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ORIGINAL ARTICLE

Pattern and Predictors of Antibiotic Prescriptions by Physicians to Paediatric Outpatients in a Nigerian Tertiary Care Hospital: A Call for Antibiotic Stewardship

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Keywords

Antibiotics;

Childhood;
Drug policy;

Inappropriate prescriptions;

Outpatient;

Paediatric patients.

ABSTRACT

Background: Irrational antibiotic use for childhood illnesses is prevalent, especially in developing countries. There is a need to provide evidence-based data for the implementation of antimicrobial stewardship programmes (ASP) in healthcare facilities. This study was conducted to describe the pattern and predictors of antibiotic prescriptions to paediatric patients at the outpatient clinic of Federal Medical Centre Umuahia Abia State, Southeast Nigeria.

Method: We conducted a retrospective review of patients' encounters in one year at the outpatient paediatric clinics (2022). An electronic data extraction form was used to collect information from patient's case notes. Descriptive, bivariate and multivariate analyses were done using SPSS version 26. The level of significance was set at 5%.

Results: Records of 722 encounters were retrieved. A total of 694 antibiotics were prescribed. The antibiotic prescription rate was 74.4% (95% CI: 71.2–77.6). The most frequently prescribed antibiotic was amoxicillin/clavulanic acid (34.9%). Most prescribed antibiotics (53.6%) were in the 'access' group of antibiotics. The commonest indication for the use of antibiotics was the treatment of respiratory infections (28.1%). The predictors of antibiotic prescription included younger age (aOR = 2.48; 95% CI: 1.50–3.80), four or more drugs prescribed (aOR = 9.43; 95% CI: 3.90–22.10), and therapeutic treatment type (aOR = 3.24; 95% CI: 1.10–9.40).

Conclusion: Irrational prescriptions of antibiotics by physicians were prevalent in the Paediatric outpatient clinic of the facility. We recommend the implementation of the ASP in the hospital to address irrational antibiotic prescriptions in line with rational drug policy.

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INTRODUCTION

Antibiotics belong to the class of drugs used in the prevention and treatment of bacterial diseases.[1] However, due to its widespread therapeutic use, its misuse has been noted by the World Health Organization (WHO) as a public health threat.[2] Inappropriate antibiotic prescriptions have been reported in about 30% of outpatient prescriptions.[3] Also, it has been documented that irrational antibiotic use for childhood illnesses is prevalent, especially in low- and middle-income countries (LMICs).[3]

Globally, up to one-quarter of the total population constitutes the paediatric population (less than 18 years) and they are prone to infectious diseases.[4] This could account for frequent use of antibiotics which is a contributory factor to the rising trend of antibiotic resistance, an emerging global health threat in the 21st century.[5] An effect of antibiotic resistance includes the inability to treat common infections such as tuberculosis, pneumonia and food poisoning.[6] Also, antibiotic resistance provides the window for persistence in the recurrence of infections, with frequent hospital visits and longer stays on admission due to missed, delayed, or wrong diagnoses and incorrect management of infectious diseases.[7] Other consequences of antibiotic misuse include adverse drug events, increased costs for more expensive antibiotics and a burden on the healthcare system.[8]

Due to childhood susceptibility to infections, antibiotics are among the classes of drugs most commonly prescribed for them.[4] It has been reported in studies that the antibiotics most commonly prescribed are amoxicillin and amoxicillin/clavulanic acid.[9,10] The most common presenting symptoms among children are those peculiar to respiratory tract infections, such as fever, cough, cold, influenza, and sore throat.[11] Most of these are viral and would be unresponsive to antibiotic therapy.[5] Some of the associated factors with antibiotic prescribing noted in studies include patient age, sex, and four or more medicines prescribed.[12] In 2017, WHO developed the Access, Watch, and Reserve (AWaRe) classification (revised in 2019 and 2021) of antibiotics to support antibiotic stewardship at all levels.[13] It serves as a guide when prescribing antibiotics and each of these groups is based on the effect of the antibiotic on Antimicrobial resistance (AMR), thus guiding their utilization.[13]

Appropriate antibiotic use in children is critical, as there are limited antibiotic formulations suitable for this population.[14] Children play a crucial role in infections within communities and act as vehicles for person-to-person transmission.[15] There is a need for pharmaco-epidemiological studies among the paediatric patients who access care in health care facilities. Such information obtained would contribute to policy formulation efforts to initiate antibiotic stewardship in healthcare facilities. The aim of this study was to describe the pattern and identify the predictors of antibiotic prescriptions by physicians for paediatric patients at the children outpatient clinic, in a tertiary health facility in Abia State.

Table 1: Characteristics of Patients' Encounters seen at the Children Outpatient Department (N=722)

Variable	Frequency (%)
Age group (years)	
0-5	515 (71.3)
6-10	90 (12.5)
11-17	117 (16.2)
Sex	
Male	362 (50.1)
Female	360 (49.9)
Period of the year	
1st Quarter	298 (41.3)
2nd Quarter	214 (29.6)
3rd Quarter	104 (14.4)
4th Quarter	106 (14.7)
Number of drugs per encounter	
1 – 4	600 (83.1)
>4	122 (16.9)

METHODOLOGY

Study design and setting

A retrospective review of case notes for paediatric patients who presented at the Children Outpatient Clinic of a tertiary health institution was undertaken in Abia State (one of the states in the southeast Geopolitical zone) from January to March 2023. The facility is located in Umuahia North Local Government Area (LGA) which is the capital territory of the state. The LGA had an estimated population of 303,787 in 2018 projected from the 2006 national population census with an annual growth rate of 2.7%. The health institution lies between latitude N5º31′14″ and longitude E7º29′36″. It is a 537-bed tertiary hospital with the triple directive of service delivery, research and training. It also serves as a referral centre for other health facilities. Antibiotics are available on the National Health Insurance Scheme (NHIS) drug list. Antibiotics are widely available as OTC (Over the counter) drugs and are sometimes dispensed without prescriptions in pharmacies within the city.

The Department of Paediatrics is a specialized department situated within the institution and is made up of 4 units: Children Emergency ward, Neonatal ward, Children Outpatient clinic and children Ward with 89 paediatrics beds. Services are rendered by the consultant paediatricians, resident medical doctors, house officers, nurses and other ancillary staff. The children's outpatient clinic provides services five days a week and an average of 944 children visit the outpatient department every month. The patient folders are stored in the medical records unit of the institution. There are no existing policies on the essential antibiotic listing for prescriptions in the hospital and enforcement of mandatory procurement of antibiotics is poor within the hospital premises.

Study population

Hospital folders of all children below 18 years who attended the paediatric outpatient clinic at the institution from January 1 and December 31, 2022 were retrieved. These folders were accessible in the medical record unit of the facility. All folders containing at least one prescribed drug were included for review. Folders with incomplete details (age and sex), prescriptions containing only vaccines, intravenous infusions and consumables and prescriptions not legible or readable were excluded. Additionally, patients' prescriptions containing only antimicrobials for Tuberculosis and cancer therapy were excluded from the study, as these medications were usually not prescribed at the CHOP clinic.

Sample size determination

WHO recommends a minimum sample size of 600 for surveys on drug use using secondary sources of data.[16] To increase the external validity of the study, we recruited a higher sample size (823 encounters) from the sampling frame of 13,011 (A total of 13,011 encounters at the children outpatient clinic from January 1st – December 31st, 2022).

Sampling technique

Simple random sampling was used to select the required sample size from the sampling frame. The random number list was generated in OpenEpi. The generated random numbers served as the serial numbers on the register and then their folder numbers were used to trace the folder in the medical records.

Study tool and data collection

Data were extracted from the case folders of the selected patients using an Open Data Kit (ODK) digital form that was adapted from WHO guidelines for drug evaluation.[16] The form was pretested at Nsukwe Primary Health Centre, a predominant outpatient facility that is an outpost of the Department of Community Medicine at FMC Umuahia. This facility was used as proxy for the other existing tertiary health facility in the state where an industrial action was on-going during the period of the pre-test. Also, the form had multiple checks to reduce data entry errors. The data was collected by three trained research assistants (MBBS Holders) under the supervision of the principal investigators. The information extracted included age, sex, folder number, date of treatment, name and number of antibiotics prescribed, diagnosis and treatment (prophylactic or therapeutic) type.

Operational definition

As adapted to this study;

Encounter: A patient encounter is recognized to refer to "the interaction between patient and health provider. Ideally, this encounter includes several components: History taking, diagnosis process: selection of non-pharmacological or pharmacological treatment, prescription (and perhaps dispensing) of treatment; and explanations about treatment and its adverse effects, follow-up, and prevention."[16]

Measurement of variables

The dependent variable was the antibiotic prescription rate. This was measured by

assigning encounters containing antibiotic(s) as 'yes' and those without antibiotic(s) as 'no'. The independent variables included age, sex, date of treatment, names of antibiotics prescribed, indications for use and AWaRe classification of antibiotics. There was no missing data in the dataset as the folder details were duly captured by the medical records and the outpatient register at the children's clinics.

Statistical analysis

The data collected on ODK was downloaded from the Kobo Collect server in Excel format. It was cleaned and exported to Statistical Package for the Social Sciences (SPSS) version 26 for analysis. Univariate analysis was used to generate frequencies, proportions, means and standard deviations. Binary logistic regression was used to assess the association between the independent variables and antibiotic prescription rate. A multivariable logistic regression analysis was done to determine the predictors of antibiotic use. A $p<0.05$ was considered statistically significant at a 95% confidence level. Appropriate tables and charts were used for data presentation.

Ethical approval and consent to participate

Ethical clearance was obtained from the Ethics and Research Committee of the Federal Medical Centre, Umuahia, Abia State (REF No: FMC/QEH/G.596/Vol.10/568).

The confidentiality and privacy of personal and medical information obtained from records and registers were maintained. Data was stored on a password-protected computer with access limited only to the principal investigator.

RESULTS

A total of 722 prescriptions were successfully analysed out of a total of 823 encounters reviewed. The median (IQR) age was 2 years (0.7, 7.0). A total of 362 (50.1%) were male patients. More than one-third of the encounters 298 (41.3%) occurred within the first quarter of the year. The total number of drugs prescribed was 2,284 and 694 (30.8%) were antibiotics. The proportion of encounters with more than four medicines was 122 (16.9%). **[Table 1]**

Amoxicillin/clavulanic acid was the most frequently prescribed antibiotic 242 (34.9%). Other antibiotics that were frequently prescribed included Ciprofloxacin 79 (11.4%), cefuroxime 46 (6.6%) and Metronidazole 45 (6.5%). **[Table 2]**

Of all encounters in which an antibiotic(s) was prescribed, the majority (72.9%) of antibiotic therapies prescribed were monotherapy.

More than half (53.6%) of the antibiotics prescribed for the patients belonged to the "access" group, while the rest (46.4%) were on the "watch" list. None were on the "reserve" list. **[Figure 1]**

The commonest indication for the use of antibiotics was respiratory infections (30.2%), followed by otolaryngological diseases (14.8%), dermatological diseases (13.6%), and gastroenterological diseases (12.7%). **[Table 3]**

Table 2: Antibiotics Prescribed in the Children Outpatient Department (n=694)

Antibiotic class	Antibiotic name	Frequency (%)
Penicillins	Amoxicillin	9(1.3)
	Ampicillin	1(0.1)
	Penicillin	11(1.6)
	Flucloxacillin	25(3.6)
Beta-lactamase inhibitor	Amoxicillin/clavulanic acid	242(34.9)
	Ampicillin/Cloxacillin	11(1.6)
	Sultamicillin	7(1.0)
Cephalosporins	Cefixime	32(4.6)
	Ceftazidime	16(2.3)
	Cefuroxime	46(6.6)
	Ceftriaxone	40(5.8)
	Cefpodoxime	22(3.2)
	Cefotaxime	1(0.1)
Macrolides	Erythromycin	9(1.3)
	Clarithromycin	6(0.9)
	Azithromycin	66(9.5)
Tetracyclines	Doxycycline	1(0.1)
Fluoroquinolones	Ciprofloxacin	79(11.4)
	Ofloxacin	1(0.1)
Imidazoles	Metronidazole	45(6.5)
Carbepenem	Meropenem	2(0.3)
Lincosamides	Clindamycin	6(1.9)
Amphenicols	Chloramphenicol	5(0.7)
Aminoglycoside	Gentamicin	2(0.3)
Sulphonamides	Cotrimoxazole	1(0.1)
	Sulfadiazine-trimethoprim	1(0.1)
Monoxycarbolic acid	Mupirocin	7(1.0)

From the binary logistic regression, patients who were within 0–5 years were more likely to have antibiotics prescribed compared to other age groups (COR = 2.50; 95% CI: 1.60–3.80). Additionally, patients who got four or more drugs had higher odds of having an antibiotic included in the prescription compared to their counterparts. (COR = 8.22; 95% CI: 3.50–19.00). Likewise, patients who received a therapeutic were more than three-fold more likely to be prescribed an antibiotic compared to those who received a prophylactic form of treatment (COR = 3.54; 95% CI: 1.20–9.90). Multivariable analysis showed that lower age (0–5 years) (aOR = 2.48; 95% CI: 1.50–3.80, p = 0.001), having a prescription with four or more drugs (aOR = 9.43; 95% CI: 3.90–22.10, p = 0.001), and treatment type (therapeutic) (aOR = 3.24; 95% CI: 1.10–9.40, p = 0.032) were the predictors of antibiotic prescriptions. **[Table 4]**

Table 3: Indications for Use of Antibiotics in the Children Outpatient Department (N=722)

Diagnosis	Frequency	Percentage
Respiratory infections	218	30.2
Gastroenterological	92	12.7
Cardiovascular	5	0.7
Genito-urinary diseases	22	3.0
Dermatological disease	98	13.6
Otolaryngological	107	14.8
Ophthalmological	13	1.8
Musculoskeletal	20	2.8
Neuro-psychiatric	31	4.3
Hematological	13	1.8
Endocrine	1	0.1
Nutritional	9	1.2
Immmunological	6	0.8
Malaria	67	9.3
Neonatal Sepsis	18	2.5
Stable/Normal	2	0.4
Total	**722**	**100.0**

DISCUSSION

This study aimed to describe the pattern and identify the predictors of antibiotic prescriptions by physicians among patients who presented at the children outpatient clinic in this facility. Antibiotic prescription was prevalent, with the pattern and independent predictors of antibiotic use identified.

The percentage of encounters with antibiotic(s) in this study was 74.4%, which is more than twice the higher range of the WHO optimal range (20.0-26.8%).[16] The rate was higher compared to recent studies in Nigeria and Abu Dhabi which reported 50.2% and 43% respectively.[17,18] However, a higher value has been reported in Nigeria (81.3%).[19] Empirical treatment with antibiotics, as seen in outpatient clinics, can lead to a high prescription rate for antibiotics. The non-use of standard treatment guidelines also contributes significantly to this rate. According to a study conducted in northern Nigeria, other reasons for this could be the absence of penalties, sales representatives' pressure and a desire to assist patients.[20]

Amoxicillin/clavulanic acid was the most commonly prescribed antibiotics. Our finding was similar to other studies in Nigeria [9,19], Ghana [21] and Italy.[22] The next most frequently prescribed antibiotic was ciprofloxacin, which is similar to the finding from a study in Ghana.[21] This differs from a study in India where cephalosporins were the most commonly prescribed antibiotics.[23] In another study, cefaclor was the most prescribed drug.[18] A study in China reported macrolides as the most prevalent antibiotics being prescribed.[14] These differences may be due to the prescribing habits of the physicians based on their varying degrees of knowledge about antibiotic prescriptions, patient characteristics, accessibility of drugs,

diagnosis, and non-compliance with or lack of standard treatment guidelines. There is a need to adhere to standard treatment guidelines in outpatient clinics to encourage the appropriate use of antibiotics for specific illnesses, thereby eliminating prescriptions based on subjectivity.

In this study, 72.9% of patients were treated with antibiotic monotherapy, this is similar to the findings from studies in Southeast Nigeria (70.6%) [9] and Northern Nigeria (71.3%).[17] These similarities might be due to the availability of antibiotics in hospitals, socio-economic concerns, and the fear of adverse drug reactions (ADRs) and drug-drug interactions (DDIs). This could also be attributed to the exposure of doctors to similar training and their subsequent clinical practice within similar environments of training. Restriction of the number of antibiotics prescribed should be practiced; however, this should be based on a proper evaluation of the patient with adequate diagnostic tools to enhance the rational prescribing of antibiotics.

More than half of the antibiotics prescribed belonged to the access group of antibiotics compared to the watch group. A study conducted in India documented a similar finding, where the most commonly used antibiotics except ciprofloxacin belonged to the access group of antibiotics.[24] However, the findings of studies in Ghana and China differed, as the majority of the antibiotics prescribed belonged to the watch group.[14,21] The access antibiotics are highly accessible and do not need as much supervision as the watch antibiotics. Based on the aforementioned reason, antibiotics belonging to the access group are likely preferred to be prescribed over the watch group antibiotics in an outpatient setting.[13]

The most common indication for the use of antibiotics in this study was respiratory infections. This observation is comparable with other published results.[14,18] It is known that most respiratory infections are viral and are unresponsive to antibiotics. The high proportion of respiratory infections could also reflect poor uptake of most childhood vaccines, poor housing conditions and a lack of hygiene. Most respiratory illnesses are also highly communicable, thereby increasing morbidity and mortality in childhood.

The highest antibiotic prescription was among patients younger than 5 years compared to other age groups. This is in resonance with the results of other similar studies.[9,25] This age group is predisposed to high rates of acute watery diarrhoea and respiratory illnesses due to their poorly developed immune makeup increasing the urge to prescribe antibiotics. There is a need to implement antimicrobial stewardship programmes (ASP), which will initiate stewardship interventions such as continuing medical education for physicians, caregiver education, the formulation of facility treatment guidelines and prospective audits.

Having more than four drugs was a predictor of antibiotic use. Similarly, other studies have shown that the likelihood of prescribing antibiotics was higher when more drugs were prescribed.[9,26] Overprescribing habits among some physicians will likely induce the

unnecessary inclusion of antibiotics. Health professionals are encouraged to prescribe drugs only when needed, using treatment guidelines.

Patients on therapeutics had higher odds of receiving antibiotics. This aligns with the reports of studies where abnormal findings on physical examinations amid diagnostic uncertainty increased the odds of an antibiotic prescription.[22,27] As much as possible, clinical diagnosis needs to be guided by laboratory investigation. Not all presenting symptoms and signs require an antibiotic course except in severe conditions. A study in New Papua Guinea demonstrated that the re-attendance rates (an indicator to assess the effectiveness of antibiotics) for children diagnosed with mild pneumonia were similar among those who received antibiotics and non-users.[28] There is a need for a more objective rapid diagnostic tool to distinguish between viral and bacterial infections, especially respiratory infections.

The strengths of this study included the retrospective nature of the study which would have eliminated the Hawthorne effect on the physicians. Furthermore, the period of review was for one year to address the seasonality of some diseases. A few limitations were observed in this study; the study was done in only one centre located in a tertiary health institution which may not be representative of the paediatric patients seen at the primary and secondary health facilities. This could affect the generalizability of the findings to the general populace. Secondly, the study was limited to only one year, so we could not ascertain the trends of antibiotic use over the years. Thirdly, this study was piloted in a primary health centre, however, it is predominantly an outpatient facility and medications are mostly prescribed by doctors. Finally, we had a few variables to add to the regression model as this was a secondary data source.

CONCLUSION

Inappropriate prescriptions of antibiotics by physicians were prevalent in the Paediatric outpatient clinic of this facility. The most prevalent indication for the use of antibiotics was respiratory infections while younger age, four or more drugs prescribed and therapeutic treatment were the predictors of antibiotic prescription. We recommend the implementation of antibiotic stewardship in the children outpatient setting through the development of antibiograms, the enforcement of standard treatment guidelines and an outpatient drug formulary to encourage the rational use of antibiotics in the clinic. There is a need to educate prescribers on the importance of rational antibiotic prescription, communication training and antibiotic counselling for the patient's caregivers.

Table 4: Predictors of Antibiotic Prescriptions in the Children Outpatient Department of FMC Umuahia Abia State (N=722)

Variable	Antibiotic prescription		COR[a] (95 CI)	P value*	aOR[b] (95 CI [c])	P value*
	Yes (%) 537 (74.4)	No (%) 185 (25.6)				
Age group						
0-5	409(79.4)	106(20.6)	2.50(1.60-3.80)	**0.001**	2.48(1.50-3.80)	**0.001**
6-10	57(63.3)	33(36.7)	1.12(0.60-1.90)	0.697	1.06(0.50-1.90)	0.857
11-17	71(60.7)	46(39.3)	1			
Sex						
Female	278(77.2)	82(22.8)	1.35(0.90-1.89)	0.081	1.45(1.00-2.00)	**0.040**
Male	259(71.5)	103(28.5)	1			
Period of the Year						
1st quarter	235(78.9)	63(21.1)	1.54(0.90-2.50)	0.091	-	-
2nd quarter	153(71.5)	61(28.5)	1.04(0.60-1.70)	0.890	-	-
3rd quarter	74(71.2)	30(28.8)	1.02(0.50-1.80)	0.949	-	-
4th quarter	75(70.8)	31(29.2)	1			
Number of medicines						
1-4	421(70.2)	179(29.8)	1			
>4	116(95.1)	6(4.9)	8.22(3.50-19.00)	**0.001**	9.43(3.90- 22.10)	**0.001**
Treatment type						
Therapeutic	481(75.6)	155(24.4)	3.54(1.20-9.90)	**0.016**	3.24(1.10-9.40)	**0.032**
Prophylactic	7(46.7)	8(53.3)	1			
Both	49(69.0)	22(31.0)	2.54(0.80-7.80)	0.106	1.76(0.50-5.80)	0.351

***P values less than 0.05 are considered significant [a] COR Crude Odd Ratio [b]aOR adjusted Odd Ratio [c] Confidence Interval**

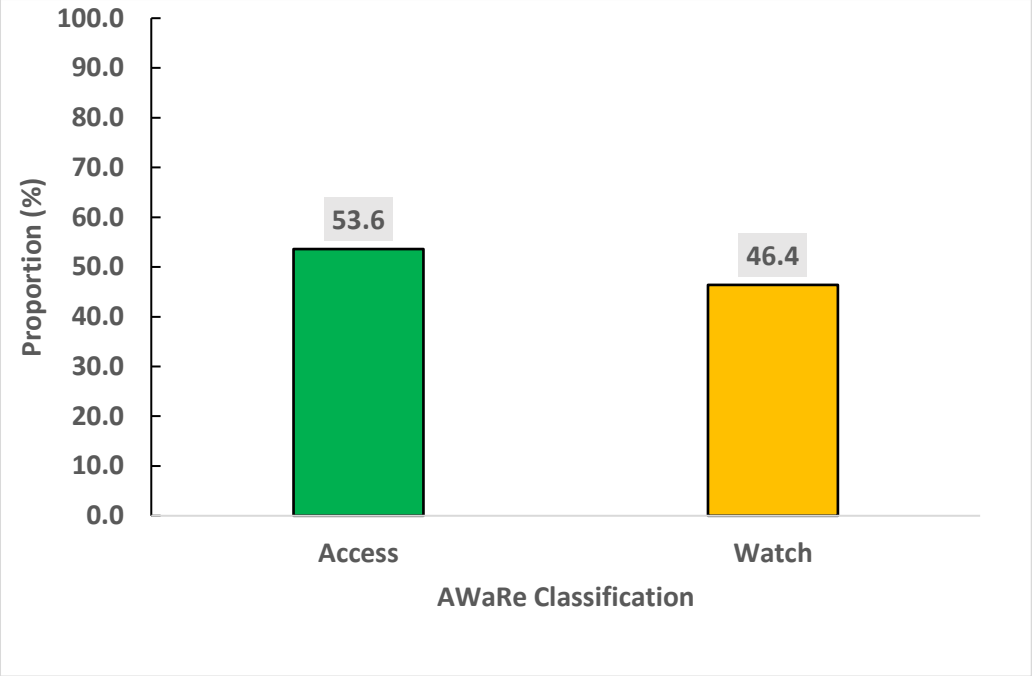

Figure 1: WHO Classification of Antibiotics Prescribed in the Children Outpatient Department (n=694)

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