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Bacteriological Profile and Antimicrobial Susceptibility Pattern of Community Acquired Urinary Tract Infection in Children: A Tertiary Care Experience

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Abstract: *This prospective cross sectional study was done with the aim to study the bacteriological profile and antimicrobial susceptibility pattern of community acquired urinary tract infection in children at a tertiary care centre in Assam. A total of 450 urine samples received in the bacteriology laboratory of children with suspected UTI were processed for wet mount microscopy and semi quantitative culture to diagnose UTI. Antimicrobial susceptibility was tested using the disc diffusion technique according to Clinical Laboratory Standards Institute guidelines. Significant bacteriuria was seen in 148 samples (32.89 %). UTI was more prevalent in the age group >1year-5 years (46.27%) and in females (44.71%). Significant pyuria was seen in 56.76% cases. Fever (64.19%) was the most common presenting symptom. Escherichia Coli (42.68%) was most commonly isolated organism followed by Klebsiella spp(16.56%) and Staphylococcus aureus (10.83%). Antibiotics active against gram negative isolates were imipenem, piperacillin-tazobactum, nitrofurantoin and gentamicin . Vancomycin, linezolid, ofloxacin and gentamicin were effective against gram positive isolates. 47.06% of Staphylococcus aureus isolates were methicillin resistant (MRSA).Uropathogens isolated showed high resistance to ampicillin, nalidixic acid and cotrimoxazole.*

Keywords: *Uropathogens, Antimicrobial Sensitivity pattern, Urinary Tract Infection*

I. Introduction

Urinary tract infection (UTI) is one of the most common diseases which are encountered by paediatricians in their practice. About 1% of boys and 2-3% of girls suffer from UTI[1]. The male:female ratio in UTI varies from around 2.8-5.4:1.0 in the first year of life to 1:10 after the second year of life[1]. However diagnosis is often difficult as young children with UTI present with nonspecific symptoms, such as poor feeding, vomiting, irritability or fever alone [2]. A study done on children presenting to an emergency department with fever found that 3.3% suffered from UTI[3]. Recurrent UTI may lead to severe complications like renal scaring which is one of the commonest reason of developing hypertension and renal failure[4]. Therefore, early diagnosis of UTI and appropriate antimicrobial treatment will help in minimising complications like renal scarring and kidney damage.

Most of UTI in children are caused by *Escherichia coli*, *Proteus* spp., *Enterbacter* spp. *and Klebsiella* spp.[5]. For majority of community acquired UTI in children, the treatment is empiric because antimicrobial susceptibility pattern of the uropathogen is available only after 48 hours of sampling. This leads clinicians to rely on urine microscopy for diagnosis of UTI. However for appropriate management of urinary tract infection, knowledge of appropriate antibiotic susceptibility pattern is essential[6].Several studies done in developing countries for finding out the antibiotic susceptibility pattern of uropathogens isolated in children have shown an increasing pattern of antibiotic resistance particularly to commonly used antimicrobials[7,8]. Studies suggest that antimicrobial susceptibility pattern of isolated microorganisms shows significant geographical variations[9] and it also varies over short period of time. As there are only a few studies regarding antimicrobial susceptibility pattern of uropathogens from northeast India, our study was done with a view to find the uropathogens causing UTI in children and their antibiotic susceptibility pattern in this part of North East India. The data obtained from this study could help in formulating proper empiric treatment for the region.

II. Materials and methods

The present study is a prospective cross sectional study carried out in a tertiary care teaching hospital in Assam for a duration of one year. A total of 450 clean catch midstream urine samples of children received in the bacteriology laboratory were included in the study after considering the following inclusion and exclusion criteria.

Inclusion criteria: Samples of children aged one month to 12 years who were clinically suspected to be suffering from urinary tract infection were included in the study.

Exclusion criteria: Samples from children with history of hospitalization in the previous month or those who had been admitted to a hospital for 48 hours or more, previous history of UTI, known urinary malformations (according to renal ultrasound), chronic illness, or current prophylactic treatment with antibiotics were excluded from the study.

Few drops of centrifuged urine were examined for white blood cells (WBCs) under high power objective(40x) for a minimum of 10 high power field (HPF). The criterion of ≥ 5WBC/HPF was taken as significant pyuria[10]. 1 µl of uncentrifuged urine samples were inoculated on MacConkey agar and Blood agar media using a calibrated nichrome loop (Semi-Quantitative method)[11] and colonies were counted after overnight incubation at 37°C. Numbers of colonies obtained were multiplied by 1000 to obtain the colony forming units (CFU)/ml. A urine culture was considered positive (significant bacteriuria) when it resulted in greater than or equal to 10^5 colonies and if there were 10^4 colonies in a symptomatic child[1]. Isolated organisms were identified by standard biochemical tests. Antimicrobial susceptibility was tested using the disc diffusion technique (Kirby-Bauer's technique) by using various antibiotic discs (Hi- media, India) according to Clinical Laboratory Standards Institute guidelines[12]. Antibiotics which were tested against the isolates include : Ampicillin(10µg), Cotrimoxazole(25µg), Cefotaxime(30µg), Ceftriaxone(30µg), Cefoxitin(30µg), Gentamicin(10µg), Ciprofloxacin(30µg), Ofloxacin(5µg), Amoxycillin/clavulanate(20/10µg), Piperacillin-tazobactum(100/10µg), Nalidixic acid(30µg), Nitrofurantoin(300µg), Linezolid(30µg) , Vancomycin(30µg), Imipenem(10µg). *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923 were used as quality control strains for antimicrobial susceptibility of gram positive and gram negative bacteria respectively.

Data was entered and analysis was performed using Microsoft excel and SPSS version 16 software. Organisms with intermediate susceptibility were considered resistant for the purpose of statistical analysis.

III. Results And Observation

A total of 450 urine samples of children with clinically suspected urinary tract infection were included in the study. Maximum numbers of samples received were in the age group of >5-10 years 40.22%(181/450) followed by >1-5 years 29.78%(134/450), >10 years 19.11%(86/450) and 1month-1year 10.89%(49/450).The study samples included were from 242(53.78%) male and 208(46.22%) female children. Out of the total sample,148 samples (32.89 %) were culture positive. Significant bacteriuria was found to be prevalent in the age group >1year-5 years 46.27%(62/134).The occurrence of culture proven urinary tract infection was 93(44.71%) in the females and 55(22.73%) in the males with a overall male: female ratio of 1:1.7. Amongst the investigated male patients, highest number of culture proven UTI were found in the age group of 1month-1year(n=10,71.43%) whereas in case of female patients, occurrence of culture proven UTI was highest in the age group of >5-10 years(n=37,69.81%)(Table 1)

Table 1: Age and sex distribution

Age Group	Sex		Culture Showing Significant Bacteriuria	Total Number Of Cases
	Male	Female		
1 month to 1 year	10 (71.43%)	4 (28.57%)	14(28.57%)	49
> 1—5 years	23 (37.10%)	39 (62.90%)	62(46.27%)	134
> 5—10 years	16 (30.19%)	37 (69.81%)	53(29.28%)	181
> 10 years	6 (31.58%)	13 (68.42%)	19(22.09%)	86

Out of the 148 cases showing significant bacteriuria, 84(56.76%) were found to have significant pyuria. Out of the 302 culture negative cases, 225(74.50%) did not have significant pyuria.(Table2). Significant pyuria was found to have sensitivity, specificity, positive predictive value and negative predictive value of 56.76%, 74.50%,51.2% and 78.2% respectively.

Table 2: Correlation between pyuria with significant bacteriuria

Pyuria	Urine culture		Total
	Significant growth(%)	Insignificant growth(%)	
Significant pyuria (>5pus cells/HPF)	84(56.76%)	77(25.50%)	161(35.78%)
Insignificant pyuria	64(43.24%)	225(74.50%)	289(64.22%)
Total	148(100%)	302(100%)	450(100%)

Regarding clinical features, fever was the most common presenting symptom, accounting for 64.19%(n=95) of patients. This is followed by abdominal pain (n=62, 41.89%), decreased appetite

(n=54,36.49%), dysuria (n=46,31.08%) and nausea/vomiting (n=29,19.59%). Other symptoms noted are increased frequency(n=18,12.16%), flank pain(n=9,6.08%), hematuria (n=9,6.08%), straining on micturition (n=6,4.05%), urgency(n=3,2.02%) and dribbling(n=3,2.02%)

Of the 148 culture proven cases, 139 cases were monomicrobial and 9 cases were bimicrobial with the isolation of 2 organisms each from the 9 bimicrobial cases. Thus a total of 157 organisms were isolated in the study. The most common pathogen isolated in our study was Escherichia Coli (67 ;42.68%) followed by Klebsiella Species(26 ;16.56%). Other organisms isolated were *Staphylococcus aureus* 17 (10.83%), *Proteus spp.*10(6.37%), *Enterococcus* spp. 8(5.09%). *Pseudomonas* spp 7 (4.46%), *Providencia* spp. 6 (3.8%), *coagulase negative Staphylococcus* spp. 6(3.8%)and *Citrobacter* spp. 3 (1.91%), *Enterobacter* spp. 2(1.27%). Six isolates of yeast cells were also obtained which were not followed up further.

The organisms isolated in the study showed varied patterns of sensitivity to the antimicrobial agents used against them. But not a single isolate was found to be resistant to all the antimicrobial agents in the study. Uropathogens isolated showed high resistance to ampicillin, nalidixic acid and cotrimoxazole. All the Gram negative isolates were sensitive to imipenem. They showed good sensitivity to piperacillin-tazobactum, nitrofurantoin and gentamicin . Gram positive isolates were 100% sensitive to linezolid and vancomycin. They also showed good sensitivity to ofloxacin and gentamicin. 47.06% of *Staphylococcus aureus* isolates were sensitive to cefoxitin. (Table 3)

Table 3: Antimicrobial susceptibility pattern of isolated uropathogens

Antimicrobials	*Escherichiaea coli*(n=67)	*Klebseilla species*(n=26)	*Staphylococcus aureus*(n=17)
Ampicillin	11(16.42)	7(26.92)	8(47.06)
Cotrimoxazole	19(28.35)	9(34.61)	6(35.29)
Cefotaxime	33(49.25)	12(46.15)	8(47.06)
Ceftriaxone	30(44.78)	10(38.46)	8(47.06)
Cefoxitin	-	-	8(47.06)
Gentamicin	41(61.19)	20(76.92)	13(76.47)
Nalidixic acid	4(5.97)	8(30.77)	-
Ciprofloxacin	34(50.74)	13(50)	11(64.70)
Ofloxacin	43(64.18)	15(57.69)	13(76.47)
Nitrofurantoin	58(86.57)	20(76.92)	-
Amoxicillin-clavulanate	-	-	8(47.06)
Piperacillin -tazobactum	54(80.60)	22(84.61)	-
Linezolid	-	-	17(100)
Vancomycin	-	-	17(100)
Imipenem	67(100)	26(100)	-

IV. Discussion

The present study shows the common uropathogens and their antibiotic sensitivity pattern in paediatric patients with suspected UTI attending a tertiary care centre. The present study comprised of 450 urine samples from children with clinically suspected urinary tract infection and out of which, significant bacteriuria was found in 32.89% of children. Significant bacteriuria was found to vary from 28.30% to 35.4% in studies done by workers elsewhere in India[13,14]. In a study done by Sharmin et al[15] percentage of culture proven UTI was 46.66%. The higher percentage of culture positivity could be due to the fact that the study included only those cases which showed >5pus cells/HPF.

Analysis of present study shows that the occurrence of culture proven UTI was highest in the age group >1 year to 5 years (46.27%). This is in accordance with the study reports of other workers[16,17].The preponderance of cases in the age group may be attributed to fact that the children in this age are not properly toilet trained leading to ascending infection of faecal flora.

The occurrence of urinary tract infection was 44.71% in females and 22.73% in males in our study. Thus occurrence was slightly higher in females and this accorded with most of the previous studies done in different countries[16,18]. In contrast to this, studies done by Rai et al[17] (53.3%)and Taneja et al[13] (77.8%) show a preponderance of UTI in male children . However, male children outnumbered female children during the first year of life with a male to female ratio of 2.5 : 1. Taneja *et al*[13] in their study found male gender and age < 1 year to be risk factors in children suffering from urinary tract infection.

Out of the 148 cases of UTI that were positive by culture, only 84(56.76%) were found to have significant pyuria. Absence of significant pyuria was seen in about 64(43.24%) cases. This discordant finding has also been seen in other studies[13,19]. Presence of pyuria in 77(25.50%) cases of insignificant or sterile growth can be due to presence of other infection and not necessarily due to UTI. Hence urine culture is essential for the diagnosis of UTI. Also there is a need to evaluate the presence of sterile pyuria for other disease conditions.

Regarding clinical presentation, fever was the most common presentation (64.19%) followed by abdominal pain (41.89%).This is similar to the study done by Sharma[20] et al . In our study, children also presented with many non specific symptoms like decreased appetite, nausea and vomiting. So, there is a need to screen the febrile children for UTI even when there is no related renal symptoms[3].

Out of the 148 culture positive cases, 139 were monomicrobial and 9 were bimicrobial with isolation of 2 organisms from each. Thus a total of 157 isolates were obtained from the study group during the study course. *Escherichia coli* was found to be the most common isolate in the present study (42.68%) followed by *Klebsiella* spp. (16.56%) which is similar with the findings of other studies done in India and other developing countries[13,15].The isolation rate of Escherichia Coli ranged from 37.3% to 87.0% in studies conducted across the world[7,8,15]. So, the most common uropathogen isolated in our study was from *Enterobacteriaceae* group which is in accordance with other studies[15,17].

Staphylococcus aureus contributing to 10.83% of the isolates. Isolation rate of staphylococcus aureus was similar in the study done by Badhan et al[21]. But unlike their study, other gram positive cocci like *coagulase negative staphylococcus*(3.8%) and *enterococcus*(5.09%) were isolated in very few numbers in our study.

Isolation of *pseudomonas* (4.46%) has seen in the present study. Badhan et al[21] in their study also found *Pseudomonas* spp.(5.8%) as a causative agent of community acquired UTI.

Escherichia coli and *Klebseilla species* isolates in our study has shown multi drug resistance to antibiotics like nalidixic acid, ampicillin and cotrimoxazole. This could be because of overuse of the drugs and their over the counter availability. High resistance patterns seen against ampicillin, nalidixic acid, cotrimoxazole was in agreement with previous studies[13,15,18,20].The isolates also showed sensitivity of 38.46-49.25% towards cephalosporins. Increasing resistance to cephalosporin has also been noted in other studies[15,17].This could be because of use of B lactam antibiotics in paediatric patients for other upper respiratory infections. Moreover, we have considered only the fully susceptible specimens as sensitive; all intermediate ones were classified as resistant, leading to lower susceptibility rates. Based on the findings of our study, imipenem, piperacillin-tazobactum, nitrofurantoin, gentamicin are highly active against the gram negative isolates. Yoon JE *et al*[22] in their study has found enterobactericeae to have lower resistance rates against Imipenem (100%) and gentamicin(79.0%) which corresponds to results of our study . In the present study, nitrofurantoin has shown a sensitivity of about 76.92-86.57%. Several studies have shown nitrofurantoin to be very active against E. coli isolates, with a susceptibility rate of 93.0% to 97.8%[8,23]. Analysis of data revealed *Esherichia coli* and *Klebseilla* species isolates have a sensitivity of about 50% to ciprofloxacin whereas ofloxacin showed sensitivity of 64.18% and 57.69% to *Esherichia coli* and *Klebseilla* species isolates respectively . In a study[24] done to identify the antibiogram pattern of isolates from UTI cases at a referral hospital in Eastern Nepal, most strains of *Escherichia coli* and *Klebsiella* spp. were resistant to ciprofloxacin. *Staphylococcus aureus* isolated in our study were 100% sensitive to vancomycin and linezolid followed by gentamicin (76%) and ofloxacin (76%). Cotrimoxazole showed least sensitivity. 47.06% of isolates were MRSA (methicillin resistant *Staphylococcus aureus*). Chander et al[25] in their study found all gram positive isolates to be sensitive to vancomycin and linezolid(100%) and 50% of *Staphylococcal* isolates to be oxacillin resistant. *Enterococcus* isolates in our study showed 100% sensitivity to vancomycin and linezolid. Sensitivity against other antibiotics like gentamicin, ciprofloxacin, ofloxacin and amoxicillin/clavulanate were 37.5%. Taneja *et al*[13] in their study found vancomycin to be the most sensitive drug against *Enterococci*. Quinolones and aminoglycosides were found to be highly resistant which is in accordance with our study. However in the present study the number of isolates were very less in number(n=8).

Thus urine cultures and sensitivity are necessary for appropriate management of UTI since treatment failure with empiric therapy is likely to occur. Also there is a need for continuous surveillance of the antimicrobial susceptibility pattern. Moreover other antibiotics not included in our work can be studied so that it can be used as an option for treatment of UTI. Our study was limited by the fact that it was conducted in patients attending a tertiary care centre and was not population based.

V. Conclusion

Urinary tract infection was found to be more in children of age > 1—5 years. Females were more prone to urinary tract infections. Both gram positive and gram negative organisms were incriminated in this condition. *Escherichia coli* was the most commonly encountered uropathogen followed by *Klebsiella* spp in the paediatric age group. Common uropathogens isolated showed high resistance to widely used antibiotics like ampicillin, nalidixic acid and cotrimoxazole. Gram negative bacteria showed good sensitivity to imipenem, piperacillin/tazobactum, gentamicin and nitrofurantoin. Gram positive bacteria showed good sensitivity to vancomycin, linezolid, ofloxacin and gentamicin. Urine culture and antibiotic susceptibility testing is therefore highly recommended to prepare standard protocol for empirical therapy of paediatric urinary tract infection. Our results will be helpful in providing useful information for the development of community acquired UTI

treatment guidelines.
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