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Comparative Cost Analysis of Treatment of Bacterial Opportunistic Infections in Patients Living with HIV/AIDS in Two Public Hospitals in Abuja, Nigeria

Paul Otor Onah[1*], Siyaka Abdul Lateef[1] and Ahmed Abdulmalik[1]

[1]Department of Clinical Pharmacy and Pharmacy Administration, University of Maiduguri, Maiduguri, Nigeria.

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. Authors SAL and AA managed the analyses of the study. Author AA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Bacterial opportunistic infections are the most frequently encountered cause of morbidity and mortality among patients living with HIV/AIDS. There has been a dramatic reduction in mortality related to HIV/AIDS infection following the introduction of highly active antiretroviral therapy (HAART). Bacterial opportunistic infections still remain a significant cause of morbidity among patients living with the virus and treatment with antibiotics is increasingly becoming less affordable for majority of patients. The rising cost of treatment is largely caused by irrational antibiotic prescriptions, high rate of treatment failure due to resistance and use of expensive innovator brands of drugs.
Aim: The purpose of this study is to identify common bacterial opportunistic infections and compare antibiotic prescription pattern and treatment cost in two public hospitals.
Method: This was a cross-sectional retrospective study using data obtained from two year medical records of patients being treated with highly active antiretroviral therapy. A sample size of 400 was

**Corresponding author: E-mail: onahpaul439@yahoo.com;*

used in each hospital for the study. Systematic random sampling was used and relevant data were extracted for analysis. The cost of antibiotic treatment was calculated from prices obtained from hospital and community pharmacies around the hospital vicinity.

Data Analysis: The data were entered into SPSS 20 for descriptive and inferential statistics. Analysis was done using students t-test and P values ≤ 0.05 was considered statistically significant.

Results and Discussion: Bacterial infections remain the most frequently encountered among patients on HAART. Antibiotic prescriptions for bacterial infections cost between one and five dollars per episode of infection. This is not affordable for majority of patients who live below the poverty line.

Conclusion: Antibiotic therapy cost is high for majority of patients, there is need to emphasize generic prescriptions and prior microbial sensitivity testing to reduce treatment cost arising from treatment failures.

Keywords: Antibiotics treatment; opportunistic infections; cost; HAART; empirical prescriptions.

1. INTRODUCTION

The introduction of highly active antiretroviral therapy (HAART) over two decades ago has significantly reduced morbidity and mortality as well as dramatically improve the quality of life of patients with HIV infection. The increasing access to life-saving antiretroviral drugs has also significantly increased the life span of victims to such an extent that their life expectancy is now close to that of uninfected persons.

In spite of the notable progress that has been made in access to life saving medications and reductions in morbidity and mortality; opportunistic infection remains a common cause of mortality among HIV/AIDS patients [1]. Opportunistic infections arise from latent or new infections from pathogenic bacteria [2,3] fungi [4,5] Protozoa [6,7] or viruses [8,9] which could be life-threatening. Bacterial opportunistic infections occur more frequently in HIV infected patients compared to un-infected patients [10]. The higher rates of infections may be related to a number of factors including immune suppression, low CD4 count (<200 cells/mm^3), poor adherence to HAART and a number of social factors such as smoking, injection drug abuse as well as chronic viral hepatitis.

In HIV infection, the most commonly encountered pathogens include *Streptococcus pneumonia* and *Haemophilus* species for community acquired pneumonia [11,12,13]. Other pathogens include *Pseudomonas aeruginosa* and *Staphylococcus aureus* [14,15]. In all cases of bacterial opportunistic infections a course of antibiotic therapy is usually indicated, and with increasing cases of resistance to older and newer generation antibiotics, there are concerns about rising cost of antibiotic therapy. There have been several reports of increasing microbial resistance to antibiotics around the world [16,17] and recently the World Health organization said it is an emerging crisis. For instance microbial resistance to Cephalosporins and Ciprofloxacin of between 9 – 24% has been reported [18] and as high as 50% resistance had been documented [19]. The rise in antibiotic resistance is associated with significant increase in healthcare costs and this would have economic and clinical implications for patients. In studies carried out in non HIV infected patients, antibiotics are said to contribute between 50 – 72% of total drug cost [20,21,22] and for patients on HAART costs of antibiotic therapy can be significantly higher.

The cost of antibiotic therapy for opportunistic infections would depend on a number of factors some of which include class of antibiotic and brand, duration of therapy, number of episodes of bacterial infection and facility. For instance, treatment of sexually transmitted infections (STI) with Cephalosporins, Quinolones and Macrolides cost 11.1%, 8.5% and 3.6% of total antibiotic treatment cost respectively [23]. The median treatment cost for one episode of an STI was reported to be about $17.8 [24] an enormous burden on majority of patients in developing countries.

There are few published research on treatment cost of bacterial infections and impact on family incomes. It's necessary to assess cost implication of antibiotic prescription practices so as to explore ways of lowering costs particularly for patients on HAART.

1.1 Aim

The aims of this study are to identify common bacterial infections, compare antibiotic

prescription pattern and treatment cost as well as assess the impact of brand prescriptions on cost.

2. METHODS

2.1 Setting

The two secondary hospitals used for the study were located at Asokoro district hospital (ADH) and Wuse district hospital (WDH) located in Abuja municipal area council of the Nigeria's capital city.

2.2 Study Design

This was a cross-sectional retrospective study using medical records of patients receiving highly active antiretroviral therapy in two hospitals between January 2015 and December 2016.

2.3 Sample size/sampling

A total of 400 medical records were selected using systematic random sampling method.

2.4 Data Collection

Selection of medical records of patients on HAART was carried out from serially arranged folders using sampling interval of 10. Data extracted included opportunistic infections and their frequency, antibiotics prescribed, generic and empirical prescriptions and demographic data among others. The cost of antibiotic treatment was computed from average prices obtained from hospital pharmacy as well as community pharmacies within the vicinity of the hospitals.

2.5 Data Analysis

The data were entered into SPSS 20 for descriptive and inferential statistics. Analysis was done using Student t-test and P values ≤ 0.05 was considered statistically significant.

3. RESULTS

Background information indicated that significant differences exist between patients receiving treatment for bacterial opportunistic infections in the two health facilities. For instance there is significant difference in number of drugs per prescription (P = <0.001), duration of antibiotic therapy (P = < 0.001) and frequency of repeat hospital visit for bacterial infections (P = 0.040).

The most frequently encountered bacterial infection was lower respiratory tract infections. This was followed by urinary tract infections occurring in over two thirds of patients, while sexually transmitted infections was diagnosed in about a third of patients. Apart from diarrhoea there were no other differences in prevalence of opportunistic infections between the two hospitals.

Hypertension was the leading co-morbidity accounting for 19% of cases followed by liver cirrhosis (12.3%) and diabetes mellitus 2 (10%). Cases of liver cirrhosis and peptic ulcer were 2 – 3 times more common in WDH.

Table 1. Demographic information

	ADH (n = 400)	**WDH (n = 400)**	**P value**
Age (yrs.)	38.3 ± 11.2	39.1 ± 12.2	0.337
Number of hospital visits	7.0 ± 2.5	7.38 ± 2.5	0.040
Duration of antibiotic therapy	15.8 ± 6.3	14.9 ± 6.3	<0.001
Number of drugs/ prescription	6.8 ± 2.6	6.9 ± 6.9	`<0.001
Gender			
Male	216 (54%)	184 (46%)	
Female	194 (48.5%)	206 (51.5%)	
Marital status			
Married	214 (53.5%)	265 (66.3%)	
Single	94 (23.5%)	58 (14.5%)	
Widow	75 (18.7%)	42 (10.5%)	
Divorced	17 (4.3%)	35 (8.7%)	

Key: ADH = Asokoro district hospital, WDH = Wuse district hospital

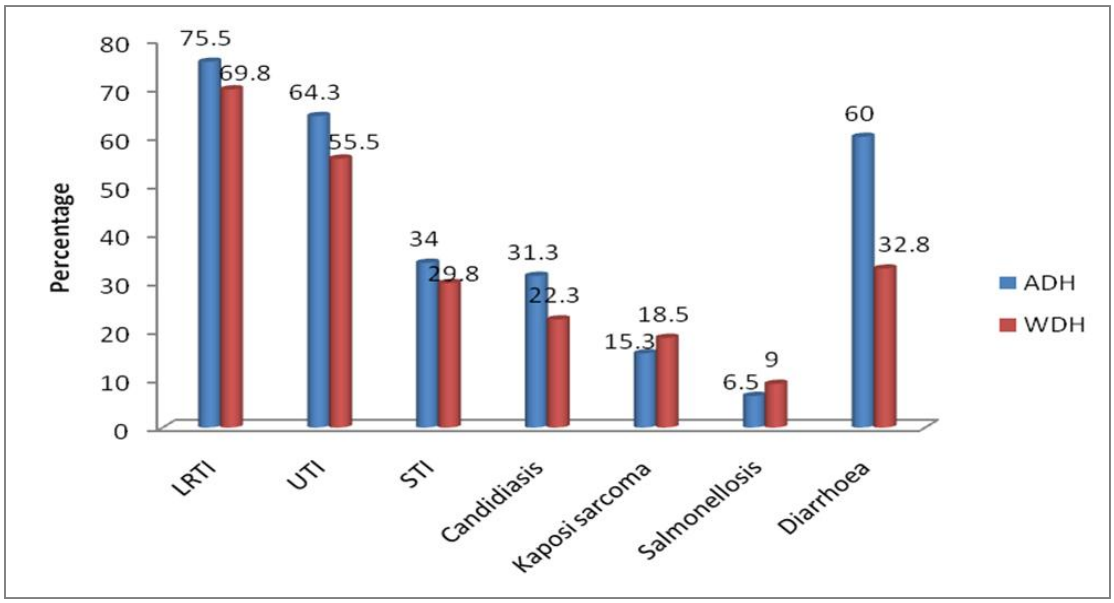

Fig. 1. Distribution of opportunistic infections

Key: LRTI = Lower respiratory tract infection, URTI = Upper respiratory tract infection, STI = sexually transmitted infection

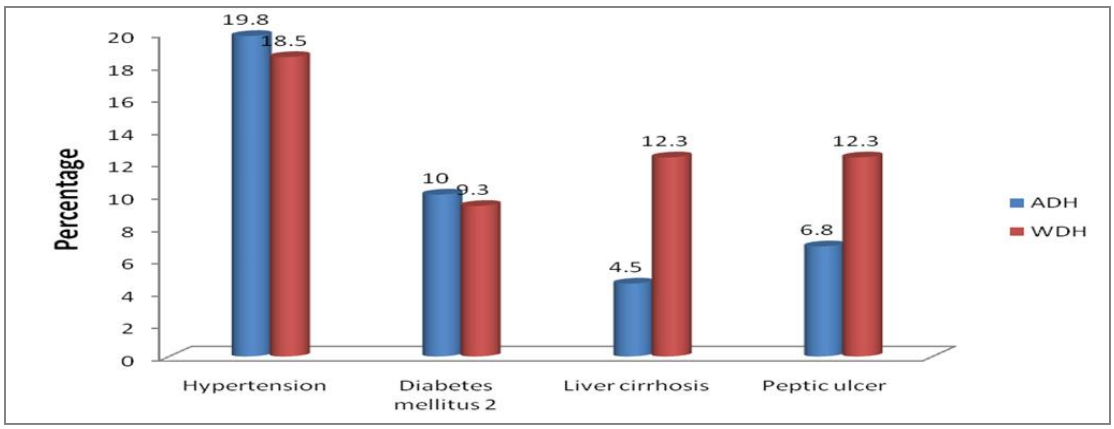

Fig. 2. Co-morbidities

Data showed that Hepatitis B, Tuberculosis and Syphilis accounted for between 19 – 28% of patients in both facilities. Differences were also noted with tuberculosis and Herpes zoster in which there were twice as many cases in WDH.

Antibiotic prescription pattern showed that Sulfonamides were prescribed for about half of all patients on HAART, followed by Macrolides (18–22%) and Penicillins (10-19%). The Quinolones and Cephalosporins had prescription rate of about 3 – 5.5%.

An empirical prescription is widely practiced in the two healthcare facilities accounting for between 70 – 100% of antibiotics. The Penicillins, Cephalosporins, Macrolides and Quinolones all had high levels of empirical use.

The cost of treating each episode of baterial infection is highest with Cephalosporins, Macrolides and Quinlones and there are significant cost differences between the facilities [P< 0.001]. The Sulfonamides were the cheapest followed by Tetracylcines, the former being the most prescribed because of its prophylactic use against Pneumocystic jirovecii infection.

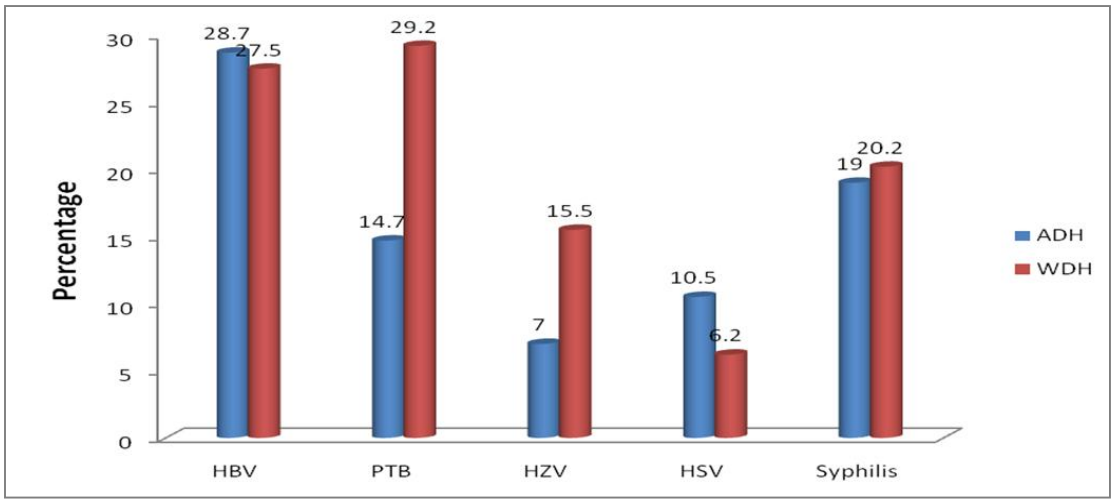

Fig. 3. Co-infections

Key: HBV = Hepatitis B virus, PTB = Pulmonary tuberculosis, HZV = Herpes zoster virus, HSV = Herpes simplex virus

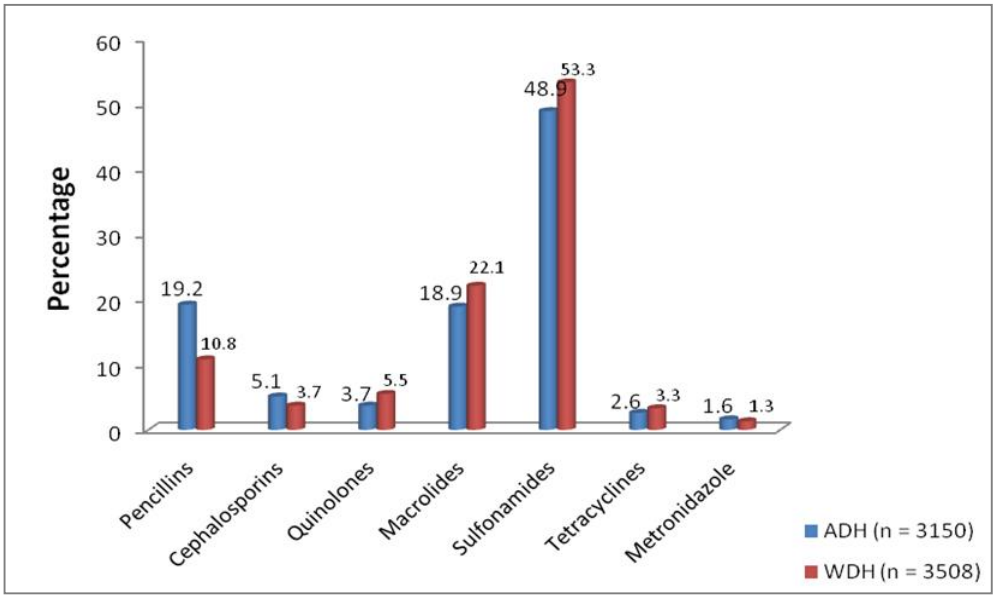

Fig. 4. Class of antibiotics prescribed for patients

Table 2. Comparism of cost of class of antibiotics prescribed

	ADH			WDH			
Antibiotic class	**n**	**Total cost($)**	**Cost ($)**	**n**	**Total cost($)**	**Cost ($)**	**P value**
Penicillins	604	4180.3	6.9± 2.3	380	2316.0	6.1±1.8	<0.001
Cephalosporins	160	6048.1	37.8±5.7	129	4515.7	35.0±4.8	<0.001
Quinolones	117	981.7	8.4±2.1	193	1543.9	7.9±1.6	0.019
Macrolides	597	6262.8	10.5±3.3	776	6333.3	8.2±3.8	<0.001
Sulfonamides	1540	998.0	0.7±0.2	1869	1197.1	0.6 ±0.1	<0.001
Tetracyclines	82	124.0	1.5 ±0.7	116	104.5	0.9±0.4	<0.001
Metronidazole	50	174.0	3.5 ± 1.6	45	25.7	0.6±0.2	<0.001

1USD = N305, no adjustment was made for inflation

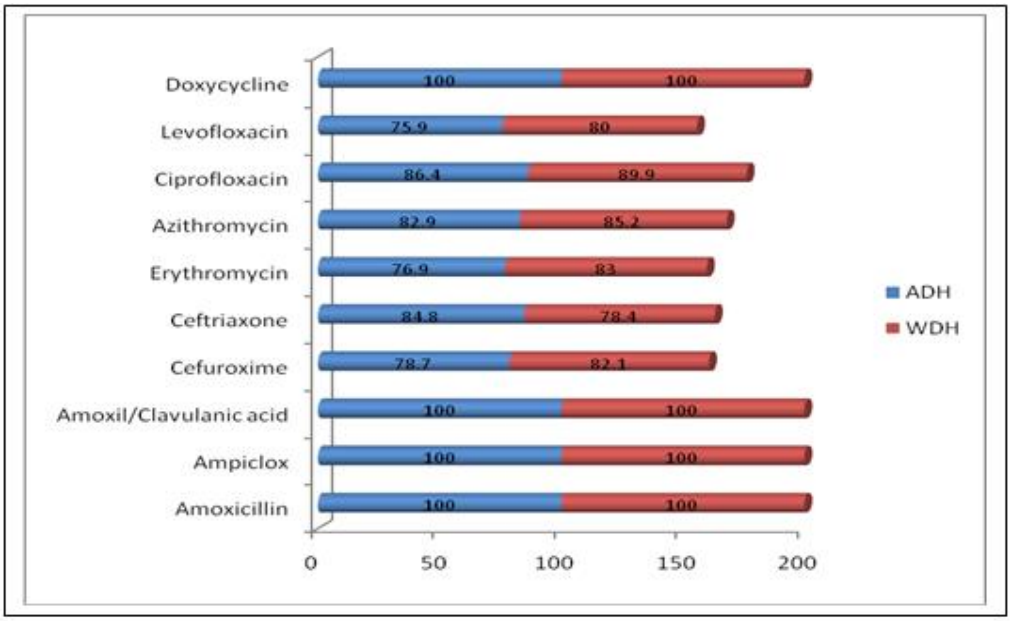

Fig. 5. Percentage of empirical antibiotic prescriptions

Comparative analysis of prices showed that innovator brands cost between 12 – 86% more than their generic versions. For instance, innovator brand of Amoxicillin/Clavulanate, Azithromycin and Ceftriaxone cost 86%, 61.4% and 49.6% more than their respective generic versions. The similar trend was observed for other antibiotics.

The cost analysis of treating bacterial infection showed that it would cost between 1 – 5 USD to treat an episode of infection. The older generation Penicillins, Tetracyclines and Sulfonamides were generally cheaper than Cephalosporins, Macrolides and Quinolone antibiotics. There were significant differences in cost of therapy with Amoxicillin (P =0.0403), Ceftriaxone (P = 0.0322) and Erythromycin (P = 0.0161) etc. The differences are likely related to the prevalence of innovator brand use.

Table 3. Comparism of cost between innovator and generic antibiotics

Antibiotic	Total cost ($)	n	IB ($)	n	LPG ($)	IB: TC ratio (%)
Ampiclox	495.2	32	200	183	295.2	40.4
Amoxicillin	1130.5	56	290.5	480	840.0	25.7
Amoxil/Clavulanate	2552.7	148	2195.5	85	357.2	86.0
Cefuroxime	1905.2	99	937.1	75	968.1	49.2
Ceftriaxone	4144.4	24	2055.5	91	2088.9	49.6
Erythromycin	2268.6	80	280.0	748	1988.6	12.3
Azithromycin	3994.3	131	2451.4	414	542.9	61.4
Ciprofloxacin	664.3	59	364.3	177	300.0	54.8
Levofloxacin	317.4	38	150.0	36	167.4	47.2
Doxycycline	59.5	8	16.6	129	42.8	27.9
Tetracycline	64.8	-	-	61	64.8	-
Cotrimoxazole	998.0	179	205.7	3200	792.3	20.6
Metronidazole	199.0	-	-	95	199.0	-

Key: IB – innovator brand, LPG – low priced generics, TC – Total cost. *1USD = 305, no adjustment was made for inflation*

Table 4. Cost of antibiotic therapy per episode of opportunistic infection

Antibiotic	ADH	WDH	P value
	Mean + SD($)	Mean + SD($)	
Ampiclox	1.49 ± 1.19	1.55 ± 1.18	0.6140
Amoxicillin	1.80 ± 0.33	1.69 ± 1.19	0.0403
Amoxil/Clavulanate	3.15 ± 1.83	2.99 ± 1.84	0.4978
Cefuroxime	2.97 ± 1.22	3.51 ± 1.82	0.0066
Ceftriaxone	3.53 ± 1.63	4.01 ± 1.53	0.0322
Ciprofloxacin	1.95 ± 0.98	1.81 ± 1.02	0.1588
Levofloxacin	2.12 ± 0.89	2.19 ± 0.79	0.6891
Erythromcyin	1.77 ± 1.18	1.91 ± 1.12	0.0161
Azithromycin	2.05 ± 1.13	1.79 ± 1.23	0.0007
Doxycycline	0.27 ± 0.15	0.28 ± 0.14	0.5751
Tetracycline	0.20 ± 0.12	0.24 ± 0.09	0.0394
Cotrimox	0.27 ± 0.11	0.29 ± 0.16	0,0001
Metronidazole	0.57 ± 0.19	0.48 ± 0.13	0.0002

1USD = N305, no adjustment was made for inflation

4. DISCUSSION

Bacterial opportunistic infections remain a major cause of morbidity and mortality among patients on HAART and treatment continue to be a significant burden on patients. Data from this study showed that there are more females on treatment than males which is consistent with several previous studies [25,26,27,28,29]. Majority of patients were married [30], while singles account for about a fifth of patients on HAART a result that is different from other findings [25] which reported that singles were the highest group of HIV/AIDS patients.

Antibiotic treatment of bacterial opportunistic infections continues to occur with regularity among patients on HAART and this study finding is no exception. The results showed that lower respiratory tract infection [LRTI] is the most commonly encountered bacterial infection which is comparable to some previous studies [31,32] though higher than previously reported in similar studies [33,34].

The second frequently observed `infection was urinary tract infection [UTI] at prevalence of 60% which is higher than 40.4% reported [35]. It is well documented that patients with HIV/AIDS experience higher frequency of UTIs compared to uninfected patients; this has been associated with low level of immunity, sexual behaviour and ineffectiveness of treatment practices.

High incidence of sexually transmitted infections among patients living with HIV/AIDS is widely reported in the literature, so the high prevalence in this study is not unexpected. The STI prevalence is much higher than 16.6% and 5.7% reported in other studies [36,37]. The incidence of diarrhoea among patients on HAART is commonly associated with pathogenic protozoa or bacteria [38,39,40,41] so the high prevalence in this study may be a reflection of repeated infections with diarrhoea causing parasites and low immune status. Prevalence of diarrhoea in this study is however comparable to a previous study [42] but higher than 25% and 28.1% reported in other studies [43,44]. Candidiasis was the most frequently encountered fungal infection found in this study and its prevalence is lower than 70.3% reported in a previous study [45]. The observed differences in prevalence in opportunistic infections are primarily due to patient characteristics, treatment practices and care setting.

Like in all chronic diseases co-morbidities the most commonly observed included hypertension, peptic ulcer and diabetes mellitus type 2 in that order of decreasing prevalence. Several studies have reported that the impact of HIV infection and HAART on blood pressure is at best minimal [46,47]. Most patients with diabetes mellitus type 2 co-morbidity are unrelated to HIV infection, though patients on protease inhibitors have a higher risk of developing diabetes mellitus.

A number of co-infections found in this study included Hepatitis B virus and prevalence found in this study is higher than 9.2 – 12.3% earlier reported [29,48]. Similarly, co-infection with pulmonary tuberculosis was more commonly seen compared to 12.7% reported [49] but lower than 44.2% reported in another study [50]. The prevalence of syphilis is comparable to 14 – 19%

reported [51], higher than 7.6 - 10% reported in previous studies [52,53]. Higher prevalence [29.1%] has been reported [54]. Other co-infections like herpes viruses were also higher than 28% [28] but lower than 62% reported in an earlier study [27].

Antibiotic prescribing pattern showed similarities [55] and differences [56]. The latter reported that Metronidazole [25%], Penicillins [19%] and Sulfonamides (12%) were the most frequently prescribed class of antibiotics, other similar studies reported that Quinolones and Macrolides were the most prescribed [56,57] which contrast with the results of this study. The differences are in the fact that HIV/AIDS dramatically alters the nature and frequency of antibiotic usage primarily because of changes in microbial sensitivity, types of pathogen and associated complications.

There is a widespread empirical prescription of all classes of antibiotics in both healthcare facilities, particularly among the older generation antibiotics. Empirical antibiotic use ranged between 75 – 100% similar to a previous study [58] though lower figure of 46.4% [23] has been reported. High level of empirical antibiotic use was also reported in several other studies [59,60]. One particular study reported that 78.4% of antibiotics were empirically given to patients and only 56.4% and 13.4% were clinically and microbiologically appropriate [60]. The high level empirical antibiotic prescriptions cast doubt on observance of rational drug principles and effectiveness of treatment.

Antibiotic therapy comes with significant cost to patients majority of who have no health insurance; one study reported that it would cost 8 USD to treat one episode of STI[23] similar to the range found in this study [0.7 – 37.8 USD]. Patients living with HIV/AIDS typically experience more frequent bacterial infections, so it's important that effective treatment at affordable cost is given due consideration.

There are valid concerns about microbial resistance to the commonly prescribed antibiotics as several studies have highlighted this problem as an emerging threat in Nigeria [16,17,18]. In sub-Saharan Africa, evidence of high level microbial resistance is emerging where resistance of enterobcteriaceae to third generation Cephalosporins may be up to 47% and 15 – 43% of Salmonella Typhi isolates were resistant to Nalidixic acid. Higher rates of resistance by gram positive pathogens responsible for most urinary tract infections, respiratory tract infections and hospital acquired infections have been reported [61].

A recent study reported that up to 43% of *Streptococcus pneumoniae* were resistant to Penicillins, and cases of multi-drug resistant invasive Salmonella Typhi to Fluoroquinolones have been also been documented [62,63]. Evidence of increasing rates of resistance by *Escherichia coli* isolates have reached 71% in women and up to 85% in men and higher rates have been reported in some countries [64]. There have been suggestions that the threat of microbial resistance is highly underestimated in Sub Saharan Africa [65] and cost of infection treatment is likely to rise as newer more expensive antibiotics become the first line choice of therapy for bacterial infections.

The cost of antibiotic therapy may also rise significantly if innovator brands are prescribed as evidence indicated that generic versions significantly cost far less. The results of this study showed that innovator brands are about 12 – 86% more expensive and treatment using these brands will considerably increase cost of treatment of opportunistic infections [66,67,68].

Irrational antibiotic therapy due to widespread empirical treatment not only encourage emergence of microbial resistance, it also erodes efficacy, increases the cost of care, increases length of hospital stay, limits options in cases of treatment failure and ultimately increase mortality [69]. It is important to discourage empirical antibiotic prescriptions not only to reduce the risk of treatment failure and save cost from repeat treatments, but also to preserve efficacy of available antibiotics. Differences in cost of therapy observed directly relates to prescribers preference for innovator brands in the erroneous belief that they are of better quality. This unnecessarily increases cost of therapies with no clear evidence of superior clinical outcomes for patients.

5. CONCLUSION

The most frequently encountered bacterial infections were lower respiratory infections, urinary tract infections and sexually transmitted infections. There was no major difference in antibiotic prescribing practices, however, cost of therapy differed significantly because of innovator brand prescriptions. The level of empirical antibiotic prescription is very high for

which clinical and microbiological appropriateness may be doubtful, so sensitivity testing should be routine for antibiotics. Generic prescription will significantly reduce cost of treatment of bacterial infections and will ultimately improve affordability.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval was obtained from health research ethics committee of Federal capital territory administration, Abuja and administrative approval from the hospitals.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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