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Original Research Article

Clinicoetiological profile of urinary tract infection in pediatric population in a teaching hospital in south India

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ABSTRACT

Background: Urinary tract infection (UTI) is one of the most common bacterial infections seen in children. A wide range of organisms with varying antibiotic sensitivity patterns have been known to cause UTI. The objective of the study was to analyse the clinical presentation of UTI in children between 1-month to15 years of age and to analyse the causative microorganism and their drug susceptibility in UTI in children between 1 month to 15 years of age.
Methods: A retrospective study was conducted in a teaching hospital in Kerala, between July 2018 and June 2020 among children 1 month to 15 years of age who presented with symptoms of UTI. Patients who had culture positive UTI were included in the study. Clinical data was obtained from inpatient and outpatient records. Antimicrobial susceptibility was done for positive urine culture by Kirby-Bauer disk diffusion method. Statistical analysis was done using Statistical package for social sciences (SPSS) software version 16.
Results: Of the 1057 urine samples analysed, 18.44% had significant bacteuria. 43.07% were children less than one year of age with male predominance. Fever and dysuria were the most common clinical presentation. *E. coli* was the most prevalent pathogen isolated followed by *Klebsiella pneumoniae. Enterococcus faecalis* was the only gram-positive bacilli isolated. Highest resistance was shown to ampicillin, third generation cephalosporins and co-trimoxazole. Least resistance was shown to nitrofurantoin, fluoroquinolones, aminoglycosides, piperacillin-tazobactam and carbapenems.
Conclusions: Regular surveillance programme is necessary for implementation of guidelines for empiric treatment of UTI.

Keywords: Children, Urinary tract infection, Antibiotic susceptibility, *Escherichia coli*

INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infection seen in pediatric population, which is a significant cause of morbidity in children.[1,2] The overall prevalence of UTIs among infants and young children is estimated to be approximately 2%–20%.[3,4] Since UTI can present with non-specific clinical features, UTI is under-diagnosed.[5,6] UTI is associated with renal parenchymal scarring in approximately 10-30% of pediatric patients presenting with febrile UTI.[7] Renal scars can result in hypertension and progressive kidney disease.[8] Hence it is necessary to clinically suspect UTI and start the children on appropriate empirical antibiotics at an early stage.

Bacteria are common causes of UTI in children with E. coli being the main isolated pathogen in pediatric age group.[9] Other bacteria that cause UTI are *Klebsiella spp, Proteus mirabilis, Staphylococcus aureus* and *Enterococci*.[10,11] Most of these pathogens are resistant to multiple antibiotics.[11-13] Effective empirical treatment requires knowledge of microorganisms involved and the antibiotic susceptibility of uropathogens in each geographic setting.[14] In this present retrospective study,

we investigated the incidence, the various clinical presentation, the microbiological profile and antibiotic sensitivity pattern at a teaching hospital in South India.

METHODS

A retrospective analysis was conducted in the department of Pediatrics in association with department of Microbiology, Pushpagiri Institute of Medical Science, Thiruvalla, on culture positive urine isolates. The study was done for a period of 2 years (July 2018 to June 2020). The study protocol was approved by the ethical committee of the institution.

The objective of the study was to analyse the clinical presentation of UTI in children between 1month to 15 years of age, to analyse the causative microorganism and their drug susceptibility in urinary tract infection in children between 1 month to 15 years of age. Children between the age group of 1month to 15 years of age with UTI who satisfy inclusion criteria during the study period, who visited both the outpatient and inpatient department was included in the study. Repeated samples from same patient who has already been included and those samples with evidence of perineal contamination was excluded from the study.

Patient details including age, sex, clinical presentation, previous history of UTI and any congenital anomaly was collected from inpatient and outpatients records and entered in the predesigned proforma. Urine culture and sensitivity report was analysed using WHONET software. Urine sample collected by clean catch midstream technique/ catheter sample was included. Urine sample showing significant growth that is more than or equal 10^5 CFU/ml of single micro-organism in presence of symptoms was considered significant and processed for further identification and susceptibility testing.[15] Data including Micturating cystourethrogram (MCU) and Dimercapto succinic acid (DMSA) scan reports were also collected from their outpatient or inpatient records.

In the presence of any potential growth, antibiotic susceptibility test was done by Kirby-Bauer disk diffusion method and interpreted according to Clinical and Laboratory Standards Institute Guidelines (CLSI) 2019 and 2020.[16] Antibiotics tested were ampicillin, cephalosporins, amikacin, gentamicin, co-trimoxazole, nitrofurantoin, piperacillin- tazobactam, fluoroquinolones and carbapenems for gram-negative organisms and ampicillin, gentamicin, nitrofurantoin, norfloxacin, linezolid and vancomycin for gram-positive organisms. Suspected ESBL isolates were tested and confirmed using combination disk method (Cephalosporin and Cephalosporin clavulanate disks). No informed consent was required as it was a non-interventional retrospective study as per national guidelines as no additional sampling was done.

Statistical analysis was done using Statistical package for social sciences (SPSS) Software version 16. Fischer's chi-square test was used for comparing numerical parameters. Probability value (p value) less than 0.05 was regarded as statistically significant.

RESULTS

A total of 1057 urine samples were obtained from pediatric patients suspected of having UTI among which 195 (18.44%) samples yielded significant bacteuria. Of them, 84 (43.07%) were infants (48 males and 36 females), 67 (34.35%) were between 1-5 years of age (32 males and 35 females), 32 (16.41%) between 6-10 years of age (19 males and 13 females), 12 (6.15%) between 11- 15 years of age (6 males and 6 females) (Figure 1).

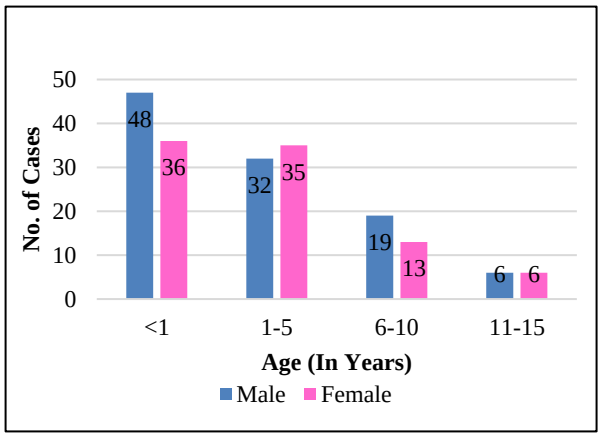

Figure 1: Age and sex distribution.

Table 1: Clinical features of UTI.

Symptoms	Culture positive cases (N)	Percentage (%)
Fever	103	52.82
Dysuria	45	23.07
Irritable cry	14	7.17
Increased frequency	4	2.05
Abdominal pain	11	5.64
Vomiting	4	2.05
Febrile seizures	12	6.15
Febrile status epilepticus	2	1.02

The most common clinical presentation of patients with UTI in our study was fever (52.82%) followed by dysuria (23.07%). Other clinical features were irritable cry (7.17%), febrile seizures (6.15%), abdominal pain (5.64%), vomiting (2.05%), increased frequency of micturition (2.05%) and febrile status epilepticus (1.02%) (Table 1). 37 (18.97%) patients had more than one clinical feature of which the main symptom was vomiting. Main symptoms among infants were fever.

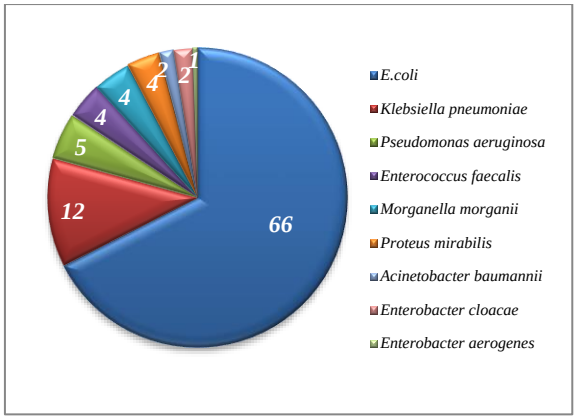

Figure 2: Percentage distribution of bacteria causing UTI in children.

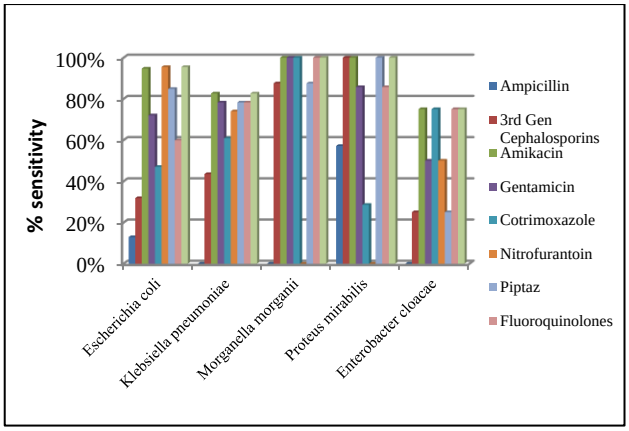

Figure 3: Percentage of antibiotic sensitivity of major uropathogens.

Table 2: *Enterococcus faecalis* - % antibiotic sensitivity (n=8).

Ampicillin	High level Gentamicin	Nitrofurantoin	Norfloxacin	Fosfomycin	Linezolid	Vancomycin
100%	38%	100%	25%	100%	100%	100%

Table 3: Comparing various studies in India.

Author, place, year	Prevalence (%)	Most common age group (In years)	Sex	Organism	ESBL + (%)	Highest sensitivity
Benachinmardi et al Bengaluru, 2015[6]	-	1-5	Male= Female	E. coli	20.4	Nitrofurantoin Amikacin Imipenem
Gupta et al Puducherry, 2014[9]	35.4	<1	Male	E. coli	-	Nitrofurantoin Aminoglycoside Cefoperazone-Sulbactum Meropenem
Badhan et al Punjab, 2016[10]	34.2	5-12	Female	E. coli	-	Nitrofuratoin Amikacin Cefotaxime
Sonkar et al, Bareilly, 2020[27]	35.75	0-5	Female	E. coli	-	Nitrofuratoin Cefaperazone-Sulbactum Amikacin Imipenem
Ramagopal et al, Tamil Nadu, 2018[32]	-	<1	Female	E. coli	-	Nitrofurantoin Amikacin
Pal et al, Calcutta, 2016[33]	24.95	5-12	Female	E. coli	3.77	Nitrofurantoin Amikacin Imipenem
Our study, Kerala, 2021	18.44	<1	Male	E. coli	43.58	Nitrofurantoin Amikacin Piperacillin-Tazobactam Carbapenem

20% patients had abnormal renal ultrasound. 15 (27.27%) patients had vesicoureteric reflux (VUR) in MCU. 40% had bilateral VUR and 60% had unilateral VUR. Isotope renogram (DMSA) revealed scarring in 14 (41.17%). 8 (4.10%) had congenital anomaly, of which three were meningomyelocele, three were dysplastic kidney, one

posterior urethral valve and one renal agenesis. Children with congenital anomaly and VUR presented with features of toxaemia along with high grade fever. 14.3% had recurrent UTI of which majority presented with fever and dysuria. 21.42% of those with recurrent UTI had congenital anomaly.

The predominantly isolated organisms from cases of pediatric UTI were *E coli* (66%), followed by *Klebsiella pneumoniae* (12%), *Pseudomonas aeruginosa* (5%), *Morganella morganii* (4%), *Proteus mirabilis* (4%), *Enterococcus faecalis* (4%), *Enterobacter cloacae* (2%), *Acinetobacter baumannii* (2%) and *Enterobacter aerogenes* (1%) (Figure 2). The most common isolated organism in recurrent UTI and congenital anomaly was *E. coli*, whereas in cases of VUR, the most common pathogen isolated was *Pseudomonas aeruginosa.*

High level of resistance to the commonly used oral urinary antibiotics such as ampicillin, third generation cephalosporins and co-trimoxazole was observed among the predominant organisms, E. coli and *Klebsiella pneumoniae.* The prevalence of ESBL producing isolates among *E. coli* and *Klebsiella pneumoniae* were 60% and 35% respectively. Acceptable levels of sensitivity to other oral antibiotics such as nitrofurantoin and fluoroquinolones was noted among all the isolated organisms. Parenteral antibiotics such as aminoglycosides and piperacillin- tazobactam showed good sensitivity for all the major pathogens isolated. There were no multi drug resistant (carbapenemase positive) pathogens among the isolates (Figure 3). *Pseudomonas aeruginosa* strains showed 100% sensitivity to all antibiotics. *Enterococcus faecalis* showed 100% sensitivity to ampicillin, nitrofurantoin, fosfomycin, linezolid and vancomycin (Table 2).

DISCUSSION

The knowledge of the sensitivity pattern of common uropathogens according to local epidemiological studies is necessary for selection of empirical antibiotic therapy. Studies recommend that the policies for UTI treatment in children should be evaluated every five years according to resistance rates.[17] The incidence of culture positive UTI among symptomatic children in our present study is 18.44% which is comparable to study conducted in Nepal, Tanzania, Nigeria and Gondar respectively.[18-20] Similar observations were noted by Kaur et al in India and Parajuli et al in Kathmandu, Nepal.[21,22] A higher incidence was reported in Italy, China and Nepal.[23,24]

The age group less than one year was the most affected in our study. This is in concordance with the study conducted in South Kerala and Bareilly in India.[26,27] Our observations are similar to Sharma et al, GK et al, Singh et al.[28-30] The age group least affected was 11-15 years. Males outnumbered females in the first year of life. This is in full agreement with other studies like Dyaneshwari et al, Ramagopal et al, Pal et al, Dash et al and Mehta et al.[31-35] The reason being uncircumcised infant boys are more likely to have UTI, as microorganisms can develop under prepuce. In our study the male: female ratio was 1.3:1 during infancy and 1:1 between 1-15 years of age. In children above one year to fifteen years of age female preponderance have been reported with a rate ranging from 6:1 to 1.33:1 depending on different sample size and difference in age group being studied.[36] In our study there was no much female preponderance after 1 year of age, may be, as only those cases presented to our hospital was taken into consideration and other UTI cases in community was not considered. Bay et al reported that the age group between 7-12 years of age was the most affected age group with female preponderance.[37] Taneja et al and Qureshi et al reported 1-5 years as the most common age group affected with a male preponderance.[38,39] Fever was the most common presenting symptom in our study population which was seen in 52.82%. This is concurrent to several other previous reports which states that fever is the most common presenting feature as Ramgopal et al, Shrestha et al, Vaidya et al, Brkic at al.[2,32,40,41] The second most common presenting complaint in our study was dysuria as reported by Anis-ur-Rehman et al.[42] Constipation was reported as an important risk factor for recurrent UTI by Rushton et al which reduced after improving the bowel habits.[43]

Gram-negative bacilli were the predominant causative group of childhood UTI accounting to 91.38% in our study. *E. coli* was the predominant organism isolated in our study (66%). This is consistent with studies reported by other authors.[2,10,11,14,33,40] *E. coli* in general was noted to account for 50-90% UTI in pediatric age group irrespective of sex, age, community or country.[2] Second common pathogen grown in our sample was *Klebsiella pneumoniae* similar to studies by Badhan et al, Vaidya et al, Pal et al.[8,33,40] A high rate of resistance was found to antibiotics such as Ampicillin, cephalosporins and co-trimoxazole in *E. coli* and *Klebsiella*. This finding correlates with the study done by Ohanu et al, Ramagopal et al, Taneja et al, Sharma et al.[14,28,32] This may be attributed to frequent use of these drugs in pediatric practice, low cost and ease of administration. The higher resistance to these oral drugs is worrisome as they will indicate the need for intravenous administration. Fluoroquinolones showed a sensitivity of 60% to *E. coli* and 78% to *Klebsiella* in our study. *E. coli* isolates were highly sensitive against Nitrofurantoin as compared to *Klebsiella* (95% and 74% respectively), similar to study by Pal et al.[33] This may be due as Nitrofurantoin is a reserved drug for treating UTI in pediatric population. Amikacin showed a sensitivity of 95% to *E. coli* and 83% to *Klebsiella* consistent with study by Elpis et al, Payel et al.[44,45] In this study Piperacillin- Tazobactam sensitivity was 85% and 78% to *E. coli* and *Klebsiella* and Carbapenem sensitivity was 95% to *E. coli* and 83% to *Klebsiella*. This is worrisome as the rate of prescription of these drugs will increase and resistance may build up over time (Table 3).

Among the gram-positive organisms, *Enterococcus faecalis* was the only isolated pathogen and it had 100 % sensitivity to ampicillin, linezolid and vancomycin. In a study by Gupta et al and Shrestha et al among the gram-positive organisms, *Enterococcus faecalis* was the most isolated pathogen.[9,2] Gram-positive organisms like *Coagulase negative Staphylococcus, Staphylococcus aureus, streptococci* have also been reported by other authors. However, these pathogens were not isolated from our samples. Lok et al and Muoneke et al reported *Staphylococcus aureus* as the second most common uropathogen isolated in their study.[14] This variation could be due to congenital anomaly or changing geographical area and ethnicity.

43.58% of gram-negative bacilli were ESBL positive, similar to studies to Akram et al (42%), Tangar et al (36.5%), Shrestha et al (40%) and Parajuli et al (38.9%).[2]

Limitations

Data was extracted retrospectively from medical and laboratory records, so no further information was obtained.

CONCLUSION

In UTI, the most common age group affected was less than 1 year with a male preponderance followed by age group between 1-5 years of age. Fever and dysuria were the most common presenting feature. *E. coli* is still the leading cause of pediatric UTI at our centre followed by *Klebsiella pneumoniae*, however there is an alarming increase in ESBL species. Gram-positive micro-organisms were not found to have a major role in our centre unlike reports elsewhere. Ampicillin, Co-trimoxazole, Cephalosporins once the mainstay of treatment, were no longer useful at our centre. As the resistance to Cephalosporins are increasing using Cephalexin as a drug for uroprophylaxis warrants revision. Nitrofurantoin can be the drug of choice when oral route is preferred. Amikacin, Piperacillin-Tazobactam and Carbapenems can be used as intravenous preparation. The pertaining issue of antimicrobial resistance among isolates calls for stronger antibiotic stewardship. Regular surveillance should be done to find out the prevalent organisms and their antibiotic susceptibility to choose empiric antibiotic therapy for UTI in children.

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