ORIGINAL ARTICLE

Susceptibility pattern of pediatric uropathogens: Insights from Mirpur Azad Jammu Kashmir Pakistan

Ammara Manzoor[1], Toqeer Ahmed[1], Syeda Tahira Batool[2], Nabia Chaudhry[2], Fatima Khurshid[3]

[1]Mohtramma Benazir Bhutto Shaheed Medical College, Mirpur Azad Jammu Kashmir
[2]Divisional Headquarters Hospital, Mirpur Azad Jammu Kashmir
[3]Shifa International Hospital Limited. Islamabad Pakistan

ABSTRACT

Background: Antibiotic resistance in pediatric urinary tract infections (UTIs) is a growing concern, necessitating the assessment of antibiotic susceptibility profiles for effective treatment strategies. The study was designed to assess the clinical profile, common uropathogens causing UTI and their antimicrobial susceptibility patterns. The study was designed to assess the frequency of pediatric UTIs along with antimicrobial susceptibility pattern of the isolated uropathogens.

Material and Methods: We conducted a retrospective review of clinical records at DHQ Hospital Mirpur AJK, Pakistan from March to September 2023, focusing on urinary tract infections in pediatric patients. We identified uropathogens and their antimicrobial susceptibility pattern to guide effective treatment strategies and address drug resistance.

Results: Data was collected from the medical records of 140 pediatric patients. of which, 49% (n=69) had positive urine cultures. Majority of these patients were males (71%). The most predominant organism was *Klebsiella pneumoniae* (32%) followed by, *Staphylococcus aureus* (26%), *Escherichia coli* (22%) and *Enterococcus faecalis* (11%). Mixed growth of uropathogens was seen in 9% of the cases. Regarding Antimicrobial susceptibility pattern, Amikacin, Vancomycin, Neomycin and Tigecycline were the most susceptible (100%), followed by chloramphenicol (90.9%), Linezolid (83.4%), Rifampicin (82%), Meropenem (77.3%), Nitrofurantoin (70%), Tazobactam (68.7%) and Imipenem (68.4%). Cephalexin (66.7%), Gentamicin (63.6%) and Cefipime (50%) showed moderate susceptibility. Whereas, Sulfamethoxazole (35%), Levofloxacin (31.4%), Cefoxitin (26.3%), Ciprofloxacin (22.2%), Tetracycline (20.5%), Cefuroxime (14.2%), Ceftriaxone (9.52%) and Amoxicillin (9.52%) were the least susceptible.

Conclusion: Our research suggests that it is important to review the use of antibiotics for treating UTIs in pediatric patients due to changes in antibiotic susceptibility and the increase in resistance among bacteria. This emphasizes the significance of antimicrobial stewardship.

Keywords: Urinary tract infections. Antimicrobial susceptibility patterns, Pediatric population

BACKGROUND

Urinary tract infection (UTI) is one of the commonest causes of febrile illness in pediatric population with a worldwide prevalence of 2–20%.[1] Untreated pediatric UTIs can lead to severe consequences like renal scarring, hypertension, and chronic renal failure. 50% of UTIs in children are not detected due to lack of symptoms, especially in infants. Early diagnosis and appropriate treatment can prevent complications, although antibiotic resistance is a growing concern worldwide.[2,3] Acute pyelonephritis is the most frequent dangerous bacterial illness in infancy, with many afflicted children, particularly newborns, experiencing severe symptoms. Most instances are easily treated if diagnosed promptly, however fever in pediatric population may take several days to subside. Approximately 7 to 8% of females and 2% of males have a UTI the first 8 years of life. Febrile UTIs are most common in both genders during the first year of life, but non-febrile UTIs occur mostly in females beyond the age of three. After infancy, urinary tract infections confined to the bladder are generally accompanied by localized symptoms and are easily treated. Fever, on the other hand, raises the chance of kidney involvement, as well as the likelihood of underlying nephro-urologic abnormalities and the risk of subsequent renal scarring.

Correspondence: Dr. Fatima Khurshid, Department of Radiology and Oncology, Shifa International Hospital Limited, Islamabad Pakistan

Email: fatimakhurshid61@yahoo.com

This article can be cited as: Manzoor A, Ahmed T, Batool ST, Chaudhry N, Khurshid F. Susceptibility pattern of pediatric uropathogens: Insights from Mirpur Azad Jammu Kashmir Pakistan. Infect Dis J Pak. 2024; 33(2): 92-96.
DOI: https://doi.org/10.61529/idjp.v33i2.283

Receiving date: **13 Jan 2024** Acceptance Date: **24 Jun 2024**
Revision date: **29 May 2024** Publication Date: **28 Jun 2024**

Kidney scarring caused by UTIs has been identified as a major source of long-term morbidity. Thus, children with established illnesses have been thoroughly investigated and treated, and they

have frequently had surgery or been given long-term antibiotic prophylaxis. Such strategies have been questioned. Several trials are now continuing to establish the best techniques for assessing and managing early febrile UTIs, as well as later therapies for them.[4,5]

Antibiotic treatment for children with febrile UTIs effectively reduces the risk of death, which was approximately 20% of hospitalized patients with pyelonephritis in the early 20th century. Nearly 50 years ago, two important studies highlighted the impact of UTIs had on children kidneys. In one study, renal parenchymal damage was detected in 210 out of 597 children with UTIs. Another study followed 72 children hospitalized for UTIs for 11 to 27 years and found that 18% died, 8% had kidney failure, and 22% experienced persistent or reinfection. However, these studies focused solely on kidney damage due to UTIs and disregarded the potential effects of kidney failure. The concept of reflux nephropathy emerged in the 1970s linking vesicoureteral reflux with pyelonephritis and subsequent renal scarring. Therefore, the evaluation of urinary tract abnormalities and long-term antibiotic use has become a routine treatment in children with UTIs, with surgical treatment of vesicoureteral reflux as the standard of care.[6, 7]

In the 1980s, two clinical trials compared immunotherapy with surgery alone or combined with immunosuppression. Surprisingly, both groups showed similar results. One study revealed a high rate of kidney scarring before treatment (38%), with low rates of new scarring and scar growth (2% and 9%). These findings highlight differences between pre-existing kidney damage and scarring from infections.[8,9]

The aim of our study was to evaluate uropathogens in terms of their antibiotic susceptibility patterns in pediatric patients admitted to DHQ Hospital Mirpur AJK over a period of 6 months. The purpose of this study is to provide insight into the appropriate selection of antibiotics to treat UTIs.

MATERIAL AND METHODS

A retrospective cohort study was carried out to examine the occurrence and antibiotic resistance of febrile UTIs in pediatric patients. The research took place at DHQ Hospital Mirpur AJK Pediatrics, from March to September 2023.The study included 140 pediatric patients who were selected through convenient sampling based on their symptoms suggesting a febrile UTI.

Criteria for inclusion and exclusion involved pediatric patients who had a confirmed fever of 38°C or higher, ≥5 white blood cells per high-power field in urine analysis, and a positive urine culture showing ≥ 10^5 Concentration of colony-forming units per milliliter. Patients who had identifiable urinary abnormalities or who were undergoing long-term antibiotic treatment were excluded in the study. Ethical approval was granted by the Institutional Ethical Review Board (IERB) of the DHQ hospital (IERB# REF. NO. 16).

Procedure of data collection involved reviewing medical records of both in-patients out-patients. Urine samples were collected through midstream catch technique for pediatric patients who were toilet-trained while, sterile bags were used for those who were not. Bacterial identification and testing for antibiotic susceptibility adhered to CLSI guidelines 2020, using standard methods such as disk diffusion and broth microdilution with standard culture media.[27]

The process of analyzing data was done using IBM SPSS Statistics version 20.0. The frequency of uropathogens and their susceptibility to antibiotics were categorized and reported in percentages.

RESULTS

Out of total of 140 pediatric patients, 69 (49%) had positive urine cultures suggestive of UTI. Of these 49 were females (71%) and 20 males (29%). Furthermore, 74% were 10 years old and above, and 26% were under 10 years of age (Table-I).

The most prevalent was Klebsiella pneumoniae accounting for 32% of cases followed by Staphylococcus aureus (26%). Escherichia coli was present in 22% of the cases, Enterococcus faecalis in 11%, and mixed growth of uropathogens in 9% (Figure-I).

Regarding Antimicrobial susceptibility pattern, Amikacin, Vancomycin, Neomycin and Tigecycline

were the most susceptible (100%), followed by chloramphenicol (90.9%), Linezolid (83.4%), Rifampicin (82%), Meropenem (77.3%), Nitrofurantoin (70%), Tazobactam (68.7%) and Imipenem (68.4%). Cephalexin (66.7%), Gentamicin (63.6%) and Cefipime (50%) showed moderate susceptibility. Whereas, Sulfamethoxazole (35%), Levofloxacin (31.4%), Cefoxitin (26.3%), Ciprofloxacin (22.2%), Tetracycline (20.5%), Cefuroxime (14.2%), Ceftriaxone (9.52%) and Amoxicillin (9.52%) were the least susceptible.

Table-I: Characteristics of pediatric patients with Positive urine cultures (n=69).

Characteristics	Frequency (%)
Gender	
Females	49 (71%)
Males	20 (29%)
Age	
>10	51 (74%)
<10	18 (26%)

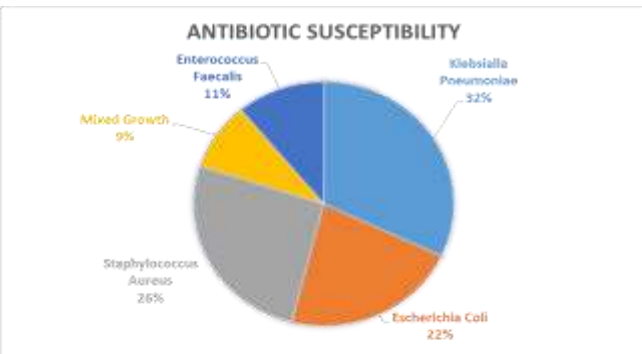

Figure-I: Pediatric uropathogens isolated among the study population (n=69).

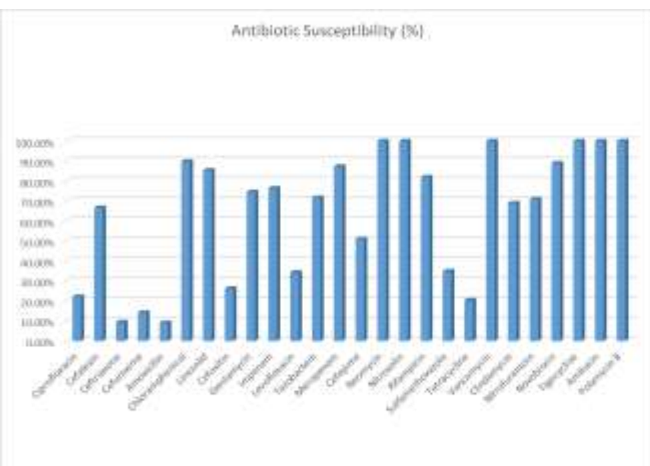

Figure-II: Antibiogram of uropathogens isolated from pediatric patients.

DISCUSSION

UTIs are a major health concern worldwide, impacting around 150 million individuals every year[49,50], with a substantial occurrence in children as well. About 3% of children in the United States are impacted annually.[10] Almost half of our study population (49%) was diagnosed with culture-proven UTI. The male-female ratio changed from 2.8-5.4:1 in the first year of life to 1:10 between ages 1-2.[11] Following early childhood, UTIs were mostly seen in females, corroborating findings of several international studies that show a higher prevalence in females.[13,14,15] *E. coli* is the leading cause of UTIs in children, accounting for 80-90%, followed by *Klebsiella pneumoniae* and *Staphylococcus aureus*. [15,16] Our results indicate a significant prevalence of *Klebsiella pneumoniae*, amounting for 32% of cases, which underscores the increasing concern regarding antibiotic-resistant bacteria. This resistance complicates the management strategies and raises the risks of morbidity and mortality in children. Urinalysis and culture are still the predominant methods for diagnosing UTIs in pediatric population with unexplained fevers.[15,16,17] Our research underscores the importance of considering local resistance patterns to steer empirical antibiotic therapy, showcasing the diverse susceptibility to different antibiotics.

Imipenem and meropenem showed relatively higher susceptibility among the isolates the most susceptible (68.4% and 77.3%).[18,19] Amikacin, an aminoglycoside, demonstrated a susceptibility rate of 100%, indicating its strong efficacy against gram-negative bacteria. Varying susceptibilities were observed with cephalosporins; cephalexin had a moderate rate of 66.7%, while ceftriaxone had lower effectiveness at 9.52%.[30] The fluoroquinolones showed decreased susceptibility, with rates of 22.2% for ciprofloxacin and 31.4% for levofloxacin.[20,21,22,23] This highlights the importance of upholding antimicrobial stewardship practices when treating pediatric UTIs. As a result, these antibiotics are excluded from the susceptibility analysis. To improve understanding, categorize the results based on types of organisms' antibiotic susceptibilities for better reader comprehension, particularly for those not well-versed in microbiology or infectious diseases.

Selecting the right antibiotic is essential for effectively treating UTIs in children, as it depends on the bacteria's susceptibility for a successful outcome. The importance of antibiotic resistance in children is a crucial factor in this situation. It should be noted that novobiocin is mainly used for diagnosis, not treatment, and CLSI recommendations advise against using polymyxin B for UTIs.

RBUS (Renal Bladder Ultrasound) and VCUG (Voiding Cystourethrogram) imaging are recommended for complex or recurrent UTIs to assist in adjusting treatments effectively. Other imaging options include DMSA (Dimercaptosuccinic Acid Scan) and NCG (Nuclear Cystogram) scans for detecting issues like vesicoureteral reflux or renal scarring.[24,25,26] Given the complexity and variability of antibiotic resistance, it is crucial to have a focused discussion on key findings.

The importance of selecting antibiotics based on specific bacteria susceptibilities is underscored by the widespread prevalence of antibiotic resistance. Enhanced management and continuous monitoring of antibiotic resistance patterns are vital for optimizing treatment efficacy and halting the spread of resistant bacteria.

The study is limited by its relatively small sample size and its regional scope, which may not accurately reflect antibiotic resistance patterns observed globally. Additionally, the retrospective design may introduce biases linked to the accuracy and completeness of medical records. Furthermore, due to the specific age range and exclusion criteria, the findings may not be applicable to all pediatric cases, such as neonates and infants, or children with ongoing antibiotic treatments. Future research should encompass larger, multi-center studies to validate these findings across broader demographics and varied geographical locations. Ongoing observation and longitudinal studies are also crucial to track the evolving patterns of resistance and assess the long-term efficacy of treatment protocols.

CONCLUSION

In conclusion, our study provides valuable insights into the antibiotic susceptibility pattern of pediatric uropathogens. To further understand the pattern of antibiotic resistance, large scale studies across diverse areas and healthcare settings are suggested. Critical is strict adherence to antimicrobial stewardship and infection control practices.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Ammara Manzoor: Study concept and design
Toqeer Ahmed: Data collection
Syeda Tahira Batool: Critical review
Nabia Chaudhry: Data collection and drafting of work
Fatima Khurshid: Manuscript write up and Data Analysis.

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