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# Study of pediatric uropathogens and their antimicrobial susceptibility pattern in a tertiary care hospital of eastern India

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**Abstract**
*Urinary Tract Infection (UTI) is one of the most common childhood bacterial infection. Early diagnosis, adequate therapy and prolonged follow-up are utmost important to reduce morbidity and long-term complications like renal scarring, hypertension, and chronic renal failure.*
**Objective:** *The study was carried out to find out the prevalent uropathogens causing pediatric UTI and their antibiotic susceptibility pattern.*
**Method:** *A total 728 urine specimens from children aged 0-12 years were processed in a tertiary care hospital from November 2015 to June 2016 . All bacterial isolates were identified by biochemical test and antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion test. Result: Prevalence of urinary tract infection was found to be 15.52% among the study population. Overall it was more common in female child. E. coli was the commonest bacteria (45.13%) isolated, followed by Enterococcus spp (31.85%), Klebsiella pneumonia (8.84%), Staphylococcus aureus (3.5%), Candida spp (3.5%), Staphylococcus saprophyticus (2.6%), Proteus vulgaris (1.76%), Pseudomonas spp (1.76 %), Morganella morganii (0.8%). Most of the oral antibiotics like cotrimoxazole, amoxyclav, ciprofloxacin, cefixime were highly resistant to urinary isolates. Nitrofurantoin was found to be the most sensitive (>65%) drug. Gram negative bacteria also showed high sensitivity to meropenem (71.22%) whereas linezolid (100%) and vancomycin were most sensitive drug for gram positive cocci (>90%)).*
**Conclusion:** *Antibiotic resistance has now become a big problem therefore it is an important issue need to be urgently addressed by the policy makers to formulate a strict antibiotics prescription policy in our country.*
**Keywords:** *Paediatric, UTI, Antibiotic sensitivity.*

## Introduction

Urinary Tract Infection (UTI) is one of the most common childhood bacterial infection in our country. Over recent decades, the importance of UTI has been increasingly recognized, in particular the role of UTI as an single most cause

of febrile illness in young children is very common now days. Screening studies in emergency departments suggest that up to 5% of children under the age of 2 years presenting with fever have underlying UTI[1]. It is associated with high morbidity and long-term complications like renal scarring, hypertension, and chronic renal failure if not detected and treated early[2]. Early diagnosis, adequate therapy and prolonged follow-up are utmost important to reduce those complications. The epidemiology of pediatric UTI varies by age, gender, race/ethnicity and other factors. Boys are more susceptible than girls during the first year of life, thereafter the incidence is substantially higher in girls[3]. About 5% of girls and 2% of boys experience at least one episode of UTI up to the age of seven years[4] and among boys, uncircumcised infants have an eightfold higher risk[5]. Gram negative enteric bacilli such as *Escherichia coli, Klebsiella spp., Proteus spp., Enterobacter spp., Pseudomonas spp., Citrobacter* spp. and Gram-positive organisms, including group B *Streptococci, Enterococcus* spp, and *Staphylococcus aureus* are commonly associated with pediatric UTI[1-5]. However, diagnosis of UTI is often delayed due to nonspecific signs and vague symptoms, particularly in infants and children of less than two years[2],[3],[6]. Moreover, it is difficult to collect urine and interpret the results to confirm the diagnosis unequivocally in this age group[3]. Hence, empirical antibiotic therapy is often given without adequate evaluation for UTI. On the other hand, the emergence of antibiotic resistant uropathogens in pediatric urology is increasing worldwide; particularly in developing countries where empirical treatment is the mainstay of treatment in the absence of proper diagnostic modalities and the availability of antibiotics over the counter[7],[8]. The antibiotic susceptibility profile of uropathogens are variable and usually depends on time, geographical location, demography and clinical characteristics of patients[9]. An updated knowledge regarding antimicrobial resistance pattern in a specific location may aid clinicians in choosing the appropriate antibiotic for empirical treatment. The study was carried out to find out the prevalent uropathogens and antibiotic susceptibility pattern of urinary isolates recovered from UTIs in children of 0–12 years age group. The study will be helpful to the clinician for timely diagnosis and proper antibiotic selection for childhood UTI.

**Materials and Methods**

The present study was carried out in the Department of Microbiology of our institution. It was a hospital based, observational and cross sectional study. After getting ethical clearance from institutional ethical committee the study was conducted during the period of 8 months from November 2015 to June 2016.Urine samples were collected both from inpatient (IPD) and outpatient (OPD) department of Pediatrics. Children under 12 years of age showing sign and or symptom of UTI were included in the present study as study population. During the study period 728 urine samples were collected from both OPD and IPD. Urine samples were collected by aseptic procedure in sterile plastic disposable containers and were immediately transported to laboratory and inoculated in MacConkey agar and UTI chromogenic media. In case of clean catch mid stream urine sample, colony count greater than $10^5$ colony forming unit (CFU) /ml of urine of a single type bacteria indicates 'significant bacteriuria'.[10] Identification of growth was done using standard biochemical methods.[11] The antibiotic susceptibility testing was carried out using Kirby- Bauer disc diffusion method following guidelines of the Clinical Laboratory Standard Institute (CLSI)[12]. The antimicrobials tested for the Gram negative bacteria were amikacin (30 µg), amoxyclav (30 µg), cefixime (30 µg), ceftriaxone (30 µg), levofloxacin (5 µg), nitrofurantoin (300 µg), ciprofloxacin (10 µg), cotrimoxazole (1.25 /23.75µg), piperacillin tazobactam (100:10 µg), and meropenem(10 µg) and for Gram positive isolates tested antibiotics were amoxyclav (30 µg), nitrofurantoin (300 µg),

levofloxacin (5 µg), ciprofloxacin (10 µg), vancomycin (30 µg), and linezolid (30 µg). Novobiocin disc was used for coagulase negative *Staphylococcus* and high concentration gentamicin (120 µg) disc was used for *Enterococcus* spp. Extended spectrum beta-lactamase (ESBL) production in Gram negative bacilli was detected by ceftazidime (30 µg), and ceftazidime-clavulanic acid(30/10 µg) disc test and Methicillin resistance in *S. aureus* (MRSA) was detected using cefoxitin (30 µg) disc according to CLSI guidelines.[12] The control strains used were *Escherichia coli* American Type Culture Collection (ATCC) 25922, *Pseudomonas aeruginosa* ATCC 27853, and *S. aureus* ATCC25923. For ESBL test control strain used was *Klebsiella* ATCC (700603). Chi square test was done to study the association between prevalence of pediatric UTI and the demographic factors. P value <0.05 was considered as significant.

**Results**

In the present study urine samples of 728 children with suspected UTI were examined. IPD and OPD ratio of suspected cases were 419:309 (1.35:1), among them 113 samples were found to be culture positive. Culture positivity rate was 15.52% (113/728) in the present study. Among the 113 culture positive cases IPD and OPD ratio of cases were found to be 77:38 (2.08:1). Overall UTI was found to be more common in female as compared to male (M:F= 1:1.56) . We found M :F ratio of 1.2 :1 in <1 year age group but it changes to 1 : 2.1 and 1 :3.3 in 1-5 years age group and >5 years age group respectively as seen in table 1. In this study, Gram negative bacilli were the predominant causative bacteria of childhood UTI accounting for 58.40% of total isolates. Whereas growth of Gram positive cocci and *Candida* spp were found to be 38.05% and 3.5% respectively . In the present study *E. coli* was the commonest isolated bacteria 45.13% (51), followed by *Enterococcus spp* 31.85% (36), *Klebsiella pneumoniae* 8.84% (10), *Staphylococcus aureus 3.5% (4),Candida spp 3.5%(4), Staphylococcus saprophyticus* 2.6% (3), *Proteus vulgaris* 1.76% (2), *Pseudomonas spp* 1.76% (2) and *Morganella morganii* 0.8% (1) as seen in table 2. Ratio of Gram negative and Gram positive organism isolated from urine was 1.53:1(66:43). Among Gram positive group *Enterococcs* spp. was most frequently isolated pathogen 83.72% (36/43). Among hospitalized patients, 77 (18.37%) samples showed significant growth and 342 (81.62%) samples were sterile. From outpatients 38 (12.29%) showed significant growth, 271 (87.70%) samples were sterile. As seen in table 3, *E. coli* and *Klebsiella* isolates were almost equally resistant to amoxyclav (86.27% and 90%, respectively). *E.coli* was more resistant than *Klebsiella* to 3rd generation cephalosporins and cefixime (84.31%, and 50%, respectively) and also to ceftazidime (74.50% and 50% respectively). Among other Gram negative bacilli, the rate of resistance to 3rd generation cephalosporins and amoxyclav was also high (> 60% and 100% respectively). Resistance to quinolones among Gram negative bacilli was also high. 84.31% of *E. coli*, 50% of *P. aeruginosa*, 50% of *P. vulgaris* showed resistance to ciprofloxacin. *Klebsiella spp* showed comparatively better sensitivity to quinolones (70%). Amikacin resistance rate among *E. coli*, *Klebsiella* spp., and *Proteus* spp were 19%, 3%, and 0% respectively. In this study *E. coli* isolates were highly sensitive to nitrofurantoin as compared to *Klebsiella* spp.(94.11% and 80%, respectively). Overall meropenem resistance rate were 35.29% for *E. coli*, and 10% for *Klebsiella pneumoniae*, whereas, other Gram negative uropathogens were found to be 100% sensitive to meropenem. Compared to other Enterobacteriaceae, *E. coli* showed higher resistance against most of the antimicrobials tested. [Table 5]. ESBL detection rate was quite high in E.coli (35.29%) compared to Klebsiella (3%). Table 4 depicts that in the case of gram positive cocci, linezolid was found to be 100% sensitive. *Staphylococcus* spp was 100% sensitive to Nitrofurantoin and vancomycin whereas

*Enterococcus spp* was 22.22% and 8.33% resistant to them respectively. *Staphylococcus saprophyticus* were more resistant (66.66%) to methicillin compared to *Staphylococcus aureus* (50%).

**Table 1** Age and Sex distribution of culture positive cases

| Age group | Male | Female | M:F | Total |
|---|---|---|---|---|
| **<1year** | 24 | 19 | 1.2 :1 | 43 |
| **1-5 yrs** | 14 | 30 | 1:2.1 | 44 |
| **>5yrs** | 6 | 20 | 1:3.3 | 26 |
| ***Total** | 44 | 69 | 1:1.5 | 113 |

*P value= 0.012

**Table 2** Distribution of culture positive cases according to microbial species

| Microbial species | No of growth | Percentage of growth |
|---|---|---|
| ***Escherichia coli*** | 51 | 45.13% |
| ***Klebsiella pneumoniae*** | 10 | 8.84% |
| ***Enterococcus* spp.** | 36 | 31.85% |
| ***Staphylococcus aureus*** | 4 | 3.5% |
| ***Staphylococcus saprophyticus*** | 3 | 2.6% |
| ***Candida*spp** | 4 | 3.5% |
| ***Morganellamorganii*** | 1 | 0.8% |
| ***Proteus vulgaris*** | 2 | 1.76% |
| ***Pseudomonas aeruginosa*** | 2 | 1.76% |
| **Total** | 113 | 100% |

**Table 3** Antibiotic sensitivity pattern of gram negative bacteria

| Organism | AMC | PIT | CFM | CAZ | CAC | MRP | CIP | AK | COT | NIT |
|---|---|---|---|---|---|---|---|---|---|---|
| ***E.coli*(51)** | 7 (13.72%) | 26 (50.98%) | 8 (15.68%) | 13 (25.49% | 31 (60.78%) | 33 (64.70%) | 8 (15.68%) | 32 (62.74%) | 12 (23.52%) | 48 (94.11%) |
| ***Klebsiella spp.*(10)** | 1 (10%) | 7 (70%) | 5 (50%) | 5 (50%) | 8 (80%) | 9 (90%) | 7 (70%) | 7 (70%) | 4 (40%) | 8 (80%) |
| ***Morganellamorganii*(1)** | 0 (0%) | 1 (100%) | 0 (0%) | 0 (0%) | 1 (100%) | 1 (100%) | 1 (100%) | 1 (100%) | 0 (0%) | 0 (0%) |
| ***Proteus vulgaris*(2)** | 0 (0%) | 2 (100%) | 1 (50%) | 1 (50%) | 2 (100%) | 2 (100%) | 1 (50%) | 1 (50%) | 0 (0%) | 0 (0%) |
| ***Pseudomonas aeruginosa*(2)** | 0 (0%) | 1 (50%) | 0 (0%) | 1 (50%) | 2 (100%) | 2 (100%) | 1 (50%) | 2 (100%) | 0 (0%) | 0 (0%) |

AMC- Amoxyclav,PIT-Piperacillin-tazobactum,CFM-Cefixime,CAZ-Ceftazidime,CAC-Ceftazidime-clavulinic acid, MRP-Meropenem,CIP- Ciprofloxacin,AK-Amikacin,COT- Cotrimoxazole, NIT- Nitrofurantoin

**Table 4** Antibiotic sensitivity pattern of gram positive bacteria

| Organism | AMC | NIT | CX | CIP | GEN (high con$^{n}$) | AK | COT | VA | LZ |
|---|---|---|---|---|---|---|---|---|---|
| ***Enterococcus* spp. (36)** | 4 (11.11%) | 28 (69.44%) | - | 3 (4.54%) | 17 (47.22%) | - | - | 33 (91.66%) | 36 (100%) |
| ***Staphylococcus aureus* (4)** | 0 (0%) | 4 (100%) | 2 (50%) | 1 (25%) | - | 4 (100%) | 1 (25%) | 4 (100%) | 4 (100%) |
| ***Staphylococcus saprophyticus* (3)** | 1 (33.33%) | 3 (100%) | 1 (33.33% | 2 (66.66%) | - | 3 (100%) | 0 (0%) | 3 (100%) | 3 (100%) |

AMC- Amoxyclav,VA-Vancomycin,LZ-Linezolid,CX-Cefixime,GEN-Gentamycin,CIP- Ciprofloxacin,AK-Amikacin,COT- Cotrimoxazole, NIT- Nitrofurantoin

**Table 5** Antibiotic resistance pattern of urinary isolates

| Name of antibiotic | Antibiotic resistance among gram negative bacteria(66) | Antibiotic resistance of *Enterococcus*(36) |
|---|---|---|
| **AMC** | 58(87.87%) | 32(88.88%) |
| **CFM** | 52(78.78%) | - |
| **CAZ** | 46(69.69%) | - |
| **CAC** | 22(33.33%) | - |
| **MRP** | 19(28.78%) | - |
| **CIP** | 48(72.72%) | 33(91.66%) |
| **AK** | 23(34.84%) | - |
| **COT** | 50(75.75%) | - |
| **NIT** | 10(15.15%) | 8(22.22%) |
| **VA** | - | 3(8.33%) |
| **GEN(high con$^{n}$)** | - | 19((52.77%) |

AMC- Amoxyclav,PIT-Piperacillin-tazobactum,CFM-Cefixime,CAZ-Ceftazidime,CAC-Ceftazidime-clavulani acid, MRP-Meropenem, CIP- Ciprofloxacin,AK-Amikacin,COT- Cotrimoxazole, NIT- Nitrofurantoin,VA-Vancomycin,LZ-Linezolid,GEN

## Discussion

The prevalence of culture-positive isolates observed in the present study was 15.52% among pediatric population, this value was quite lower compared to the finding of 34.5% by Dash *et al*., and 36.6% by Mehta *et al*.[13,14] However, this was concordant with another study conducted by Mohanty *et al*.(14.7%) at the All India Institute of Medical Sciences, New Delhi, India[15], and the rate is higher than the study done by Saravanan *et al*(11.3%) [16 ].The similarities and difference in the type and distribution of uropathogens may be due to different age groups and environmental conditions of different geographical regions. The present study showed that overall female child were more commonly infected with UTIs compared to male child (M:F-1:1.56). But males outnumbered females during the 1st year of life only with a ratio of 1.26:1. After the age of 1 year risk was increased in girls. This ratio (M:F) in 1-5 years was 1:2.14 and it increased to 1:3.3% in >5 years age group. This finding was statistically significant with p value 0.012. This was in full agreement with other studies by different authors[14-17]. In this study, *E. coli* was the predominant uropathogen, accounted for approximately 45.13% of all clinically significant urinary isolates .This is consistent with the findings of previous studies in which *E. coli* was the predominant pathogen isolated around worldwide[13-17]. However we found uropathogens like *Klebsiella* pneumoniae, *Pseudomonas* aeruginosa , *proteus vulgaris* and *morganella morganii* to be very less in numbers when compared to their study . Present study showed *Enterococci spp.* to be the predominant (31.85%) Gram positive uropathogen whereas infection by *Staphylococcus* was low *(3.5%).* It was noted that a high proportion of strains of *E. coli* were resistant to orally administered drugs such as amoxiclav (>85%), co-trimoxazole (>75%) and ciprofloxacin (>84%). Third generation cephalosporin have also shown high degree of resistance (>70%) for *E.coli*. This high degree of resistance by *E.coli* was also noted by other studies done by Sood *et* al[18] and Pal *et al*[19]. But in contrast to their studies *Klebsiella spp* showed less resistance to 3rd generation cephalosporin and fluroquinolone (50% and 30% respectively) in the present study. ESBL production rate among *E.coli* (35.2%) were also high than *Klebsiella* spp (3%) in this study. ESBL production rate among *Klebsiella* spp were comparatively low than that was reported by Akram *et al* (27.3%)[17] but quite similar to study done by Pal *et al* (4.17%)[19] and Sood *et al* ( 8.69%)[18].This difference could be due to the geographic difference in antibiotic usage. Nitrofurantoin and meropenem were most sensitive drug (84.84% and 71.21% respectively) followed by amikacin (62.74%) for *E.coli*. Which was also reported by most of the similar study. Nitrofurantoin was the drug with least resistance (3%) to *E. coli* and it was 2$^{nd}$ most sensitive drug for *Klebsiella* spp. However, this drug

demonstrated a very high resistance (100%) to non-fermenters and other enterobacteriaceae. Overall meropenem was the most sensitive drug (71.21%) for gram negative bacilli in our study. Higher resistance rate to all oral antibiotics like amoxyclav, cotrimoxazole, cefixime and ciprofloxacin could be explained by uncontrolled empirical consumption of these antibiotics without doing any culture sensitivity test. In most developing countries, it is the standard practice to treat febrile child empirically with an antibiotic as symptoms are nonspecific and specimen collection is difficult from this age group. Among gram positive cocci *Enterococcus* spp. were highly resistant to amoxyclav (88.88%) and ciprofloxacin (91.66%). Linezolid was 100% sensitive drug among gram positive cocci followed by vancomycin (>90%). Only 3 *Enterococcus* spp showed resistance to vancomycin (8.33%). Vancomycin resistance by *Enterococcus* spp also reported by Sood *et al*[18] and many others..In this study, nitrofurantoin showed low level of resistance in both gram negative and gram positive isolates which makes this drug a reasonable alternative in management of uncomplicated UTI . This might have been due to its multiple mechanisms of action, underusage and narrow-spectrum nature of the drug. However, it cannot be used to treat UTI in complicated and febrile infants because it is excreted in the urine and does not achieve therapeutic concentrations in the blood stream[20].

## Conclusion

In our centre prevalence of pediatric UTI was 15.52%. Risk of UTI was higher in male child than female within 1year age and the risk was found in a higher rate in girls thereafter. As expected *E.coli* was the most common etiological agent isolated. Most of the isolates including *E.coli* has become resistant to commonly used oral antibiotics like cotrimoxazole, cefixime, ciprofloxacin and amoxyclav. Nitrofurantoin remained susceptible to most of the isolates. It should be used for uncomplicated UTI. Most of the gram negative isolates were sensitive to meropenem and amikacin., Gram positive cocci were more sensitive to vancomycin and linezolid than other drugs but it should not be given without antibiotic sensitivity test. Antibiotic resistance has now become a big problem as because only limited or no drugs are left to be used against multidrug resistant organism. Therefore, antibiotic resistance is an important issue need to be urgently addressed by the policy makers to formulate a strict antibiotics prescription policy in our country and to stop over the counter sale of antibiotics.

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