

## Original Article

## Emerging Antimicrobial Resistance Patterns in Pediatric Urinary Tract Infections: A Tertiary Care Perspective

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## ABSTRACT

**Background:** Urinary tract infections (UTIs) are a common pediatric concern that can lead to significant morbidity if improperly managed. The objective of this study is to determine the etiological profile and antimicrobial resistance patterns of uropathogens in children aged 1 month to 5 years. **Methodology:** A prospective observational study was conducted in a tertiary care government medical college involving 96 children between 1 month to 5 years of age presenting with UTI. Aetiology was confirmed using standard microbiological methods, and antimicrobial susceptibility testing was conducted [1]. **Results:** Of the 96 children, 50 showed significant bacterial growth. *Escherichia coli* (66%) and *Klebsiella pneumoniae* (18%) were the predominant pathogens. Multi-drug resistance was observed in 75% of *E. coli* and 66% of *Klebsiella* isolates. Sensitivity remained high for Amikacin and Imipenem. **Conclusion:** The high prevalence of multidrug-resistant uropathogens underscores the importance of antibiotic stewardship and region-specific antibiogram-based empirical therapy in children [2, 3].

**Key words:** Urinary Tract Infections, Multidrug resistance, *Escherichia coli*, *Klebsiella*, Empiric therapy, Microbial sensitivity

Urinary tract infection (UTI) is a common yet potentially serious condition in children, with approximately 3% of females and 1% of males experiencing an episode before 5 years of age [4, 5]. UTIs in children may signify underlying anatomical anomalies and can progress to renal scarring, hypertension, or end-stage renal disease if undiagnosed or improperly treated. The clinical presentation of UTI varies widely from subtle irritability and fever in infants to more specific symptoms such as dysuria and frequency in older children. Among pathogens, *Escherichia coli* is the predominant organism, responsible for 80–90% of pediatric UTI cases.

A concerning trend has been the rise in antimicrobial resistance among uropathogens, particularly *E. coli* and *Klebsiella* species, limiting effective treatment options [6, 7]. This study was conducted to better understand current patterns of antimicrobial resistance among pediatric UTI isolates and help inform empiric treatment protocols. UTIs are among the most common bacterial infections in children, particularly affecting those under five years of age. In India, the prevalence of UTIs in this age group varies, with studies reporting rates

ranging from 3.5% to 6.5% among febrile children [8, 9]. The incidence is notably higher in females, attributed to anatomical and physiological factors.

The clinical presentation of UTIs in young children is often nonspecific, including symptoms such as fever, irritability, vomiting, and poor feeding. These vague symptoms can lead to delays in diagnosis and treatment, increasing the risk of complications like renal scarring and hypertension. Therefore, prompt recognition and appropriate management are crucial to prevent long-term sequelae.

*Escherichia coli* (*E. coli*) is the predominant uropathogen responsible for pediatric UTIs, accounting for approximately 78% of cases. Other common pathogens include *Klebsiella spp.*, *Enterococcus spp.*, and *Proteus spp.* [9]. The emergence of antimicrobial resistance (AMR) among these pathogens poses a significant challenge to effective treatment. In particular, resistance to commonly used antibiotics such as ampicillin, cefuroxime, and trimethoprim-sulfamethoxazole has been observed [10].

A study conducted in Vadodara, India, highlighted the high resistance rates of *E. coli* and *Klebsiella spp.* to

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fluoroquinolones, penicillin sub-classes, and cephalosporins. Conversely, nitrofurantoin and phosphonic acid antibiotics demonstrated lower resistance rates, suggesting their potential efficacy in empirical therapy [11]. These findings underscore the importance of local antimicrobial susceptibility data in guiding appropriate antibiotic selection.

The Indian Society of Pediatric Nephrology (ISPN) has updated its guidelines to address the evolving landscape of pediatric UTIs and AMR. The revised recommendations emphasise the need for accurate diagnosis through urine culture and sensitivity testing, judicious use of antibiotics, and consideration of underlying anatomical anomalies such as vesicoureteral reflux (VUR) and bladder-bowel dysfunction (BBD) [12].

In conclusion, pediatric UTIs remain a significant health concern, compounded by the growing threat of antimicrobial resistance. Timely diagnosis, informed antibiotic selection based on local resistance patterns, and adherence to updated clinical guidelines are essential strategies to manage UTIs effectively and mitigate the impact of AMR in the pediatric population.

## MATERIALS AND METHODS

This was a prospective, observational study conducted in the paediatric ward of a tertiary care medical college over 1.5 years after getting human ethical committee clearance (IEC: 601/2020). All children aged 1 month to 5 years, admitted with one or more episodes of urinary tract infections (UTIs), were included. Written informed consent was obtained from parents or guardians. Those who had catheter-associated UTIs, known immunodeficiency and polymicrobial growth in urine cultures were excluded.

Midstream urine was collected and processed within 2 hours. For infants, sterile catheterisation and suprapubic aspiration techniques were used. Samples were inoculated onto cysteine lactose electrolyte deficient (CLED) agar and incubated at 37°C for 18–24 hours. Antimicrobial Susceptibility Testing (AST) was performed using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar, following the guidelines outlined by the Clinical and Laboratory Standards Institute (CLSI), 2020 [13]. Additionally, selected urine isolates were processed using the VITEK 2 Compact system [14], an automated system that provides rapid and standardised interpretation of minimum inhibitory concentrations (MICs).

The antibiotics tested included: Amikacin (30 µg), Amoxicillin-Clavulanate (20/10 µg), Ampicillin (10 µg), Ceftriaxone (30 µg), Cotrimoxazole (1.25/23.75 µg), Gentamicin (10 µg), Norfloxacin (10 µg), Cefoperazone-Sulbactam (75/30 µg), Imipenem (10 µg), and Piperacillin-Tazobactam (100/10 µg).

Interpretation of results—based on zone diameters (Kirby-

Bauer) and MIC values (VITEK)—was done as sensitive, intermediate, or resistant, adhering to CLSI 2020 breakpoints. For quality control, standard ATCC strains such as *E. coli* ATCC 25922 and *K. pneumoniae* ATCC 700603 were used during testing. Antimicrobial susceptibility was tested using the Kirby-Bauer disc diffusion method as per CLSI (Clinical and Laboratory Standards Institute) guidelines.

Definite Urinary Tract Infection is defined as evidence of pyuria with a positive urine culture report ( $>10^5$  CFU/ml of an uropathogen), whereas probable Urinary Tract Infection is evidence of positive nitrite and/or leucocyte esterase result with pyuria, in a culture-negative setting. Recurrent urinary tract infection (UTI) refers to  $\geq 2$  infections in six months or  $\geq 3$  infections in one year [15].

## Statistical analysis

Data was entered in Microsoft Excel and was analysed using SPSS-27. Frequency was noted as numbers & percentages among categorical variables. The percentage with a 95% confidence interval was calculated for the primary outcome variable. Mean with standard deviation or median with IQR was used for continuous variables, depending on the normality of the data. The comparison of continuous variables was done using the t-test and the Mann-Whitney U test according to the normality of the data. Chi-square or Fisher Exact test was used, wherever applicable, to find out the significance of the association, and the strength of the association was calculated with relative risk and its 95% confidence interval. A p-value of  $<.05$  was considered significant throughout the analysis.

## RESULTS

96 children were enrolled in the study after fulfilling the inclusion and exclusion criteria [Figure 1]. The median (IQR) of age (months) of the children enrolled in the study was 12.00 months (6.7-24). Excess crying while passing urine was the most common symptom, reported in 32 children  $< 2$  years of age (59.2%). Dysuria was reported in 9 children aged  $> 2$  years (21.4%). The other manifestations include urgency and increased frequency of micturition and oliguria. A poor stream of urine was reported in 8 out of 54 male children. In the present study, the most common presenting symptom was fever, observed in 61 children (63.5%). Other common symptoms were irritability, vomiting and lethargy.

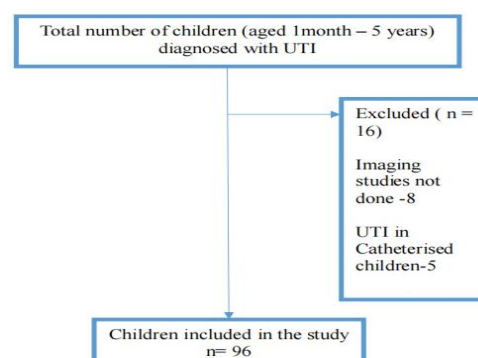


Figure 1: Study selection process

In the present study, the occurrence of first-time UTI was 85.4%. The most common Gram-negative urinary pathogens isolated were *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Enterobacter aerogenes*, and *Citrobacter koseri*. The frequency of the various uropathogens encountered is mentioned in Table [1]. The common urinary pathogens, such as *Escherichia coli*, *Coli* and *Klebsiella pneumoniae* showed high resistance when they were tested against amoxicillin/clavulanic acid, ceftriaxone, cotrimoxazole and norfloxacin. In comparison, low resistance rates were found against cefoperazone-sulbactam, piperacillin and imipenem. Multiple resistance was high among the isolated urinary pathogens. Of note, *Escherichia. Coli* demonstrated >50 % resistance rate to at least 6 common antimicrobial agents [Table 2], while *Klebsiella pneumoniae* had > 50% resistance rate to 5 common antimicrobial agents [Table 3].

**Table 1: Distribution of Microorganisms in the urine culture (n=50)**

Micro Organism	n	Frequency (%)
E. coli	32	64.0
Klebsiella	9	18.0
Enterococcus	2	4.0
Proteus	2	4.0
Pseudomonas	2	4.0
Citrobacter	2	4.0
Enterobacter	1	2.0

Of the microorganisms, 24 of 32 (75%) *E. coli* isolates were multidrug resistant. The *Escherichia coli* isolates were sensitive to Gentamicin (65.6%), Piperacillin-Tazobactam (66.7%), Cefoperazone-Sulbactam (76.7%), Imipenem (96.7%) and Amikacin (96.9%). The sensitivity to Ampicillin, Amoxicillin, Amoxicillin-Clavulanic Acid, Cotrimoxazole, Ceftriaxone and Norfloxacin ranged from 6.2- 37.5%.

**Table 2. Antibiotic Susceptibility of E. Coli (n=32)**

Antibiotic	Sensitive n (%)	Resistant n (%)
Amikacin	7 (77.7)	2 (22.3)
Amoxicillin-Clavulanate	1 (11.1)	8 (88.9)
Ampicillin/Amoxicillin	0 (0)	9 (100)
Ceftriaxone	2(22.2)	7 (77.8)
Cotrimoxazole	2 (22.2)	7 (77.8)
Gentamicin	7 (77.7)	2 (22.3)
Norfloxacin	2 (22.2)	7 (77.8)
Cefoperazone-Sulbactam	6 (66.6)	3 (33.4)
Imipenem	6 (66.6)	3 (33.4)
Piperacillin-Tazobactam	6 (66.6)	3 (33.4)

**Table 3. Antibiotic Susceptibility of Klebsiella (n=9)**

Antibiotic	Sensitive n (%)	Resistant n (%)
Amikacin	7 (77.7)	2 (22.3)
Amoxicillin-Clavulanate	1 (11.1)	8 (88.9)
Ampicillin/Amoxicillin	0 (0)	9 (100)
Ceftriaxone	2(22.2)	7 (77.8)
Cotrimoxazole	2 (22.2)	7 (77.8)
Gentamicin	7 (77.7)	2 (22.3)
Norfloxacin	2 (22.2)	7 (77.8)
Cefoperazone-Sulbactam	6 (66.6)	3 (33.4)
Imipenem	6 (66.6)	3 (33.4)
Piperacillin-Tazobactam	6 (66.6)	3 (33.4)

*Proteus* isolates (2/50) and *Citrobacter* isolate (1/50) demonstrated good sensitivity (>70%) to Amikacin, Amoxicillin-Clavulanic Acid, Ampicillin, Ceftriaxone, Cotrimoxazole, Gentamicin and Norfloxacin. *Enterococcus* isolates (2/50) demonstrated multidrug resistance against Amikacin, amoxicillin-clavulanate and Ampicillin. These isolates were sensitive to Gentamicin (100%), Ceftriaxone (50%) and Cotrimoxazole (50%). *Pseudomonas* isolates (2/50) were sensitive to Amikacin (100%), Gentamicin (50%) and Norfloxacin (50%). The sole *Enterobacter* isolate in the study showed resistance against Amoxicillin-clavulanate, Ampicillin and Norfloxacin, with sensitivity to Amikacin, Ceftriaxone, Cotrimoxazole and Gentamicin.

During the analysis, it was observed that empirical therapy was started in 28 cases. Among the 32 children, in 15 cases Cefoperazone-sulbactam was used, in 9 cases Amikacin, in 8 cases Cotrimoxazole was used, and in a child Ceftriaxone was used as primary therapy, with other antibiotics added on, which included Gentamicin, Ampicillin and Amoxicillin. In our study among 96 children, 18.7% showed urine nitrite positive and 63.5% showed leucocyte esterase test positive.

## DISCUSSION

Urinary tract infection (UTI) is one of the most common bacterial infections in children, often presenting with nonspecific symptoms that make diagnosis challenging, especially in infants and young children. Prompt identification of the uropathogen and appropriate antimicrobial therapy is crucial to avoid complications such as renal scarring and the development of antimicrobial resistance [16].

In our study, the male-to-female ratio was 1.28:1, with 56.2% of children under the age of two. This is consistent with studies such as Gupta et al. and Taneja et al., which reported a higher incidence of UTI among male infants, likely due to anatomical and physiological differences, including lack of

circumcision [15, 17].

Fever was the most common presenting symptom (63.5%), followed by irritability and vomiting. These findings are in line with the observations by Sharma *et al.*, who also identified fever and dysuria as the predominant clinical features [18]. Leung *et al.* conducted a meta-analysis that found unexplained fever to be the most frequent symptom in children under two years of age [19].

*E. coli* was the predominant pathogen in our study (66%), followed by *Klebsiella* (18%). This distribution aligns with global trends where *E. coli* is consistently the most frequent causative organism in pediatric UTIs [20]. The higher prevalence of gram-negative bacilli may reflect colonisation patterns of the periurethral area and ascending infection routes in children.

Urinalysis showed a positive leucocyte esterase test in 63.5% and a positive nitrite test in 18.7% of cases. The low nitrite positivity can be explained by the need for urine to remain in the bladder for at least 4 hours to accumulate detectable levels—an issue also documented in pediatric UTI evaluations [21].

In our study, 52.1% had culture-confirmed UTI. This is higher than the 35.4% culture positivity reported by Gupta *et al.*, possibly due to stricter inclusion criteria or different urine collection techniques [15].

A major concern in our findings was the high rate of antimicrobial resistance, particularly among *Escherichia coli*. *Coli* and *Klebsiella* isolates. More than 70% of these isolates showed resistance to multiple antibiotics. Similar trends have been documented in other Indian and global studies, reflecting the overuse of empirical broad-spectrum antibiotics, especially third-generation cephalosporins [6].

Aminoglycosides such as gentamicin and amikacin showed the lowest resistance rates among *Escherichia coli*. Isolates. This observation has also been reported in studies from both developed and developing countries, likely due to their limited use in outpatient settings and the need for parenteral administration.

The use of automated systems like the VITEK 2 Compact improved the speed and accuracy of organism identification and susceptibility profiling. Studies have shown that VITEK can provide reliable MICs in a time-efficient manner, which supports tailored therapy [14].

The incidence of recurrent UTI was 14.6%, which falls within the reported global range of 10–30%, depending on the presence of underlying vesicoureteral reflux or bladder dysfunction [22]. Our findings reinforce the need for early imaging and consideration of prophylactic strategies in recurrent cases.

The variation in antibiotic susceptibility between studies further underscores the importance of region-specific pediatric

antibiograms, which are crucial in guiding empirical therapy. Over-the-counter availability and unsupervised use of antibiotics like cotrimoxazole likely contributed to the high resistance observed in our cohort, a pattern also highlighted in antimicrobial surveillance data across South Asia [23].

Parental education, counselling on treatment adherence, and public health strategies aimed at curbing antibiotic misuse remain critical. The development of rapid diagnostic tools such as point-of-care molecular assays could help in early, targeted treatment and resistance containment [24].

## CONCLUSION

The diagnosis of UTI in children remains a clinical challenge due to nonspecific symptoms, especially in younger age groups. A high index of suspicion and prompt urine testing are essential. Our study highlights the growing burden of multidrug-resistant uropathogens and the urgent need for antimicrobial stewardship. The findings underscore the importance of routine culture-based diagnosis, local antibiogram monitoring, and the integration of rapid diagnostic platforms to optimise therapeutic outcomes in pediatric UTI.

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