PATTERN OF ANTIBIOTICS PRESCRIPTION IN A TERTIARY HOSPITAL IN DELTA STATE, NIGERIA

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ABSTRACT

Background: *Antibiotics are drugs commonly used in hospitals but are prescribed inappropriately in most cases. This has led to the emergence of bacterial resistance and an increase in the cost of treatment. Drug utilization studies are intended to provide information on prescription patterns to ensure rational drug use.*

Objective: *The study aimed at describing antibiotic prescription patterns in Delta State University Teaching Hospital, Delta State, Nigeria.*

Methods: *A retrospective cross-sectional study was conducted on antibiotic prescriptions pattern at Delta State University Teaching Hospital using 17 core quantitative prescribing indicators which determined the availability of a Standard Treatment Guidelines and Essential Medicine List at the facility. The study was conducted for a period of six months. A total of 420 prescriptions were studied. Data collected was analyzed using SPSS version 23. Results were presented as frequency (percentages), mean, tables and charts.*

Results: *The average number of antibiotics prescribed per encounter (ANAPE) was found to be 1.49, with an average cost of NGN 2404 per hospitalization. The percentage of prescriptions by generics was 58.65%. The prevalence of inappropriate prescription was found in 67.5% of patients. The most commonly prescribed class of antibiotics were Cephalosporin 149(23.8%), Nitroimidazole 150(23.93%), and Penicillin 134(21.36%). In-depth interviews of the health professionals revealed factors that influenced antibiotic prescription pattern including: diagnosis uncertainty, doctor's hierarchy, external influence by manufacturer among others.*

Conclusion: *There was inappropriate prescription of antibiotics with increased risk of developing resistance hence increasing financial burden on patient. Intervention programs, strategies, policies, and reforms should be put in place to address this problem*

Keywords*: Antibiotic, drug utilization, rational drug prescription, healthcare professionals*

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INTRODUCTION

Antibiotics are drugs used to suppress or destroy the growth of pathogens.[1]It has been identified that antibiotics are one of the drugs most prescribed by physicians but in most cases are prescribed inappropriately. For example, studies [2,3]stated that 85% of all prescriptions generated by physicians are antibiotics.

One of the main goals of medical practice is to ensure the appropriate use of antimicrobial agents.[1] It has been identified that many health facilities in developing countries are faced with the problem of irrational antibiotics prescription.[4]These inappropriate prescriptions include (but are not limited to) the unnecessary use of antibiotics to treat non-responsive conditions and the suboptimal use of antibiotics for treating responsive conditions; incorrect use of drugs, their dosing and duration; excessive use of broad agents, and poor adherence.[5]The widespread irrational use of antimicrobial agents has led to an emergence of antibiotics resistance.[6]Rational use of drugs has been defined by the world health organization as patients receiving appropriate medication for their clinical needs at the appropriate dose designed to meet their personal needs for an appropriate period of time and at the lowest cost to them and their community.[7]Irrational prescribing of antimicrobial agents is a global problem that has drawn the attention of health authorities in many countries because of its adverse bearing on the development of resistance, increase in healthcare cost, morbidity, and mortality.[8]

Drug utilization studies assess the appropriate use of drug therapy by evaluating drug use and comparing data obtained against predetermined criteria and standards. The main objective of drug utilization studies is to promote the rational use of drugs in populations. [1]These studies provide information on how drugs are being used thereby providing means of managing the adverse effects and economic problems emanating from inappropriate use of drugs.

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Studies have been carried out on drug utilization of antibiotics in different hospitals all around the world. [9,10,1,11]In developing counties, regulating drug use is not as strict as in developed countries and this has given rise to inappropriate prescription and use of antibiotics with the emergence of antibiotics resistance. [1] To reduce antimicrobial resistance in hospitals, interventions should be put in place such as monitoring the use of antibiotics, evaluating prescription patterns, developing and implementing antimicrobial stewardship to suit the peculiar needs of the hospital amongst others. This study, therefore, evaluated the pattern of antibiotic prescription in Delta State University Teaching Hospital, Delta State, Nigeria.

METHODS

Ethical consideration: The study protocol was approved by the research and ethical committee of Delta state teaching hospital (DELSUTH/HREC/2019/024/0386). Full access to the patient folder and all documents needed for the study was granted. Study codes were generated and used instead of the direct reference of the patient's name or folder number

Study setting/Location: This study was carried out in Delta State Teaching Hospital (DELSUTH), a tertiary healthcare facility located in Oghara, Delta State, Nigeria. This study was carried out using records from the out-patient department, medicine, surgery, orthopedic, pediatric and obstetrics, and gynecology departments as well as the main pharmacy department of DELSUTH

Study design: This is a retrospective, cross-sectional (descriptive) study of the antibiotics prescription pattern among physicians in Delta State University Teaching Hospital, Delta State. The study was conducted in the five different wards of DELSUTH as well as the outpatient department from January to June 2019. The study population was antibiotics prescriptions collected from the In-patients and Out-patients folders of patients that visited the health facility within the 6 months. The Sample size was calculated using the formula

$$n = \frac{z^2 \times P(1-P) \div e^2}{1 + \left[\frac{Z^2 \times P(1-P)}{e^2 N}\right]}$$

The population size was 622 prescriptions. A total of 420 prescriptions out of the 622 prescription collected met the inclusion criteria. Antibiotics prescriptions were selected through cluster sampling from the recording unit while systematic sampling was used to ascertain each case note and the antibiotic prescribed. Inclusion criteria include all patients' folders admitted into medicine, surgery, orthopedic, pediatric, obstetrics, and gynecology with complete patient information containing antibiotics prescription and folders of patients that visited the out-patient department for the study period. Folders of antenatal patients, folders containing other antimicrobial agents other than antibiotics and those that have antibiotics prescribed together with other antimicrobial agents were excluded from the study.

Study procedure Data collection: Two trained research assistants and the primary researcher were involved in the data collection process. Data relevant to the objective of the study were retrieved from the folder of each patient using a pre-designed standard data collection form. These include patient demography, name, and number of the antibiotics prescribed, dosage regimen (dosage form, strength, dose, dosing frequency and duration of administration), number of days of hospitalization, patient's antimicrobial culture sensitivity test results, cost of prescribed and administered antibiotics treatment.

The financial and drug inventory record or stock books from the hospital pharmacy were also reviewed. Data obtained from these records include; the amount of money spent for the purchase of antibiotics, the total amount of money spent on overall medicines purchase, and the number of essential antibiotics in-stock and out-of-stock within the study period. Purchase prices of the hospital drugs were collected. Other information assessed includes the existence of a drug therapeutic committee (DTC), essential medicine list (EML), and standard treatment guidelines (STGs). (See appendix for data collection forms).

In-depth interview: In depth interview was conducted among randomly selected healthcare professionals in the healthcare facility. The healthcare professionals interviewed included physicians, pharmacists and medical lab scientists. The interview addressed the pattern of antibiotic prescription in the health facility, the presence and use of standard treatment guideline and essential medicine list. A structured questionnaire was adapted and tailored to suit the objectives of the study. The questionnaire was subjected to face and

content validity by consulting 4 healthcare professionals and a statistician. The feasibility of the instrument was assessed on ten healthcare professionals who were not included in the main study. Interviews were audio-recorded and transcribed verbatim after obtaining consent from the participants. Each interview lasted for an average of 20 minutes and the confidentiality of the participants were maintained throughout the process.

Data analysis: The data obtained were coded and checked for completeness and consistency. Microsoft Excel (Microsoft Corporation, USA) was used for the data analysis. Data collected were summarized using a frequency (percentage), mean and standard deviation. Interview audio records were transcribed, and the transcripts obtained from the interview were analyzed thematically using the framework method. [12] The transcripts were first screened against the audio recording for completeness and accuracy and then codes were assigned, this transcript was also sent to two other researchers to cross-check.

RESULTS

Demographics of folders surveyed: Among the 622 patient's folders with complete information reviewed, 420 contained antibiotics. Patient characteristics are shown in Table 1. There were 51.7% male patients and 48.3% female patients out of which 14.5% are children. The admissions from five (5) wards and the out-patient department were distributed by ratio to the total sample size. The prevalence of antibiotic prescription was 67.5% (420/622 multiply by 100).

Table 1: Characteristic of antibiotics prescription pattern (n=420)

Variable	Frequency	Percentage
Gender		
Male	188	44.8
Female	171	40.7
Male children	29	6.9
Female children	32	7.6
Age group(years)		
0-10	50	11.9
11-20	21	5.0
21-30	76	18.1
31-40	95	22.6
41-50	78	18.6
51-60	47	11.2
61-70	27	6.4
71-80	19	4.5
81-90	5	1.2
91-above	2	0.5
Ward		
Medicine	118	28.1
Surgery	77	18.3
Orthopedic	44	10.5
Pediatric	17	4.0
Obstetrics and Gynecology	22	5.2
Outpatient Department	142	33.8

Drug use pattern

The type and number of prescribed antibiotics across wards of study

A total of 32 different types of antibiotics were prescribed either alone or in different combinations amongst the 420 antibiotics prescriptions reviewed.

Table 2 shows the type, number, and percentage of antibiotics prescribed during the study. Metronidazole was the most prescribed antibiotic from the health facility with 142 (22.65%) of all antibiotic prescriptions. This was followed by Amoxicillin and Clavulanate Potassium 91 (14.5%) and ciprofloxacin 81 (12.9%) of all antibiotic prescriptions. The least prescribed antibiotics were Cephalexin, Lincomycin, Flucloxacillin, Meropenem, all with a frequency of 1 (0.16%).

The outpatient department recorded Amoxicillin and Clavulanate Potassium as the most frequently prescribed antibiotic 43(24), followed by Ciprofloxacin 36(20), Metronidazole 33(18.9), and Amoxicillin 23(12.5). The analysis is shown in Table 2.

	Antibiotic used	**In-patients**					**Out-patients**		
S/N	***Antibiotics***	***MD***	***SG***	***OTH***	***PD***	***O&G***	***OUT PXT (%)***	***TOTAL***	***%***
1	Cefuroxime	18	19	11	4	7	11 (6.1)	70	11.2
2	Rifampicin	0	0	2	0	0	0 (0)	2	0.32
3	Ciprofloxacin	25	11	3	1	5	36 (20)	81	12.9
4	Ofloxacin	0	1	3	0	0	0 (0)	4	0.64
5	Ceftriaxone	9	34	18	2	0	2 (1.1)	65	10.37
6	Cefixime	3	1	2	1	0	2 (1.1)	9	1.44
7	Levofloxacin	10	2	1	0	0	8 (4.4)	21	3.35
8	Amoxicillin/ Clav	22	5	6	4	11	43 (24)	91	14.5
9	Imipenen	1	0	1	0	0	0 (0)	2	0.32
10	Clarithromycin	1	2	2	0	0	3 (1.7)	8	1.28
11	Clindamycin	1	1	6	0	0	0 (0)	8	1.28
12	Amoxicillin	11	0	0	2	0	23 (12.5)	36	5.74
13	Penicillin V	1	0	0	0	0	0 (0)	1	0.16
14	Azithromycin	5	0	0	1	0	3 (1.7)	9	1.43
15	Metronidazole	32	47	19	0	11	33 (18.3)	142	22.65
16	Erythromycin	5	0	0	1	0	3 (1.7)	9	1.43
17	Gentamycin	4	19	8	1	0	0 (0)	32	5.1
18	Doxycyclin	3	0	0	0	3	4 (2.2)	10	1.59
19	Meropenem	1	0	0	0	0	0 (0)	1	0.16
20	Cephalexin	0	0	0	0	0	1 (0.6)	1	0.16
21	Cotrimoxazole	2	0	0	0	0	3 (1.7)	5	0.8
22	Nitrofuranton	1	2	0	0	0	1 (0.6)	4	0.64
23	Vancomycin	1	0	0	0	0	1 (0.6)	2	0.32
24	Cefotaxime	2	0	0	1	0	0 (0)	3	0.47
25	Ampicillin/ cloxacillin	0	0	0	0	0	2 (1.1)	2	0.32
26	Bezyl Penicillin	0	1	0	0	0	0 (0)	1	0.16
27	Ampicillin/fluclox acillin	0	2	0	0	0	0 (0)	2	0.32

28	Tinidazole	1	0	1	0	0	0 (0)	2	0.32
29	Flucloxacillin	1	0	0	0	0	0 (0)	1	0.16
30	Lincomycin	0	0	0	0	0	1 (0.6)	1	0.16
31	Ceftazidine	0	1	0	0	0	0 (0)	1	0.16
32	Ofloxacin/Tinidazole	0	1	0	0	0	0 (0)	1	0.16
	TOTAL	**160**	**83**	**149**	**18**	**37**	**180 (100%)**	**627**	**100**

The 420 antibiotics prescriptions reviewed in all wards of DELSUTH were from the ten major classes of antibiotics (see Figure 1 below). The cephalosporin's were the most commonly prescribed class of antibiotics 149 (35.5%) followed by the nitroimidazole 144 (41.1%) and penicillin 134 (39.5%).

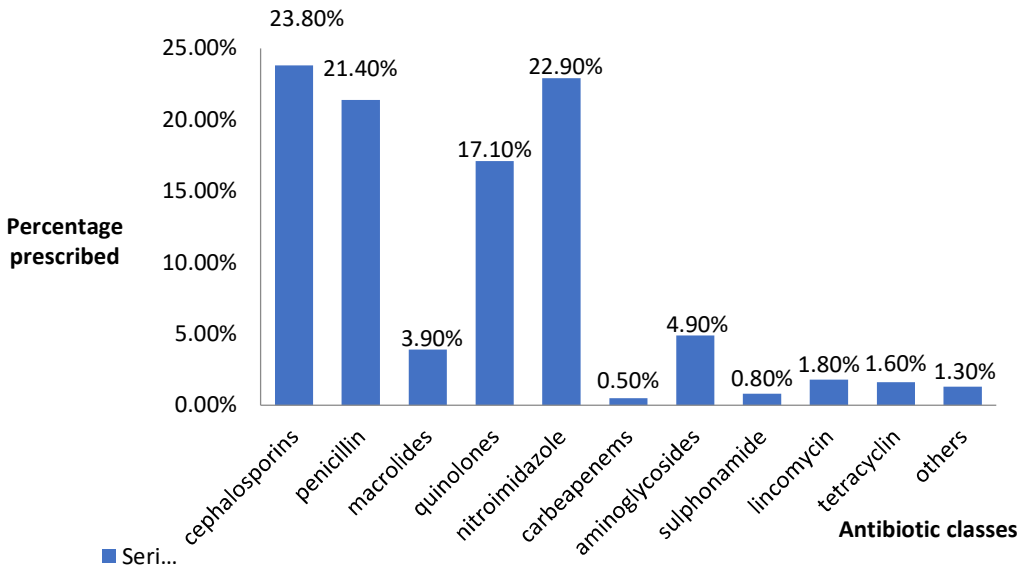

Figure 1: percentage classes of antibiotic prescribed (n=420)

Cost of antibiotic per class: A total of N 1,009,844.00 (one million, nine thousand eight hundred and forty-four naira) was spent by the patient admitted within the study period on the purchase of antibiotics, translating to NGN2404 naira as the cost for each prescribed dose of antibiotics per hospitalization with an average number of 1.49 antibiotics prescribed for hospitalization

(Table 3) The Cephalosporin's class of antibiotics accounted for the highest percentage cost, (39.59%) of the overall antibiotic cost while penicillin had the second-highest percentage, (22.09%) of the overall cost of prescribed antibiotics during the study (Table 3).

Antibiotic class prescribed	Antibiotic cost (naira)	Percentage of antibiotics cost (%)
Penicillins	223080	22.09
Cephalosporins	399845	39.59
Quinolones	132040	13.08

Macrolides	29870	2.96
Nitroimidazole	77900	7.71
Carbapenems	81000	8.02
Aminoglycoside	23020	2.28
Lincomycins	22770	2.25
Tetracyclines	2312	0.23
Sulphonamides	4710	0.47
Others	13297	1.32
TOTAL	**1009844**	**100**

The prices are the price of antibiotics sold in the hospital pharmacy.

QUALITY OF PRESCRIPTION

Inappropriate antibiotic prescribing: Inappropriate antibiotic prescribing was found in 65.2% of patients studied. This value represent antibiotics misuse, overuse, abuse (use of antibiotics when they are not necessary), and use of trade names. Deviation from one or more of these was regarded as inappropriate antibiotic prescribing (Figure 2)

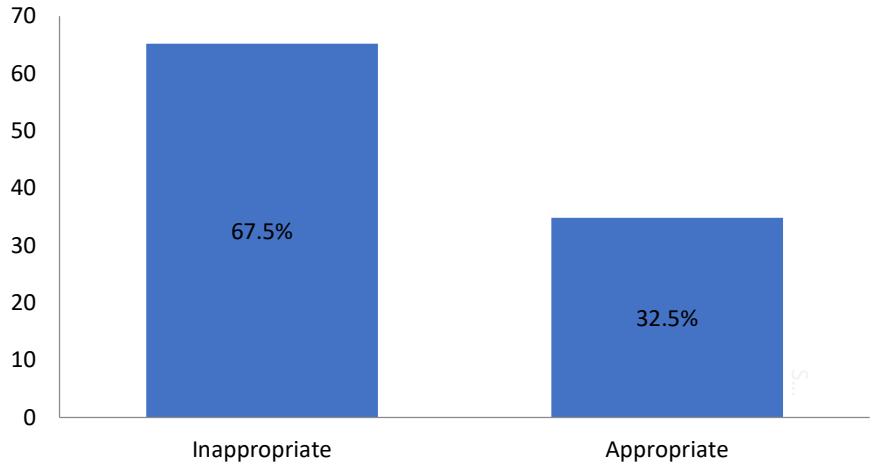

Figure 2: Percentage inappropriate antibiotic prescribing (n=420)

Table 4: Summary of the result of 17 antibiotics use indicators assessed in DELSUTH

NO	Standard indicators	Study values	Previously derived in Nigeria	Previously derived in southern Nigeria Remedies,2018 (unpublished)	WHO Ideal (SPS,2012)
1	Existence of standard treatment guidelines (STGs)	Available	Not available	Not available (unpublished)	Available
2	Availability of an Essential Medicine List /date last reviewed	Available (7/15)	Not avalable [13]	Available (unpublished)	Available
3	Percentage of key antibiotics available	78.3%	83.3% [14]	62.2% (unpublished)	100%
4	The average number of days out of stock of key antibiotics	46 days	N/A	61 days (unpublished)	0 days
5	Percentage of total drug expenditure on antibiotics in	61.7%	62%	13% (unpublished)	Minimal

	DELSUTH				
6	Percentage of antibiotic prescribed per hospitalization	67.5%	63.3-86.6%	68.8% (unpublished)	ALAP
7	The average number of antibiotics prescribed per hospitalization	1.49	2.4 [13]	2.9 (unpublished)	Minimal
8	Percentage of prescribed consistent with the hospital's EML	84%	92.75% [15]	84.2% (unpublished)	100%
9	Average cost of antibiotic prescribed per hospitalization	NGN 2,404($6.67)	USD 9.05(SD = USD 6.89) [15]	N 13,632 (SD=14,957) (unpublished)	ALAP
10	The average duration of prescribed antibiotic treatment	10.09 days	N/A	7.0 days (unpublished)	5-7days
11	Percentage of patients who received surgical antimicrobial prophylaxis for cesarean section in accordance with STG	100%	N/A	89.0% (unpublished)	100%
12	The average number of doses of prophylactic antibiotics prescribed for Surgeries procedures	0.3	N/A	1.3 (unpublished)	1.0*
13	Percentage of patients with pneumonia whom antimicrobial agents were prescribed	80%	N/A	75.0% (unpublished)	100%
14	The percentage of antimicrobials prescribed by generic	58.7%	45.3% [15]	39.9% (unpublished)	100%
1 5	Percentage of doses of prescribed antimicrobial administered	97.6%	N/A	88.9% (unpublished)	100%
16	The average duration of hospital admission of patients who received antibiotics	4.7 days	7.13 [15]	10-9 days (unpublished)	5-7 days
17	Percentage of antimicrobial drugs sensitivity tests reported per hospital admission with curative antibiotics prescribed	14 %	4.2% [13]	52.7% (unpublished)	100%

FINDING FROM IN-DEPTH INTERVIEW OF THE HEALTH PROFESSIONAL

Fifteen health professionals participated in the interview. These include eight (8) physicians, five (5) pharmacists, one (1) nurse, and one (1) laboratory scientist. There are eight (8) males and seven (7) females. Nine were less than 50 years of age while six were 50 years and above. Ten of them had been in clinical practice for 5-15 years; four(4) of the participant had 16- 25 years of practice experience while one (1) of the participant had spent more than 25 years of practice experience.

Eight major themes relating to antibiotics use emerged from the interview with these participants which provided a better understanding of the current antibiotics used in the health care facility. The highlighted key challenges to antibiotics use include: Diagnostic uncertainty, Patient expectation and demands from physicians, Practice sustainability and financial burden, Low staff strength and overcrowding, Palliative measure and susceptibility, External influence on prescriber, Doctor Hierarchy, and Near- Expires.

BACK-END OR POST PRESCRIPTION APPROACH DIAGNOSTIC UNCERTAINTY

It is difficult for clinicians to diagnose infections at early stage especially cases of upper respiratory infections, diarrhea and causes of fever especially when patients present with high temperature. To deal with this uncertainty, physicians usually employ back-end or post prescription approach where antibiotics are prescribed for the patient with de-

escalation once the susceptibility profile of the pathogen determined.

PATIENT EXPECTATIONS AND DEMANDS FROM PHYSICIANS

Many doctors succumb to patient expectations and demand for an antibiotics prescription. Some patients demand specific antibiotics that were previously prescribed for them. Some others want a new class of drugs to be prescribed for them. Patients on a long queue for consultation were not satisfied with just paracetamol for fever without the addition of antibiotic

PRACTICE SUSTAINABILITY AND FINANCIAL BURDEN

Doctors stated that they do not want to employ a wait-and-watch policy. They wanted to use their clinical judgment. The wait-and-watch policy as they stated might take a toll on patients who are not financially stable and so the inclusion of antibiotics might prevent hospital re-visit by the patients.

LOW STAFF STRENGTH AND OVERCROWDING

Doctors complain that due to time constraint, they could not go through all the patients' case files for past medical and medication history or do any proper physical examination. A physician stated that they only have 5 to 10 minutes to attend to each patient and as such, they cannot effectively educate patients on their drug therapy needs. Some doctors, therefore, prescribe antibiotics to save time without considering their irrational use.

PALLIATIVE MEASURE AND SUSCEPTIBILITY

The health professionals stated that they prescribe antibiotics as preventive measures against infections even when it was not indicated for the patient. They stated that it was a result of the patient's high susceptibility to infections due to their unhygienic conditions.

EXTERNAL INFLUENCE ON PRESCRIBER

Many pharmaceutical representatives present the doctors with biased studies in favor of the antibiotics they market. As one of the health professional rightly put in, these pharmaceutical representatives only promote the good views of their drugs to instigate physicians to prescribe these antibiotics.

DOCTOR HIERARCHY

Junior physicians are strongly influenced by the antibiotic prescribing behavior of senior physicians. One participant rightly put in that he would prescribe the antibiotics his senior colleague usually prescribes.

NEAR-EXPIRY DRUGS

The hospital gets all their medication from the central pharmacy. Some of the physicians reported that drugs that are near their expiry dates were prescribed often (antibiotics inclusive), even when alternatives would be have been preferred.

DISCUSSION

Appropriate drug utilization contributes immensely to a global reduction in morbidity and mortality as a result of its medical, social, and economic benefits. [16]This study described the antibiotic prescription pattern in Delta State University Teaching Hospital, Delta State, Nigeria. It was a retrospective cross-sectional study conducted on both in-patients and out-patients that visited the hospital within 6 months. In-depth interview was conducted on the antibiotics prescribing pattern in the healthcare facility. There was overprescribing of antibiotics within the healthcare facility, measured by the percentage of antibiotics encountered. Physicians need to be obliged to abandon empirical treatment for the more acceptable evidence-based medicine practices to reduce the over-prescription of antibiotics.

The percentage of antibiotics encountered in this study was high compared to other studies in Nigeria.[17,18] The average number of drugs per encounter obtained in this study was minimal when compared with the ideal WHO standard of less than 2.[19] This contrasts with higher values reported in similar studies carried out in Nigeria [15,13]and in Ghana.[20]

This study revealed that the majority of antibiotics prescribed in this facility were from the essential medicine list (EML). This is similar to the results of other studies reported in Nigeria. [22,23,14] WHO however recommended prescriptions to be 100% based on the essential medicine list.[21] This study revealed minimal inappropriate antibiotic prescription. This contradicts with result of a study[1] where high levels of inappropriate antibiotics were reported. A similar study in Nigeria [24] revealed a lower level of inappropriate antibiotic prescribing. A high level of inappropriate antibiotic prescribing can lead to an increased risk of complication, increased length of stay in the hospital, worsening of disease condition, increase health care cost and mortality. [25]

The overall antibiotic prescription in this facility was high as revealed from this study. This is consistent with findings from studies conducted in other developing countries.[26,27,28] The studies showed that antibiotics were prescribed in 40% to 65% of all clinical encounters although WHO.[19] recommended antibiotic prescription rate of less than 30%

The generic prescription rate of antibiotics revealed from this study was far lower than previous studies by WHO in other countries.[21 This implies that health professionals in this facility still prescribe using brand names. This is consistent with studies carried out in Nigeria and India. [15, 29] A study in Sierra Leone [30] revealed high use of generic names in antibiotics prescription. This contradicts the result obtained from this study. Professional bodies must collaborate with regulators to positively influence the standard practice in the African region.

This study shows that patients spent NGN 2400 only on antibiotics prescription on an average duration of 7 days. This translates to about NGN343 only on antibiotics per day which is half of the minimum wage an average Nigerian worker earns daily. According to the World Bank Report 2007, a significant number of Nigerians live below the poverty line of USD1.90. This means that majority of the Nigerian population who live below USD 2.14 per day may not be able to afford antibiotics treatment or complete the course of their treatment. This will lead to an increased risk of developing antimicrobial resistance which invariably necessitates the use of expensive antibiotics for common infections[31,7]thus creating an increased financial burden on the patient as well as a prolonged hospital stay.[7] At present, the mortality due to antimicrobial resistance is 100,000 per year globally and it is estimated to increase in coming years.[32] It is, therefore, necessary to put in place measures, including an antibiotic stewardship program (ASP) to optimize antibiotic utilization and curtail cost. There are no implementation plans at present in Nigeria, despite the existence of a national policy on rational antibiotic use. Most public hospitals do not have a fully functional antibiotic control stewardship program. This has resulted in scarce data on antimicrobial stewardship programs.[33] Rational antimicrobial use can be achieved through antibiotics stewardship.

This study had possible limitations. The retrospective nature of the current study, the limited period of time the data was collected, and the small sample size could be possible limitations of this study. Facility upgrade and renovation work at the hospital caused the reduction in admission rate within the hospital which affected the sample size.

CONCLUSION

There was prevalence of inappropriate prescription of antibiotics in DELSUTH. Structure intervention programs, strategies, policies, and reforms should be put in place to address this problem and all healthcare teams should be willing to embrace such programs and policies to improve the rational use of antibiotics, improve quality of care and ultimately curtail healthcare costs.

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Conflict of interest: The authors declare none

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