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Bacteriology of urinary tract infection and antimicrobial sensitivities in under-five children in Enugu

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Abstract: *Background:* Urinary tract infection (UTI) is one of the serious bacterial infections in febrile young children, which may cause chronic morbidities. Studies from different parts of Nigeria have shown varying pattern in its bacteriology and antibiotic sensitivities. Antimicrobial resistance rate among uropathogens is an increasing problem limiting therapeutic options, and underscores the need to determine local bacteriological pattern that will guide empiric antibiotic choices.

Objectives: To identify the bacterial pathogens responsible for UTI in febrile under-five children in Enugu as well as their antibiotic sensitivity patterns.

Methods: A cross-sectional descriptive hospital based study of eligible febrile children aged one to 59 months. Urine samples were collected using mid-stream and suprapubic aspiration methods. Standard laboratory procedures were used to culture the urine specimens, identify the bacterial pathogens as well as their antibiotic sensitivity patterns. Descriptive statistics were used to analyse the outcome.

Results: Significant bacteriuria occurred in 22 (11%) of the 200 samples. *Escherichia coli* isolates were the most common organisms in 7(31.8%) of the 22 positive samples. Others were *Staphylococcus aureus*, Klebsiella spp and *Streptococcus faecalis* isolated in 5 (22.7%), 3(13.6%), and 3(13.6%) of the positive samples respectively. Most of the isolates were sensitive to ofloxacin (90.9%), ciprofloxacin (81.8%), nitrofurantoin (77.3%) and ceftriaxone (72.7%). High levels of resistance to ampicillin, cotrimoxazole, amoxicillin, nalidixic acid and clavulanate-potentiated amoxicillin were observed.

Conclusion: Escherichia coli is the most common cause of UTI in febrile under-five children studied. Ciprofloxacin and ceftriaxone showed better sensitivities are advocated for the empiric treatment of febrile UTI in Enugu.

Key words: UTI, under-fives, bacterial pathogens, antibiotic sensitivities

Introduction

Urinary tract infection is an important cause of morbidity and mortality in the paediatric age group[1]. Symptomatic (febrile) UTI is associated with renal parenchymal involvement which predisposes to renal scarring with devastating consequences such as hypertension, chronic renal failure and end-stage renal disease[2]. Delay in initiating appropriate antibiotic therapy during UTI episodes is a known risk factor for development of renal scars which is more marked in under-five children[3]. Prompt diagnosis and early initiation of appropriate antibiotics in such children would reduce the morbidities associated with UTI.

In suspected UTI cases, it is appropriate to begin empiric treatment after collecting urine specimensfor culture and sensitivity. The selection of antibiotics should be based on, amongst other factors, the pattern of urinary pathogens and their antimicrobial sensitivities in the local environment. Although *Escherichia coli* has been reported to account for most of the cases of symptomatic UTI in children[4], studies from some parts of Nigeria however, have shown a changing trend in the bacteriology of UTI[5,6,7]. While *Escherichia coli* was the most common urinary isolate in studies in Benin[8] and Maiduguri[9], Klebsiella predominated in studies in Port Harcourt[5] Ibadan[6] and Abakiliki[7]. Also the antimicrobial resistance rates among uropathogens is on the increase thus limiting therapeutic options[7,10,11]. The rate and manner of resistance varies with the setting either in developing or developed countries. This variation in bacteriology and antibiotic sensitivities warrants different usage of antibiotics for empirical treatment of the disease in various localities to minimize the evolution of bacterial antibiotic resistance and at the same time ensure adequate and effective treatment. There is no reported study in Enugu that evaluated urinary tract pathogens and their antimicrobial sensitivity patterns in children with symptomatic UTI so as to guide empiric antibiotic choice and prompt treatment. A study done in Enugu over two decades ago documented the urinary pathogens isolated from asymptomatic preschool children[12]. It is possible there may have been a changing pattern in the bacteriology of UTI in Enugu over time. Also the bacterial pathogens implicated in asymptomatic UTI may differ from that of symptomatic UTI. Against this background, this study was carried out to identify the prevalent bacterial pathogens causing UTI in febrile under-five children seen at UNTH, Enugu as well as the antibiotic sensitivity patterns. It is envisaged that the resultant findings would improve case management of such children and perhaps provide basis for the development of guidelines that could be used in Enugu as well as similar centres subsequently.

Materials and methods

The study was conducted at the University of Nigeria Teaching Hospital (UNTH), Enugu, in Nigeria, catering for patients predominantly from the South-Eastern region of the country. Ethical approval was obtained from the hospital's Health Research and Ethics Committee as well as caregivers' written informed consent prior to subject enrolment. It was a cross-sectional descriptive study with subjects recruited consecutively from the Children's Outpatient Clinic of the hospital between February and April 2010. Relevant information such as age, sex, place of domicile, symptoms, past medical and drug history was obtained. Furthermore, physical examination to elicit clinical signs of chronic illnesses such as severe protein energy malnutrition (PEM), sickle cell disease, malignancies, nephrotic syndrome and HIV/ AIDS were performed before enrolment. Children with such chronic diseases were excluded as well as those with history of antibiotic treatment less than seven days to the study. The urine samples of eligible children were collected in sterile bottles, containing boric acid, using suprapubic aspiration in subjects younger than two years and midstream collection in older children. Urine culture was done within one hour of collection employing the quantitative method as described by Guttman and Stokes[13]. Each uncentrifuged urine sample was well mixed and inoculated unto plates of cystine lactose electrolyte deficient (CLED) medium and blood agar as described by Uqurhart and Gould[14], and incubated aerobically at 37^0C for 24 hours after which the colonies were counted with a colony counter. A pure growth of $\geq 10^5$ colony forming units per ml from midstream urine sample or growth of any number of uropathogen from urine obtained by suprapubic aspiration was considered as significant bacteriuria[4]. In cases with significant bacteriuria, the bacterial isolates were identified based on colony morphology characteristics, Gram stain reaction and biochemical tests using standard techniques.[15] Antibiotic sensitivity pattern of the isolates were determined by the disc diffusion method in accordance with the National Committee for Clinical Laboratory Standards,[16] using diagnostic sensitivity test agar (International diagnostic group PLC, Topley house, Bury Lancashire, BL9 6AU, UK) and antibiotic multidiscs (Abtek)with the following antibacterial agents: ampicillin 25mcg, gentamicin 10mcg, nalidixic acid 30mcg, nitrofurantoin 200mcg, cotrimoxazole 25mcg, amoxicillin 25mcg, augmentin (amoxicillin-clavulanate) 30mcg, ofloxacin 5mcg. Others were ciprofloxacin 5mcg, ceftriaxone, cefuroxime 30mcg, and ceftazidime 30mcg. The discs were placed onto the agar surface and incubated for 24 hours. After incubation, the diameter of the zone of inhibition was measured and compared with a zone diameter interpretative chart to determine the sensitivity of the isolates to the antibiotics. *Staphylococcus aureus* (ATCC 29213) and *Escherichia coli* (ATCC 35218) were employed in the antibiotic sensitivity testing as control.

The data obtained were analysed using the Statistical Package for the Social Sciences (SPSS) software version 15.0 for Windows® (SPSS Inc.2006 Chicago, Illinois USA). Descriptive statistics was used to describe the frequency, mean and standard deviation of continuous variables. Categorical variables were tested for association using Pearson Chi square and Fisher exact test as appropriate. Significant level was set at p value of 0.05.

Results

General characteristics of the study population

One hundred and twelve (56%) of the 200 children enrolled were males with a male female ratio of 1.3:1.
Table 1 shows the age and sex distribution of the study population. The mean age was 31.14 ±17.96 months.The mean temperature was 38.3 ± 0.69^0C. Significant bacteriuria occurred in 22(11%) of the patients comprising 8 males and 14 females. Females had a higher prevalence of UTI than males (15.9% [14/88] vs. 7.1% [8/112]; odds ratio [OR] = 2.5 [confidence interval (CI) = 0.9 to 6.9] $\chi^2 = 3.87$, $P = 0.049$). UTI occurred more in infants compared with non-infants (21.1% [8/38] vs. 8.6% [14/162]; odds ratio [OR] = 2.8 [confidence interval (CI) = 1.1-7.3] $\chi^2 = 4.84$, $P = 0.028$)

Table 1: Age and Sex distribution of study population

Age group in months	Gender Male	Female	Total (%)
<12	23	15	38 (19)
12-23	23	17	40 (20)
24-35	27	13	40 (20)
36-47	14	16	30 (15)
48-59	25	27	52 (26)
All ages	112	88	200 (100)

Isolated Bacterial Pathogens

Escherichia coli isolates were the most common, grown in 7(31.81%) of the positive urine cultures. Other pathogens isolated were *Staphylococcus aureus* (22.73%), Klebsiella species (13.63%) and *Streptococcus faecalis* (13.63%). Proteus species, Pseudomonas species, Enterobacter species and Serratia species each accounted for 4.55% of the isolates. There were no mixed infections. Table 2 shows the distribution of the various isolates according to sex.

Antibiotic Sensitivity Pattern of isolated pathogens

Sensitivity of the bacterial isolates for the respective antibiotics were ofloxacin (90.9%), ciprofloxacin 81.8%, nitrofurantoin 77.3%, ceftriaxone 72.7%, gentamicin 63.6%, ceftazidime 50%. Sensitivity was poor to cotrimoxazole (4.5%), amoxicillin (9.1%), nalidixic acid (18.2%), cefuroxime (31.8%) and clavulanate potentiated amoxicillin (40.9%). No pathogen was sensitive to ampicillin. Table 3

Table 2: Sex distribution of the isolated pathogens

Bacterial isolates	Males	Females	Total (%)
Escherichia coli	0	7	7(31.81)
Staphylococcus aureus	4	1	5(22.73)
Klebsiella spp	2	1	3(13.63)
Streptococcus faecalis	1	2	3(13.63)
Proteus spp	1	0	1(4.55)
Pseudomonas spp	0	1	1(4.55)
Enterobacter spp	0	1	1(4.55)
Serratia spp	0	1	1(4.55)
All pathogens	8	14	22(100.00)

Table 3: Bacterial isolates and their antibiotic sensitivity patterns

Number (%) of Sensitive Bacterial Isolates												
Bacterial Isolates (n)	OFL	CIP	NIT	CTZ	GEN	CAZ	AUG	CRX	NA	AMX	COT	AMP
Escherichia coli (7)	7(100)	5(71.4)	7(100)	6(85.7)	4(57.1)	4(57.1)	3(42.9)	3(42.9)	2(28.6)	0(0.0)	1(14.3)	0(0.0)
Staphylococcus aureus (5)	5(100)	5(100)	3(60)	4(80)	4(80)	5(100)	2(40)	2(40)	1(20)	0(0.0)	0(0.0)	0(0.0)
Klebsiella spp (3)	2(66.7)	3(100)	3(100)	2(66.7)	3(100)	1(33.3)	1(33.3)	0(0.0)	0(0.0)	1(33.3)	0(0.0)	0(0.0)
Streptococcus faecalis(3)	2(66.7)	2(66.7)	2 (66.7)	2(66.7)	3(100)	0(0.0)	2(66.7)	2(66.7)	0(0.0)	1(33.3)	0(0.0)	0(0.0)
Proteus spp (1)	1(100)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Pseudomonas spp (1)	1(100)	1(100)	0(0.0)	1(100)	0(0.0)	1(100)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Enterobacter spp (1)	1(100)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Serratia spp. (1)	1(100)	1(100)	1(100)	1(100)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(100)	0(0.0)	0(0.0)	0(0.0)
All Pathogens (22)	20 (90.9)	18 (81.8)	17 (77.3)	16 (72.7)	14 (63.6)	11 (50)	9 (40.9)	7 (31.8)	4 (18.2)	2 (9.1)	1 (4.5)	0 (0.0)

OFL= Ofloxacin	CIP= Ciprofloxacin	NIT=Nitrofurantoin
CTZ= Ceftriaxone	GEN=Gentamicin	CAZ=Ceftazidime
AUG= Clavulanate potentiated amoxicillin	CRX= Cefuroxime	NA=Nalidixicacid
AMX= Amoxicillin	COT= Cotrimoxazole	AMP= Ampicillin

Discussion

The high rate of UTI (11%) in this study is comparable with the figures documented in studies[8,9] among children of similar ages in Nigeria.

Escherichia coli, *Staphylococcus aureus*, Klebsiella and *Streptococcus faecalis* were the organisms most frequently isolated from the urine samples in our study. This finding is similar to what have been documented in other centres in Nigeria[7,8,9,11,17,18]. However while *E. coli* was the most common organism causing UTI in our series as was also reported in Benin[8] and Maiduguri,[9] Klebsiella was the dominant organism isolated in studies in Portharcourt,[5] Ibadan[17] and Abakiliki[7]. These studies irrespective of the site have shown the dominance of gram negative organisms as important causative agents in urinary tract infections. This reflects the origin of the bacterial pathogens, which are usually from the microflora of the intestine, and perineum[4]. The study design and subject selection used by the different studies may also be responsible for the differences in the spectrum of uropathogens from these studies. In Benin[8] and Maiduguri[9] as well as in our series children below the age of five years were enrolled, while the study in Portharcourt,[5] Ibadan[17] and Abakiliki[7] included older children above five years of age. In Abakiliki it was a case series review, which may not have given an exact representation as some cases may have been excluded. Some of the children in their study may also have had other chronic morbidities, which were excluded in our study. The finding from our study agrees with previous finding in Enugu that showed *E. coli* as the most predominant organism in asymptomatic preschool children. The similarity of pathogenic agents may suggest that these organisms, which are present in the genitourinary tract, become pathogenic given a prevailing circumstance. The differences regarding which organism predominates underscore the need for identifying the organisms responsible for childhood UTI in the local environment.

Escherichia coli infections occurred only in females in our study and accounted for 50% of all infections in females. Studies have reported the preponderance of *E. coli* infections in females, accounting for 75 to 90% of all urinary infections in females[19-21]. This has been ascribed to the proximity of the urethra to the anus in females which encourages contamination and ascent into the urinary tract of faecal flora of which *E. coli* is the most common.[21]

The large contribution of *Staphylococcus aureus* as second most common causative organism in this study was also demonstrated in other centres. Ibadin[22] in Benin, and Adeleke and colleague[23] in Kano documented a high frequency of *S. aureus* isolates. These studies however were among patients with nephrotic syndrome and may have accounted for the observed trend. In high-income countries, *Escherichia coli* constitute a high majority (up to 90%) of uropathogens in children[24,25]. unlike in low-income countries where other organisms along with *E. Coli* contribute largely as urinary isolate,[8,26] as was demonstrated in our study.

The flouroquinolones showed better sensitivities against the pathogens as was observed in other studies[6,8,9,11,18,26,27] In Maiduguri,[11] Benin[8] and Ilorin,[18] more than 80% of the *E. coli* isolates was sensitive to ciprofloxacin. *S. aureus* was 100% sensitive to this drug in Maiduguri.[11] The higher sensitivity to this class of drugs may be attributable to their infrequent use in the treatment of childhood infections. Initially the use of the flouroquinolones in children was restricted by their potential to induce cartilage toxicity in immature animals[28]. Ciprofloxacin however has been found to be relatively safe in children as no arthropathy has been reported[29]. Ciprofloxacin could therefore be safely utilized for empirical treatment of febrile UTI in children.
The good sensitivity shown by Nitrofuratoin although commendable and similar to what was reported by other studies,[30] may not be applicable in practice. The drug is formulated in tablet form, does not achieve optimal blood levels,[2] and thus is not recommended in those with renal parenchymal injury.

The good sensitivity of urinary isolates to ceftriaxone in this study is similar to findings by Mava et al[11]in Maiduguri where more than 80% of both *E. coli* and *S.aureus* isolates were sensitive to this drug. In Benin also, comparable sensitivity for this drug was reported where about 70% and 100% of *E. coli* and *S. aureus* isolates respectively were found to be sensitive[8]. The explanation for the persisting good sensitivity of urinary isolates to this drug in our environment may be due to the fact that it is expensive and must be administered parenterally, therefore less likely to be abused by patients. This good sensitivity suggests that ceftriaxone will be safely used in the empiric treatment of febrile UTI.

Gentamicin was active against 64% of the isolates (57% of *E. coli*). The moderate activity of gentamicin against urinary pathogens in the present study is comparable to finding in Maiduguri and Ilorin where less than 70% of E. coli isolates were sensitive to this drug.[9,18] Variable sensitivities of urinary isolates to this drug have been documented in different centres. Higher sensitivity of 80% was recorded in Benin[8] while studies in Ibadan documented very low sensitivities.[6,17] In South Africa[31] all gram negative pathogens were 100% sensitive to this drug. The use of gentamicin in the treatment of UTI should be considered when it is based on local sensitivity report.

Only 41% of the urinary isolates (42.9% of *E. coli* and 40% of *Staph. aureus*) were sensitive to clavulanate potentiated amoxicillin in the present study. This figure is lower than the 81% sensitivity (50% of *E. coli* and 100% of *Staph. aureus*) obtained in Benin[8]. However later studies demonstrated poor sensitivities of 22% and 31% to this drug in Ibadan[17] and in Maiduguri[9] respectively. The increasing resistance of the urinary pathogens (especially *E. coli*) to this drug indicate that clavulanate potentiated amoxicillin may no longer be useful in the empiric treatment of UTI among children in Enugu.

Ampicillin, cotrimoxazole, amoxicillin and nalidixic acid were the antibiotics with the highest level of resistance noted in this study. Similar observation had been made by other workers in Nigeria[7,9,11,17]. The practice of self-medication and the possible use of fake and substandard drugs as well as drug abuse may perhaps be responsible for the observed trend[32]. These older drugs are readily available, accessible and relatively affordable in patent medicine shops. The oral route of administration also favours their risk of abuse. With the high level of resistance to these common antimicrobials observed in this study, it will be inappropriate to recommend the use of these older drugs in the empirical treatment of UTI in this environment.

Conclusions

Escherichia coli is the predominant cause of UTI in febrile under-fives in our series. Ciprofloxacin and ceftriaxone showed better sensitivities and should be recommended for empirical treatment of UTI in under-five children in Enugu.

Authors' contribution

ICA: Conception and designing of the study, collecting, analyzing and interpreting the data, manuscript writing, revising and approval of the work.

OT: Design of study, manuscript writing, revising, and approval of the work.

IAN, OHU, OUC: Design of study, manuscript review, and approval of the work.

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