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Antibiotic Prescription Pattern in Bacterial Opportunistic Infections among Patients Stabilized on HAART in a Tertiary Healthcare Facility in North-East Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author POO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author SAL managed data collection, data analysis and author AYK managed literature search, editing and jointly wrote the final draft of manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: The violent insurgency in northeast Nigeria has uprooted people from their homes and means of livelihood and has made it increasingly difficult to afford the cost of HIV/AIDS care services. Bacterial infections are the most frequently encountered opportunistic infection among patients stabilized on highly active antiretroviral therapy [HAART]. It is critical that antibiotics remain affordable to ensure patients can have financial access to effective treatment.
Objectives: To determine the prevalence of bacterial opportunistic infections, identify commonly prescribed antibiotics and quantify the cost of antibiotic treatments.
Methods: This was a cross-sectional retrospective carried out in 600 bed University of Maiduguri teaching hospital. A sample size of 360 (Andrew Fisher method) was used for the study. Data was obtained from randomly selected medical records of patients on HAART. Data were entered into SPSS 21 for descriptive statistics.

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Results and Discussion: Bacterial opportunistic infections accounted for more than two-thirds of all infections (65.4%) and the majority has been on HAART for 5 – 10 years. The most prevalent bacterial infections were upper respiratory tract infections, sexually transmitted and urinary tract infections accounting for 74.6% of all bacterial infections. Antimicrobial therapies using generic brands cost less than half of the cost of innovator brands. It would take 1 – 14 days of wages of the least paid a government employee to afford treatment of an episode of bacterial infection thus making it unaffordable.
Conclusion: Bacterial infections remain a significant source of morbidity and treatment is largely unaffordable to the majority of patients.

Keywords: HIV/AIDS; opportunistic infections; affordability; antibiotics; cost.

1. INTRODUCTION

The last few years have witnessed a violent insurgency that has displaced millions from their homes in the northeastern part of Nigeria; people have been uprooted from their homes and means of livelihood. The violence not only destroyed healthcare infrastructure and social services but also forced people to live in internally displaced camps set up on the fringes of major towns. The large-scale displacement has been particularly hard on the poor, farmers, unemployed and people living with chronic diseases including HIV/AIDS most of who find it extremely difficult to pay for lifesaving essential medicines. Those who are still able to access antiretroviral drugs in healthcare facilities in major towns are faced with the problem of inability to pay for non-antiretroviral drugs including those for treatment of opportunistic infections.

Opportunistic infections are common among patients living with HIV infection because microorganisms take advantage of the weakened immune system to cause localized and/or systemic infections. These infections may range from bacterial, fungal or Protozoal in origin often coexisting together. Immunosuppression is caused by high viral replication which selectively attacks and destroys CD4 cells – a key component of cellular immunity. The selective destruction of CD4 cells results in progressive loss of immunity leaving the body susceptible to infections from microorganisms. Majority of bacterial opportunistic infections include respiratory tract infections, gastroenteritis and systemic infections which together contribute the greatest burden on morbidity [1]. Bacterial opportunistic infections occur with greater frequency and severity in HIV infected compared to uninfected persons. Among the bacterial infections commonly seen with HIV/AIDS is bacterial pneumonia; it is the most frequent cause of hospital admission; patients typically experience two or more episodes within one year [2].

Although there has been a general decline in the prevalence of bacterial opportunistic infections in patients stabilized on highly active antiretroviral therapy [HAART], they remain at high risk of infection either from reactivation of latent infections or new primary infection [3]. Patients on antiretroviral treatment have sustained suppression of viral replication which allows for immune reconstitution, increase in CD4 count, resolution of clinical symptoms and reduction in morbidity and mortality. Despite these benefits of HAART, bacterial opportunistic infections remain a frequent source of disease often requiring hospitalization. Several pathogens have been implicated in respiratory tract infections some of which include *Streptococcus pneumonia*, *Haemophilus* species and atypical pathogens such as *Mycoplasma pneumonia* and *Legionella pneumophila* etc [4,5,6].The most frequent invasive bacterial infections are *Streptococcus* and *Haemophilus* species; together they account for over half of all systemic infections [7]. Bacterial enteric infections are more than ten-fold higher in HIV infected patients compared to the general population and are often associated with high morbidity and mortality [8,9]. Other bacterial isolates encountered among patients with HIV/AIDS included *Shigella* species, *Campylobacter* species, *Clostridium difficile*, and entero-aggregative *Escherichia coli* [10,11,12].

In all cases of bacterial infection in patients living with HIV/AIDS, a course of antibiotic therapy is indicated either for prophylaxis or treatment of acute infection. While there is no general consensus on the duration of therapy for bacterial infections, one to two weeks is regarded as adequate in most cases [2], though longer duration of therapy has been recommended in special cases [13]. The rise in cases of microbial

resistance makes a case for reconsidering prophylactic prescription of antibiotics. Recently there have been reports that 35% of bacterial isolates were resistant to Fluoroquinolones and 17% to Azithromycin [14].

In Nigeria studies have reported resistance of *Pseudomonas aeruginosa* to Sparfloxacin and Ceftazidime to be about 94.3% and 97% respectively. Also reported were multiple resistances of 2 – 9 commonly used antibiotics against bacterial isolates obtained from HIV infected patients [15]. A combination of resistance to cheap older generation antibiotics, increased frequency of infections and therapy with newer expensive generation antibiotics is sure to increase cost of treatment. In this region, private healthcare facilities play a dominant role in the provision of drugs to the population, so prices vary according to the facility where medicines are obtained. This has obvious negative implications for treatment affordability as patients are exposed to wide price fluctuations and market forces.

Profit oriented private hospitals and community pharmacies generally charge higher fees for services and drugs compared to public health facilities [16,17]. Affordability of antibiotics is critical to sustenance of effective treatment of bacterial infections and reduction in morbidity and mortality among patients on HAART.

1.1 Objectives

- To determine the prevalence of bacterial opportunistic infections
- To identify commonly prescribed antibiotics
- To quantify the cost of antibiotics therapy
- To compare affordability between innovator brands and generic versions

2. METHODS

Setting: The study was carried out in the antiretroviral clinic of University of Maiduguri teaching hospital. The hospital is a 600-bed tertiary healthcare facility that provides comprehensive HIV/AIDS care services to patients.

Study design: This was a cross-sectional retrospective study that uses data obtained from the medical records of patients, Pharmacy records and prices of drugs provided by the hospital as well as from community pharmacies within Maiduguri metropolis.

Sample size: This was determined using Andrew Fisher method of determining sample size for infinite populations. A total of 360 patient medical records were reviewed for the study.

Data collection: The data collected included HAART regimen, bacterial opportunistic infections, antibiotic prescription pattern, duration of antibiotic therapy, empirical antibiotic prescriptions, number of bacterial infections, diagnosis, demographic data and prices of drugs prescribed. The study period was October 2016 – September 2017. The prices of various formulations of antibiotics were obtained from three hospitals and community pharmacies and the average was used for analysis.

Data analysis: The data entered into SPSS 21 for descriptive and inferential statistics. Students - test and one way ANOVA were used for analysis as appropriate. Median price ratios were calculated by dividing international reference price of antibiotic by retail price in local currency. P values ≤ 0.05 was considered to be statistically significant.

3. RESULTS

The results showed that females were about twice as many as the males and the majority of patients were married (59.4%). About a quarter of patients were single and unemployed, while patients with secondary education (35.6%) and illiterate (32.2%) constituted about two third of the patient population.

Table 1. Background information

Gender	Number	Percentage
Male	135	37.5%
Female	225	62.5%
Marital status		
Married	214	59.4%
Single	87	24.2%
Divorced	21	5.8%
Widow	38	10.6%
Occupation		
Civil servant	106	29.4%
Self-employed	77	21.4%
Farming	66	18.3%
Housewife	43	11.9%
Private sector employed	68	18.9%
Education		
Primary	34	9.4%
Secondary	128	35.6%
Tertiary	82	22.8%
Illiterates	116	32.2%

Age distribution showed that majority of patients is below 50 years with a mean age of 41.9±9.8. The age group with the most prevalence was between 35 – 45 years (34.7%) and the least was 55 – 65 years.

Bacterial infections had the highest prevalence of 65.4% which is twice the rate for fungal infections (30.5%). Viral opportunistic infections had the least prevalence (4.4%).

Majority of patients have been on HAART for 5 – 10 years (6.4±2.2 years), accounting for 68.4% of patients.

Upper respiratory tract infection was the most frequent bacterial infection (36.1%) followed by sexually transmitted infections (20.2%) and urinary tract infections (18.3%). These infections accounted for two thirds of all bacterial infections.

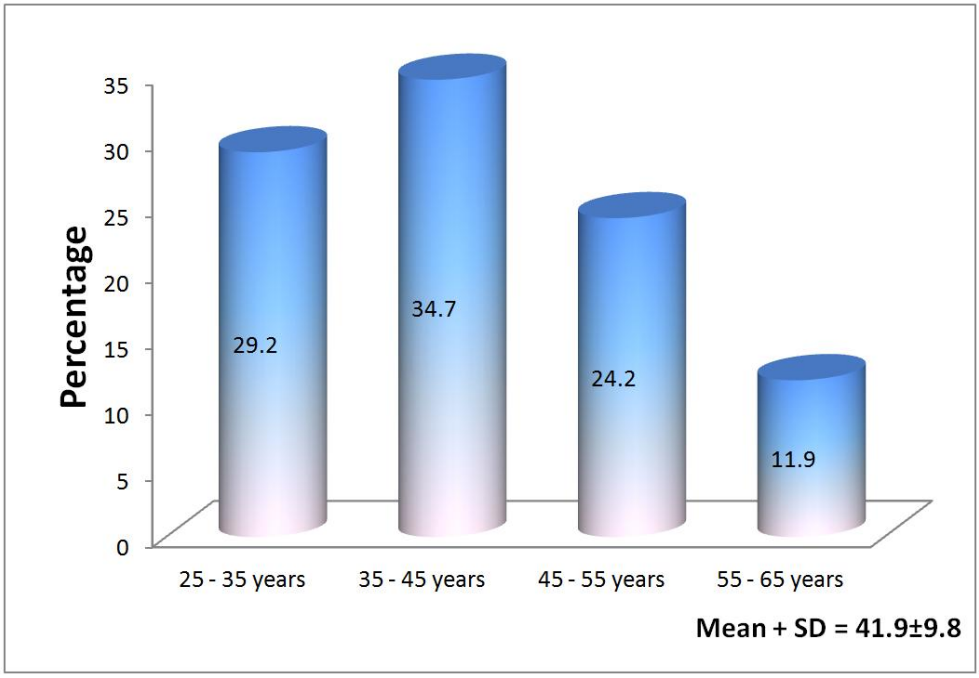

Fig. 1. Age distribution

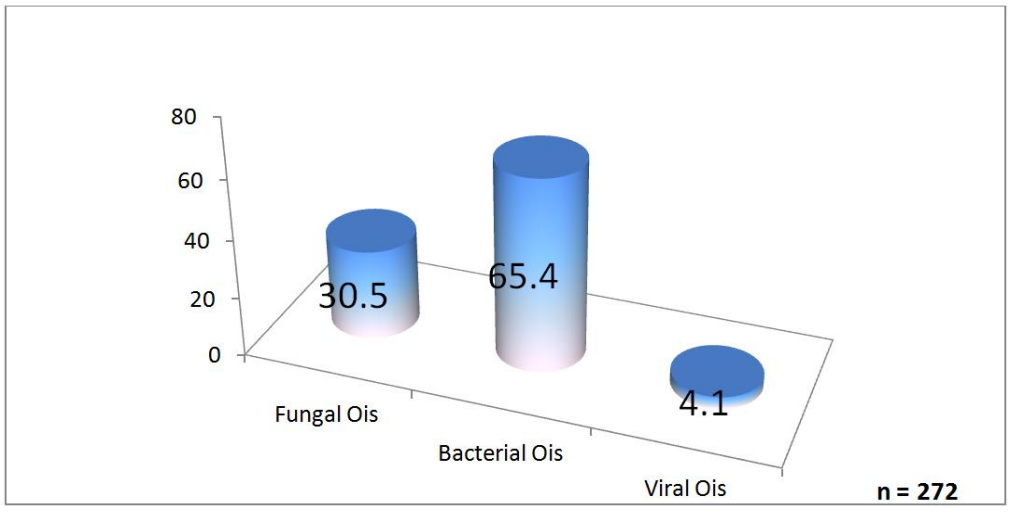

Fig. 2. Distribution of opportunistic infections
key = OI – opportunistic infections

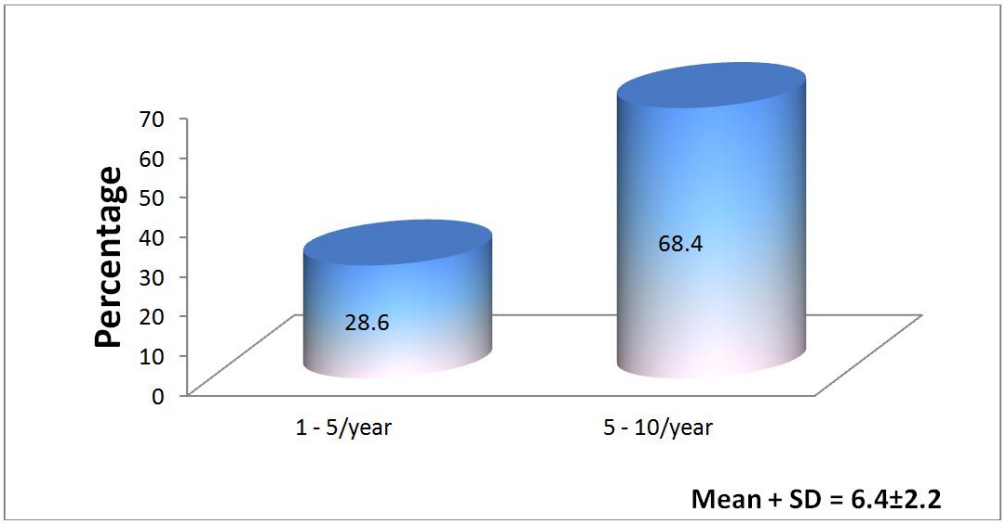

Fig. 3. Duration of HAART regim

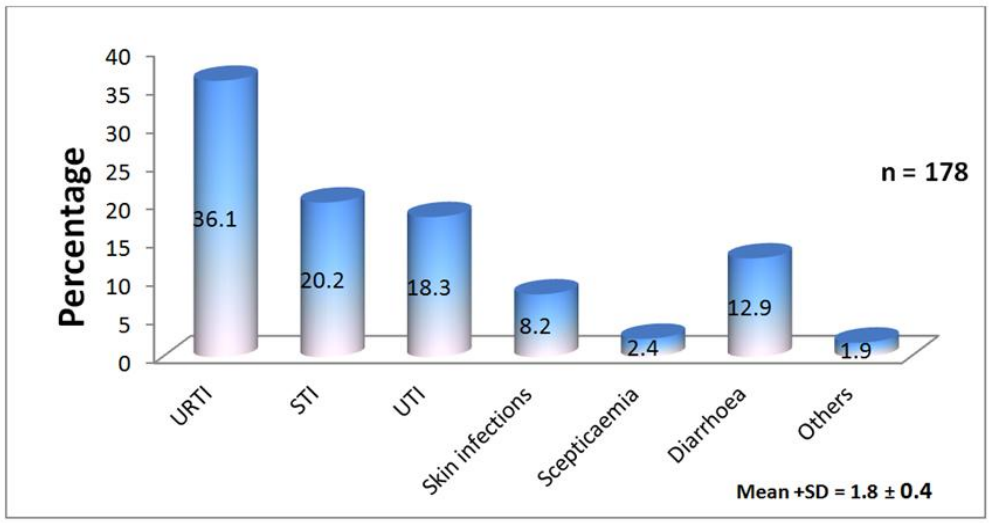

Fig. 4. Distribution of bacterial opportunistic infections

Key: URTI – Upper respiratory tract infection, STI – Sexually transmitted infection, UTI – Urinary tract infection

The most frequently prescribed antibiotics include Cotrimoxazole (20.8%), Metronidazole (15,9%) and Ciprofloxacin (14.2%) and together accounted for about half all antibiotic prescriptions.

Cost of antibiotics vary widely within and between sectors, the median price ratios (MPR) showed that innovator brands were 2 – 3 times as expensive compared to generic versions of the same drug. Variability in prices of both innovator and generic brands between pharmacies are not significant.

Prices of antibiotics in both public and private hospitals showed small variability.

A comparison of prices of innovator and generic antibiotics between hospitals and community pharmacies shows similar price pattern. Generally generics versions were about three times cheaper in hospitals and community pharmacies.

Antibiotic therapies took between 5 – 14 days and cost between 0.3 - 55.6 USD per episode of infection depending on the brand and class of antibiotic. While innovator brands cost between

0.5 – 55.6 USD, the generics cost less than half of this cost for the same duration of treatment. Innovator brands were far less affordable than generic versions.

4. DISCUSSION

Antibiotics are central to the treatment and management of bacterial opportunistic infections and their non-affordability remains a challenge for the poor and most vulnerable patients. This may be further compounded by increasing cases of microbial resistance to commonly used antibiotics that necessitate the use of more expensive newer generation antibiotics for treatment.

The results of this study showed that majority of patients were less than 50 years of age; there were twice as many females as males. This may

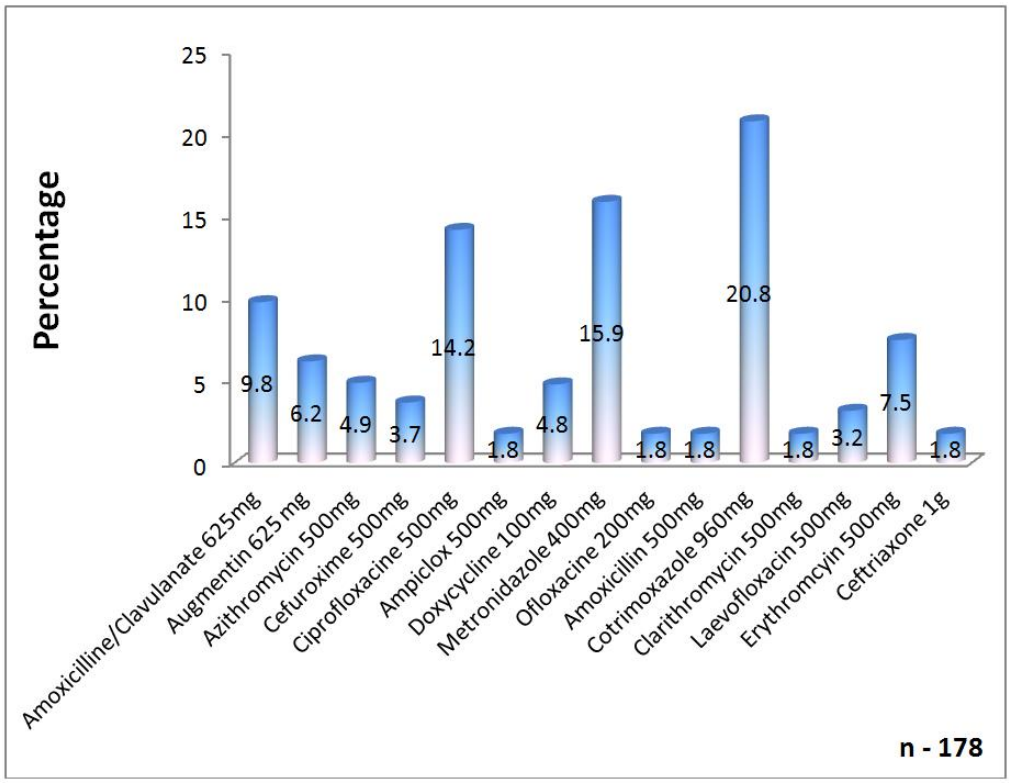

Fig. 5. Antibiotic prescription pattern

Table 2. Variability of prices (MPR) in pharmacies

Name	Pharmacy 1		Pharmacy 2		Pharmacy 3	
	IB	LPG	IB	LPG	IB	LPG
Tab Ciprofloxacin 500 mg	4.9	1.7	4.7	1.5	4.2	1.9
Tab Levofloxacin 500 mg	3.9	2.0	3.4	2.5	3.2	1.9
Tab Amoxil/Clavulanate 625 mg	10.1	4.7	9.4	4.2	8.1	5.0
Tab Azithromycin 500 mg	6.1	5.3	5.4	4.6	4.9	4.0
Tab Erythromycin 500 mg	5.5	1.6	5.2	1.2	4.4	0.6
Tab Cefuroxime 500 mg	8.8	5.7	9.2	4.6	8.3	4.5
Inj Ceftriaxone 1 g	20.9	2.5	21.2	2.6	22.3	2.8
Cap Amoxicillin 500 mg	3.1	0.8	2.6	0.7	2.8	0.6
Cap Ampiclox 500 mg	4.5	1.3	4.8	1.0	4.1	0.8
Tab Metronidazole 400 mg	0.6	0.2	0.4	0.1	0.3	0.1

Key: IB = innovator brands, LPG = low priced generics

Table 3. Variability of prices [MPR] in hospitals

	Hospital 1		Hospital 2		Hospital 3	
	IB	LPG	IB	LPG	IB	LPG
Tab Ciprofloxacin 500 mg	5.2	1.5	4.2	1.7	3.9	1.2
Tab Levofloxacin 500 mg	4.1	2.5	3.7	2.9	3.2	2.1
Tab Amoxil/Clavulanate 625 mg	9.7	4.6	10.4	5.5	9.8	4.3
Tab Azithromycin 500 mg	5.8	5.0	6.9	4.7	4.9	4.2
Tab Erythromycin 500 mg	5.8	1.0	6.1	0.8	4.7	0.6
Tab Cefuroxime 500 mg	9.0	5.2	8.2	4.9	7.5	5.0
Inj Ceftriaxone 1g	21.0	2.2	25.0	1.8	20.2	1.6
Cap Amoxicillin 500 mg	3.2	0.7	2.7	0.8	2.5	0.6
Cap Ampiclox 500 mg	4.8	1.2	4.3	1.1	4.0	0.8
Tab Metronidazole 400 mg	0.5	0.2	`0.3	0.1	0.4	0.1

Key: IB = innovator brands, LPG = low priced generics

Table 4. Variability of prices [MPR] across sectors

	Hospital		Pharmacy		IB:LPG ratio
	IB	LPG	IB	LGP	
Tab Ciprofloxacin 500 mg	4.4	1.3	4.3	1.7	2.9
Tab Levofloxacin 500 mg	3.7	2.4	3.5	2.1	1.6
Tab Amoxil/Clavulanate 625 mg	9.3	4.8	9.0	4.7	1.9
Tab Azithromycin 500 mg	5.9	4.8	5.5	4.6	1.2
Tab Erythromycin 500 mg	5.5	0.8	5.0	1.1	5.5
Tab Cefuroxime 500 mg	8.2	5.1	8.8	4.9	1.7
Inj Ceftriaxone 1g	22.4	1.9	22.1	2.1	22.2
Cap Amoxicillin 500 mg	2.8	0.6	2.0	0.7	3.7
Cap Ampiclox 500 mg	4.3	1.0	4.5	1.2	4.0
Tab Metronidazole 400 mg	0.3	0.1	0.4	0.1	3.5

Key: IB = innovator brands, LPG = low priced generics

Table 5. Cost of therapy and affordability

	Duration of therapy	Cost ($)		Affordability (days)	
	Mean (days)	IB	LPG	IB	LPG
Tab Ciprofloxacin 500 mg	9.5 ± 3.9	13.3	4.4	7.0	2.3
Tab Levofloxacin 500 mg	8.7 ± 4.7	9.2	5.8	4.8	3.0
Tab Amoxil/Clavulanate 625 mg	8.5 ± 2.1	13.7	7.6	7.2	4.0
Tab Azithromycin 500 mg	7.5 ± 4.5	12.2	10.2	6.5	5.3
Tab Erythromycin 500 mg	7.3 ± 2.8	20.8	9.9	10.9	5.2
Tab Cefuroxime 500 mg	9.1 ± 4.9	24.4	15.3	12.8	8.0
Inj Ceftriaxone 1g	5.4 ± 1.7	55.6	26.8	29.3	14.1
Cap Amoxicillin 500 mg	8.9 ± 3.7	8.0	2.1	4.2	1.1
Cap Ampiclox 500 mg	9.2 ± 3.6	16.5	3.6	8.7	1.9
Tab Metronidazole 400 mg	6.9 ± 3.3	0.9	0.5	0.5	0.3

NB: N305 = 1USD was used for calculations. No provision was made for price fluctuations. Least paid government employee earns $1.9 per day

be largely due to widespread practice of polygamy and traditional practices that put women in polygamous relationships at increased risk of infection. The prevalence of bacterial opportunistic infections was about twice in a year which is comparable to earlier reported [2], Their prevalence was also twice the rate of fungal infections [18]; lower respiratory tract infections (LRTI) accounted for a third of all cases [19]). The incidence of urinary tract infections (UTI) and sexually transmitted infections (STI) is about a fifth of all bacterial infections which is lower than previously reported [20,21].

The prevalence of LRTI in this study is much higher than 9.1% and 12.5% earlier reported [22,23], but lower than 55.6% reported [15]. Similarly the incidence of UTI in this study is lower than earlier reported [23,24]. Several studies reported between 25.3% and 41% prevalence which is considerably higher than the result of this study [24,25]. The prevalence of diarrhoea was comparatively higher and skin infections lower than result from previous study [26].

The wide variation in prevalence in bacterial opportunistic infections may be related to patient characteristics, setting, and presence of co-morbidities as well as level of immuno-competence [27,28]. Generally, patients who have better nutritional status and good immune recovery following HAART comparatively experience lower incidence of opportunistic infections [29].

The most widely prescribed antibiotics were Cotrimoxazole, Metronidazole, Ciprofloxacin and Amoxicillin/Clavulanic acid in that order of decreasing frequency. There have been several reports of increasing resistance to these antibiotics among HIV/AIDS patients, so empirical prescription of antibiotics should be a matter of concern [15]. Microbial resistance will increase the risk of treatment failure, increase cost of care and ultimately result in higher morbidity and mortality.

Antibiotic therapy is not covered under the antiretroviral treatment program in Nigeria, so patients have to pay for treatment as out of pocket expenditure; this brings concerns about accessibility and affordability among the internally displaced and other vulnerable groups. Prices of antibiotics vary widely depending on whether they are innovator brands or generic versions as well as the facility from where patients obtained them. Patients pay between 2 – 22 times the international reference prices for innovator brands and 2 – 5 times for generic version. The median price ratios (MPR) also vary between and within sectors and between public and private health facilities though the differences were not statistically significant [30]. This result is similar to earlier reports which concluded that antibiotics are more expensive in private health facilities compared to public facilities [31]. Similarly innovator brands are more expensive compared to generic versions and therefore less affordable [30].

The results of this study showed that antibiotic therapies for bacterial opportunistic infection are not affordable to majority of patients. There is need to improve prescription practices with emphasis on generic products and sensitivity testing. This will reduce incidence of treatment failure, relapses and ultimately reduce cost of care for patients. Health authorities should consider subsidizing treatment of opportunistic infections to the internally displaced and most vulnerable groups of patients.

5. CONCLUSION

Bacterial opportunistic infections remain the highest cause of morbidity in patients on HAART; antibiotics used in treatment are generally not affordable for majority of patients. Innovator brands of antibiotics are generally more expensive and therefore less affordable than their generic versions.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It was obtained from the health research ethics committee of the University of Maiduguri teaching hospital, Maiduguri.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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