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Research Article

Evaluation of Antibiotic Prescription and Utilization amongst Hospitalized Children in a Tertiary Facility in Sokoto, North-Western Nigeria

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ABSTRACT

Background: Antibiotics are the most widely utilized therapeutic agents. Inappropriate use causes increase cost and antibiotic resistance. The World Health Organization recommends assessment of antibiotics use to guide prescribing practices.

Objective: To describe the pattern of antibiotic usage among paediatric inpatients aged > 1 month to 15 years in a tertiary hospital in Sokoto, Nigeria.

Methods: Febrile children were recruited prospectively by systematic random sampling from January to October 2018. Socio-demographics, diagnosis, antibiotics administered were obtained from case notes. The WHO indicators of use of antibiotics were employed for evaluation. Data was analysed with SPSS version 23.

Results: Out of 352 children, 318 (90.3%) received antibiotics; commonest being Ceftriaxone in 155/318 (48.7%), Cefuroxime in 74 (23.2%), and Metronidazole in 29 (9.1%). Average number of antibiotics per patient was 2.3 ± 1.1 with treatment duration of 4.3 ± 1.4 days. Antibiotic consumption was 937.2 days of antibiotic therapy/1000 patient days (DOT/PD). Generic name was used in 92.3% while 100% of the drugs were on the essential medicine list. Frequent diagnoses were severe malaria 98/352 (27.8%), respiratory infections 39 (11.1%) and severe malnutrition in 38 (10.8%). Only 6 (1.7%) patients had microbiologic evidence of infection.

Conclusion: Utilization of antibiotics is higher than recommended. There is need for improved diagnostic facilities to avoid antibiotic overuse and its consequences.

Keywords: antibiotics, prescription, utilization, children, inpatients, DOT

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INTRODUCTION

Antibiotics are chemical substances that destroy or inhibit the growth of microorganisms in the body.^[1] They are used for empirical treatment, definitive treatment and prophylactic or preventive treatment of infections.^[2] Antibiotics are the most commonly prescribed drugs in children and irrational use is a global issue.^[3] The irrational use of antibiotics could be practiced in the form of overuse, underuse, and misuse of prescription or over-the-counter drugs. It could also be due to the poor quality of antibiotic prescription and use of antibiotics in nonbacterial diseases.^[4]

Children and adolescents constitute a significant proportion of the population especially in developing countries where they are also exposed to a plethora of pathogenic organisms resulting in acute febrile illnesses.^[5] They also have a developing immune system so are prone to multiple

infections^[6] and thus presentations in the emergency unit leading to numerous exposure to antibiotics.^[7] In many instances, these infections may be viral or parasitic infections that do not necessitate antibiotic therapy or may be malaria in endemic regions.^[5, 8] These issues lead to unnecessary exposure to antibiotics generally especially if diagnostic facilities to distinguish such infections are not readily available or are not appropriately utilized.

Unnecessary exposure to antibiotics results to increase in health care costs, prolonged hospitalization, superinfections and emergence of antibiotic resistance.^[9] Judicious use of antibiotics has been advocated and one of the ways is to establish institutional guidelines based on local pattern of diseases.^[9] Accordingly, the WHO together with International Network of Rational Use of Drugs (INRUD) developed a manual on how to investigate antibiotic use in hospitals and this provides a standardized concise way to

assess antibiotic utilization for improvement as needed by practitioners.^[3]

The WHO prescribing indicators are the basic minimal standard for promoting rational drug use, monitoring, and evaluation of drug utilization.^[3] Also, the Centre for Disease Control and Prevention recommends antibiotic stewardship programmes (ASPs) in health institutions to protect and preserve the power of antibiotics.^[10] The quantitative parameters recommended by WHO include days on therapy per 1000 patient days (DOT/PD) and defined daily dose (DDD). DOT is more recommended in paediatrics because it is not dependent on drug dose unlike DDD.^[11] It is useful in evaluating the total burden of antimicrobial use and is based on the number of drugs given as well as the number of days of drug exposure.^[12] DOT is useful in comparing volume antibiotic use between facilities and also in monitoring interventions to reduce antibiotic use within a facility.^[13]

There are few studies on antibiotic use in paediatric in patients in Nigeria ^[14, 15] both of which showed the commonest antibiotic used amongst paediatric in-patients was Gentamicin. A study among inpatients in Gambia revealed a high antibiotic consumption of 670.7 DOT/PD.^[16] It is important to document antibiotic prescribing practices in children who are predisposed to multiple childhood illnesses and repeated use so as to identify areas of intervention, hence this study assessed the antibiotic prescription pattern by WHO parameters at point of admission, the intensity of antibiotic use during admission and antibiotics prescribed at point of discharge from the hospital.

METHODOLOGY

Study area

The study was carried out in the Emergency Paediatric Unit (EPU) of the Department of Paediatrics, Usmanu Danfodiyo University Teaching Hospital located in the capital of Sokoto State. It is the major tertiary health facility in the state providing care to children from Sokoto as well as neighbouring states of Zamfara, Kebbi, Niger as well as the neighbouring countries Republics of Niger and Benin.

The EPU is a 25 bedded facility where children with acute illnesses aged > 1 month to 15 years are admitted and managed.

Study design

This was a cross-sectional study conducted over 8 months from 1st January to 31st October 2018.

Study population

Comprised children aged > 1 month to 15 years

Inclusion criteria

Those with febrile illness of < 7 days.

Exclusion criteria

Those who had been referred for admission from another facility and had already been commenced on antibiotics and those who spent less than 24 hours on admission. Patients who died on admission were also excluded.

Sample size determination

Prevalence of children presenting to the emergency given antibiotics of 49.5% in a study by Lawal in Zaria was used in a standard formula as follows.^[15]

$$n = \frac{z^2 pq}{d^2}$$

Where n = minimum sample size

z = Standard normal deviate set at 1.96

p = Prevalence of antibiotic use

q = (1 - p) = (1 - 0.495) = 0.505

d = degree of accuracy desired = 0.05

n = (1.96 x 1.96 x 0.495 x 0.505 / 0.0025) = 384.1

These figures were corrected for the average number of admissions in a year in the EPU of approximately 2500.

The formula is:

$$n = \frac{no}{1 + (no - 1)/N}$$

Where n° = initial sample size calculated

n = sample size with finite correction for population size

N = Population size

n = 384/1+ (384 - 1/2500) = 334; which was corrected for 95% response; 339/0.95

= 352 patients.

The above number was recruited by systematic random sampling as they met the inclusion criteria.

Instrument of data collection: A proforma based developed for the study was used to derive information on antibiotics prescription and use from the medication charts in recruited patients' folders who were followed up till the point of discharge. Also, the nurse's documentation records were used.

The proforma included the age, gender, initials, serial number of the patient. Also captured was the diagnosis, name of antibiotic used on admission and at discharge, route of administration and duration of therapy.

The following items were entered: number of drugs per prescription, percentage of encounters with antibiotics, percentage of drugs prescribed by generic name, number of drugs prescribed from essential drug list, percentage of encounters with injection, percentage of combination drugs given.

Antibiotics were classified as drugs such as antibacterial used to treat a recent diagnosis of infective aetiology but did not include antifungals, antimycobacterial and anti-inflammatory medications. Prophylactic antibiotics were not included.

A copy of the Nigerian Drug Formulary is available within the pharmacy which is located within the EPU.

Days of therapy per 1000 patient days (DOT/1000PDs):

This is a quantitative measure of antibiotic use which is calculated for all admissions in a unit and it provides a measure of the intensity of use. It comprises a numerator which is total number of days on antibiotics and calculated for each antibiotic and summed up. One DOT is counted when a single antibiotic is administered to an individual patient on a calendar day regardless of the number of administrations, resulting in whole day counts even for partial days of exposure.^[12, 13] This data is easily gotten from records which are electronic because it is more tedious

counting from manual records^[13] especially with antibiotic combinations as was done in this study.

The denominator which is patient days (PD) is gotten from a manual or electronic count of the patients taken at the same time of the day, every day throughout the period under study.^[17] It can also be estimated from the total number of admissions multiplied by average length of hospital stay.^[13] This ratio of the DOT:PD is multiplied by 1000 to get the DOT/1000PDs.

In this study, the DOT was counted from the number of drugs administered in a day from the drug charts while the PD was calculated at the end of the study from the total number of admissions multiplied by average length of hospital stay.

Data analysis

Responses were entered into SPSS version 23 and Microsoft Excel version 2016. Categorical variables such as gender, socioeconomic class, number on antibiotics including respective types were expressed as ratios, proportions and percentages while continuous variables such as age range, duration of antibiotics, duration of hospital stay were expressed as mean and standard deviation. Bar charts were used to present some discrete variables.

DOT was expressed as a ratio per 1000PD.

Ethical approval

Ethical approval for the study was obtained from the Ethics Committee of Usmanu Danfodiyo University Teaching Hospital, Sokoto.

RESULTS

Sociodemographic characteristics

352 children were recruited and their data was analysed. They comprised 234 (66.5%) males and 118 females (33.5%). The age range was 1 month to 180 months (1month to 15 years) with mean and SD of 56.5±49.7 months. Majority 230 (65.3%) were of lower socioeconomic class while only 14 (4%) were of upper socioeconomic class. Sociodemographic characteristics are shown in Table 1.

Diagnosis and antibiotic use on admission

318 (90.3%) received antibiotics while 34 (9.7%) did not receive any antibiotic. The commonest antibiotic prescribed was Ceftriaxone in 155 (48.7%), Cefuroxime in 74 (23.3%), and Metronidazole in 29 (9.1%). Figure 1 shows the drugs given according to Antibiotic classes.

The most frequent diagnosis was severe form of malaria in 98/352(27.8%), acute respiratory infections in 39 (11.1%) and severe malnutrition in 38 (10.8%). Table 2 shows the different diagnoses and drugs used.

From the table 2 it is seen that the 2 most frequent uses of Ceftriaxone as per diagnosis were severe malaria and febrile convulsions (81 and 13 patients respectively). For Cefuroxime, the 2 most frequent uses were Malnutrition and diarrhoeal diseases (22 and 21 patients respectively), while Metronidazole was most frequently used in Malnutrition and tetanus (7 and 5 patients respectively). The 2 most frequent diagnosis associated with Ciprofloxacin was Enteric fever and Sickle cell anaemia while for Amoxicillin, it was respiratory tract infection (Pneumonia).

Prescribing indicators for antibiotic use among the subjects

The average number of antibiotics per patient was 2.3 ± 1.1 with average duration of treatment of 4.3±1.4days. Generic name of prescribed antibiotics was used in 92.3% while 100% of the drugs were available on the essential medicine list as shown in Table 3.

DOT/1000PDs

The total antibiotic consumption was 937.2 DOT/1000 PD. The total days on antibiotic therapy (DOT) was 1360, while the total patient days on admission were 1451 days. Details of the individual antibiotics are shown in Table 4. Ceftriaxone had the highest volume of consumption of 470DOT/1000PD followed by Cefuroxime and Metronidazole with 196 and 74.4 DOT/1000PD respectively.

Type of oral antibiotic prescribed on or before discharge.

All patients who had parenteral antibiotics were converted to oral before or on discharge. The most frequently prescribed during at discharge was Amoxicillin followed by Amoxiclav, Cefuroxime, Cefixime, Metronidazole, Cotrimoxazole and others as shown in the Figure 2 below.

Microbial tests done on admission

Of the total subjects only 6 (1.7%) had positive microbiological culture during the period of admission. Out of these, the commonest isolate was *Escherichia coli* in 4 specimens, while *Staph aureus* accounted for 2 of the isolates. Urine sample accounted for 4 positive isolates while cerebrospinal fluid accounted for the remaining 2. Two of the *E.coli* isolates were resistant to all the tested antibiotics. The antibiogram showed Augmentin and Amoxicillin had the highest resistance profile. While the highest sensitivity rate was recorded with the Quinolones tested predominantly Ofloxacin.

Malaria parasitaemia was present in 192 (54.5%) of the patients. Those with features of severity (98/352---27.8%) were treated for severe malaria with intravenous Artesunate or Quinine while others received oral antimalarial therapy with artemisinin combination therapy (ACT).

Table 1: Showing the sociodemographic characteristics

Parameter	Frequency	Percentage
Gender		
Male	234	66.5
Female	118	33.5
Age category		
>1 months – 5 years	232	65.9
>5 years to 15 years	120	34.1
Socioeconomic class		
Upper	14	4
Middle	110	30.7
Lower	230	65.3

Table 2: showing the different diagnoses and antibiotics used

Drug/∕ Diagnosis	Ceft	Cefu	Metr	Cipro	Amox	Gent	Cefo	Am/Cl	Xtap	Other ∞	None	Total	% of 352 (total)
Severe malaria	81	14	-	2	-	-	1	-	-	-	23	98	27.8
Resp. infection ¹	9	10	1	-	9	3	-	3	2	2	2	39	11.1
Malnutrition	9	22	7	-	-	-	-	-	-	-	-	38	10.8
Diarr. Disease ²	4	21	5	-	-	-	-	-	-	5	6	35	9.9
SCA ³	6	4	5	6	1	-	-	2	-	1	3	25	7.1
Sepsis	11	1	-	1	-	2	2	-	-	-	-	17	4.8
Enteric fever	5	1	3	6	-	1	-	1	-	-	-	17	4.8
Feb.convulsion ⁴	13	-	-	-	-	-	-	-	-	-	-	13	3.7
Meningitis	8	-	-	-	-	-	3	-	-	-	-	11	3.1
Tetanus	1	1	5	-	-	-	-	-	2	-	-	9	2.6
UTI ⁵	7	-	-	-	-	-	-	-	-	-	-	7	1.9
Bone &soft tx ⁶	1	-	3	2	-	1	-	-	-	-	-	7	1.9
ARF ⁷	-	-	-	-	1	-	-	-	1	-	-	2	0.6
Total	155	74	29	17	11	7	6	6	5	8	34		
%tage of those on antibiotics (318)	48.7	23.3	9.1	5.3	3.5	2.2	1.9	1.9	1.6	2.5	9.7		

1=Respiratory infections (Bronchopneumonia, Pharyngotonsillitis, Bronchiolitis, Otitis media)

2=Diarrhoeal disease; 3=Sickle cell anaemia; 4=Febrile convulsion; 5=Urinary tract infection; 6=Bone &soft tissue infection; 7= Acute rheumatic fever

*Ceft=Ceftriaxone; Cefu=Cefuroxime; Metr=Metronidazole; Cipro=Ciprofloxacin; Amox=Amoxycillin; Gent=Gentamicin; Cefo=Cefotaxime; Amoxcl=Amoxiclav; Xtap=Xtapien; Azith=Azithromycin

∕=Combinations not counted separately

∞=Others include oral antibiotics- Azithromycin, Cotrimoxazole, and oral metronidazole

Table 3: Showing the status of WHO prescribing indicators in the study population (n=318)

WHO/INRUD Prescribing indicators	Standard	Result
Average number of antibiotics per patient	1.6-1.8	2.3 ± 1.1
Percentage of drugs prescribed by generic name	100%	92.3%
Percentage of drugs on the essential medicines list	100%	100%
Percentage of patients on antibiotics	≤10%	90.3%
Percentage on parenteral antibiotics	≤30%	97.5%

Table 4: Showing the DOT of the different antibiotics

Antibiotic	Proportion treated (%)	DOT	DOT/1000PD Total PD = 1451
Ceftriaxone	155 (48.7)	683	470
Cefuroxime	74 (23.3)	284	196
Metronidazole	32 (10.1)	108	74.4
Ciprofloxacin	17 (5.3)	120	82.7
Amoxycillin	11 (3.5)	83	57.2
Gentamicin	7 (2.2)	17	11.7
Cefotaxime	6 (1.9)	11	7.6
Amoxiclav	6 (1.9)	15	10.3
Benzylpenicillin	5 (1.6)	18	12.4
Azithromycin	3 (0.9)	10	6.9
Cotrimoxazole	2 (0.6)	11	7.6
Total	318 (100)	1360	937.2

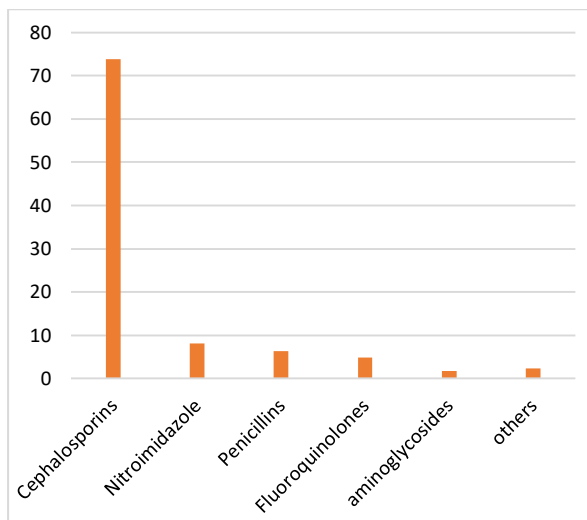


Figure 1: Showing class of antibiotics prescribed on admission

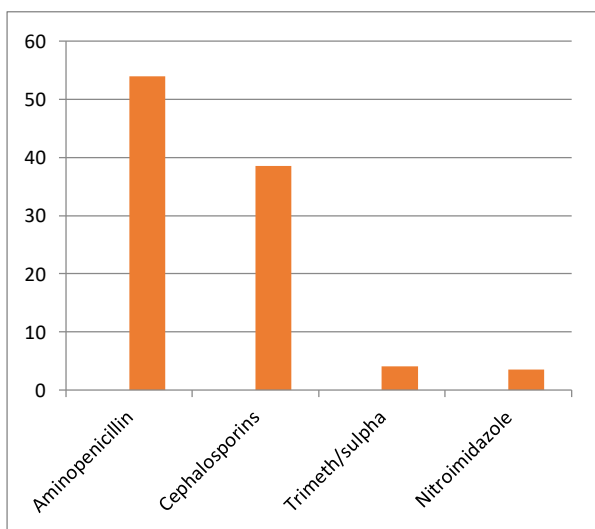


Figure 2: Showing the class of antibiotics given at discharge

DISCUSSION

The WHO prescribing indicators used to assess antibiotic prescription pattern revealed suboptimal performance with regards to the percentage of patients on antibiotics and injections which were more than the recommended 30% and 10% respectively, however, a better performance was seen with regards to the compliance with the essential medicine list and use of generic name which were all over 90%.^[3] The mean number of antibiotic per patient of 2.3 was also higher than 1.6-1.8 recommended which supports over prescription of antibiotics.

There was a high use of antibiotics in this study as evidenced by the percentage of those who received antibiotics (90.3%) and the high DOT (937.2DOT/PD) compared to a study among hospitalized children in a Gambian tertiary hospital^[16] where it was reported that 54.1% of admissions received antibiotics with a DOT of 676/1000PD. The volume of the individual antibiotics by DOT in this study was higher for all the drugs with exception of Gentamicin and Benzylpenicillin when compared to the Gambian study which also included neonates unlike this study. Another study from a developed country^[11] reported a lower DOT/PD of 483.6 with a percentage antibiotic use in hospitalized children of 30.6%. Likewise, the percentage of admitted patients on antibiotics in this study was higher than that reported from a similar

study by Lawal^[15] in Zaria, North-western Nigeria where the prescription records were examined and 49.5% of the admitted children received antibiotics.

The most frequently prescribed antibiotic was Ceftriaxone (48.7%) followed by Cefuroxime (23.3%), also in the same class. This finding is similar to other studies in India^[18-20] amongst hospitalized children where Cephalosporins were the most commonly prescribed especially Ceftriaxone in an average of about 50% of patients probably due to its broad spectrum nature, while other African studies reported Gentamicin as the most frequently prescribed.^[15, 16, 21] Two studies, one from North-Western and another from South-South Nigeria reported Cefuroxime as the most commonly prescribed antibiotic.^[22, 23] These differences may be due to different policies of antibiotic use in different centres based on common diseases seen, their local sensitivity pattern and clinical response profile.

The high rate of use of antibiotics in this study is reflective of what predominates in developing countries where there are multiple problems like late presentation to emergency departments with very sick children and lack of financial resources on part of parents to commence critical investigations due to lack of health insurance.^[24] Given the most frequent diagnosis of severe malaria (parasitic infection) in this study compared to the other quoted studies^[15, 16] where pneumonia (viral or bacterial infection) was the most common infection also lays credence to possible over prescription of antibiotics in this centre. Reasons that could possibly be responsible include the lack of rapid tests (like C-reactive protein and antibody tests) to differentiate bacterial from non-bacterial infections. Also, even though samples for microbiological tests were taken from some patients, the delay in getting results has probably led to over indulgence in empirical antibiotic therapy over time in children presenting with fever who are also suspected to have bacterial infection on account of presenting with other systemic symptoms.^[14]

Severe infections commonly result to systemic symptoms and organ dysfunction which can rapidly lead to disability and death without prompt treatment. Frequently, bacterial infections coexist with severe malaria in endemic areas with overlap of presenting features.^[25] Due to this, paediatricians usually commence empirical antibiotic treatment for severe malaria cases.^[25] In a study in Tanzania^[26] on predictors of treatment of febrile children with antimalarials and antibiotics, it was found that due to lack of laboratory facilities, physicians tend to deal with all possibilities by giving both drugs.

From this study, aside from Ceftriaxone being prescribed for many cases diagnosed as severe malaria, other antibiotics used (Cefuroxime, Metronidazole, Aminopenicillins) appeared to be more rational as seen from the topmost indications of those antibiotics in the study population. This finding therefore emphasizes the need to properly diagnose all cases because those who were treated as severe malaria with a combination of antimalarials and antibiotics might as well have sepsis which was not diagnosed. The cost implication of this antibiotic should also not be overlooked. Although not assessed in this study, financial metrics^[27] is also an important aspect of antibiotic stewardship programs and it is worth noting that majority from this study were from the lower socioeconomic class. A study in Lagos, Nigeria had reported that Ceftriaxone was the most frequently missed drug in up to 40% cases due to affordability issues.^[14]

The commonest drug prescribed at discharge was oral Amoxicillin unlike Cefixime which was most favoured in the

study from Lagos.^[14] This was also in discordance with the class of the commonest prescribed antibiotic while subjects were on admission and may be preferentially selected by the prescribers due to its lower cost since on discharge most symptoms may have subsided. Only few of the patients had microbial culture which could also support sepsis presumptively similar to other studies in the country limiting proper comparison^[14, 22], however, Quinolones were the most sensitive as reported by Ahmed^[22] also in North West Nigeria while resistance was high to Amoxicillin similar to other studies in the region.^[16]

Limitations of this study include the lack of preferable electronic records though manual compilation of the DOT was done as the patients were on admission to minimize errors. In conclusion, the high use of antibiotics in this study calls for more prudence and intervention to improve the ability for prompt diagnosis of sepsis as early as possible to reduce the blind use of antibiotics. More multi-centred antibiotic stewardship programs are recommended in the region.

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Authors' contributions

KOI conceptualized the study. KOI and OBO contributed to the data collection. UMS, BGI, UMW, AA, FBJ and MAS contributed to the manuscript development. All the authors have contributed to the final version of this manuscript.

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