DOI: https://doi.org/10.53350/pjmhs020241848

ORIGINAL ARTICLE

Spectrum of Urinary Tract Pathogens and their Antimicrobial Susceptibility Pattern in Paediatric patients

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ABSTRACT

Aim: To investigate the current spectrum and determine the age-related sensitivity or resistance patterns of bacterial uropathogens to commonly used antibiotics in children aged two months to twelve years.
Methods: This cross-sectional study was carried out at the Pediatrics Department of Shaheed Mohtarma Benazir Bhutto Medical College (SMBBC) Lyari and Dr. Ziauddin Hospital Keamari, KDLB using a consecutive sampling technique from December 30th, 2022, until June1st, 2023. The diagnosis was based on a colony count of 105/ml of a single pathogen in a symptomatic child. Within 1 hour after the initial collection, samples were sent to the laboratory and were cultured in 5% sheep blood agar and MacConkey's media.
Results: Our study included 100 children with a "positive" urine culture, aged ranged from 2 months to 12 years. Thirty (30%) were males and seventy (70%) were females. E. coli was the most prevalent urinary pathogen, accounting for 52 (52%), followed by Klebsiella (29%), Proteus (9%), Pseudomonas (8%), and Enterococcus faecalis (2%). The majority of pathogens were sensitive to Amikacin, Imipenem, and Piperacillin/Tazobactam. Cefoperazon, Nitrofurantoin, and Ciprofloxacin were shown to be intermediately sensitive, whereas Amoxicillin-clavulanate, Ceftazidime, and Ceftriaxone were resistant.
Conclusion:UTI is a source of morbidity in children, which requires regular studies to identify the organism and its sensitivity from time to time and recommend prompt empirical treatment to bring down the UTI-related morbidity and mortality in children.My study reflects a lack of in-vitro sensitivity to commonly used oral forms of antibiotics.
Keywords: Spectrum, urinary pathogens, paediatric patients, urinary tract infection.

INTRODUCTION

Urinary tract infection is a common problem in children[1]. The incidence varies according to the age, race, and sex of children. Recurrence rates of UTIs vary between 8% and 30%. In high-income nations, UTIs affect around 2.8% of children annually. Approximately 8% of the girls and 2% of the boys experience at least one episode of UTI within the first 8- years of life[2]. The symptoms of UTI usually remain nonspecific in children; among children 2–24 months of age with a fever without an obvious source, the prevalence of UTI is about 5%. In older children, UTI can present with "symptoms of the urinary tract," while in infants and young children, the clinical presentation ranges from fever to gastrointestinal manifestations as well as upper and lower urinary tract symptoms[3,4,5].

Early diagnosis and treatment can reduce the risk of renal scarring and its long-term sequelae, such as hypertension and end-stage renal failure[1]. The treatment of acute UTI depends on the local pattern of causative pathogens and their antimicrobial resistance. The changing antimicrobial susceptibility pattern of bacterial pathogens is a growing problem and a matter of concern. It is especially true for developing countries where antibiotics are prescribed irrationally, not only by medical practitioners, but the antibiotics can be purchased directly from chemists without a prescription[6].

Among the causative agents identified as bacteria, Escherichia coli accounts for 80–90% of UTIs in children and is most common in young infants. Some other organisms include Enterobacteraerogenes, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus spp., and Serratia spp. The uropathogenic E. coli has been found to be resistant to a number of antibiotics, including beta-lactams (57.4%), co-trimoxazole (48.5%), quinolones (74.5%), gentamicin (58.2%), amikacin (33.4%), cefuroxime (56%), and nalidixic acid (77.7%)[3,7]. UTI due to drug-resistant E. coli increases the cost of treatment, morbidity, and mortality, especially where antibiotic misuse is the norm of the day[8,9].

This study was conducted to investigate the current spectrum and to obtain the sensitivity and resistance patterns of bacterial uropathogens to the most commonly used antimicrobials in children aged 2 months to 12 years.

MATERIALS AND METHODS

This was a cross-sectional study carried out using the non-probability consecutive sampling technique. The study was carried out in the out-patient, accident and emergency, and in-patient pediatric department of Shaheed Mohtarma Benazir Bhutto Medical College (SMBBC) Lyari and Dr. Ziauddin Hospital Keamari, KDLB Karachi, Pakistan. The duration of the study was 6 months. The enrolment of patients was started on December 30th 2022, and data collection was completed by June 1st2023. The sample size was estimated using the WHO'S sample size calculator. The confidence interval level was considered to be 95%. And absolute precision was taken as 10% by choosing the population proportion as 43.3%. The sample size comes out to be 100 patients (50 from SMBBC and 50 fromDr. Ziauddin Hospital Keamari) with proven UTIs through urine culture who fulfilled the inclusion criteria were included in the study. Inclusion criteria: children of either gender between 2 months and 12 years of age; children with two or more clinical findings of UTI (fever, irritability, increased urine frequency, dysuria, and abdominal pain). A case

was classified as a UTI when the urine culture had >100000 colonies of a single pathogen or if there were 10000 colonies in a symptomatic child. Exclusion criteria: prior use of antibiotics within the previous 48 hours; those with known urinary anomalies; urinary tract stones; and chronic co-morbid illnesses.

After permission from hospital Ethical Review Board, an informed consent was attained from the parents or guardian. Children were recruited through the OPD, accident and emergency, and in-patient pediatric departments of SMBBC Lyari and Dr. Ziauddin Hospital Keamari. In infants and children, the urine was collected in a urine collection bag or sterilized container. After washing the genital region with soap and water, the midstream, clean catch specimen was delivered to the laboratory within 24 hours of collection. SPSS version 24.0 was used to analyze the data. The mean and standard deviation were calculated for numerical data, e.g., age. Frequencies and percentages were calculated and presented for gender, organisms, and their susceptibility patterns.

RESULTS

Our study enrolled 100 children with positive urine cultures. The age of the patients ranged from 2 months to 12 years. The mean age was 5.1±3.6 years. 28(28%) were below 2 years of age, 30(30%) were between 2 to 5 years of age, and 42(42%) were above 5 years of age (Table 1). 30(30%) were males, and 70(70%) were females (Table 1). In the age group of < 2 years, among 28 children, 12 (42.8%) were males and 16 (57.2%) were females. In the age group of 2–5 years, among 30 children, 6 (20%) were males and 24 (80%) were females. In the age group of >5 years among 42 children, 12 (28.6%) were males and 30 (71.4%) were females (Table 1). The commonest urinary pathogen was E. coli in 52 (52%), followed by Klebsiella in 29 (29%), Proteus in 9 (9%), Pseudomonas in 8 (8%), and Enterococcus faecalis in 2 (2%) (Table 1).

In children < 2 years of age, 15 (53.6%) had E. coli, 9 (32.1%) had Klebsiella, 3 (10.7%) had Pseudomonas, and 1 (3.6%) had Proteus. In children 2–5 years of age, 18 (60%) had E. coli, 5 (16.7%) had Klebsiella, 4 (13.3%) had Proteus, and 3 (10%) had Pseudomonas. In children >5 years of age, 19(45.2%) had E. coli, 15(35.7%) had Klebsiella, 4(9.5%) had Proteus, 2(4.8%) had Pseudomonas, and 2(4.8%) had Enterococcus faecalis (Figure 1). Among the male children, 15(50%) had E. coli, 9(30%) had Klebsiella, 3 (10%) had Proteus, and 3 (10%) had Pseudomonas. Among the female children, 37 (52.9%) had E. coli, 20(28.6%) had Klebsiella, 6(8.6%) had Proteus, 5(7.1%) had Pseudomonas, and 2(2.9%) had Enterococcus faecalis.

Figure 1: Percentage distribution of organism among all the enrolled children by age groups (n=100).

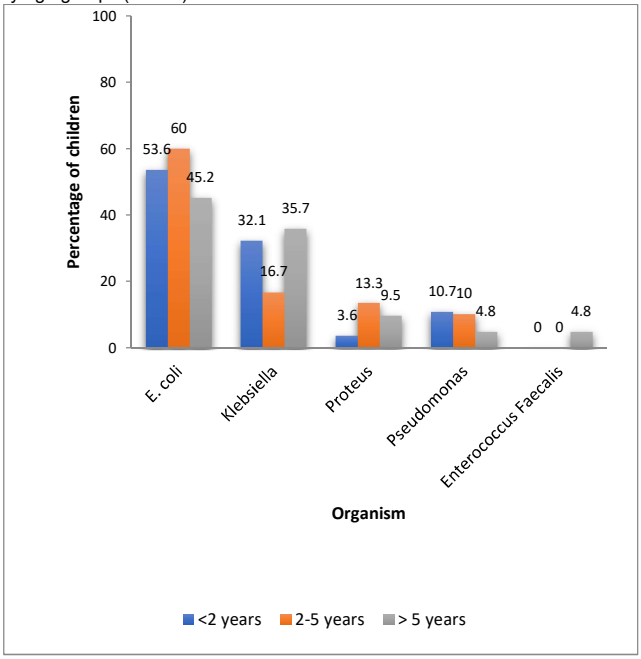

Table 1: Age distribution and pathogen of all the enrolled children (variable=100, 5.1±3.6 Mean ± SD)

	n%	
Age group		
<2 years	28 (28%)	
2-5 years	30 (30%)	
> 5 years	42 (42%)	
Age group and gender		
<2 years	Male	12(42.8%)
	Female	16(57%)
2-5 years	Male	06(20%)
	Female	24(80%)
>5 years	Male	12(28.6%)
	Female	30(71%)
Urinary pathogens		
E. Coli	52 (52%)	
Klebsiella	29 (29%)	
Proteus	9 (9%)	
Pseudomonas	8 (8%)	
Enterococcus Faecalis	2 (2%)	

Table 2:Spectrum of culture sensitivity (percentage) of different pathogens among all the enrolled children (n=100)

Antibiotics	**E. coli (n=52)**	**Klebsiella (n=29)**	**Proteus (n=9)**	**Pseudomonas(n=8)**	**Enterococcus (n=2)**
Amikacin	95%	72.20%	88.9%)	100%	100%
Amoxicillin-clavulanate	10%	30.70%	22.20%	-	0%
Cefoperazon&Sulbactam	58.80%	85.70%	100%	83.30%	50%
Ceftazidime	37.20%	42.80%	55.50%	62.50%	0%
Ceftriaxone	26.90%	48.30%	22.20%	20%	
Imipenem	100%	100%	-	100%	100%
Nitrofurantoin	74%	86.60%	100.00%	-	-
Norfloxacin	40.50%	47%	28.60%	60%	-
Piperacillin and Tazobactam	81.50%	100%	100.00%	75%	-
Ciprofloxacin	72.80%	70%	0.00%	66.60%	0%
Aztreonam	66.60%	50%	-	-	-
Nalidixic acid	18%	32%	-	-	-
Pipedemic acid	48%	58.80%	28.60%	-	-

The susceptibility pattern of antimicrobials is shown in Table 2. Among 52 children infected with E. coli, 41 had sensitivity to Amikacin, 39 (95%) were sensitive, and 2 (5%) were resistant. Fifty had sensitivity to Amoxycillin-clavulanate, 5 (10%) were sensitive, and 45 (90%) were resistant. Seventeen had sensitivity to Cefoperazon /Sulbactam and 10 (58.8%) were sensitive and 7 (41.2%) were resistant. Fifty-one had sensitivity to Ceftazidime, 19 (37.2%) were sensitive, and 32 (62.8%) were resistant. All 52 had sensitivity checked to XCeftriaxone, and 14 (26.9%) were sensitive and 38 (73.1%) were resistant. Sixteen had sensitivity to Imipenem, and all (100%) were sensitive. Twenty-seven had sensitivity to Nitrofurantoin, 20 (74%) were sensitive, and 7 (26%) were resistant. Thirty-seven had sensitivity to Norfloxacin, 15 (40.5%) were sensitive, and 22 (59.5%) were resistant. 38 had sensitivity to Piperacillin/Tazobactam or Tazobactam, 31 (81.5%) were sensitive, and 7 (18.5%) were resistant. 11 had sensitivity to Ciprofloxacin, 8 (72.8%) were sensitive, and 3 (17.2%) were resistant. 9 had sensitivity to Aztreonam, and 6 (66.6%) were sensitive, and 3 (33.3%) were resistant. 33 had sensitivity to Nalidixic acid, and 6 (18%) were sensitive, and 27 (82%) were resistant. 33 had sensitivity checked to Pipedemic acid, and 16 (48%) were sensitive and 17 (52%) were resistant. Among 29 Klebsiella patients, 18 had sensitivity to Amikacin, 13 (72.2%) were sensitive, and 5 (27.7%) were resistant. 26 had sensitivity to Amoxicillin-clavulanate; 8 (30.7%) were sensitive, and 18 (69.2%) were resistant. 7 had sensitivities to Cefoperazon/Sulbactam, 6 (85.7%) were sensitive, and 1 (14.2%) were resistant. Twenty-eight had sensitivity to Ceftazidime, and 12 (42.8%) were sensitive and 16 (57.2%) were resistant. All 29 had sensitivity to Ceftriaxone, 14 (48.3%) were sensitive, and 15 (51.7%) were resistant. 5 had sensitivity checked for Imipenem, and all (100%) were sensitive. 15 had sensitivity to Nitrofurantoin, 13 (86.6%) were sensitive, and 2 (13.4%) were resistant. 17 had sensitivity to Norfloxacin; 8 (47%) were sensitive, and 9 (53%) were resistant. 20 had sensitivity checked for Piperacillin/Tazobactam and all (100%) were sensitive. 10 had sensitivity checked to Ciprofloxacin, and 7 (70%) were sensitive and 3 (30%) were resistant. 12 had sensitivity toAztreonam, and 6 (50%) were sensitive, and 6 (50%) were resistant. Twenty-five had sensitivity checked to Nalidixic acid, and 8 (32%) were sensitive and 17 (68%) were resistant. 17 had sensitivity to Pipedemic acid, 10 (58.8%) were sensitive, and 7 (41.2%) were resistant. Among 9 Proteus patients, all had sensitivity checked to Amikacin, and 8 (88.9%) were sensitive and 1 (11.1%) were resistant. All had sensitivity checked to Amoxicillin-clavulanate, and 2 (22.2%) were sensitive and 7 (77.8%) were resistant. One had sensitivity checked for Cefoperazon/Sulbactam, and it was (100%) found to be sensitive. All had sensitivity checked to Ceftazidime, and 5 (55.5%) were sensitive and 4 (44.5%) were resistant. All 9 had sensitivity checked to ceftriaxone, and 2 (22.2%) were sensitive and 7 (87.8%) were resistant. None had sensitivity checked to Imipenem. Four had sensitivities checked to Nitrofurantoin, and all (100%) were sensitive. Seven had sensitivities checked to Norfloxacin, 2 (28.6%) were sensitive, and 5 (71.4%) were resistant. All 9 had sensitivity checked to Piperacillin or Tazobactam, and all (100%) were sensitive. Two had sensitivity checked to Ciprofloxacin, and both (100%) were resistant. Seven had sensitivities checked to Pipedemic acid, 2 (28.6%) were sensitive, and 5 (71.4%) were resistant. Among 8 Pseudomonas patients, 5 had sensitivity checked to Amikacin, and all (100%) were sensitive. None had sensitivity checked for amoxicillin-clavulanate. Six had sensitivity checked to Cefoperazon/Sulbactam, and 5 (83.3%) were sensitive and 1 (16.7%) was resistant. All had sensitivity checked to Ceftazidime, and 5 (62.5%) were sensitive and 3 (37.5%) were resistant. Five had sensitivity checked to Ceftriaxone, and 1 (20%) was sensitive and 4 (80%) was resistant. Three had sensitivity checked for Imipenem, and all (100%) were sensitive. None had sensitivity checked for Nitrofurantoin. Five had sensitivity checked to Norfloxacin, and 3 (60%) were sensitive and 2 (40%) were resistant. All 8 had sensitivity checked to Piperacillin/Tazobactam, and 6 (75%) were sensitive and 2 (25%) were resistant. Three had sensitivity checked to ciprofloxacin, 2 (66.6%) were sensitive, and 1 (33.3%) was resistant. Among 2 Enterococcus faecalis patients, both had sensitivity checked to Amikacin, and all (100%) were sensitive, while both (100%) were resistant to Amoxicillin-clavulanate. All had sensitivity checked to Cefoperazon/Sulbactam, and 1 (50%) was sensitive and 1 (50%) was resistant. Both had sensitivity checked to Imipenem, and all (100%) were sensitive, while both (100%) were resistant to Ceftazidime, Ceftriaxone, and Ciprofloxacin. Sensitivity to Nitrofurantoin, Norfloxacin, Nalidixic acid, and Pipedemic acid was not checked.

DISCUSSION

UTI is not an uncommon infection in paediatric practice, an important cause of morbidity and mortality in children, and an important cause of gram-negative bacteremia, particularly in young infants. Infection generally occurs with the colonization of Gram-negative microorganisms, which may extend up to the bladder and kidney, depending on the pathogen's characteristics[10]. Prompt diagnosis and management of UTI can reduce the consequences. It is important to know the causative pathogens and their sensitivity for appropriate management.

The age group of 13–60 months is more susceptible to UTI due to their toilet training period, as per many literatures[16].

The majority of patients (42%) belonged to the >5-year age group in this study, whereas studies from Turkey, Saudi Arabia, Australia, and Kuwait show that the majority of children belong to the 1–5-year age group[10,11,13,14]. Female predominance (70%) was in concurrence with other studies[10,11,14].

During the first year of life, male patients dominated in number, as reported by all other researchers as well. In our study, the commonest urinary pathogen was E. coli (52%), followed by Klebsiella (29%), Proteus (9%), Pseudomonas (8%), and Enterococcus faecalis (2%). The spectrum of urinary pathogens and gender were similar to those in other studies. The frequency of Pseudomonas was higher among children in our study than in the study by Autore G et al[12] i.e., uncommon in paediatric UTIs, but it is associated with more severe infections.

The distribution of organisms was similar among different age and gender groups in our study. It was reported in many papers that Proteus mainly affects males, with a high incidence in them. This has been explained by the ability of the Proteus species to swarm the long urethra of the males and ascend to cause the infection. The urinary infections caused by Staphylococcus ranged from 0.7% to 8.5% in different studies. However, staphylococcus was not identified in our study.

As regards the sensitivity pattern of organisms to different antibiotics, the results were also quite similar to those of other studies mentioned in this article. In our study, the majority of the pathogens showed good sensitivity to amikacin, imipenem, piperacillin, and tazobactam. Intermediate sensitivity was shown against Cefoperazon/Sulbactam, Nitrofurantoin, and Ciprofloxacin. While substantial resistance was shown to amoxicillin-clavulanate, ceftazidime, ceftriaxone, and nalidixic acid.

In our study, the resistance rates to amoxicillin-clavulanate were 90%, 69.3%, and 87.8% among E. coli, Klebsiella, and Proteus, respectively. The overall resistance rates to ampicillin

were found to be 61.2% and 100% among children from Turkey and Africa, respectively[10,15]. However, the differences in vivo versus in vitro sensitivities and resistance is a recognized fact. In our study, a very low resistance of 5% was reported by E. coli against Amikacin, 27.8% against Klebsiela, and 11% against Proteus. In the study by Mohammed, Deena et al. [13] from Bahrain, 3.9% of the E. coli were resistant to aminoglycosides.

In our study, nitrofurantoin also had a good sensitivity profile, and 26%, 14%, and 0% resistance were found among E. coli, Klebsiella, and Proteus, respectively.

A retrospective study of the bacterial profile of the uropathogens and patterns of antibiotic resistance was carried out in Kuwait from January 1, 2017 to December 31, 2017. Significant isolates from symptomatic pediatric patients with UTIs were detected using both conventional techniques and the VITEK 2 identification card technology. 13.7% of the 9,742 urine samples were positive for bacteriuria. Escherichia coli accounted for 67.3%, followed by Klebsiellapneumoniae (8.9%), Proteus spp. (5.7%), and Enterococcus spp. (7.4%). The enterobacteria were found to have high resistance rates to trimethoprim-sulfamethoxazole, ampicillin, cephalothin, nitrofurantoin, and amoxicillin/clavulanic acid. E. coli and K. pneumoniae that produce ESBLs were prevalent at 26% and 55%, respectively. Among the antibiotics evaluated for Gram-negative pathogens, Gentamicin, Amikacin, piperacillin/tazobactam, and Meropenem were the most sensitive, while the antibiotics tested for Gram-positive organisms were vancomycin, ampicillin, linezolid, and nitrofurantoin[14].

Comparing our results with the published data, we observed a higher resistance to cephalosporins and quinolones, which indicates an excessive use of this class of antibiotic in our community. The resistance to cephalosporins is explained through enzymatic mechanisms and efflux pumps. The resistance rate to aminoglycoside (amikacin) in our study was low, which was similar to above mentioned studies made on urine samples of children with UTIs. According to our study, the first line of antibiotics to be used for the treatment of UTIs when the causative pathogen is unknown should be beta-lactam/beta-lactamase inhibitor combinations (Piperacillin/Tazobactam), Cefoperazon & Sulbactam, Amikacin, or Imipenem. However, all these are parenteral use agents and are difficult to use for uncomplicated UTI children. Fluoroquinolones are, however, oral agents, and Nitrofurantoin and Ciprofloxacin show a sensitivity rate of about 70%. Imipenem is a broad-spectrum beta-lactamase antibiotic, active against a broad spectrum of bacteria (gram-positive and Gram-negative bacteria, aerobic and anaerobic organisms). It is mainly effective and used for pseudomonas; selective use is advised to avoid the emergence of resistance to carbapenems.

Paediatric urinary tract-colonizing bacteria are becoming increasingly resistant to commonly used antibiotics. Increasing resistance to the 3rd generation is due to the frequent acquisition and expression of extended spectrum beta-lactamase (ESBL). The phenotypes of extended spectrum beta-lactamase (ESBL) have become more complex due to the production of multiple enzymes, including inhibitor-resistant TEM enzymes, AmpC, enzyme hyperproduction, and porin loss. The high resistance levels found could be explained by the high frequency of Cephalosporins used for both prophylactic and therapeutic treatment of hospitalized children. This practice may have exerted selective pressures leading to the emergence of multidrug-resistant strains, which in turn may have stimulated the acquisition of genes encoding resistance mechanisms via horizontal transfer mechanisms between bacterial strains within the hospital environment. Genotypic methods based on enzyme assays, PCR, and others are not suitable for routine clinical testing. The clinical manifestations of ESBLs are extremely severe; hence, sensitive diagnostic methods are urgently required to guide therapy. Monitoring resistance development and implementing intervention strategies are a must. The results of this study showed that the rate of resistance to widely used antibiotics was high for Gram negative bacteria. The most effective antibiotics against Gram-negative bacteria were Carbapenems, beta-lactam/beta-lactamase inhibitor combinations, and aminoglycosides. Cephalosporins have intermediate sensitivity, while most strains are resistant to Amoxicillin-clavulanate. The primary reason for resistance to antibiotics is the widespread use of antibiotics in hospitals. In order to prevent or decrease resistance to antibiotics, the use of antibiotics should be kept under supervision and always evaluated thoroughly before initiating therapy; further, it should be given in appropriate doses for an appropriate period of time and infection.

CONCLUSION

In our study, the majority of the children (72%) with UTI were between 2 and 12 years of age. Overall, UTI was more common among female children, with a male: female ratio of 1:2.3. The most commonly isolated urinary pathogen was E. coli, followed by Klebsiella and Proteus. The majority of organisms showed good sensitivity to Amikacin, Imipenem, and Tazobactam, while great resistance was seen against Amoxicillin-clavulanate, Nalidixic acid, Ceftazidime, and Ceftriaxone.

Recommendation: The high rate of multidrug-resistant bacteria seen in our study points to the fact that frequent and excessive use of antibiotics should be avoided in day-to-day practice to provide a better healthy future for children of all ages.

Authorship and contribution declaration: Each author of this article fulfilled following Criteria of Authorship:

1. Conception and design of or acquisition of data or analysis and interpretation of data.
2. Drafting the manuscript or revising it critically for important intellectual content.
3. Final approval of the version for publication.

All authors agree to be responsible for all aspects of their research work.

Funding: No funding was provided for this research.

Conflict of interest: There is no conflict of interest.

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This article may be cited as: Chandio MA, Anwar T, Rehman A, Safdar S, Qaisrani S, Fatima S, Ahmed Z, Shafique R, Haider S, Shabbir A: Spectrum of Urinary Tract Pathogens and their Antimicrobial Susceptibility Pattern in Paediatric patients. Pak J Med Health Sci, 2024; 18(4): 29-33.