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Original Article

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The evaluation of children hospitalized with the diagnosis of urinary tract infection

Abstract

Aim: The aim of this study was to investigate the factors that cause urinary tract infections (UTI) and antibiotic susceptibility profiles with epidemiological and clinical features among children hospitalized with the diagnosis of UTI.
Materials and Methods: This study was retrospective and evaluated the clinical and laboratory features of 216 patients aged 0-15 years old evaluated, who were hospitalized with a diagnosis of UTI in a single center.
Results: The mean age of patients with confirmed UTI was 3.75±3.73, with a male-to-female ratio of 2:1. Fever was the most common symptom observed. In patients with confirmed UTI, urine nitrite positivity and high leukocyte positivity were significantly elevated (p=0.0001). Urine culture yielded positive results in 43% of the patients, with *Escherichia coli* (*E. coli*) being the most frequently detected pathogen. High rates of resistance were observed for the antibiotics ampicillin, cefuroxime, ceftriaxone, and trimethoprim-sulfamethoxazole (TMP-SMX), while resistance to aminoglycosides, nitrofurantoin, and carbapenems was less frequently encountered.
Conclusion: Urine nitrite and high leukocyte positivity may be suggestive of a diagnosis of UTI in patients without positive urine culture results.

Keywords: Urinary tract infection, children, antibiotics, epidemiology, pediatric healthcare, antibiotic resistance

INTRODUCTION

Urinary tract infections (UTIs) are the second most common infections in childhood, following upper respiratory tract infections. The prevalence of UTIs in children varies by age and gender. The rate of UTIs in infants aged 2-12 months with fever has been reported as 5.6%, while the rate of UTIs in neonates under two months of age is 4.6%. UTIs are more common in girls, except during the neonatal period when they are more common in boys (1,2). The accurate frequency of UTIs remains uncertain due to symptom variability, potential oversight of asymptomatic bacteriuria, and the challenge of distinguishing colonization from infection. Escherichia coli is the most frequently identified bacteria in pediatric UTIs, accounting for approximately 80% of cases, although fungi can also be causative agents (3). In cases of suspected UTIs, treatment should commence with empirical antibiotics effective against the most commonly implicated microorganisms. However, such treatment should only begin after obtaining a urine culture. Unfortunately, inappropriate antibiotic use has led to the development of resistance in many of the common pathogens responsible for UTIs.

If UTI involves the kidney parenchyma, it can lead to acute pyelonephritis, a condition of significant clinical concern and complexity. The definitive diagnosis of UTI is made by the identification of a causative agent in urine cultures. However, in patients whose urine culture cannot be performed, there is a need to identify other informative laboratory tests that will provide good evidence for clinical intervention.

The aim of this study was to assess epidemiological data regarding pediatric patients hospitalized with a diagnosis of UTI. This assessment included an examination of their clinical findings, symptoms, diagnostic methods, laboratory tests, and the outcomes of various imaging techniques to identify clinically relevant information. Additionally, the study aimed to investigate the profiles and antibiotic susceptibilities of the agents responsible for confirmed UTIs.

MATERIALS AND METHODS

In this retrospective study, clinical and laboratory data of pediatric patients hospitalized with the diagnosis of UTI in the

Ministry of Health Okmeydanı Training and Research Hospital Pediatrics Service between September 2009 and September 2012 were extracted from patient case files and analyzed. Patients between the ages of 0-16 were included in the study. Age and gender, symptoms at presentation, personal and family medical history, clinical findings, and blood tests for leukocyte count and C-reactive protein (CRP) and urinary levels of nitrite (in complete urinalysis), leukocyte esterase, leukocyte count, leukocyte clusters, and pH were collected. In addition, the results of urine culture, urinary tract, renal ultrasonography (USG), and Technetium 99m dimercaptosuccinic acid (DMSA) scintigraphy were recorded. Finally, the antibiotics used in treatment and antibiotic resistance identified in cultured agents were assessed.

Patients were divided into two groups, either definite UTI or probable UTI. The criterion for definite UTI (DUTI) was positive reproduction of a pathogenic agent in urine culture. Patients were classified as probable UTI (PUTI) when there was no growth in urine culture, but clinical and other laboratory tests supported a diagnosis of UTI.

Ethical approval for the study was granted by Okmeydanı Training and Research Hospital Clinical Research Ethics Committee, dated 07/05/2013, decision number 91.

Statistical Analysis

Statistical analysis of data was performed using the Statistical Package for the Social Sciences (SPSS), version 15.0 (IBM Inc., Armonk, NY, USA) and GraphPad InStat demo version. The chi-square test, Fisher exact test, Student T test, Mann Whitney U test, Kruskal Wallis test and Dunn's test were used for this study. The results were evaluated at the 95% confidence interval, and thus a $p<0.05$ was assumed to indicate statistical significance.

RESULTS

Out of the 330 patients admitted to the Pediatrics Service with a diagnosis of UTI, 216 patients who met the inclusion criteria were included in the study. Among these 216 patients, the mean age was 3.75±3.73 years, and 142 (65.7%) were female. When patients were subdivided by age, there were significantly more patients ($p=0.015$) in the 0-2-year-old age group, with 39 (41.9%) patients, compared to 23 (24.7%) in the 2-5 age group and 31 (33.3%) in the over 5 years group.

The symptoms at the presentation are summarized in Table 1. The sensation of burning while urinating was significantly more common in the DUTI group ($p=0.030$). Clinical findings in the DUTI and PUTI are listed and compared in Table 2. In patients with DUTI, costovertebral angle sensitivity was found more often ($p=0.028$). Urinalysis findings based on DUTI or PUTI are shown in Table 3. Urine nitrite and urine leukocyte cluster positivity were also more common in the DUTI than in the PUTI group ($p=0.0001$, $p=0.020$, respectively) (Table 3).

Table 1. Symptoms according to definite or probable urinary tract infection

	Definite urinary tract infection		Possible urinary tract infection		Chi-square	p
	N	%	n	%		
Fever	p	69.9	60	72.3	0.122	0.726
Bloody urine	4	4.3	10	12.0	3.595	0.058
Urinary incontinence	2	2.2	1	1.2	-	0.999
Burning while urinating	17	18.3	6	7.2	4.714	**0.030***
Smelly urine	0	0	1	1.2	-	0.472
Frequent urination	3	3.2	2	2.4	-	0.999
Abdominal pain	13	14.0	10	12.0	0.144	0.704
Backache	0	0	1	1.2	-	0.999
Flank pain	1	1.1	0	0.0	-	0.999
Vomiting	31	33.3	28	33.7	0.003	0.955
Constipation	0	0	2	2.4	-	0.221
Restlessness	10	10.8	12	14.5	0.550	0.458
Asymptomatic	7	7.5	5	6.0	0.156	0.693

Table 2. Clinical findings according to definite or probable urinary tract infection

	Definite urinary tract infection		Possible urinary tract infection		Chi-square	p
	n	%	n	%		
Concomitant respiratory infection	15	16.1	14	16.9	0.017	0.895
Abdominal tenderness	4	4.3	3	3.6	-	0.999
Costovertebral angle tenderness	12	12.9	3	3.6	4.854	**0.028***
Phimosis	1	1.1	3	3.6	-	0.344
Hypospadias	1	1.1	1	1.2	-	0.999

Table 3. Urinalysis findings according to definite or probable urinary tract infection

	Definite urinary tract infection		Possible urinary tract infection		Chi-square	p
	n	%	n	%		
Nitrite in urine	37	39.8	12	14.5	14.004	**0.0001**
Urine leukocyte esterase	80	86.0	63	75.9	2.947	0.086
Leukocytes in urine	78	83.9	62	74.7	2.268	0.132
Cluster of leukocytes in the urine	44	47.3	25	30.1	5.438	**0.020**
Fungus in the urine	5	5.4	5	6.0	-	0.999

Table 4. Urine culture results

	n	%
There is growth in the urine culture	93	43.1
No growth in urine culture	83	38.4
Contamination	23	10.6
Not studied	17	7.9

Table 5. Microorganisms grown in culture.

	n	%
E. coli	61	34.7
ESBL *E. coli*	20	11.4
Klebsiella	9	5.1
ESBL Klebsiella	2	1.1
Staphylococcus	1	0.6

Urine pH ranged from 5 to 8, and most of the patients had urine pH below 6. Urine pH was significantly lower in the DUTI group compared to the PUTI group (p=0.025).

There was growth in the urine culture in 43.1%, while contamination was detected in 10.6% (Table 4). The most commonly cultured organism was *E. coli* (Table 5). Positive urine culture was more common in the 2-5 age group than in the 0-2 age group (p=0.015). *E. coli* was more commonly cultured when the urinary pH was above 6.

USG was performed in 121 (56%) of 216 patients. Among the pathological findings reported were: pelvicaliectasis at 6% (n=13); calculus at 3.7% (n=8); increase in echogenicity at 1.9% (n=4); and hydronephrosis at 0.9% (n=2). DMSA scanning was performed in only 28 (13%) patients. In DMSA scans with pathological findings, a hypoactive area was reported in 1 patient (3.6%), and unilateral/bilateral scarring was found in 2 patients (7.1%).

The most commonly used antibiotics, in order of frequency, were Ceftriaxone (69%), Ampicillin (20.8%), Cefotaxime (18.1%), Amikacin (10.6%), Gentamicin (4.6%), Ampicillin-sulbactam (4.2%), Meronem (3.2%), Sulperazone (2.3%), Netilmicin (0.9%), and Ceftazidime (0.5%). Combined antibiotic therapy was administered to 44 (20.4%) patients.

The use of Ceftriaxone was significantly lower in the 0-2 age group compared to other age groups (p=0.0001), but the use of Ampicillin-Cefotaxime was significantly higher (p=0.0001) in the youngest age group. Gentamicin was significantly less frequently used in the over 5 years age group compared to the 0-2 age group (p=0.028).

Antibiotic resistance rates for *E. coli*, ESBL-positive *E. coli*, Klebsiella, and ESBL-positive Klebsiella were as follows:

- Ampicillin: 41.7%, 70%, 88.9%, and 100%, respectively.
- Cefazolin: 8.3%, 85%, 11.1%, and 33.3%, respectively.
- Gentamicin: 13.3%, 11%, 11.1%.
- Ampicillin-sulbactam: 16.7%, 35%, 30%, and 33.3%, respectively.
- TMP-SMX: 26.7%, 70%, 11.1%, 0%.
- Nitrofurantoin: 1.7%, 5%, 50%, and 55.9%, respectively.
- Cefuroxime: 11.7%, 85%, 0%, and 0%, respectively.
- Ceftriaxone: 90%-100%.
- Cefixime: 3.3% and 10%.

Notably, resistance to imipenem and meropenem was not observed.

DISCUSSION

The mean age of children with UTI has previously been reported as 6.5 years (4,5). The lower mean age in this study of 3.75 years may be due to the fact that the patients in the earlier studies were recruited from outpatient departments while the population of the present study was inpatients. The most common symptoms in children diagnosed with UTI were reported to be abdominal pain (94.6%) and vomiting (72.1%) (6). In another study, fever (62.7%) and vomiting (46%) were the most common reasons for admission (7). Similarly, in the present study undertaken in an inpatient population, the most common complaints were fever (67.6%) and vomiting (33.3%).

Positive culture rates vary widely in studies, ranging from 10% to 43% (4,6,10). In the present study, urine cultures were positive in 43.1% of the patients. Similarly, rates of urine contamination vary between 20.58% and 22.1% in previous studies (4,11). In contrast, the present study observed a notably low contamination rate of 10.6%.

Studies conducted in different countries have reported the frequency of *E. coli* isolation in children, ranging from 45.1% to 89.9% (4,10,12-22). In this study, the rate of *E. coli* isolation was

at the lower end of this range, with 46.1%.

Furthermore, almost 70% of patients with positive cultures in our study were female. This finding aligns with Yolbas et al., who reported a proportion of female patients at 78.7%. This gender difference can be attributed to female's increased susceptibility to bacterial colonization due to the anatomical structure of the urethra. Inadequate perineum hygiene in females can lead to recurrent infections and subsequently higher morbidity rates (23).

Ampicillin resistance was found to be 50-53% in studies conducted abroad (21,22) while in the present study, ampicillin resistance varied from 41.7% to 100% for different bacteria. We suggest that ampicillin may not be the most appropriate antibiotic choice for suspected UTIs in Turkey. Second-generation cephalosporins are frequently used in UTIs due to their appropriate spectrum of action and relatively few side effects. In the present study, resistance to cefuroxime was very variable ranging from 0% to 85%. In some studies, cefuroxime resistance was found to be as low as 7% and 10% although high resistance rates have also been reported at 38.2-39% (4,24-26). Aminoglycosides have a high potential for side effects, but they are effective when used alone in UTIs. In the present study, the resistance rate was 11.1-30% for different bacteria. It has been reported that amikacin resistance varies between 0-8% in different studies (4,10,29,27-30). Resistance to imipenem, one of the carbapenem group antibiotics, is still low (4,10,27,31). It was notable that no resistance to imipenem or meropenem was observed in the present study. Nitrofurantoin is one of the antibiotics commonly used in the empirical treatment of UTIs. Nitrofurantoin resistance has been reported to range from 8.2% to 67.3% in different studies (35-39), while resistance was 1.7%-55.9% in the present study, depending on the organism cultured.

In the present study, high urine nitrite levels and urine leukocyte clusters were significantly more likely in the DUIT group compared to the PUTI group (p=0.0001 and p=0.02, respectively). We suggest that these tests may help in diagnosing UTI in patients whose urine culture cannot be performed, or an agent cannot be identified.

CONCLUSION

In conclusion, UTIs are common infections in childhood and are important because they may cause severe complications. A full understanding of each country's epidemiological data, common UTI-causing agents, and the likely antibiotic resistance will be important for preventing complications and guiding both treatment and prophylaxis.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
According to the decision of Okmeydanı Training and Research Hospital Clinical Research Ethics Committee dated 07/05/2013 and numbered 91, it was found ethically appropriate.

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