CLINICO-BACTERIOLOGICAL PROFILE OF URINARY TRACT INFECTIONS IN CHILDREN AND RESISTANCE PATTERN OF UROPATHOGENS- A STUDY FROM SOUTH INDIA


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ABSTRACT

BACKGROUND
Urinary tract infection is a common problem in children. Early diagnosis and prompt treatment is very important for preventing its complications like renal parenchymal disease. Emergence of multidrug-resistant bacteria has made treatment of urinary tract infection a challenge in children. The aim of the study is to determine the clinico-bacteriological profile of urinary tract infections in children and resistance pattern of uropathogens.

MATERIALS AND METHODS
A cross-sectional study was conducted in children ≤12 years with suspected urinary tract infections from October 2011 to February 2012 in a tertiary care centre. Urine samples were collected for urinalysis and culture. Antibiotic susceptibility test was performed as per the Clinical and Laboratory Standards Institute (CLSI) guidelines.

RESULTS
Out of 550 children studied significant bacteriuria detected in 90 (16.4%) cases. Males constituted 60% and females 40%. Infants (31.2%), 1-5 years (35.5%) and 5-12 years (33.3%) were the age distribution. Fever was present in 93.4% and specific urinary symptoms in 48.9% children. Blood culture was positive in 4.8%. E. coli (57.8%), Klebsiella spp. (22.3%), Proteus (6.7%), Pseudomonas spp. (6.7%), Enterobacter (4.4%) and methicillin-resistant staphylococcus aureus (2.2%) were the uropathogens. Multidrug-resistant isolates were 65.6%. Sensitivity and specificity of pyuria was 71.2% and 76.6%, respectively.

CONCLUSION
Urinary tract infection should be ruled out in all febrile children with no obvious focus of infection. MDR uropathogens should be considered while initiating treatment in children with UTI.

KEYWORDS
Children, Multidrug-Resistance, Urinary Tract Infections, Uropathogens.


BACKGROUND
Urinary Tract Infections (UTI) are one of the most common bacterial infections of children seen in primary care level with 8% of girls and 2% of boys having at least one episode by seven years of age.1 The risk of having a UTI before the age of 14 years is approximately 1-3% in boys and 3-10% in girls.2 UTI has been increasingly recognised as an occult cause of febrile illness in young children.3 The diagnosis of UTI is often missed and treatment may be delayed in infants and young children as the urinary symptoms are minimal or nonspecific and reliable specimens for culture cannot be obtained without invasive methods.

Antibiotic susceptibility of uropathogens in both the community and hospitals have been changing and drug resistance has become a major problem.4-7 Following first episodes of UTI, 3 to 15% of children develop renal parenchymal disease.1 Early diagnosis and initiation of appropriate treatment is very important in preventing the renal scarring, resultant hypertension and progressive renal damage.8

There are only limited studies available on the prevalence of drug resistance in children with UTI. It is important to know the type of uropathogens in the locality and their resistance pattern to commonly used antimicrobials, because treatment is often started...

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empirically. Updating the knowledge and situation of the prevailing Multidrug-Resistant (MDR) pathogens is also of prime importance in making the treatment policies in referral centres like ours. The present study was conducted to find out the clinical and bacteriologic profile of UTI in children and also the resistance pattern of uropathogens to commonly used antimicrobials in a Government Medical College, which cater six northern districts of Kerala.

MATERIALS AND METHODS
A cross-sectional study was conducted including all consecutive children ≤12 years with suspected UTI attending OPD or hospitalised in Department of Paediatrics, Government Medical College, Kozhikode, Kerala, India, from October 2011 to February 2012. Institutional Ethics Committee approval and consent from parents were obtained. Infants below 28 days old were excluded. Urine specimen for urinalysis, culture and sensitivity were collected in separate sterile tubes through suprapubic aspiration in children not attained bladder control or a clean catch midstream sampling in those who attained bladder control.

Urine culture was done by semiquantitative technique on Cysteine-Lactose Electrolyte-Deficient medium (CLED) agar (HiMedia, Mumbai).\(^9\) One μl urine was cultured using a calibrated bacteriological loop by surface streaking on CLED agar and colonies counted after overnight incubation at 37°C. A-10\(^5\) CFU/mL bacterial growth of a single type was taken as threshold for significant bacteriuria. For suprapubic samples, any number of colonies were considered significant. Isolates were preliminarily identified on the basis of morphology and Gram staining. Motility test or routine biochemical reactions were applied as required. Antibiotic sensitivity was put up by the Kirby-Bauer method following the Clinical and Laboratory Standards Institute (CLSI) guidelines.\(^10\) All isolates belonging to the Enterobacteriaceae family were tested against ampicillin, gentamicin, amikacin, ceftriaxone, cefotaxime, nitrofurantoin, co-trimoxazole, nalidixic acid and ciprofloxacin. They were tested against higher order antibiotics like cefoperazone, sulfactam and/or piperacillin-tazobactam when found resistant to all the initially tested antibiotics or when requested by the treating physician. Pseudomonas aeruginosa was tested against amikacin, gentamicin, cefazidime, piperacillin-tazobactam and ciprofloxacin. Methicillin-Resistant Staphylococcus Aureus (MRSA) was tested against vancomycin, gentamicin, amikacin, co-trimoxazole, ciprofloxacin and linezolid. MDR was defined as resistance to three or more of the structurally different class of antimicrobials.\(^11\)

Urinalysis was done within half an hour of sampling. Ten ml of the urine was centrifuged at 3000 rpm for one minute. Unstained specimen of the sediment was examined microscopically for pus cells and result reported as number of cells per High-Power Field (HPF). Significant pyuria was defined as >5 pus cells/hpf.\(^2\)

Children with significant bacteriuria were diagnosed as having UTI. Detailed physical examination, CBC, blood urea and creatinine were performed in all of them. Blood cultures were performed in children with temperature ≥38°C. One sample of 2-5 mL blood is collected in 50 or 100 mL bottles containing broth and incubated. Growth is identified as per the CLSI guidelines.\(^10\)

Statistical analysis was done using the statistical software package SPSS version 16. Age, gender, symptomatology, organisms isolated, their antibiotic resistance, risk factors for UTI and urinalysis findings were included as variables in the model. The results were described using frequencies and proportions. Sensitivity and specificity of pyuria for UTI were calculated.

RESULTS
Out of 550 patients enrolled, significant bacteriuria was detected in 90 (16.4%) cases. There were 54 (60%) males and 36 (40%) females and the male:female ratio was 1.5:1. Age distribution is given in Table 1 and clinical features in Table 2.

<table>
<thead>
<tr>
<th>Age</th>
<th>Total ‘n’ and %</th>
<th>Male ‘n’ and %</th>
<th>Female ‘n’ and %</th>
<th>Male Female Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 Year</td>
<td>28 (31.2%)</td>
<td>22 (78%)</td>
<td>6 (21.4%)</td>
<td>3.7:1</td>
</tr>
<tr>
<td>1-5 Years</td>
<td>32 (35.5%)</td>
<td>16 (50%)</td>
<td>16 (50%)</td>
<td>1:1</td>
</tr>
<tr>
<td>5-12 Years</td>
<td>30 (33.3%)</td>
<td>16 (53.3%)</td>
<td>14 (46.7%)</td>
<td>1:1.1</td>
</tr>
</tbody>
</table>

Table 1. Age and Gender Distribution of UTI (n=90)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Total n=90</th>
<th>&lt;1 Year n=28</th>
<th>1-5 Years n=32</th>
<th>5-12 Years n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>84 (93.4%)</td>
<td>28 (100%)</td>
<td>30 (93.8%)</td>
<td>26 (86.7%)</td>
</tr>
<tr>
<td>*Specific urinary symptoms</td>
<td>44 (48.9%)</td>
<td>4 (14.3%)</td>
<td>16 (50%)</td>
<td>24 (80%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>25 (27.8%)</td>
<td>15 (53.6%)</td>
<td>9 (30%)</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Deranged renal function</td>
<td>14 (15.6%)</td>
<td>10 (35.7%)</td>
<td>4 (12.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Poor stream</td>
<td>10 (11.2%)</td>
<td>3 (10.8%)</td>
<td>6 (18.8%)</td>
<td>1 (3.4%)</td>
</tr>
<tr>
<td>Palpable renal mass</td>
<td>8 (8.9%)</td>
<td>0</td>
<td>6 (18.8%)</td>
<td>2 (6.7%)</td>
</tr>
<tr>
<td>Dribbling</td>
<td>6 (6.7%)</td>
<td>2 (14.3%)</td>
<td>2 (6.2%)</td>
<td>0</td>
</tr>
<tr>
<td>Febrile seizure</td>
<td>4 (4.5%)</td>
<td>2 (7.1%)</td>
<td>2 (6.2%)</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Total n=90</th>
<th>&lt;1 Year n=28</th>
<th>1-5 Years n=32</th>
<th>5-12 Years n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 2. Clinical Features of Children with UTI</td>
<td></td>
<td></td>
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</tbody>
</table>

*Specific urinary tract symptoms included dysuria, frequency, gross haematuria, smelly urine, flank or abdominal pain.

A 46 (51.5%) febrile children with UTI were not having specific urinary symptoms. Profile of uropathogens is given in Table 3 and their resistance pattern in Table 4. Among the uropathogens isolated, 59 (65.6%) were MDR.
Numbers without parentheses indicate resistant isolates by number of isolates tested for sensitivity and those within parentheses indicate percentage of resistance † indicates not tested. Enterobacter was showing 100% resistance to ampicillin, gentamicin, cefotaxime, co-trimoxazole and nitrofurantoin. It was 100% sensitive to amikacin, ciprofloxacin and piperacillin-tazobactam. Two isolates of each E. coli and Klebsiella were tested for susceptibility to cefoperazone, sulbactam and all were sensitive to it. Four out of 6 Klebsiella, 10 E. coli and 2 pseudomonas isolates tested for susceptibility to piperacillin-tazobactam were found sensitive to it.

Out of 550 children included 172 had pyuria in which 64 children were having UTI and 108 not having UTI. Among 378 children with no pyuria, 26 had UTI and 352 were not having UTI. Sensitivity and specificity of pyuria for diagnosing UTI were 71.2% and 76.6%, respectively.

Blood culture was positive in 4 (4.8%) children of which E. coli was the isolate in 3 cases and Klebsiella in one. Isolates from blood and urine were concordant in all cases.

**DISCUSSION**

In the present study, 16.4% of symptomatic children were having culture proven UTI, which is relatively a low detection rate. Many Indian studies has shown a detection rate of 28.5% to 35.4% in children with compatible symptoms. Since symptoms of UTI are nonspecific, children with discordant illness might also have included in the study contributing to this low detection rate.

Due to longer course of urethra and the bacteriostatic action by prostatic secretions in them, the incidence of UTI is low in boys. Present study showed an overall male preponderance of UTI, which was maximum in infants. As this study was conducted in a tertiary centre, gender distribution may not be comparable with general population. Other hospital-based Indian studies also had demonstrated similar gender distribution.

In the present study, UTI was more common in children of 1-5 age group, which was in concordance with other Indian studies. Ineffective toilet training and the resultant ascending infection from urethra maybe predisposing children of this age group with UTI. The prevalence of UTI among children presenting with fever without focus is reported as 3.5 to 5.5%. It is recommended that all febrile children below 2 years of age with no obvious cause of infection should be evaluated for UTI. In the present study, most of the children with UTI were having fever as the presenting symptom and specific urinary symptoms were present in less than half of UTI cases. These observations may indicate that clinical presentations play only a minor role in detecting UTI. E. coli was the commonest isolate, Klebsiella being the second most common in our study, which was in concordance with many Indian studies. Concurrent resistance to antimicrobials of different structural classes is on the rise among pathogenic bacteria. This can complicate the treatment of infections, including those of the urinary tract. Empirical antibiotic therapy, overuse and incomplete course of antibiotics are the major contributing factors for multidrug-resistance. Availability of antibiotics over-the-counter also contribute to this. Multidrug-resistance was demonstrated by more than half of the isolates and it was uniformly high among all types of uropathogens in our study. Other studies also reported high incidence of multidrug-resistance among uropathogens.
E. coli were resistant to commonly used antimicrobials like ampicillin, co-trimoxazole, ceftriaxone, cefotaxime, ciprofloxacin, gentamicin and nalidixic acid. Nitrofurantoin was the only oral antimicrobial to which most of the E. coli were susceptible.

Owing to its antibiotic resistance property, Klebsiella infections are far more commonly encountered than previously. The ability of MDR Klebsiella to spread easily has made them an important nosocomial pathogen. They exhibited high resistance against commonly used antimicrobials like ampicillin, co-trimoxazole, cefotaxime, ceftriaxone and gentamicin in our study, which was in concordance with previous studies. Klebsiella was sensitive to amikacin, ciprofloxacin and higher order antibiotic-like cefoperazone and sulbactam in the present study.

A third generation cephalosporin is the preferred antibiotic of choice in the empiric treatment of UTI in children as per most of the guidelines. In the present study, almost all types of uropathogens were showing high resistance to ceftriaxone and cefotaxime, which are the empiric antibiotics of choice in complicated UTI in our center. Similar resistance pattern to these antibiotics were shown by other Indian studies.

Intravenous therapy with single daily dose of aminoglycosides is recommended as safe and effective in children with acute pyelonephritis. Highlighting the relevance of this recommendation, present study showed very high sensitivity by all the uropathogens (except pseudomonas) to amikacin. Many Indian studies also show high sensitivity of uropathogens to amikacin.

In children, oral ciprofloxacin is an alternative agent for UTI by resistant microorganisms, particularly pseudomonas. Widespread use of quinolones as first line agent by physicians in view of the increased resistance to ampicillin and co-trimoxazole contributes to increasing resistance to quinolones. Ciprofloxacin resistance was high in most of the isolates, including pseudomonas spp. in our study.

Leukocyturia occurs in conditions like fever, nephritis, renal stones or foreign body in the urinary tract other than UTI. Sensitivity and specificity of conventional pyuria of >5 pus cells/hpf for diagnosing UTI are 73% and 81%, respectively. In our study, sensitivity (71.2%) was in concordance with this, but specificity was low (76.6%). Being a referral center, significant number of children in the study might have received prior antibiotics leading to higher proportion of them having sterile pyuria and the resultant low specificity.

Bacteremia has been reported in 15-25% of patients with complicated UTIs, which was more common in young infants. In many guidelines for the management of UTI, routine blood culture is not recommended as they may provide little additional diagnostic value over urine cultures. In our study, 4.8% of febrile children with UTI had positive blood cultures. We performed blood culture in all febrile children, which included simple and complicated UTI. This may explain the low yield of blood culture in our study.

In a similar study by Pitetti RD and Choi S, the prevalence of bacteremia in febrile patients was 5.6%.

CONCLUSION
UTI should be ruled out by urine culture in all febrile children without any other focus of infection. MDR uropathogens should be considered while initiating treatment in children with UTI. For empirical therapy of UTI in children, amikacin maybe more effective than third generation cephalosporins. Routine blood culture is not needed in the evaluation of a febrile child with suspected UTI.

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REFERENCES


