeal – n (%)*	*Eye – n (%)*	*Others* – n (%)*	
L01XA01	Cisplatin	36 (6.9)	59 (41.3)	140 (33.7)	19 (19.6)	43 (13.9)	19 (31.1)	9 (16.4)	93 (10.5)	418 (16.8)
L01DB01	Doxorubicin [a]	138 (26.5)	2 (1.4)	18 (4.3)	8 (8.2)	67 (21.6)	-	4 (7.3)	160 (18.0)	397 (15.9)
L01AA01	Cyclophosphamide	135 (25.9)	-	15 (3.6)	-	65 (21.0)	-	4 (7.3)	92 (10.4)	311 (12.5)
L01BC02	Fluorouracil	18 (3.5)	45 (31.5)	102 (24.6)	17 (17.5)	18 (5.8)	10 (16.4)	9 (16.4)	56 (6.3)	275 (11.0)
L01CD01	Paclitaxel	109 (20.9)	14 (9.8)	81 (19.5)	-	10 (3.2)	11 (18.0)	5 (9.1)	11 (4.3)	268 (10.8)
L01CA02	Vincristine	6 (1.2)	-	10 (2.4)	-	26 (8.4)	7 (11.5)	9 (16.4)	91 (10.2)	149 (6.0)
L01CA01	Vinblastine	16 (3.1)	-	-	-	36 (11.6)	-	-	52 (5.9)	104 (4.2)
L01DC01	Bleomycin	2 (0.4)	-	17 (4.1)	-	3 (1.0)	7 (11.5)	4 (7.3)	70 (7.9)	103 (4.1)
L01XA02	Carboplatin	2 (0.4)	21 (14.7)	8 (1.9)	-	5 (1.6)	-	2 (3.6)	42 (4.7)	80 (3.2)
L01BA01	Methotrexate	5 (1.0)	-	3 (0.7)	-	8 (2.6)	7 (11.5)	5 (9.1)	36 (4.1)	64 (2.6)
L01CB01	Etoposide	6 (1.2)	-	7 (1.7)	3 (3.1)	1 (0.3)	-	3 (5.5)	33 (3.7)	53 (2.1)
L01CD02	Docetaxel	18 (3.5)	-	13 (3.1)	-	9 (2.9)	-	-	11 (1.2)	51 (2.0)
L01AX04	Dacarbazine	-	-	-	-	2 (0.6)	-	-	44 (5.0)	46 (1.8)
L01BC05	Gemcitabine	12 (2.3)	-	-	-	-	-	-	29 (3.3)	41 (1.6)
L01AA06	Ifosfamide	6 (1.2)	-	1 (0.2)	-	10 (3.2)	-	1 (1.8)	18 (2.0)	36 (1.4)
L01BC06	Capecitabine [b]	8 (1.5)	-	-	16 (16.5)	-	-	-	6 (0.7)	30 (1.2)
L01DB03	Epirubicin	4 (0.8)	2 (1.4)	-	8 (8.2)	-	-	-	13 (1.5)	27 (1.1)
L01XA03	Oxaliplatin	-	-	-	16 (16.5)	-	-	-	-	16 (0.6)
L01DA01	Actinomycin	-	-	-	-	7 (2.3)	-	-	4 (0.5)	11 (0.4)
L01DC03	Mitomycin	-	-	-	10 (10.3)	-	-	-	-	10 (0.4)
	Total	521 (100.0)	143 (100.0)	415 (100.0)	97 (100.0)	310 (100.0)	61 (100.0)	55 (100.0)	888 (100.0)	2,490 (100.0)

ATC Code = Anatomical Therapeutic Chemical (ATC) Classification Code; * Bone, Ear, GIT, Ovarian, Virginal, Parotid cancers et c; [a] Adriamycin; [b] Xeloda;
**$\chi^2_{(19)}$=2,676.5, p<0.001

Table 4: Combinations of Chemotherapeutic Agents Used in Managing Different Cancer Types*, N = 955

Table 4a: Breast Cancer

Combinations	*n (%)*
Doxorubicin + Cyclophosphamide + Paclitaxel	85(45.7)
Doxorubicin + Cyclophosphamide + Vinblastine	16(8.6)
Doxorubicin + Cyclophosphamide + Fluorouracil	11(5.9)
Doxorubicin + Cyclophosphamide + Docetaxel	11(5.9)
Doxorubicin + Cyclophosphamide	7(3.8)
Others Combinations (<3.8% occurrence)	56(30.1)
Total	***186(100.0)***

Table 4b: Cervical Cancer

Combination	*n (%)*
Cisplatin + Fluorouracil	26(29.2)
Cisplatin	25(28.1)
Carboplatin + Fluorouracil	13(14.6)
Cisplatin + Paclitaxel	6(6.7)
Carboplatin + Paclitaxel	5(5.6)
Others Combinations (<5.6% occurrence)	14(15.8)
Total	***89(100.0)***

Table 4c: Nasopharyngeal Cancer

Combination	*n (%)*
Cisplatin + Fluorouracil + Paclitaxel	44(27.7)
Cisplatin + Paclitaxel	30(18.9)
Cisplatin + Fluorouracil	25(15.7)
Cisplatin + Fluorouracil + Docetaxel	12(7.5)
Cisplatin + Fluorouracil + Bleomycin	11(6.9)
Others Combinations (<6.9% occurrence)	37(23.3)
Total	***159(100.0)***

Table 4d: Anorectal Cancer

Combination	*n (%)*
Oxaliplatin + Capecitabine	16(34.8)
Mitomycin + Fluorouracil	8(17.4)
Cisplatin + Epirubicin	8(17.4)
Cisplatin+ Doxorubicin+ Fluorouracil	8(17.4)
Others Combinations (<13.0% occurrence)	6(13.0)
Total	***46(100.0)***

Table 4e: Hand and Foot Cancer

Combination	*n (%)*
Doxorubicin + Cyclophosphamide + Vinblastine	36(31.6)
Cisplatin + Cyclophosphamide	14(12.3)
Cisplatin + Fluorouracil	13(11.4)
Gemcitabine + Docetaxel	9(7.9)
Actinomycin + Doxorubicin + Cyclo + Vincristine	7(6.1)
Others Combinations (<6.1% occurrence)	35(30.7)

Table 4f: Oropharyngeal Cancer

Combination	*n (%)*
Cisplatin + Paclitaxel	9(346)
Cisplatin + Fluorouracil	8(30.8)
Bleomycin + Methotrexate + Vincristine	7(26.9)
Cisplatin + Fluorouracil + Paclitaxel	2(7.7)

Table 4g: Eye Cancer

Combination	*n (%)*
Cisplatin + Fluorouracil	6(28.6)
Bleomycin + Methotrexate + Vincristine	4(19.0)
Cisplatin + Fluorouracil + Paclitaxel	3(14.3)
Doxorubicin + Cyclophosphamide + Vincristine	3(14.3)
Carboplatin + Etoposide + Vincristine	2(9.5)
Others Combinations (<9.5% occurrence)	3(14.3)
Total	***21(100.0)***

Table4h: Other Cancers like Bone, Ear, GIT, Ovarian, parotid

Combination	*n (%)*
Bleomycin + Doxorubicin + Dacarb + Vinb	40(12.7)
Cyclo + Doxorubicin + Vincristine	28(8.9)
Carboplatin + Etoposide + Vincristine	24(7.6)
Cyclo+ Doxorubicin + Fluorouracil	16(5.1)
Cisplatin + Gemcitabine	14(4.5)
Others Combinations (<4.5% occurrence)	192(61.2)
Total	***314(100.0)***

***** in the hospital, the combinations were given in cycles and every cycle is 3 weeks; Cyclo = Cyclophosphamide; Dacarb = Dacarbazine; Vinb =Vinblastine

Table 5: Prescribed Daily Doses (PDDs) of the Chemotherapeutic Agents Used in the Facility by Cancer Type

			PDD (mg) per patient per day (*Mean ± SD*)								
			Breast	*Cervical*	*Nasopharyngeal*	*Anorectal*	*Hand & Foot*	*Oropharyngeal*	*Eye*	*Others**	Overall
L01DA01	Actinomycin	0.5	-	-	-	-	1.9 ± 0.2	-	-	2.8 ± 0.3	2.6 ± 0.2
L01DC01	Bleomycin	15 IU	18.2 ± 5.3	-	15.0 ± 0.0	-	20.0 ± 20.0	16.7 ± 2.9	15.0 ± 0.0	17.3 ±7.3	17.5 ± 9.5
L01BC06	Capecitabine[a]	150	750.0±353.6	-	-	1500.0±707.1	-	-	-	2566.7±513.2	2015.4±803.0
L01XA02	Carboplatin	150	450.0 ± 0.0	360.0±174.6	437.5 ± 25.0	-	266.8 ± 230.7	-	320.0±75.0	300.3±259.4	356.3 ± 170.0
L01XA01	Cisplatin	50	72.5 ± 19.4	71.2 ± 21.2	61.5 ± 17.0	70.0 ± 28.3	68.1 ± 22.4	57.5 ± 11.7	58.3 ± 7.6	67.2 ± 19.7	65.6 ± 18.9
L01AA01	Cyclophosphamide	500	793.3±190.8	-	633.3 ± 153.8	-	860.0 ± 263.2	-	766.7±202.1	702.9±280.8	754.8 ± 226.9
L01AX04	Dacarbazine	200	-	-	-	-	1600.0±200.0	-	-	1600.0±400.0	1600.0±500.0
L01CD02	Docetaxel	80	120.8 ± 32.6	-	120.0 ± 40.0	-	115.0 ± 25.8	-	-	130.0 ± 70.7	122.6 ± 38.0
L01DB01	Doxorubicin[b]	50	67.0 ± 18.3	50.0 ± 0.0	61.4 ± 14.9	90.0 ± 0.0	64.2 ± 14.7	-	60.0 ± 8.7	63.6 ± 19.1	64.7 ± 17.4
L01DB03	Epirubicin	50	50.0 ± 0.0	75.0 ± 11.3	-	50.0 ± 0.0	-	-	-	75.0 ± 34.4	66.7 ± 28.9
L01CB01	Etoposide	100	900.0±173.2	-	950.0 ± 100.0	1000.0 ± 0.0	750.0 ± 353.6	-	680.0 ± 0.0	493.3±321.0	830.0 ± 253.9
L01BC02	Fluorouracil	500	1000.0 ± 0.0	750.0±288.1	800.0 ±259.4	750.0 ± 435.9	670.0 ± 236.1	800.0±264.6	583.3±453.7	667.5±311.8	735.2±290.9
L01BC05	Gemcitabine	200	100.0 ± 0.0	-	-	-	-	-	-	44.5 ± 38.4	36.0 ± 32.4
L01AA06	Ifosfamide	500	200.0 ± 0.0	-	100.0 ± 0.0	-	200.0 ± 0.0	-	100.0 ± 20.0	750.0±212.0	439.0 ±277.9
L01BA01	Methotrexate	25	50.0 ± 0.0	-	65.0 ± 0.0	-	55.0 ± 12.5	50.0 ± 0.0	50.0 ± 0.0	50.5 ± 26.4	51.6 ± 19.2
L01DC03	Mitomycin	5	-	-	-	40.4 ± 22.4	-	-	-	-	40.4 ± 22.4
L01XA03	Oxaliplatin	100	-	-	-	110.9 ± 35.1	-	-	-	-	110.9 ± 35.1
L01CD01	Paclitaxel	100	134.1 ± 44.7	141.7 ± 46.5	131.0 ± 40.4	-	136.0 ± 43.4	100.0 ± 0.0	100.0 ± 0.0	148.8 ± 48.8	134.8 ± 43.2
L01CA01	Vinblastine	10	85.0 ± 16.5	-	-	-	90.0 ± 15.0	-	-	10.0 ± 0.0	90.0 ± 58.3
L01CA02	Vincristine	1	1.4 ± 0.0	-	1.3 ± 0.3	-	1.2 ± 0.3	1.1 ± 0.2	1.0 ± 0.0	1.5 ± 0.4	1.4 ± 0.4

ATC Code = Anatomical Therapeutic Chemical (ATC) Classification Code; MMD = Minimum Marketed Dose; PDD = Prescribed Daily Dos e; SD = Standard deviation; [a]Xeloda; [b]Adriamycin; * Bone, Ear, GIT, Ovarian, Virginal, Parotid cancers etc;

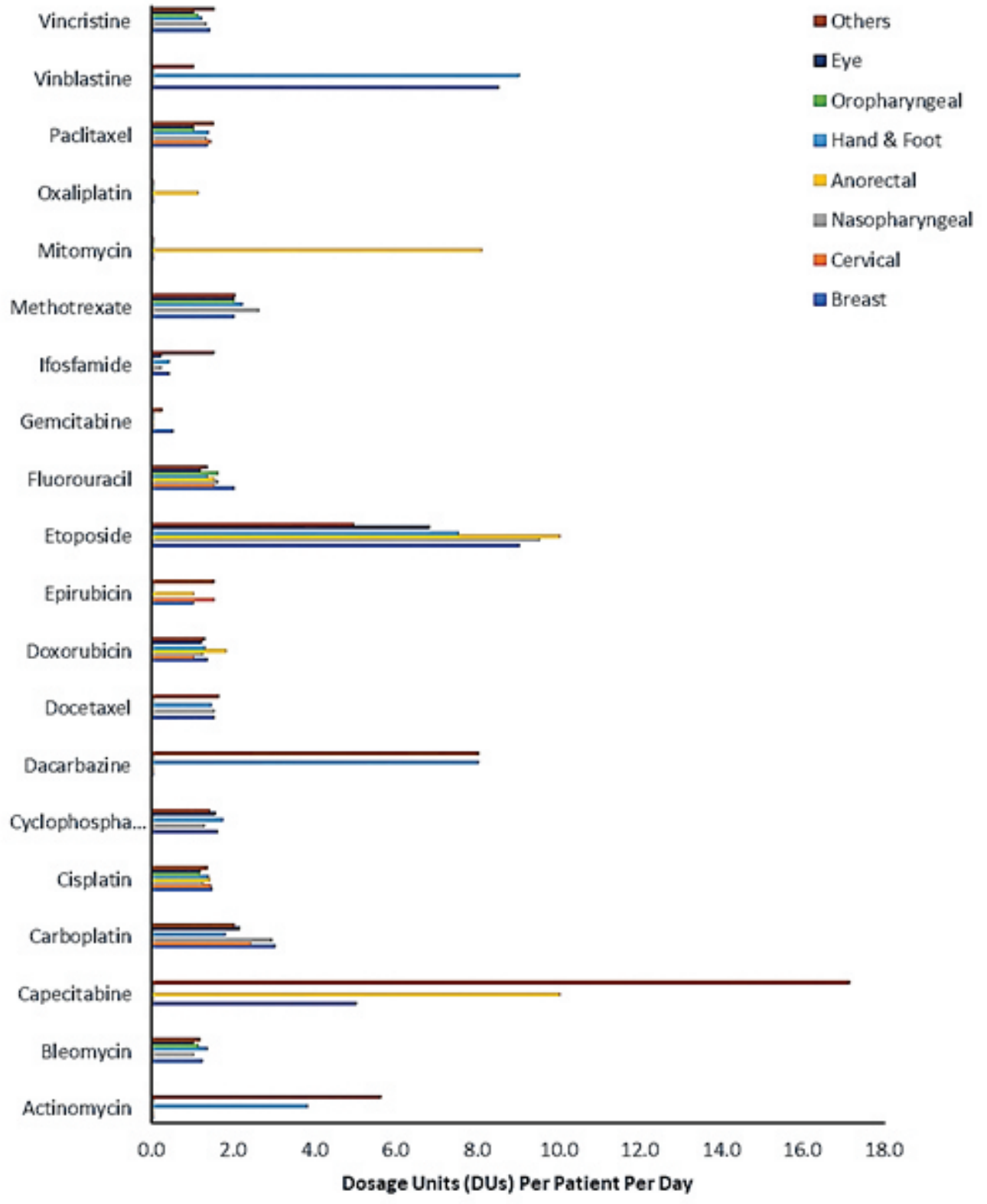

Figure 1: Dosage Units (DUs) of Chemotherapeutic Agents

Table 6: Indicators of Chemotherapeutic Agents' Use

Variables	*Breast*	*Cervical*	*Nasopharyngeal*	*Anorectal*	*Hand & Foot*	*Oropharyngeal*	*Eye*	*Others**	Total
Number of encounters	186.0	89.0	159.0	46.0	114.0	26.0	21.0	314.0	955.0
Total No of Anticancer drugs used	521.0	143.0	415.0	97.0	310.0	61.0	55.0	888.0	2,490.0
Average No of Anticancer per Encounter	2.8	1.6	2.6	2.1	2.7	2.3	2.6	2.8	2.6
Prescriptions by generic (%)	71.4	98.6	95.7	75.3	78.4	100.0	92.7	81.3	82.9
Encounters with Antibiotic (%)	46.8	70.3	58.8	28.6	58.3	40.0	77.8	59.4	60.4
Encounters with Injections (%)	98.5	100.0	100.0	83.5	100.0	100.0	100.0	99.3	98.8
Prescriptions from EDL (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Average Cost of anticancer per Prescription *(NGN; 1 NGN = 382 USD as @ 13/08/2020)*	28,174.9	23,307.5	28,016.6	18,447.5	32,659.5	16,109.6	17,463.3	25,371.0	26,275.8

* Bone, Ear, GIT, Ovarian, Virginal, Parotid cancers etc; EDL = Essential Drug List; NGN = Nigerian Naira; USD = United State Doller

4. Discussion

The result of this study shows that the patients were middle-aged, reflecting how cancer affects the younger population. The fact that females were slightly higher than their male counterparts could be because breast and cervical cancers, which mainly affect females were observed in this study to be the predominant cancer types after nasopharyngeal cancer. This finding shows the extent to which cancer slightly affects more females than males. These findings are consistent with global cancer statistics[2] and some related studies within[7] and outside Nigeria.[13]

The result also shows that the most utilised chemotherapeutic agents in the facility were cisplatin, doxorubicin, cyclophosphamide, fluorouracil, paclitaxel and vincristine. This could be connected to their therapeutic benefits, physicians experience, and recommendations from guidelines. Some similar studies conducted outside Nigeria reported cisplatin, cyclophosphamide, paclitaxel, carboplatin, fluorouracil and oxaliplatin as the most utilised anticancer drugs which is consistent with our finding.[14,15]
It was observed that different cancer types had different anticancer drug utilisation pattern, though there could be some few drugs in common. For example, the findings of our studies showed that the three most common drugs for managing breast cancer (doxorubicin, cyclophosphamide and paclitaxel) were different from that of cervical cancer (cisplatin, fluorouracil and carboplatin). A related study conducted in Nigeria among breast and cervical cancer patients also reported similar finding; the study shows that cisplatin, fluorouracil and paclitaxel were among the drugs used in managing the two disease states.[8] The anticancer drugs for managing patients with breast cancer in this facility is similar to that of a study conducted in India.[16] Overall, the pattern of anticancer drug utilisation for cancer chemotherapy in the facility is in agreement with international guidelines for cancer therapy like the National Comprehensive Cancer Network (NCCN)[4] and the American Society of Clinical Oncology (ASCO).[3]
Chemotherapeutic agents were prescribed in different combinations depending on the type of cancer to be managed. The most frequently used combination was doxorubicin + cyclophosphamide + paclitaxel which is used for managing patients with breast cancer. However, some studies reported the use of fluorouracil + epirubicin + cyclophosphamide (FEC) among breast cancer patients which disagrees with our finding.[7,17] The difference could be attributed to the difference in patients' preferences (like tolerability, cost, patient's comorbid state), physicians' preference or experience. However, what is common between them is that anthracyclines (doxorubicin or epirubicin) and cyclophosphamide (AC) are common in combinations used for managing patients with breast cancer. Hence, the popular use of AC could suggest good treatment outcomes from their use.

The result of this study also shows the prescribed daily dose (PDD) for all the chemotherapeutic agents used in the facility. This can be used to understand different doses of the same anticancer agent which depends on the cancer to be treated. These doses could be used to improve the quality of patients' treatment and possibly the quality of existing guidelines. Furthermore, due to the lack of defined daily doses (DDDs) for anticancer drugs,[10] continuous study of PDDs could lead to the future development of DDDs for these chemotherapeutic agents.

The result of this study also shows that the dosage units (DUs) for most of the chemotherapeutic agents were ≤ 2. This is a reflection of the multiple units of the anticancer agents per patients used in the facility. Only a few of the

drugs have a high DU of up to 8. The difference could be because doses are chosen based on the evidence of effectiveness, thus, every drug has its range of dosages hence the dosage units. Also, some anticancer agents might be available in different dosage units. When the lower dosage unit is used (MMD), multiple of that unit is needed to achieve the same result. For example, the MMD of capecitabine in the study setting is 150 mg but its PDD can be as high as 1500 mg, making the DU to be 10. If the MMD were to be 500 mg, the DU would have been 3.

The WHO prescribing indicators for chemotherapeutic agents in the facility shows that an average of 2.6 drugs were used per encounter, which shows that combinations of anticancer drugs were used in the facility. Also, almost all the drugs were observed to be injections, suggesting that oral cytotoxic drugs are rare. Encounters with about 60% antibiotic could suggest that most of the patients suffered co-infection with bacteria during their treatment. Almost all the prescriptions were done with generic names and all the prescribed drugs were from essential drug list, suggesting rational prescribing. Rational prescribing among cancer patients was also reported by many studies.[18]

The cost of chemotherapeutic agents per prescription was observed to be 26,275.8 NGN (68.8 USD). This cost does not include the costs of other adjuvant therapy, targeted therapy, consumable, other hospital bills, some direct non-medical costs and indirect cost. This shows the expensive nature of managing cancer especially in a low-income country like Nigeria which has many people leaving below 1 USD per day. This finding exposed the need for governmental and non-governmental intervention towards supporting cancer patients in Nigeria.

The limitation of this study is that a cross-sectional design was used. Hence, trends of anticancer use between years could not be seen. Other limitations are the use of a single centre and descriptive statistical analysis only to analyse the drug utilisation data. The study did not also evaluate the outcomes of the drugs utilised, hence, a cause-effect relationship cannot be established from this study. However, despite these limitations, this study has quality findings that will go a long way in adding value to existing literature and form a base for further studies that could improve future practice.

5. Conclusion

The most utilised chemotherapeutic agents in the facility were cisplatin, doxorubicin, cyclophosphamide, fluorouracil, paclitaxel and vincristine. The average number of chemotherapeutic agents per encounter was 2.6, with doxorubicin + cyclophosphamide + paclitaxel and cisplatin + fluorouracil + paclitaxel combinations as the most commonly used combination. There was rational prescribing of chemotherapeutic agents in the facility. The average cost of chemotherapeutic agents per prescription is 26,275.8 NGN (68.8 USD). These findings should be used by clinicians and policymakers to keep track of anticancer drug utilisation in the facility.

Conflict of Interest

We declare that there is no conflict of interest to disclose.

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