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PRIMARY UROPATHOGENS RESPONSIBLE FOR PEDIATRIC UTIS AND THEIR ANTIBIOTIC RESISTANCE PATTERNS

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ABSTRACT

Background: Pediatric urinary tract infections (UTIs) are common bacterial infections that can lead to significant morbidity if inadequately treated. The rise in antibiotic resistance complicates management, particularly in regions with high empirical antibiotic use, such as Pakistan.
Objective: This study aimed to identify primary uropathogens causing pediatric UTIs and evaluate their antibiotic resistance patterns to support effective treatment protocols at Sami Medical Center, Abbottabad.
Methods: A retrospective analysis was conducted on 100 pediatric UTI cases. Urine samples were cultured, and antibiotic sensitivity was tested using the Kirby-Bauer disk diffusion method. Patient demographics and resistance patterns were analyzed.
Results: Most cases occurred in females (68%) and in children under five years of age (66%). Escherichia coli was the predominant pathogen (85%), followed by Klebsiella pneumoniae (11%). The highest sensitivity was observed with piperacillin-tazobactam (94%) and nitrofurantoin (87%), while co-amoxiclav (24%) and co-trimoxazole (20%) showed the lowest activity.
Conclusion: The findings demonstrate considerable resistance to commonly used first-line agents. Piperacillin-tazobactam and nitrofurantoin appear to be the most reliable options for empirical treatment of pediatric UTIs in this setting. Regular surveillance of resistance trends is recommended to support evidence-based prescribing.
Keywords: Urinary Tract Infections, Escherichia coli, Antibiotic Resistance, Pediatrics, Pakistan Drug Sensitivity Tests

INTRODUCTION

Urinary tract infections (UTIs) are among the most frequent bacterial illnesses in children and continue to represent a significant health burden worldwide [1]. Clinical presentations vary from asymptomatic bacteriuria to severe infections of the upper urinary tract, such as pyelonephritis. If inadequately treated, these conditions may lead to renal scarring, hypertension, or long-term kidney disease [2,3]. Timely recognition and appropriate antimicrobial therapy are therefore critical for preventing complications.
The occurrence of pediatric UTIs follows a bimodal distribution, with peaks in infancy and adolescence, and is more common in girls. Studies estimate that up to 8% of girls and 2% of boys experience at least one episode during childhood, with female predominance largely explained by anatomical features such as a shorter urethra [4]. Uncircumcised male infants are also considered at higher risk [5]. Escherichia coli accounts for the majority of cases, responsible for roughly 75–90% of community-acquired infections, while other pathogens such as Klebsiella pneumoniae, Proteus mirabilis, Enterococcus species,

Pseudomonas aeruginosa, and Staphylococcus aureus are implicated less frequently, often in recurrent or complicated infections [6,7].

Beyond anatomy, several factors influence the risk of UTI in children. These include vesicoureteral reflux (VUR), dysfunctional voiding, and behavioral habits such as poor hygiene, infrequent urination, or challenges with toilet training [8,9]. In low-resource environments, inadequate sanitation and limited access to clean water further contribute to disease burden [10,11].

Antimicrobial resistance has become a pressing challenge in UTI management, particularly in South Asia. In Pakistan and neighboring countries, empirical prescribing without culture testing remains common and has fueled rising resistance rates [3,12–14]. Recent local studies confirm that agents once considered first-line, including penicillins and co-trimoxazole, now show limited effectiveness [15–20].

Management in Pakistan is complicated further by the lack of national treatment guidelines and restricted availability of culture facilities. As a result, clinicians frequently depend on empirical regimens, which may no longer match prevailing resistance profiles. This practice undermines treatment outcomes and accelerates the spread of resistant organisms.

The present study was conducted at Sami Medical Center in Abbottabad to address this gap by documenting the pathogens most often responsible for pediatric UTIs and their susceptibility to commonly used antibiotics. The findings aim to provide locally relevant data that can inform empirical prescribing practices, improve clinical care, and contribute to ongoing antimicrobial stewardship efforts.

MATERIALS AND METHODS

This retrospective analysis was carried out at Sami Medical Center in Abbottabad, Pakistan. Medical and laboratory records were reviewed for children diagnosed with urinary tract infections (UTIs) between January and September 2024. Eligible patients were those aged 3 months to 16 years who presented with clinical features consistent with UTI, including fever, dysuria, or flank pain. A confirmed diagnosis required a positive urine culture, defined as bacterial growth of at least 10,000 colony-forming units (CFU) per milliliter. Exclusion criteria included patients with known structural anomalies of the urinary tract (as identified through imaging), recent antibiotic use within 48 hours (which could alter culture results), and those undergoing immunosuppressive or prolonged corticosteroid therapy, due to the potential impact on infection risk and microbial patterns.

These inclusion and exclusion criteria were carefully selected to focus the analysis on typical pediatric UTI cases and to control for confounders that might bias the findings.

Urine samples were collected using sterile methods suitable to the patient's age to minimize contamination. For infants, urine was obtained via catheterization or suprapubic aspiration, while midstream urine samples were collected from older children. Samples were promptly processed using standard bacterial culture media, including CLED (Cystine-Lactose-Electrolyte-Deficient) agar, which inhibits swarming of Proteus species, and EMB (Eosin Methylene Blue) agar, which differentiates between lactose fermenting and non-lactose fermenting gram-negative organisms. Both media are widely used in clinical microbiology for isolating and identifying uropathogens in urine samples. After 24–48 hours of incubation at 37°C, bacterial isolates were identified based on colony morphology, Gram staining, and biochemical reactions specific to uropathogens. The antibiotic sensitivity of isolated pathogens was determined using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar. Antibiotics tested included frequently prescribed agents such as co-amoxiclav, co-trimoxazole, amikacin, nitrofurantoin, cefoperazone-sulbactam, and piperacillin-tazobactam. The zones of inhibition around each antibiotic disk were measured in millimeters, and sensitivity was classified according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Descriptive statistics were calculated to summarize patient demographics, pathogen frequency, and antibiotic sensitivity. The prevalence of pathogens and the percentage of resistance to each antibiotic were presented as proportions. Chi-square tests were performed to assess significant differences in antibiotic sensitivity rates across pathogens, with a p-value of <0.05 considered statistically significant. Data were analyzed using SPSS software to ensure accurate and detailed statistical reporting.

RESULTS

The study included 100 pediatric patients diagnosed with UTI. Of these, 68% were female, and 32% were male, yielding a female-to-male ratio of approximately 2:1. The mean age of the study population was 6.56 years, with an age range spanning from 3 months to 16 years. Most children (66%) were under five years of age, which aligns with established patterns showing higher susceptibility to UTIs among young children.

Distribution of patients by age

The mean age of the patients in study was 6.56 $\pm$ 7.68 years [range 3 months – 16 years]. There were 31 (31%) patients of age range of 3 months – 2 years, 35 (35%) patients of age range of 2 – 5 years, 21 (21%) patients of age range of 6 – 10 years and 13 (13%) patients of age range of 11 – 16 years (Table 1).

Table 1: Distribution of patients by age (n= 100)

Age in years	No. of patients
3 months – 2 years	31
2 – 5 years	35
6 – 10 years	21
11 – 16 years	13
Mean ± SD	6.56 ± 7.68
Range	3 months – 16 years

Distribution of patients by sex

There were 32(32%) male patients and 68(68%) female patients in the present study. The male to male ratio was 1: 2.12 (Figure 2).

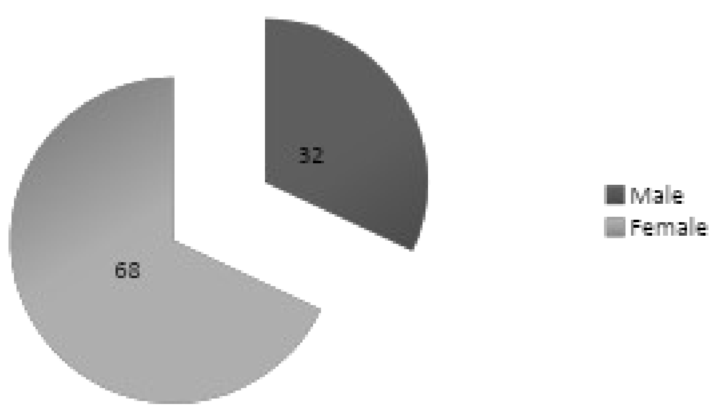

Figure 1: Distribution of patients by sex (n=100)

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Figure 2: Specimen No. 5. Growth of *E coli* on MacConkey medium

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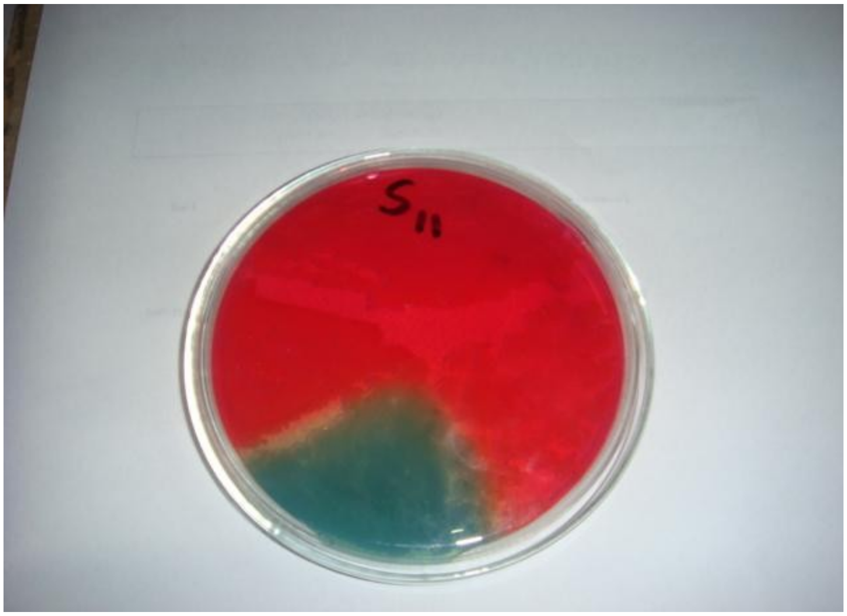

Figure 3: Growth of *E. coli* on CLED medium

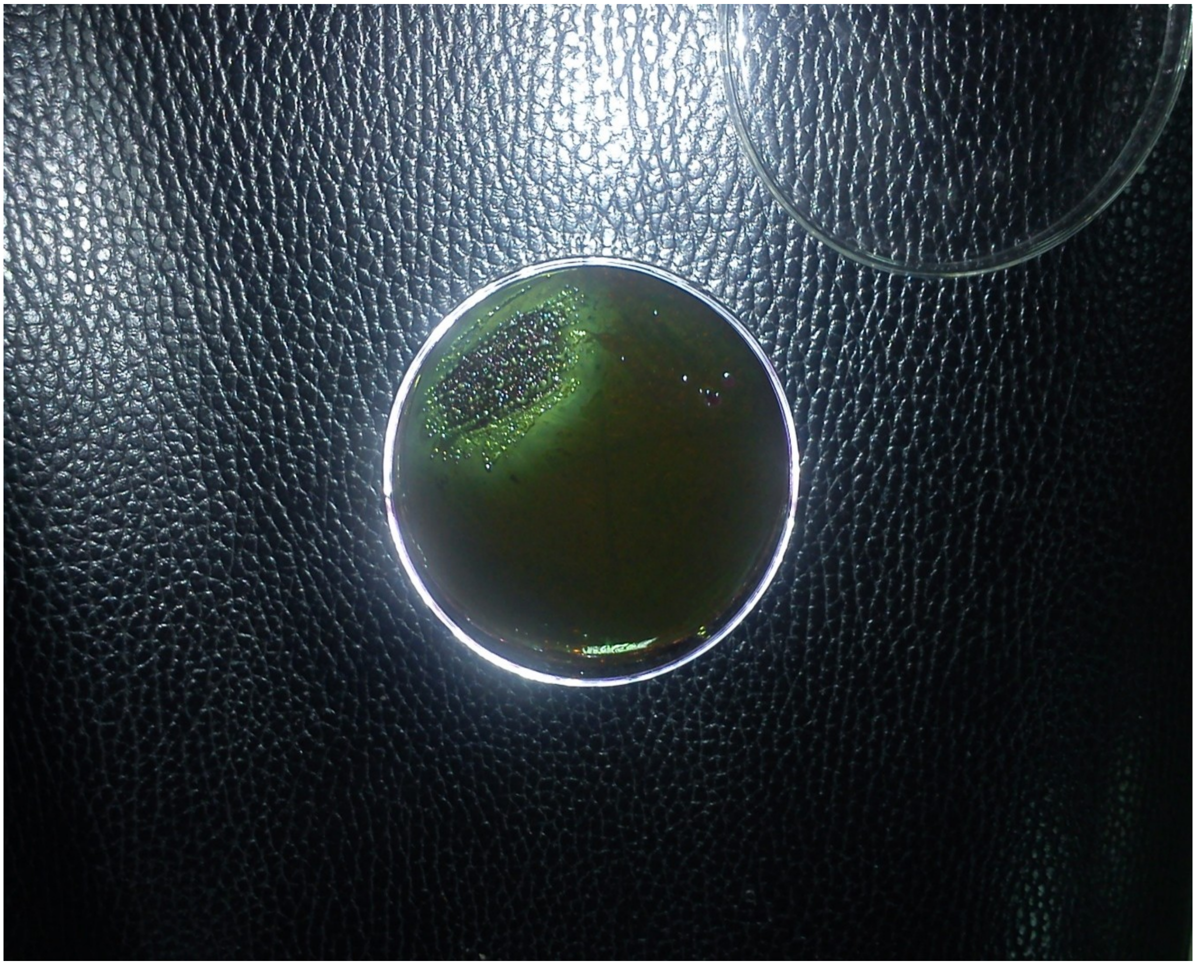

Figure 4: Growth of *E. coli* on EMB agar

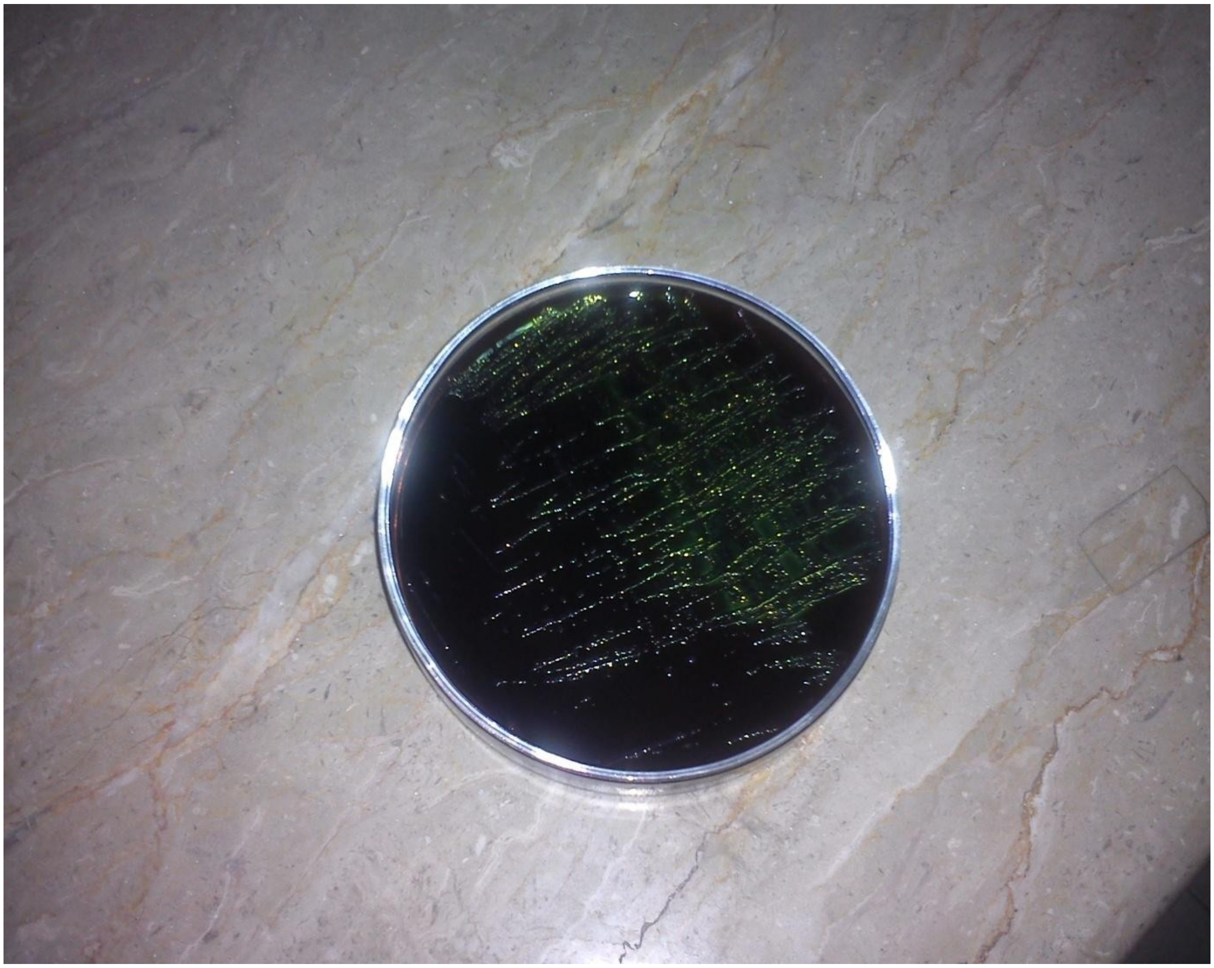

Figure 5: Growth of *E. coli* on EMB agar

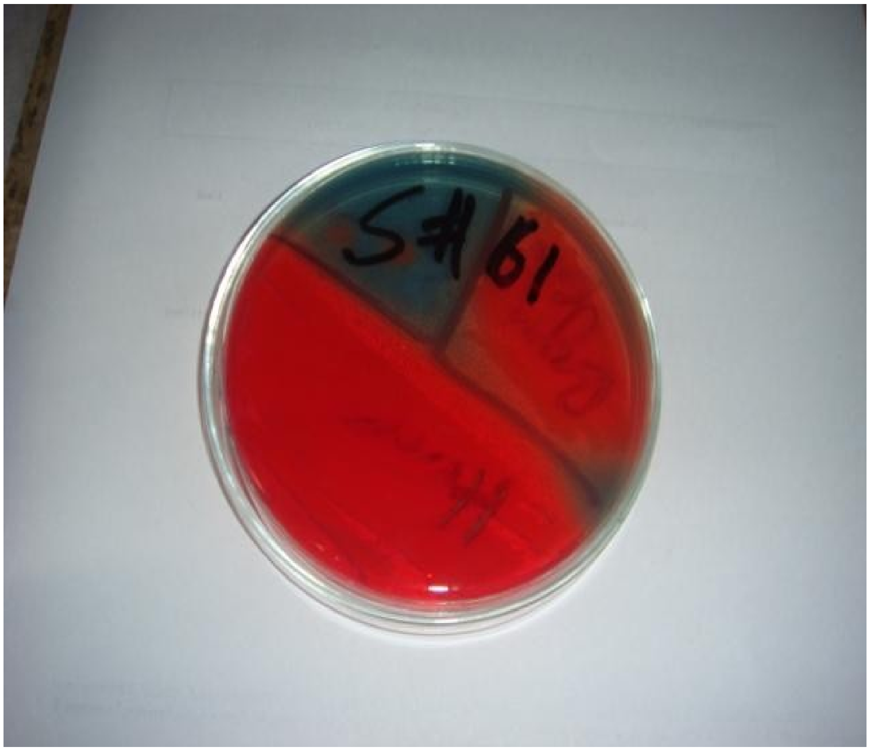
Figure 6: Growth of *E. coli* on CLED medium

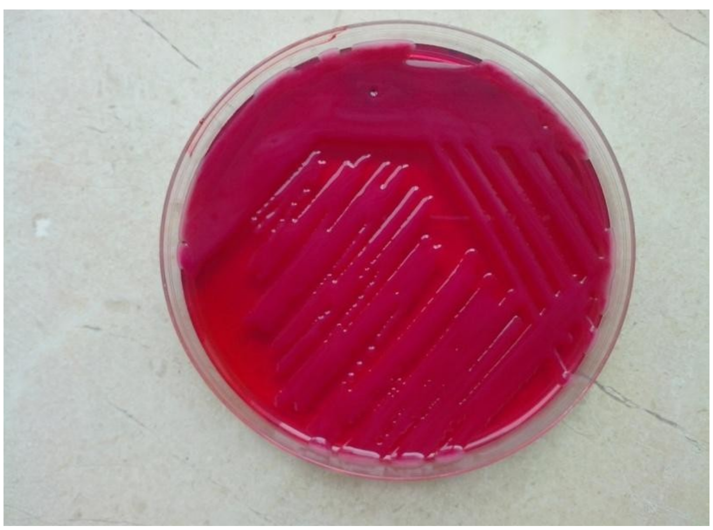
Figure 7: Growth of *klebsiella* on MacConkey medium

Pathogen Distribution

Urine cultures identified *Escherichia coli* as the predominant pathogen, isolated in 85% of cases. *Klebsiella pneumoniae* was the second most common organism, found in 11% of samples, followed by *Proteus*

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mirabilis in 2% and *Staphylococcus aureus* in 2%. This distribution of pathogens aligns with regional and international data indicating *E. coli* as the leading causative agent in pediatric UTIs.

Antibiotic Sensitivity Patterns

To provide clarity and ease of comparison, the sensitivity of each uropathogen to the tested antibiotics is summarized below. Sensitivity rates were determined based on the percentage of isolates that were susceptible to each antibiotic, following CLSI breakpoints.

- **Piperacillin-tazobactam**: Highly effective, with an overall sensitivity rate of 94%.
- **Cefoperazone-sulbactam**: Demonstrated 87% sensitivity, indicating it as a viable alternative for treating resistant infections.
- **Nitrofurantoin**: Showed high sensitivity at 87%, making it a strong candidate for empirical therapy.
- **Amikacin**: 84.8% sensitivity against *E. coli*, suggesting good efficacy, particularly for intravenous use in hospital settings.
- **Co-amoxiclav**: Notably low sensitivity, effective in only 24% of cases.
- **Co-trimoxazole**: Exhibited the lowest efficacy, with a sensitivity rate of only 20%.

A breakdown of sensitivity patterns for each pathogen provides additional context for clinical treatment choices:

- **E. coli**: Demonstrated high sensitivity to piperacillin-tazobactam (94.9%), nitrofurantoin (91.1%), and cefoperazone-sulbactam (87.3%). However, resistance was significant for co-amoxiclav (25.3%) and co-trimoxazole (20.3%).
- **Klebsiella pneumoniae**: This pathogen was less sensitive to standard oral antibiotics, with only 14.3% sensitivity to co-amoxiclav and 28.6% to co-trimoxazole. However, it showed favorable sensitivity to amikacin (78.6%) and nitrofurantoin (78.6%).
- **Proteus mirabilis**: Displayed 100% sensitivity to piperacillin-tazobactam, with moderate sensitivity to amikacin and nitrofurantoin (75% each).
- **Staphylococcus aureus**: Exhibited complete sensitivity to piperacillin-tazobactam and cefoperazone-sulbactam (100%), although sensitivity to co-trimoxazole was negligible.

Comparative Analysis with Existing Literature

The observed sensitivity rates align closely with studies from similar regions. For example, *E. coli*'s high prevalence and resistance to co-amoxiclav and co-trimoxazole are consistent with reports from South Asia, where empirical use of these antibiotics has contributed to increased resistance levels. Studies from Pakistan and India similarly highlight declining sensitivity to first-line oral agents, emphasizing the need for updated empirical therapy guidelines in both hospital and community settings.[18,19]

Table 1: Antibiotic Sensitivity Rates Across Pathogens (selected values for reference)

Pathogen	Piperacillin-tazobactam	Cefoperazone-sulbactam	Nitrofurantoin	Co-amoxiclav	Co-trimoxazole
Escherichia coli	94.9%	87.3%	91.1%	25.3%	20.3%
Klebsiella pneumoniae	85.7%	85.7%	78.6%	14.3%	28.6%
Proteus mirabilis	100%	80%	75%	Not tested	Not tested
Staphylococcus aureus	100%	100%	Not tested	Not tested	0%

This table highlights the comparative effectiveness of antibiotics across different pathogens, providing clear insights for clinical decision-making. The high efficacy of piperacillin-tazobactam and cefoperazone-sulbactam supports their potential as preferred empirical options, particularly in cases where resistance to conventional treatments is suspected.

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Overall, these findings underscore a clear need to adapt treatment protocols to local resistance profiles. The significant resistance rates to commonly used antibiotics, such as co-amoxiclav and co-trimoxazole, emphasize the importance of utilizing antibiotics with proven efficacy, such as piperacillin-tazobactam and nitrofurantoin, for empirical treatment of pediatric UTIs.

DISCUSSION

Urinary tract infections (UTIs) remain one of the most prevalent bacterial infections in infants and children. Early diagnosis and timely antibiotic treatment are essential, as delays can lead to severe renal complications, including scarring and potential loss of kidney function.[15] Unfortunately, the overuse and misuse of antibiotics contribute to bacterial resistance, altering the natural intestinal flora and complicating the management of UTIs.[16] The Enterobacteriaceae family, a group of gram-negative, facultative anaerobic bacilli, encompasses the most frequently isolated pathogens in pediatric UTIs.[15-20] Among these, *Escherichia coli* (E. coli) is the leading cause, responsible for approximately 90% of community-acquired and over 30% of hospital-acquired UTIs.[16] The increased prevalence of UTIs among females is likely due to anatomical factors, such as a shorter urethra, facilitating bacterial ascent.[15,16]

This study provides new insights into the primary pathogens causing pediatric UTIs and their antibiotic susceptibility patterns in a local context. Conducted at Ayub Teaching Hospital, the study aimed to identify prevalent uropathogens and evaluate their resistance to commonly used antibiotics, providing recommendations based on culture and sensitivity results. Our findings revealed *E. coli* as the most common pathogen, detected in 85% of cases, followed by *Klebsiella pneumoniae* (11%), *Proteus mirabilis* (2%), and *Staphylococcus aureus* (2%). Piperacillin-tazobactam emerged as the most effective antibiotic, with sensitivity observed in 94% of cases. Cefoperazone-sulbactam and nitrofurantoin also demonstrated high sensitivity rates, effective in 87% of cases each. Conversely, the lowest sensitivity was noted with co-amoxiclav (24%) and co-trimoxazole (20%).

Demographic analysis indicated that the average age of patients in this study was 6.56 years, with the majority (66%) under five years old. This finding is consistent with other studies reporting a higher incidence of UTIs in younger children due to age-related anatomical and immune system factors. A study by Khan & Shakeel documented a similar mean age of 4.6 years among children with UTIs[16], while Mumtaz & colleagues observed a slightly higher mean age of 7±1.8 years.[18] This early onset of UTI underscores the vulnerability of infants and toddlers, as noted in other studies from the region.[15,17,19–21]

Gender distribution in our study, with females accounting for 68% of cases, aligns with previous reports. This female predominance is observed in similar studies, such as those by Muzamil & colleagues, which documented a 70% female prevalence[19], and Khalily and colleagues, with a 62% female majority.[20] Similarly, Khan and Shakeel found a female prevalence rate of 80% recently in Karachi.[16] Such data support the established risk of UTIs in female children, attributed to anatomical factors conducive to bacterial ascent.

The high prevalence of *E. coli* (85%) as the primary causative agent in this study mirrors results from both regional and international research.[11,13–16,20,21] For instance, a study by Iqbal and colleagues from Lahore, Pakistan reported *E. coli* and *Klebsiella* as the leading organisms responsible for pediatric UTIs in the 0-6 year age group.[15] Similarly, *E. coli* was identified as the predominant pathogen in studies by Khan & Shakeel and Mumtaz & colleagues, with respective prevalence rates of 73.9% and 59.1%.[16,18] Research from other countries in the region further supports *E. coli*'s dominance in pediatric UTIs, though prevalence rates for secondary pathogens vary across studies, suggesting geographical differences in pathogen distribution and risk factors.[12-14]

Antibiotic resistance, particularly in *E. coli*, presents a significant challenge in managing pediatric UTIs. In this study, *E. coli* exhibited high resistance to co-amoxiclav and co-trimoxazole, both of which are frequently prescribed as first-line treatments. Injectable antibiotics such as cefoperazone-sulbactam and amikacin showed greater efficacy, with sensitivity in over 84% of cases. These results align with findings by Mumtaz et al., who observed high sensitivity of *E. coli* to amikacin but notable resistance to first-line drugs like amoxicillin and ofloxacin.[18] A similar decline in *E. coli* susceptibility to penicillins and co-trimoxazole has been documented in other reports from this region[11,13,15,17,20], suggesting a broader trend of increasing resistance over time, likely exacerbated by widespread empirical antibiotic use.

Klebsiella pneumoniae, the second most common pathogen identified in this study, displayed low sensitivity to traditional oral antibiotics, with only 14.3% and 28.6% sensitivity to co-amoxiclav and co-trimoxazole, respectively. However, *Klebsiella* showed favorable sensitivity to amikacin and nitrofurantoin, with sensitivity rates of 78.6% for each. These results are consistent with studies from this region[18,20,21], which also noted significant resistance in *Klebsiella* to first-line antibiotics, underscoring the importance of antibiotic stewardship to prevent resistance development in non-*E. coli* pathogens.

Overall, piperacillin-tazobactam, cefoperazone-sulbactam, and nitrofurantoin emerged as the most effective antibiotics, with resistance observed primarily in co-amoxiclav and co-trimoxazole. These findings are comparable to results from other cities of the country reported in recent years[15,18–20], which each highlighted the limitations of penicillins, cepahlosporins and other empirical antiobiotics due to high resistance rates.

This study reinforces *E. coli*'s role as the predominant uropathogen in pediatric UTIs in Pakistan and highlights considerable resistance to first-line treatments, such as co-amoxiclav and co-trimoxazole. The data underline the need for continuous surveillance of local resistance patterns, especially in areas where empirical treatment is common. We recommend revising current treatment protocols to reflect local antimicrobial susceptibility patterns. In particular, nitrofurantoin remains a practical oral choice for uncomplicated infections, while piperacillin-tazobactam appears more appropriate for severe presentations. These results highlight the value of using treatment strategies that reflect local resistance data and support wider efforts to promote antimicrobial stewardship.

CONCLUSION

This study provides insight into the causative organisms and resistance profiles of pediatric UTIs in Abbottabad, Pakistan. Escherichia coli was the dominant pathogen and showed marked resistance to commonly prescribed first-line antibiotics, including co-amoxiclav and co-trimoxazole. The data underline the importance of evidence-based prescribing adapted to local resistance patterns. Given the observed susceptibility, nitrofurantoin, piperacillin-tazobactam, and cefoperazone-sulbactam represent more reliable choices for both empirical and targeted therapy. By generating locally relevant evidence, this study contributes to regional surveillance efforts and supports more informed clinical decision-making in pediatric UTI management.

Study Limitations

Several limitations should be acknowledged. As a retrospective analysis from a single healthcare facility, the findings may not fully reflect the broader epidemiological trends of pediatric UTIs across Pakistan. The study also lacked molecular characterization of resistant strains, which would have provided more detailed insight into resistance mechanisms. Furthermore, the absence of follow-up data restricts the ability to evaluate treatment outcomes. Additionally, variables such as prior antibiotic exposure were not consistently controlled. Future research involving multiple centers and prospective designs is recommended to build a more comprehensive understanding and inform national treatment guidelines.

Future Recommendations

Short-term Priorities:

1. Establish antibiotic stewardship initiatives focused on reducing inappropriate empirical prescribing in pediatric populations, thereby limiting the development of resistance.

2. Update local treatment guidelines to reflect the high efficacy of nitrofurantoin, piperacillin-tazobactam, and cefoperazone-sulbactam, aligning empirical choices with current sensitivity patterns.
3. Encourage the use of culture and sensitivity testing for UTI diagnosis, wherever possible, to minimize the overuse of broad-spectrum antibiotics.

Long-term Recommendations:

1. Conduct continuous surveillance studies to monitor changing resistance patterns in pediatric uropathogens, ensuring that empirical treatment protocols remain effective.
2. Expand research to include molecular studies of resistant strains, which could uncover resistance mechanisms and guide more targeted antibiotic development.
3. Explore non-antibiotic preventive measures, such as probiotics and behavioral interventions, to reduce the incidence of recurrent UTIs and the reliance on antibiotics.

In summary, these actions could significantly enhance pediatric UTI management in Pakistan and similar regions, improving patient outcomes and contributing to global efforts to combat antibiotic resistance.

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