International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

Original Research Article.

Spectrum of Uropathogens and Their Antibiotic Susceptibility Patterns Among Pediatric Patients with Urinary Tract Infections in a Tertiary Emergency Department Setting

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ABSTRACT

Introduction: Urinary tract infection (UTI) is common in children and accounts for a large proportion of emergency department (ED) visits annually. The spectrum and antimicrobial susceptibility of pathogenic bacteria varies across institutions and patients. We aim to determine the spectrum of Uropathogens and their antibiotic sensitivities among pediatric UTI patients presenting to tertiary level University Hospital in Riyadh, Saudi Arabia.

Method: Retrospective chart review of patients aged 0-14 years who presented during the study period (May 2015 to April 2017) with a positive urine culture was conducted and the spectrum of uropathogens and their antibiotic sensitivities were recorded.

Results: A total of 578 patients (154 males and 424 females) were included in the study. Patients' mean age was 4.84 (3.94) months. *Escherichia coli* was the most frequent bacterial isolate found in 360 patients (62.3%), followed by *Klebsiella pneumonia* (17.0%), *Pseudomonas aeruginosa* (5.4%), *Proteus mirabilis* (2.9%), and *Enterococcus faecalis* (2.2%). Moreover, 77.8% of *E. coli* were resistant to ampicillin. More than half of the *K. pneumonia* and *P. mirabilis* isolates were resistant to ampicillin, whereas 76.9% of *E. faecalis* isolates were resistant to ampicillin. *E. coli* was the most sensitive to nitrofurantoin (88.6%) and gentamicin (76.4%). *P. aeruginosa, K. pneumonia,* and *P. mirabilis* were the most sensitive to co-amoxiclav (69.4%) and gentamicin (70.6%).

Conclusion: A high percentage of children diagnosed with UTI showed resistance to commonly used antibiotics. The data emphasize the importance of locally reported antibiotic resistance patterns for the treatment of UTIs.

Keywords: Urinary Tract Infection, Pediatrics, Antibiotic Resistance.

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Article History:

Received: 28-09-2021, **Revised:** 26-10-2021, **Accepted:** 20-11-2021

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2021.7.6.005	

INTRODUCTION

Urinary tract infections (UTI) are one of the most common infections in children, with a cumulative incidence of 3%-7% in girls and 1%-2% in boys.[1,2] In the United States, UTIs in children result in more than 500,000 emergency department (ED) visits annually, corresponding to 7% of all febrile presentations.[1,3,4]

Escherichia coli is the most commonly reported uropathogen.[5-10] Other pathogens include *Enterococcus faecalis*, *Klebsiella pneumonia*, *Proteus spp.*, and *Pseudomonas aeruginosa*.[5-8, 11,12]

A review of literature shows that the reported antimicrobial susceptibility of pathogenic bacteria varies across different geographic locations and institution. Studies found that common uropathogens were variably resistant to ampicillin (68%-87.3%), co-trimoxazole (54%-60.8%), cefuroxime (71.6%), and amoxicillin/clavulanic acid (30%).[6,7,13] On the other hand, a lower resistance to antibiotics like nitrofurantoin, piperacillin/tazobactam, imipenem, meropenem, amikacin, and cefoperazone/sulbactam was reported by Demir et al.[7]

Parenteral cephalosporins.[5,11] was found to be highly active against *E. coli*. Another study demonstrated a high *E. coli* sensitivity to cephtizoxin, gentamicin, and ciprofloxacin.[14]

Gram-negative isolates exhibit sensitivity to imipenem, amikacin, and ceftazidime.[15,16] *Klebsiella* were found to be highly sensitive to ceftazidime and imipenem whereas *Pseudomonas* was sensitive to carbapenem, aminoglycoside and ciprofloxacin.[16-19]

In our search of literature, we found a lack of studies reporting local antibiotic resistance pattern in children with UTI from the middle east region. We therefore conducted this study in the emergency department of a tertiary level hospital in Saudi Arabia to determine the local spectrum of uropathogens and antibiotic sensitivities of bacterial isolates from urine cultures of pediatric patients.

MATERIALS AND METHODS

We conducted a retrospective chart review of all pediatric patients aged 0-14 years who received a diagnosis of UTI based on urinary analysis and culture examinations. These patients were seen at the pediatric ED of tertiary level University Hospital of Saudi Arabia from May 2015 to April 2017. Any pediatric ED patient who presented within the study period with a positive urine culture, defined as >100,000 CPF/ml by clean catch or >1000 CPF/ml by catheterization, was included in the study. Patients with negative urine culture and those aged >14 years were excluded from the study.

Patients' demographic and clinical characteristics, including age, sex, underlying conditions [vesicoureteric reflux (VUR), neurogenic bladder), history of UTI, symptoms presented (e.g., fever, abdominal pain, hematuria, painful micturition, urinary smell change, signs of neonatal sepsis), urine sample technique (e.g., use of catheter, use of a urine bag, suprapubic aspiration, clean catch, vesicostomy), and results of urinary analysis, urine culture, and antibiotic sensitivity, were collected using a preformed case report form.

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 23.0 (SPSS Inc., IBM, Armonk, New York, USA). The results are reported as the mean and standard deviation for continuous variables and as the number and percentage of the total for categorical variables. The study was approved by the Ethics Review Board for Research Involving Human Subjects of the College of Medicine, King Saud University, Riyadh, Saudi Arabia.

RESULTS

A total of 578 patients [154 (26.7%) male and 424 (73.4%) female) were included in the study. The mean age was 4.84 (3.94) months (range: 4 days–16 years). The most commonly identified underlying condition was VUR (n=62, 10.7%). There were 229 patients (39.6%) with a previous UTI. A total of 154 patients (26.6%) received antibiotic UTI prophylaxis and 257 (44.5%) had recent or current antibiotic treatment. The most common presentation was fever (n=225, 44.1%). Most samples were clean-catch midstream urine (n=236, 40.8%). There were 421 samples that showed drug resistance (n=72.8%). Table 1 shows the detailed frequencies of the variables.

Table 2 shows the frequency of bacterial uropathogens from the urine culture results. *E. coli* was the most frequent bacterial isolate found (62.3%). *K. pneumonia*, *P. aeruginosa*, *Proteus mirabilis*, and *E. faecalis* were other commonly isolated organisms. Resistance frequencies of isolates is summarized in Table 3. Of note, a high percentage of isolates were resistant to commonly used antibiotics. About 65% isolates showed resistance to ampicillin, 28% to trimethoprim-sulfamethoxazole, 22% to cefuroxime, 17% to amoxicillin/clavulanic acid and 10% to nitrofurantoin.

Table 1: General demographic characteristics of 578 patients

Demographic profile	n	%
Sex		
Male	154	26.6
Female	424	73.4
With underlying conditions		
VUR	62	10.7
Neurogenic bladder	48	8.3
Posterior urethral valve	21	3.6
Had previous UTI	229	39.6
Had prophylaxis	154	26.6
Recent/current antibiotic	257	44.5
Presenting symptoms		
Foul-smelling urine	58	10.0
Fever	255	44.1
Abdominal pain	146	25.3
Hematuria	49	8.5
Dysuria	94	16.3
Sepsis screening	7	1.2
Sample collection methods		
Catheter	225	38.9
Urine bag	80	13.8
Suprapubic aspiration	19	3.3
Clean catch	236	40.8
Others	18	3.1
Nitrite positive	225	38.9
Antibiotic resistance present	421	72.8
ESBL	127	22.0

VUR: Vesico-uretetic reflux; ESBL, Extended spectrum betalactamase resistance; UTI: urinary tract infection

Table 2: Frequency of culture isolates from 578 pediatric patients diagnosed with urinary tract infection

Culture isolates	n	%
Escherichia coli	360	62.3
Klebsiella pneumoniae	98	17.0
Pseudomonas aeruginosa	31	5.4
Proteus mirabilis	17	2.9
Enterococcus faecalis	13	2.2
Enterobacter cloacae	8	1.4
Klebsiella oxytoca	7	1.2
Yeast	7	1.2
Morganella morganii	5	0.9
Staphylococcus aureus	5	0.9
Citrobacter freundii	4	0.7
Citrobacter koseri	4	0.7
***Salmonella* serogroup D**	2	0.3
Staphylococcus epidermidis	2	0.3
Enterobacter aerogenes	2	0.3
Acinetobacter lwoffii	1	0.2
Acinetobacter baumannii	1	0.2
Enterococcus avium	1	0.2
Proteus rettgeri	1	0.2
Serratia marcescens	1	0.2
***Streptococcus* group B**	1	0.2
Staphylococcus sciuri	1	0.2

Table 3: Percentage of isolates that are resistant to antibiotics in 578 children with urinary tract infection

Antibiotics	N (%)
Ampicillin	378 (65.4)
Trimethoprim/sulfamethoxazole	163 (28.2)
Cefuroxime	130 (22.5)
Cefazolin	129 (22.3)
Amoxicillin /clavulanate	102 (17.7)
Cefepime	89 (15.4)
Gentamicin	84 (14.53)
Nitrofurantoin	59 (10.2)
Ciprofloxacin	55 (9.5)
Piperacillin	33 (5.7)
Cefotaxime	31 (5.4)
Levofloxacin	23 (3.9)
Cefoxitin	22 (3.8)
Meropenem	20 (3.5)
Ceftazidime	17 (2.9)
Imipenem	17 (2.9)
Amikacin	12 (2.1)
Cefixime	10 (1.7)
Tobramycin	10 (1.7)
Ceftriaxone	7 (1.2)
Fosfomycin	7 (1.2)
Moxifloxacin	1 (0.2)
Tetracycline	1 (0.2)
Clindamycin	1 (0.2)
Vancomycin	1 (0.2)

Table 4: Number and percentage of resistance of the commonly isolated uropathogens to antibiotics

Antibiotics	*E. coli* N=360 N (%)	*P. aeruginosa* N=31 N (%)	*K. pneumonia* N=98 N (%)	*P. mirabilis* N=17 N (%)
Ampicillin	280 (77.8%)	3 (9.7%)	51 (52.0%)	9 (52.9%)
Amox/Clav	56 (15.6%)	3 (9.7%)	25 (25.5%)	3 (23.5%)
Cefazolin	80 (22.2%)	3 (9.7%)	24 (24.5%)	4 (23.5%)
Cefepime	70 (19.4%)	1 (3.2%)	12 (12.2%)	2 (11.8%)
Cefuroxime	88 (24.4%)	2 (6.5%)	30 (30.6%)	3 (17.6%)
Nitrofurantoin	14 (3.9%)	3 (9.7%)	31 (31.6%)	9 (52.9%)
Trim/Sulfa	110 (30.6%)	2 (6.5%)	40 (40.8%)	5 (29.4%)

Table 5: Number and percentage sensitivity of the commonly isolated uropathogens to antibiotics

Antibiotics	*E. coli* N=360 N (%)	*P. aeruginosa* N=31 N (%)	*K. pneumoniae* N=98 N (%)	*P. mirabilis* N=17 N (%)
Amoxicillin/ clavulanic acid	126 (35.0%)	3 (9.7%)	68 (69.4%)	8 (47.1%)
Ampicillin	131 (36.4%)	2 (6.5%)	7 (7.1%)	4 (23.5%)
Cefuroxime	129 (35.8%)	2 (6.5%)	16 (16.3%)	6 (35.3%)
Ciprofloxacin	147 (40.8%)	12 (38.7%)	27 (27.6%)	8 (47.1%)
Gentamicin	275 (76.4%)	22 (70.9%)	45 (45.9%)	12 (70.6%)
Nitrofurantoin	319 (88.6%)	2 (6.5%)	37 (37.8%)	1 (5.9%)
Trimethoprim-sulfamethoxazole	165 (45.8%)	1 (3.2%)	28 (28.6%)	4 (23.5%)

Table 4 shows the bacterial isolate specific percentage resistance to the most common isolates to some antibiotics. Although 77% of *E. coli* isolates were resistant to ampicillin, there was relatively lower antibiotic resistance noted for *E. coli* isolates to the other antibiotics. *P. aeruginosa* isolates showed an almost uniform resistance spectrum in all tested antibiotics ranging between 3%

to 9% resistance. More than half of the *K. pneumonia* and *P. mirabilis* isolates were resistant to ampicillin (52% and 53%, respectively), whereas 76.9% of *E. faecalis* isolates were resistant to ampicillin.

Table 5 shows the percentage of isolate sensitivity of *E. coli*, *P. aeruginosa*, *K. pneumonia,* and *P. mirabilis* to antibiotics. *E. coli* was most sensitive to nitrofurantoin (88.6%) and gentamicin (76.4%). *P. aeruginosa* was most sensitive to gentamicin (70.9%), whereas *K. pneumonia* and *P. mirabilis* were most sensitive to co-amoxiclav (69.4%) and gentamicin (70.6%), respectively.

DISCUSSION

We investigated the spectrum of uropathogens and the antimicrobial resistance to the most commonly isolated uropathogens in the pediatric population in one of the first such study of its kind from Saudi Arabia. The distribution and profile of the bacterial species are relevant to the present study population, because UTIs are very prevalent in this age group. Therefore, performing a culture and sensitivity test is important for disease management.

Consistent with previous studies, the most common uropathogens isolated were *E. coli*, *K. pneumonia,* and *E. faecalis,* which are part of the normal intestinal flora, together with *P. aeruginosa* and *P. mirabilis*.[5-12] *E. coli* was the most frequently isolated uropathogen, found in 62.3% of patients.

In this study, we found that *E. coli* was most sensitive to nitrofurantoin (88.6% of isolates) with 3.9% resistance. The other antibiotics that showed a greater action against *E. coli* included trimethoprim-sulfamethoxazole, cefuroxime, and amoxicillin/clavulanic acid. On the other hand, *E. coli* isolates showed more resistance to ampicillin (77.8%). This is consistent with the finding of the pooled prevalence of resistance of *E. coli* and other uropathogens by Bryce et al., to ampicillin (53.4%), trimethoprim-sulfamethoxazole (23.6%), co-amoxiclav (8.2%), and ciprofloxacin (2.1%).[20] Furthermore, the findings of the present study were consistent with those of Bryce et al. who reported that *E. coli* exhibited the lowest resistance and the highest sensitivity to nitrofurantoin.[20] The resistance of *E. coli* to ampicillin and trimethoprim-sulfamethoxazole, which are the most commonly used empirical treatments for UTI, was also high at 77.8% and 30.6%, respectively. This is consistent with the findings of Alanazi et al. who reported 82.76% and 51.72% resistance for ampicillin and trimethoprim-sulfamethoxazole, respectively[21], and many other studies that were conducted in Saudi Arabia.[22-25]

The most commonly isolated uropathogens that caused UTIs among children in our study are consistent with the findings of other studies.[5-12] However, we cannot deduce and/or refute the influence of geographical variation in this study to assess contrast or conformance with other studies, because we only studied a sample of patients from a single tertiary center.[26-28] This study showed that the empirical treatment with co-trimoxazole or cephalexin may be inadequate; thus, there is a need for the identification of the causative microorganism to establish the most effective antimicrobial treatment.

The present study has some limitations. The study was conducted only among children seen at the emergency room, which may not represent the entire population of children who are diagnosed with a UTI in a healthcare setting. Furthermore, the patients were not followed up to monitor the outcomes of the observed resistance and to verify whether these patients received another antibiotic after confirmation of the culture and sensitivity results. Therefore, a large prospective study is warranted to determine the extent of bacterial resistance and sensitivity among children diagnosed with UTI.

CONCLUSIONS

A high percentage of children diagnosed with UTI showed resistance to the more commonly used antibiotics, including ampicillin, cefuroxime, and trimethoprim-sulfamethoxazole. The present study suggests a need for the re-evaluation of the empirical treatment for UTIs among children, and the need for urine culture and sensitivity testing to institute the utmost antimicrobial treatment for these patients.

ACKNOWLEDGEMENTS/ DECLARATIONS

The study was approved by the Ethics Review Board for Research Involving Human Subjects of the College of Medicine, King Saud University, Riyadh, Saudi Arabia. We do not identify and conflict of interest. We did not receive any funding for conducting the study or employ any writing assistant for writing the manuscript. The study was approved by the Ethics Review Board for Research Involving Human Subjects of the College of Medicine, King Saud University, Riyadh, Saudi Arabia.

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Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Syed A. Ahmad, Tariq A. Althobaiti. Spectrum of Uropathogens and Their Antibiotic Susceptibility Patterns Among Pediatric Patients with Urinary Tract Infections in a Tertiary Emergency Department Setting. Int J Med Res Prof. 2021 Nov; 7(6): 25-29. DOI:10.21276/ijmrp.2021.7.6.005