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Empiric antibiotic prescription among febrile under-five Children in the University of Port Harcourt Teaching Hospital, Rivers State, Nigeria.

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Abstract: *Background:* More than 97% of febrile infants and young children have self-limiting viral infection and therefore, would not require antibiotics. Over prescription of antibiotics increases antibiotics exposure and development of resistance among patients. There is need to evaluate empiric antibiotic prescription in order to limit its use to only febrile children with bacterial infection.

Aim and Objectives: The aim of this study was to determine the prevalence of empiric antibiotic prescription among febrile under-five, post neonatal children presenting in the children outpatient clinic of the University of Port Harcourt teaching hospital.

Method: Febrile Children aged 29 days to <60 months who presented in the outpatient clinic were recruited from September 2010 to January 2011. Their weight, biodata, symptoms, Physician's diagnosis, and names of antibiotic prescribed were entered into a predetermined proforma and analysed.

Result: A total of 362 children with male to female ratio of 1.03:1 were studied. Two hundred and eighty three (78.2%) febrile children received empiric antibiotic prescriptions. The most frequent antibiotic prescribed was amoxicillin 80 (28.3%). Children aged 1-12months received the highest number of prescriptions 113 (80.7%). There was no significant relationship between age, temperature level, weight for age, number of symptoms and frequency of antibiotic prescription ($p>0.05$). Upper respiratory tract infection (83.7 %) and diarrhea (55.9%) were significantly associated with empiric antibiotic prescription ($P=0.05$ and 0.002 respectively).

Conclusion: Empiric antibiotic prescription for febrile under-five children is a common practice in UPTH. Physicians should therefore reduce the frequency of antibiotics prescription in febrile children unless there is clinical evidence of bacterial infection.

Key words: Empiric Antibiotics, Fever, post neonatal under-five, Nigeria

Introduction

Acute febrile illness among infants or young children is a common clinical scenario, accounting for up to 30% of paediatric clinic consultation[1]. More than 97% of non-toxic but febrile infants and young children have self-limiting viral infection therefore would not require antibiotics[2]. In Uganda, antibiotic was prescribed empirically to 59.5% of febrile, under-five children while in Netherland, it was prescribed to 26.5% of febrile children aged 1month to 6years[3,4].

The Integrated management for childhood illnesses (IMCI) guideline for management of febrile children in Malaria endemic areas recommended use of antibiotics when any of the following is present: General danger signs, stiff neck or any sign of severe malaria[5]. The National institute for health and clinical excellence (NICE) guide lines for management of febrile children in the United Kingdom recommends empiric antibiotic be given to children with suspected serious bacterial infection.[6] Considering that the prevalence of bacterial infections among febrile children in ambulatory clinic setting is 1.1% in the United States of America, few febrile children would actually require empiric antibiotics prescription[7].

It is important to monitor antibiotic usage in order to protect their efficacy[8]. This is because improper antibiotic usage, increases antibiotic exposure among humans and animals. This directly increases antibiotic resistance by promoting emergence of resistant bacteria strains.[9,10]

If this continues unchecked it would ultimately cause increased mortality from treatable diseases. In management of the febrile child, there is a need to evaluate empiric antibiotic treatment in order to limit its use to only children at risk of bacterial infection[11].

The aim of this study was to determine the prevalence of empiric antibiotic prescription among febrile under-five, post neonatal age children presenting in the children outpatient clinic of the University of Port Harcourt teaching hospital. We also set out to identify the factors on which physicians base their decision to prescribe empiric antibiotics and to identify the pattern of antibiotics prescription. It is hoped that consideration of findings from this study may lead to better founded and consequently, diminished empiric antibiotic prescriptions. This will ultimately help to protect available antibiotics from the emergence of resistant bacteria strains, threatening to render them ineffective.

Subjects and Methods

This was a prospective study that was carried out in the Children's outpatient clinic (CHOP) of the University of Port Harcourt Teaching Hospital (UPTH) between September 2010 and January 2011. The University of Port Harcourt Teaching hospital is a tertiary hospital located in Southern part of Nigeria. The children outpatient clinic runs both general and specialist paediatric services. The general paediatric clinic is covered mostly by Resident doctors and House officers with access to review cases with the Consultant Paediatrician. Ethical clearance for the study was obtained from the Ethics Committee of the University of Port Harcourt Teaching Hospital. Written informed consent was obtained from parents or guardian. The minimum sample size of 362 was calculated using a bacteraemia prevalence rate of 38.2% among febrile infants in a children emergency ward in Nigeria[12]. All the children that presented to the clinic and met the inclusion criteria within the study period were consecutively recruited. The criteria for inclusion into the study was age one month to < 5years, and axillary temperature ≥ 37.5°C. Children that had initially received antibiotic were excluded. The temperature and weight of all the children were measured and recorded in a structured data collection form. Each child was given a code prior to their scheduled consultation by the physician. In order not to influence the patients' prescription, the attending physicians were not informed that their prescriptions were being recorded. After being attended by the physician, they were seen in a separate room where data was collected by interviewing the caregivers. Sociodermographic information regarding age, sex, address was obtained. Clinical information including the number of symptoms the subject presented with, Physician's diagnosis, number and names of antibiotic prescribed if any was obtained from the patient files. The questionnaire was filled by the investigator. Any antibiotic prescribed prior to laboratory evidence of any bacterial infection was defined as Empiric antibiotic prescription.

Their nutritional status was determined using the Gomez classification[13].

Statistical analysis was done using EP Info version 3.5. Chi- squared test and Fishers Exact test were used to test for significant associations between proportions. Comparison of means was done with the student's t test. A p value of 0.05 or less was considered statistically significant

Result

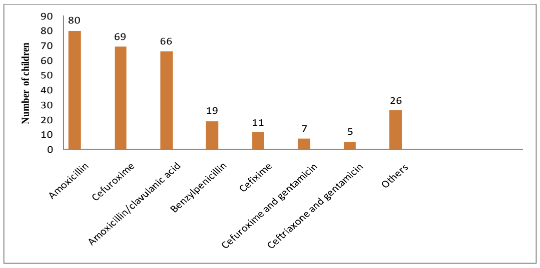
Three hundred and sixty two children who met the inclusion criteria were enrolled into the study. There were 184 (50.8%) males and 178 (49.2%) females, giving a male to female (M:F) ratio of 1.03: 1. They were aged 1 to < 60 months (mean 21.1 ± 15.4 months). The mean age of the male subjects was 20.8 ± 15.07 months, while that of the females was 21.4 ± 15.8 months (p=0.15). The median age for all the subjects was 18 months and the modal age was 24months. Two hundred and fifty eight (71.3%) children were aged ≤ 24months. The mean temperature of the study population was 38.2 ± 0.6°C (range 37.5 - 40.8 °C). One hundred and ninety children had axillary temperatures within the range of 37.5 - 38 °C. Seven had temperature >40°C(Table 1).

Table 1: Temperature and age distribution of the study population

Temp (°C)	Age in months (%)					Total (%)
	1-12	>12-24	>24-36	>36-48	>48-<60	
37.5-38.0	85(44.7)	54(28.4)	31(16.3)	10 (5.3)	10(5.3)	190(100)
>38.0-38.5	31(35.6)	29(33.3)	12(13.8)	5(5.7)	10 (11.5)	87(100)
>38.5-39.0	13(34.2)	16(42.1)	6(15.8)	1(2.6)	2(5.3)	38(100)
>39.0-39.5	9(30.0)	11(36.7)	8(26.7)	1(3.3)	1(3.3)	30(100)
>39.5-40.0	2(20.0)	5(50.0)	0(0)	0(0)	3(30.0)	10(100)
>40.0	0(0)	3(42.9)	1(14.3)	1 (14.3)	2(28.6)	7(100)
Total (%)	140 (38.7)	118 (32.6)	58(16.0)	18 (5.0)	28(7.7)	362(100)

Two hundred and sixty seven (73.8%) children had normal nutritional status. 1st, 2nd and 3rd degree malnutrition was seen in 72(19.9%), 21(5.8%) and 2(0.6%) respectively. The mean weight of the study population was 11.2 ± 4.5kg. Two hundred and eighty three (78.2%) febrile children received prescription for empiric antibiotics from the consulting physician. The most frequent antibiotic prescribed was amoxicillin in 28.3% of children (Fig 1). Antibiotics prescribed less than five times were grouped under others and they include ampicllox, ceftazidime, ceftriaxone, cephalexin, ciprofloxacin, erythromycin, septrin, ampicillin/ sulbactam and chloramphenicol. Most children 257(90.8%) received one antibiotic while two antibiotics were prescribed in 25(8.8%) and 3 in a single prescription.

Fig 1: Names of Empiric antibiotics and frequency



Children aged 1-12months received the highest number of prescriptions (80.7%) and frequency of antibiotic prescription decreased with age (Table 2). Although the difference was not statistically significant (P=0.76).

Table 2: Age distribution of children given empiric antibiotics

Age (months)	Empiric antibiotics Yes (%)	Empiric antibiotics No (%)	Total
1-12	113(80.7)	27(19.3)	140(100)
>12-24	93(78.8)	25(21.2)	118(100)
>24-36	44(75.9)	14(24.1)	58(100)
>36-48	13(72.2)	5(27.8)	18(100)
>48-<60	20(71.4)	8(28.6)	28(100)
Total	283(78.2)	79(21.8)	362(100)

χ^2 =1.86 df=4 P=0.76

All children with temperature >39.5-40.0°C received empiric antibiotics (Table 3). There was however, no significant relationship between temperature level and the frequency of empiric antibiotic prescription (P=0.2)

Table 3: Relationship between temperature and empiric antibiotic prescription

Temperature range (°C)	Empiric antibiotic Yes(%)	Empiric antibiotic No(%)	Total
37.5-38.0	143(75.3)	47(24.7)	190(100)
>38.0-38.5	71(81.6)	16(18.4)	87(100)
>38.5-39.0	31(81.6)	7(18.4)	38(100)
>39.0-39.5	24(80.0)	6(20.0)	30(100)
>39.5-40.0	10(100)	0(0)	10(100)
>40.0	4(57.1)	3(42.9)	7(100)
Total	283(78.2)	79(21.8)	362(100)

χ^2 =6.4, df=5, P=0.2

Children with second degree malnutrition received the highest number of prescriptions for empiric antibiotics (Table 4). Only two children however had third degree malnutrition. Nutritional status was not significantly related with the frequency of prescriptions (P=0.55)

Children that presented with 3 and ≥5 symptoms received the highest number of empiric antibiotics prescription (Table 5), while 72.75% of children that presented with fever and no other symptom where given empiric antibiotic prescription. The number of symptoms the patient presented with was not significantly related to the frequency of empiric antibiotic prescription.

Table 4: Nutritional status and empiric antibiotic prescription

Nutritional status (Gomez)	Empiric antibiotic Yes(%)	Empiric antibiotic No(%)	Total
Normal	210(78.7)	57(21.3)	267(100)
1^{st} degree malnutrition	54(75.0)	18(25.0)	72(100)
2^{nd} degree malnutrition	18(85.7)	3(14.3)	21(100)
3^{rd} degree malnutrition	1(50.0)	1(50.0)	2(100)
Total	283(78.2)	79(21.8)	2(100)

χ^2 =2.0, df=3, P=0.55

Table 5: Number of symptoms excluding fever and antibiotic prescription

No of symptoms excluding fever	Empiric antibiotic Yes(%)	Empiric antibiotic No(%)	Total
0	16(72.7)	6(27.3)	22(100)
1	55(76.4)	17(23.6)	72(100)
2	108(77.1)	32(22.9)	140(100)
3	70(83.3)	14(16.7)	84(100)
4	29(76.3)	9(23.7)	38(100)
≥5	5(83.3)	1(16.7)	6(100)
Total	283(78.2)	79(21.8)	362(100)

χ^2 =2.08, df=5, P=0.83

Febrile Children who had upper respiratory tract infection (URTI) presenting only as either cough or catarrh or both were given empiric antibiotic prescription in 83.7% of their consultations. Those who had diarrhoea received prescription for empiric antibiotics in 55.9% of their consultations (Table 6). Diagnosis that occurred in less than 9%(32) of the study population was not evaluated because of the small sample size. URTI and diarrhoea were significantly associated with increased antibiotic prescription (P=0.05 and 0.002 respectively).

Table 6: Clinical diagnosis and frequency of antibiotic prescription

Clinical diagnosis	Empiric antibiotic Yes(%)	Empiric antibiotics No(%)	P value
URTI	118(83.7)	23(16.3)	0.05
Tonsillitis	41(87.2)	6(12.8)	0.1
Pneumonia	33(86.8)	5(13.2)	0.2
Diarrhoea	19(55.9)	15(44.1)	0.002

Discussion

An overall frequency of 78.2% for empiric antibiotic prescription among febrile under-five children is high. This high frequency of antibiotic prescription is similar to 72.2% reported among similar age group in Tanzania, another African country[14]. African countries with developing economies could have similar challenges in their health sector. In such settings, challenges with laboratory services ranges from delay in laboratory results to complete absence of laboratories. Results of laboratory investigations to confirm infection usually takes more than 24 hours. This necessitates a second visit or often the patient is lost to follow up. This situation makes the physician to opt for empiric antibiotic prescription. A study done in the Netherland among febrile children reported a lower antibiotic prescription rate of 26.5%[4]. In the Netherland study a practice guideline for the management of febrile children was used.[15] This guideline does not recommend routine use of antibiotics in children with fever without an apparent source. This adherence to the guideline could have contributed to the lower frequency of antibiotic prescription. Also the mean temperature of the Netherlands study was lower than our study (37.9 vs 38.2°C respectively). The lower temperature could mean that the study population in the Netherlands study was at a lower risk of bacterial infection than our study population. Previous studies have demonstrated that high temperatures in association with young age increases the likelihood of bacterial infection[6,16].

Amoxicillin and cefuroxime were the most frequently prescribed antibiotics in this study. Amoxicillin, a narrow spectrum penicillin has been reported in Tanzania, Nigeria and America as one of the common antibiotics used in paediatric practice[14,17,18]. The high use of cefuroxime, a broad spectrum cephalosporin in our study shows a growing pattern of clinicians choosing more expensive and broader spectrum antibiotics in their practice. Similar trend has also been reported in USA and it raises serious concerns about the overuse of broad-spectrum antibiotics, particularly for patients for whom antibiotic therapy is not indicated at all[18]. The recommended principle for rational antibiotic prescription includes: Choosing a drug that has efficacy in treating or preventing the disease but leaves other bacteria in the body intact and one that is available, convenient and inexpensive[19,20].

The risk of bacterial infection is higher in younger children due to immaturity of the immune system.[21] knowledge of this fact may encourage physicians to prescribe empiric antibiotics more often in this age group. However, even among febrile young children there is an urgent need for classification based on risk for bacterial infection using clinical guidelines. In Europe and America these guidelines are already available[6,15,22]. These guidelines use both clinical and laboratory parameters in risk assessment for bacterial infection. This is based on the assumption that results of these laboratory tests are available to the physician during the index consultation. In a resource poor setting however, this is not the case, so an assessment for risk of bacterial infection in a febrile child is often made without the use of any laboratory results.

The highest antibiotic prescription rate was found among children with temperature range of 39.5-40°C. The combination of young age and hyperpyrexia may have contributed to the 100% antibiotic prescription seen in this group of children. This is because in our study, children with temperature range of 39.5-40°C were much younger (70% < 24mths) while those with temperature >40°C were older (57% > 24mths), as shown in Table 1. Although hyperpyrexia has been documented to be associated with higher risk for sepsis, guidelines on management of febrile children recommends that, height of body temperature alone should not be used to identify children with high risk for bacterial infection but the age of the child should also be taken into account[6,7,16].

Febrile Malnourished children could receive higher antibiotic prescriptions as they have a higher risk of bacterial infection[23]. This was the case in our study as children with 2nd degree malnutrition received the most antibiotics. The number of symptoms did not significantly affect the rate of antibiotic prescriptions. This finding is not surprising as increased symptoms could have meant more system involvement in the on-going pathology but does not differentiate between viral and bacterial aetiology.

In our study 83.7% of children who had common cold were prescribed antibiotics. This directly contravenes WHO and IMCI treatment guidelines, which discourages the use of antibiotics in children with common cold[5,24]. In Tanzania 68.9% of children with common cold were prescribed antibiotics, while in USA 29.6% of children received antibiotic for acute respiratory tract infections when it was not indicated[14,18]. Antibiotics do not reduce the severity or duration of illness in viral infections. Thus their use in viral illness exposes a patient to the risks of side effects from a medication without any benefit. Antibiotics are also not recommended for acute watery diarrhoea[5,24]. Our study however reported 55.9% antibiotic prescription rate in management of diarrheal diseases. Similar high frequency of antibiotic prescription has been reported in other low income countries.[14,25,26]

Conclusion

In conclusion, empiric antibiotic prescription for febrile under-five children is very high in UPTH. This finding has also been reported in studies conducted in other low income countries. Such high rate of empiric antibiotic prescription would lead to increased development of resistant strain of bacteria to the present antibiotics and threatens the end of antibiotic era. There is a need to protect available antibiotics by rational prescription only when they are indicated. The use of available practise guidelines in the management of febrile children would help reduce inappropriate antibiotic prescription in febrile children. The campaign to protect these antibiotics needs to be actively brought to low income countries. These countries have a higher prevalence of infectious diseases and as such would have greater mortality should these drugs be rendered inactive.

We recommend implementation of current evidence based practice that advocates for prior documentation of evidence of bacterial infection by laboratory testing before antibiotic prescription for febrile children. The febrile child at urgent need for empiric antibiotic should however receive it while laboratory testing to document bacterial infection is being done. We acknowledge the need for locally useful clinical detector/screening tools which could be used in the absence of sophisticated laboratory methods to identify the febrile child at risk of serious bacterial infection. There is no doubt that classifying children based on their risk assessment for bacterial infection prior to commencing antibiotics will, identify the small group of children that need urgent commencement of empiric antibiotics and at the same time, limit the irrational use of antibiotics. This practice may reduce development of antibiotic resistance and reduce the cost of healthcare.

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