HEALTH SCIENCES QUARTERLY

Volume: 4
Issue: 4
2024

E-ISSN: 2791-6022
https://journals.gen.tr/jsp

Received: 2023-08-18
Accepted: 2024-09-18

ORIGINAL ARTICLE

The relationship between uropathogens and clinical characteristics of children with urinary tract infection

Emre Leventoğlu[1] **Mustafa Soran**[1] **Şadiye Kübra Tüter Öz**[2]
Elif Böncüoğlu[2] **Zafer Bağcı**[3]

[1] Department of Pediatric Nephrology, Konya City Hospital. Konya / Türkiye
[2] Department of Pediatric Infectious Diseases, Konya City Hospital. Konya / Türkiye
[3] Department of Pediatrics, Konya City Hospital. Konya / Türkiye

Abstract

Urinary tract infections (UTI) are common bacterial infections in children. This study aimed to examine the relationships between different microorganisms and both clinical and laboratory findings in pediatric patients with UTIs. We conducted a retrospective evaluation of children with UTI between 2019 and 2024. Patients were divided into four main groups as normal anatomy, vesicoureteral reflux (VUR), ureteropelvic junction obstruction (UPJO), and neurogenic bladder (NB). Information on clean intermittent catheterization (CIC) and prophylactic antibiotic use was recorded. Laboratory results were compared across these patient groups. The study included 266 patients, with a female predominance (female/male ratio: 7.33). NB was the most common urinary tract condition (43.3%), followed by VUR (10.9%) and UPJO (9%). Prophylactic antibiotics were used by 9% of the patients. Acute phase reactants in patients with CIC were significantly higher (p=0.023 for white blood cell (WBC) and p=0.002 for C-reactive protein (CRP) levels). They were also higher in patients with prophylactic antibiotics compared to those without (p=0.001 for both). The most frequently detected bacteria in urine cultures were *E. coli* (65%), followed by *Klebsiella spp.* (18.8%), *Pseudomonas spp.* (7.5%), and *Proteus spp.* (4.9%). *Klebsiella spp.*, *Enterococcus spp.*, and *Morganella spp.* were not isolated from patients receiving prophylaxis (p=0.022). Risk factors for UTIs need to be carefully assessed for every patient, and treatment should be customized according to clinical and laboratory results. Individual patient factors should guide drug selection, and treatment plans should account for potential resistance patterns.

Keywords: Antibiotic resistance, children, urinary tract infection, uropathogen

Citation: Leventoğlu E, Soran M, Tüter Öz ŞK, Böncüoğlu E, Bağcı Z. The relationship between uropathogens and clinical characteristics of children with urinary tract infection. Health Sci Q. 2024;4(4):293-304. https://doi.org/10.26900/hsq.2502

Corresponding Author:
Emre Leventoğlu
Email: dremrelevent@gmail.com

Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections in pediatrics [1]. Due to the rising antibiotic resistance among uropathogens, UTI is now considered a public health concern [2]. Although diagnosing and treating UTI might seem straightforward, there are important points that cause confusion in pediatrics. The clinical manifestations are highly varied, including symptoms such as dysuria, frequent urination, incontinence, fever, or flank pain [3]. UTIs are most prevalent in infancy, with another peak occurring in the toddler years and third rise during adolescence. UTIs affect 2% of boys up to the age of 7 years, 4 times more in girls. Additionally, UTI recurs at least once in up to 30% of children who experience it [2,4]. The frequency of UTIs and the likelihood of recurrence increase significantly, particularly in the presence of anatomical abnormalities in the urinary system [5]. Urine sampling plays a crucial role in diagnosing UTI. A positive urinalysis for nitrite or nitrite combined with leukocyte esterase is highly specific for diagnosing UTI and for initiating empirical antibiotic therapy [6]. Antibiotic selection is one of the most important aspects of UTI treatment and should be guided by previously established resistance patterns in the relevant region [7]. Antibiotic prophylaxis may be indicated for patients who have a history of recurrent UTIs, defined as three or more infections per year or those with high-grade vesicoureteral reflux (VUR) (grades 4-5). Although there is a recent trend to minimize the use of prophylactic antibiotics, using them in certain situations can help avert long-term issues like hypertension and chronic kidney disease [8]. In this study, the potential correlations between clinical and laboratory characteristics and causative microorganisms in pediatric patients diagnosed with UTI were evaluated.

Materials and Methods

In this study, we retrospectively evaluated children who admitted to Pediatric Nephrology/ Infection departments of Konya City Hospital between January 2019 and January 2024 with UTI with a single microorganism growth in urine culture. Patients with no growth in urine culture, or in whom growth was considered as contamination, and patients with known immunodeficiency were excluded. In infants during their first year, the symptoms of a urinary tract infection (UTI) have been characterized by fever, hypothermia, apnea, bradycardia, lethargy and vomiting. For older children, lower urinary tract symptoms included dysuria, stranguria, increased frequency of voiding, foul-smelling urine, incontinence, hematuria, and suprapubic pain, while upper urinary tract symptoms were characterized by fever and flank pain [9]. For patients with recurrent UTIs, only the results from the most recent infection episode were included in the analysis. Additionally, it was recorded whether the patients underwent clean intermittent catheterization (CIC) for urinary drainage and whether they received prophylactic antibiotics for UTI prevention. The results of urinary ultrasonography (USG), voiding cystoureterography (VCUG) and Tc-99m mercaptoacetyltriglycine (MAG-3) imaging, if performed previously, were analyzed for possible urinary system anomalies. Patients were divided into four main groups: normal anatomy, vesicoureteral reflux (VUR), ureteropelvic junction obstruction (UPJO) and neurogenic bladder (NB). Urine samples were collected through either midstream urine or bladder catheterization, with patients whose samples were obtained using a collection bag excluded from the study. Urinalysis was conducted using the LabUMat & Urised Complete Urine Analysis System, recording leukocyte count, presence of bacteriuria, and results for leukocyte esterase and nitrite. Pyuria was characterized by a leukocyte count of 5/HPF or more in urinalysis and/or leukocyte esterase positivity in the dipstick test [4,6]. Bacteriuria was detected with an automated urine analyzer utilizing digital imaging. Quantitative urine cultures were established through standard microbiological methods. A positive urine culture from midstream urine was defined as one showing growth of a single organism at least 100,000 cfu/mL or ≥50,000 cfu/mL accompanied by pyuria [9]. Additionally, a UTI was diagnosed when bladder catheterization yielded growth of a single microorganism at least 10,000 cfu/mL [10]. Since it is not sufficient to diagnose UTI in patients with CIC by depending solely on

pyuria or urine culture results, the diagnosis in these patients was made with the presence of symptoms compatible with UTI and an increase in acute phase reactants in addition to pyuria and culture positivity [11,12]. Antibiograms were performed using the disk diffusion method. The antibiogram panel included ampicillin, amikacin, ceftriaxone, cefixime, carbapenem, trimethoprim-sulfamethoxazole (TMP-SMX), nitrofurantoin, and ciprofloxacin. The extended-spectrum beta-lactamase (ESBL) positivity was noted based on antibiogram results, and antimicrobial susceptibility test results was noted. The results of acute phase reactants, specifically white blood cell (WBC) and C-reactive protein (CRP), obtained at the time of hospital visits when patients were diagnosed with UTI, were recorded. Normal reference ranges are 4000-1000/uL for WBC and <0.5 mg/dL for CRP [13]. The results of blood and urine tests, anatomical and functional pathologies of the urinary system detected by imaging methods, whether or not CIC was performed, and whether or not antibiotic prophylaxis was used were compared. In addition, we analyzed whether there was a difference between blood and urine test results according to the microorganisms in urine culture. Antibiogram results of uropathogens were also evaluated, and their resistance status was analyzed according to underlying anatomical or functional pathologies. Whether hospitalization for UTI treatment was performed was noted and the laboratory results were compared with the hospitalization status. The study received approval from the Education Planning Commission of Konya City Hospital and KTO Karatay University, Faculty of Medicine Ethics Committee (Date: 30.01.2024, No: 77856).

Statistical Analysis

Descriptive statistics were reported as counts and percentages for categorical variables, and as medians for continuous variables that did not follow a normal distribution. Continuous variables with a normal distribution were presented as means with standard deviations. The Chi-square test was employed to analyze categorical variables. Differences between two groups for non-normally distributed continuous variables were evaluated using the *Mann-Whitney U test*, whereas the Student's t-test was applied to normally distributed ones. Data analysis was performed using IBM SPSS Version 25.0, and a *p*-value below 0.05 was deemed statistically significant.

Results

The study involved a total of 266 children diagnosed with UTIs. The majority were female (n=234, 88%). The mean age was 6.87 ± 4.66 years (median: 7 years old, min-max: 0.25-16.5 years old). Among the patients, 62 (23.3%) had not yet completed toilet training due to their young age. NB was the most prevalent urinary tract condition, affecting 116 patients (43.3%). Of the patients with NB, 91 (78.4%) had undergone surgery for meningomyelocele, and 53 (45.7%) were using CIC for urination. Prophylactic antibiotics for UTIs were administered to 24 patients (9%), all of whom were NB patients undergoing CIC. Other urinary system anomalies included VUR in 29 patients (10.9%) and UPJO in 24 patients (9%). As anticipated, the median levels of WBC, CRP, and urinary leukocytes were elevated. Median WBC count was 11459/uL, CRP was 12.1 mg/dL and median urine leukocyte count was 61/HPF. (Table 1).

In our study, when analyzed according to UTI risk factors, median acute phase reactants were highest in patients with UPJO (median WBC 15800/uL, median CRP 100.3 mg/dL) and lowest in patients without pathology (median WBC 8300/uL, median CRP 6.7 mg/dL) (p=0.004 for WBC and p=0.049 for CRP). In urinalysis, median leukocyte count was higher in patients with NB (117/HPF) compared to other pathologies and it was the lowest in the VUR group (25/HPF) (p=0.006). Leukocyte esterase positivity (91.7%, p=0.204) was more frequent in UPJO, nitrite positivity (54.3%, p=0.004) in NB and bacteriuria (86.2%, p=0.001) in VUR compared to other pathologies. The median WBC and CRP were elevated in CIC compared to non-CIC group (median WBC: 17100/uL vs 11100/uL, p=0.023 and median CRP: 89 mg/dL vs 10.8 mg/dL, p=0.002). Leukocyte esterase, nitrite positivity and bacteriuria were similarly found more frequently in patients who performed CIC compared to patients who did not (p=0.013, p=0.122 and p=0.002, respectively).

Table 1. Laboratory values according to patient characteristics.

	Blood						Urine									
	WBC			CRP			Leukocyte			LE		Nitrite		Bacteriuria		
	Median - IQR	Min-Max	*p* value	Median - IQR	Min-Max	*p* value	Median - IQR	Min-Max	*p* value	n (%)	*p* value	n (%)	*p* value	n (%)	*p* value	
General	11459 - 8210	4640 - 39690	-	12.1 - 72.7	0.6 - 314.1	-	61 - 356	0 - 4466	-	204 (76.7)	-	124 (46.6)		170 (63.9)	-	
Urinary system pathology																
NB *(n=116)*	11600 - 6355	5890 - 28100	**0.004**	29 - 72.6	0.61 - 284.4	**0.049**	117 - 657	0 - 4466	**0.006**	85 (73.3)	0.204	63 (54.3)	**0.004**	81 (69.8)	**0.001**	
VUR *(n=29)*	9185 - 9440	5400 - 30560		8 - 80.9	0.66 - 172		28 - 171	1 - 4098		23 (79.3)		15 (51.7)		25 (86.2)		
UPJS *(n=24)*	15800 - 5797	8080 - 34010		100.3 - 167.8	1.5 - 200		51 - 67	2 - 723		22 (91.7)		4 (16.7)		10 (41.7)		
No pathology *(n=97)*	8300 - 8055	4640 - 39640		6.7 - 44.7	0.6 - 314.1		46 - 210	0 - 2544		74 (76.3)		42 (43.3)		54 (55.7)		
CIC																
Patients who performed *(n=53)*	17100 - 7830	6610 - 20290	**0.023**	89 - 139.6	0.61 - 284.4	**0.002**	79 - 1057	1 - 2449	0.763	47 (88.7)	**0.013**	29 (54.7)	0.122	43 (81.1)	**0.002**	
Patients who did not *(n=213)*	11100 - 7010	4640 - 39690		10.8 - 64.3	0.6 - 314.1		55 - 266	0 - 4466		157 (73.7)		95 (44.6)		127 (59.6)		
Prophylaxis																
Patients who used *(n=24)*	19240 - 3200	9270 - 20290	**0.001**	103.6 - 95	0.61 - 284.4	**0.001**	105 - 1754	3 - 2449	0.147	22 (10.8)	**0.050**	13 (10.5)	0.286	20 (11.8)	**0.028**	
Patients who did not *(n=242)*	11360 - 7252	4640 - 39690		10.5 - 64.4	0.6 - 314.1		55 - 312	0 - 4466		2 (3.2)		11 (7.7)		4 (4.2)		
Uropathogens																
E.coli *(n=173)*	11360 - 8560	4640 - 28100	**0.000**	34.9 - 95.5	0.6 - 314.1	**0.021**	65 - 355	0 - 3795	0.500	140 (80.9)	**0.001**	86 (49.7)	**0.000**	119 (68.8)	**0.013**	
Klebsiella spp. *(n=50)*	11480 - 2200	5890 - 21380		3.9 - 38.4	0.91 - 152.4		50 - 569	0 - 4466		36 (72)		30 (60)		30 (60)		
Proteus spp. *(n=13)*	10840 - 11065	5450 - 34010		1.4 - 137.4	0.86 - 166.9		39 - 157	1 - 2446		12 (92.3)		4 (30.8)		7 (53.8)		
Enterococcus spp. *(n=8)*	10595 - 4863	7290 - 12750		8.2 - 22.5	0.6 - 29		87 - 179	11 - 210		2 (25)		0 (0)		6 (75)		
Pseudomonas spp. *(n=20)*	17010 - 21660	8000 - 39690		9.6 - 29.1	1.52 - 54.4		44 - 189	0 - 4098		14 (63.6)		4 (18.1)		6 (27.2)		

WBC, White blood cell; CRP, C-reactive protein; LE, Leukocyte esterase; NB, Neurogenic bladder; VUR, Vesicoureteral reflux; UPJS, Ureterovesical junction stenosis; CIC, Clean intermittent catheterization. Bolded *p* values are statistically significant.

Table 2. Growth rates of uropathogens according to patient characteristics.

	E.coli	*Klebsiella spp.*	*Proteus spp.*	*Enterococcus spp.*	*Pseudomonas spp.*	*Morganella spp.*	*p* value
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
General	173 (65)	50 (18.8)	13 (4.9)	8 (3)	20 (7.5)	2 (0.8)	-
Urinary system pathology							
NB *(n=116)*	63 (54.3)	34 (29.3)	6 (5.2)	3 (2.6)	8 (6.9)	2 (1.7)	**0.004**
VUR *(n=29)*	20 (69)	2 (6.9)	0 (0)	3 (10.3)	4 (13.8)	0 (0)	
UPJS *(n=24)*	16 (66.7)	6 (25)	2 (8.3)	0 (0)	0 (0)	0 (0)	
No pathology *(n=97)*	74 (76.3)	8 (8.2)	5 (5.2)	2 (2.1)	8 (8.2)	0 (0)	
CIC							
Patients who performed *(n=53)*	41 (77.4)	6 (11.3)	2 (3.8)	0 (0)	4 (7.5)	0 (0)	0.139
Patients who did not *(n=213)*	132 (62)	44 (20.7)	11 (5.2)	8 (3.8)	16 (7.5)	2 (0.9)	
Prophylaxis							
Patients who used *(n=24)*	20 (83.3)	0 (0)	2 (8.3)	0 (0)	2 (8.3)	0 (0)	**0.022**
Patients who did not *(n=242)*	153 (63.2)	50 (20.7)	11 (4.5)	8 (3.3)	18 (7.4)	2 (0.8)	

NB, Neurogenic bladder; VUR, Vesicoureteral reflux; UPJS, Ureterovesical junction stenosis; CIC, Clean intermittent catheterization. Bolded *p* values are statistically significant.

Table 3. Antibiotic resistance status of common uropathogens according to patient characteristics.

	Ampicilin		**Amikacin**		**Ceftriaxone**		**Cefixime**		**TMP-SMX**		**Nitrofurantoin**		**Carbapenem**		**Ciprofloxacin**	
Uropathogens	**n (%)**	***p* value**	**n (%)**	***p* value**	**n (%)**	***p* value**	**n (%)**	***p* value**	**n (%)**	***p* value**	**n (%)**	***p* value**	**n (%)**	***p* value**	**n (%)**	***p* value**
E.coli																
General	122 (70.5)	-	5 (7.5)	-	58 (58.5)	-	72 (63.7)	-	79 (45.6)	-	6 (3.7)	-	2 (2.6)	-	35 (34.6)	-
CIC (+)	31 (75.6)	**0.030**	1 (7.6)	0.055	11 (73.3)	**0.025**	15 (71.4)	**0.032**	30 (73.1)	**0.000**	2 (5.1)	0.324	0 (0)[c]	0.323	8 (38.1)	0.296
CIC (-)	91 (68.9)		4 (7.5)		47 (55.9)		57 (61.9)		49 (37.1)		4 (3.2)		2 (3.2)		27 (33.7)	
Prophylaxis (+)	16 (80)	**0.028**	1 (16.6)	0.092	6 (66.6)	**0.033**	8 (72.2)	**0.044**	13 (65)	**0.004**	0 (0)[b]	0.456	0 (0)[d]	0.266	3 (27.2)	0.565
Prophylaxis (-)	106 (69.3)		4 (6.6)		52 (57.7)		64 (62.7)		66 (43.1)		6 (4.1)		2 (2.9)		32 (35.5)	
Klebsiella spp.																
General	50 (100)	-	6 (15.7)	-	26 (68.4)	-	28 (70)	-	28 (56)	-	28 (56)	-	0 (0)[e]	-	20 (50)	-

Table 3. (continued) Antibiotic resistance status of common uropathogens according to patient characteristics.

CIC (+)	6 (100)	**0.000**	0 (0)[a]	0.221	2 (50)	0.082	2 (100)	0.080	2 (33.3)	0.226	2 (33.3)	0.440	0 (0)[f]	0.247	0 (0)[i]	0.160
CIC (-)	44 (100)		6 (17.6)		24 (70.5)		26 (68.4)		26 (59)		26 (59)		0 (0)[g]		20 (55.5)	
Prophylaxis (+)	-	-	-	-	-	-	2 (100)	0.151	-	-	-	-	-	-	-	-
Prophylaxis (-)	50 (100)		6 (15.7)		26 (68.4)		28 (70)		28 (56)		28 (56)		0 (0)[h]		20 (50)	

[a] n=4, [b] n=19, [c] n=15, [d] n=8, [e] n=40, [f] n=2, [g] n=38, [h] n=40, [i] n=4

TMP-SMX, Trimethoprim-sulfamethoxazole; CIC, Clean intermittent catheterization.

Bolded *p* values are statistically significant.

The median WBC and CRP values were elevated in patients who used antibiotic prophylaxis compared to those who did not (median WBC: 19240/uL vs 11360/uL, and median CRP: 103.6 mg/dL vs 10.5 mg/dL, *p*=0.001 for both) (Table 1).

The most common bacteria grown in urine culture was *E. coli* (n=173, 65%), followed by *Klebsiella spp.* (18.8%), *Pseudomonas spp.* (7.5%) and *Proteus spp.* (4.9%). Based on the anatomical structure, the prevalence of *E. coli* was 76.3% in patients without any pathology, followed by *Klebsiella spp.* with a frequency of 8.2%. While *E. coli* is still the most common uropathogen in NB and UPJO (54.3% and 66.7%, respectively), *Klebsiella spp.* are also quite prevalent in these conditions (29.3% and 25%, respectively). *Morganella spp.* grew in 2 patients and these patients were patients with NB who did not perform CIC or did not use prophylaxis (*p*=0.004). There was no notable difference of microorganisms between patients with and without CIC. However, the incidence of *E. coli* was higher among patients who used antibiotic prophylaxis than in those who did not use prophlaxis. *Klebsiella spp.*, *Enterococcus spp.*, and *Morganella spp.* were not isolated in patients

Table 4. ESBL rates according to patient characteristics.

	ESBL positivity	
	n (%)	***p* value**
General	108 (40.6)	-
Urinary system pathology		
NB *(n=116)*	47 (40.5)	**0.002**
VUR *(n=29)*	9 (31)	
UPJS *(n=24)*	14 (58.3)	
No pathology *(n=97)*	38 (39.2)	
CIC		
Patients who performed *(n=53)*	19 (35.8)	0.097
Patients who did not *(n=213)*	89 (41.8)	
Prophylaxis		
Patients who used *(n=24)*	9 (37.5)	0.111
Patients who did not *(n=242)*	99 (40.9)	
Uropathogens		
E.coli (n=173)	76 (43.9)	**0.000**
Klebsiella spp. (n=50)	28 (56)	
Proteus spp. (n=13)	4 (30.8)	
Enterococcus spp. (n=8)	0 (0)	
Pseudomonas spp. (n=20)	0 (0)	

ESBL, Extended-spectrum beta-lactamase; NB, Neurogenic bladder; VUR, Vesicoureteral reflux; UPJS, Ureterovesical junction stenosis; CIC, Clean intermittent catheterization.

Bolded *p* values are statistically significant.

who used prophylaxis (p=0.022) (Table 2).

When comparing uropathogens identified in urine cultures with laboratory data, it was found that the median WBC count was higher in infections caused by *Pseudomonas spp.* (17010/uL), while the CRP level was elevated in *E. coli* infections (63.9 mg/dL) compared to other microorganisms (p=0.000 and p=0.021, respectively) (Table 1).

In the evaluations made to compare uropathogen and antibiotic resistance, most of the *E.coli* were resistant to ampicillin, ceftriaxone and cefixime antibiotherapies (70.5%, 58.5% and 63.7%, respectively); TMP-SMX and ciprofloxacin resistance was 45.6% and 34.6%, respectively, while amikacin, nitrofurantoin and carbapenem resistance remained at low levels (7.5%, 3.7% and 2.6%, respectively). It was noticed that all *Klebsiella spp.* were ampicillin resistant and, carbapenem resistance was not observed. Ampicillin, ceftriaxone, cefixime and TMP-SMX resistance rates of *E. coli* were markedly higher in patients who performed CIC compared to those who did not. Similarly, resistance rates to the same antibiotics were higher in patients who used antibiotic prophylaxis compared to those who did not. The overall TMP-SMX resistance rate in the study was 44.7% and increased to 54.5% in patients receiving TMP-SMX prophylaxis (p=0.044) (Table 3).

ESBL positivity was observed in 40.6% of all patients. In the evaluation according to anatomical stractures, it was most frequently (58.3%) observed in the UPJO and lowest in VUR (31%) (p=0.002). ESBL positivity was not observed in *Enterococcus spp.* and *Pseudomonas spp.* infections, while 56% in *Klebsiella spp.*, 43.9% in *E.coli* infection and 30.8% in *Proteus spp.* (p=0.000). No significant correlation was found between the CIC/prophylactic antibiotics for ESBL positivity (Table 4).

The number of patients requiring hospitalization for UTI was 93 (34.9%). The largest proportion of hospitalized patients (n=46, 49.4%) were diagnosed with NM. While 39.6% (n=46) of patients with NM, 31% (n=9) of patients with VUR and 79.1% (n=19) of patients with UPJS were hospitalized, 19.5% (n=19) of patients with no underlying pathology were hospitalized (p=0.035). Also, 39 (73.5%) of the patients who performed CIC were hospitalized due to UTI, only 7 (3.2%) of the patients who did not perform CIC were hospitalized (p=0.001). The rate of hospitalization due to UTI was significantly higher in patients who used antibiotic prophylaxis than in patients who did not use prophylaxis (62.5% vs 32.2%, p=0.025). Median WBC and CRP values of inpatients were significantly higher than outpatients (13350/uL vs 7580/uL for WBC, p=0.001 and 35.4 mg/dL vs 16.4 mg/dL for CRP, p=0.005). Similarly, the pyuria was higher in hospitalized patients (177/HPF vs 41/HPF, p=0.002). Furthermore, hospitalization was required in 26.5% (n=46) of patients with *E.coli*, 56% (n=28) of patients with *Klebsiella spp.*, 15.3% (n=2) of patients with *Proteus spp.* and 85% (n=17) of patients with *Pseudomonas spp.* (p=0.023).

Discussion

Urinary tract infection is a significant cause of antibiotic use and hospitalization among children. While UTIs are more common in male infants younger than 12 months of age, the gender ratio shifts, with females being more affected after the age of one year [14]. In one study, 89% of patients with symptomatic UTIs were girls [15]. Our study also found a similar female predominance, with 88% of patients being female. Gram-negative bacteria are the primary culprits of UTIs, with the frequency of *E. coli* reported between 68.5% and 90% in previous studies [15-18]. Consistent with existing literature, *E. coli* was the most common bacteria in our study, followed by *Klebsiella spp.*, *Pseudomonas spp.*, and *Proteus spp*. Acute phase reactants are increased in UTI as in all infections [19]. When there is an anatomical disorder in the urinary system such as obstruction, hydronephrosis, fistula, when there is a foreign body such as ureteric stent, suprapubic tube or urethral catheterization, or when antibiotic resistance is high due to recurrent UTI, the risk of complicating UTI is high and a higher increase in acute phase reactants is expected [20,21]. In this study, WBC and CRP, which are acute phase markers, were measured at the lowest levels in patients without urinary tract anatomical disorders. Acute phase

reactants were found to be higher when UTI developed in patients who performed CIC or used prophylactic antibiotics. Pyuria is a key diagnostic criterion for UTIs, but in the absence of pyuria, the patient should be considered as UTI if clinical findings are compatible and urine culture shows significant growth [22,23]. In our study, although urine leukocyte levels increased up to >4000/HPF in some patients, no pyuria was detected in some of them. Because, our patients continued to be monitored at regular intervals, were admitted to the hospital without delay in case of any symptoms compatible with UTI, and urine samples were collected before an increase in urinary tract inflammation. In our study, the mean leukocyte count in urine during a UTI was higher in NB compared to those with other urinary tract anatomical disorders. However, a previous study demonstrated that pyuria could be seen in NB even in the absence of UTI and it was reported that additional markers besides pyuria are necessary to diagnose as UTI [11]. Another study showed that pyuria was more common in patients requiring CIC [12]. In our study, the mean urinary leukocyte count was higher in patients with CIC compared to those without, although not statistically significant. Similarly, pyuria levels during UTI were higher in patients with prophylactic antibiotics compared to those without. It is notable that the antibiotic resistance rates of microorganisms, especially in *E. coli* infection, were higher in patients who performed CIC or used antibiotic prophylaxis in our study. It may be considered that urinary system inflammation is higher in these patients due to resistant microorganisms and pyuria may be at higher levels as in acute phase reactants. Nitrite positivity is highly specific in the diagnosis of UTI, but it is not seen in some microorganisms such as *Enterococcus spp* [24]. In our study, nitrite positivity was not detected in *Enterococcus spp.* infection. Therefore, it should not be ignored that patients with nitrite negative findings may also have UTI. Bacterial positivity in a fresh urine sample that has not been centrifuged indicates that >100000 CFU bacteria will grow in urine culture. Bacteriuria is found more frequently in *E. coli* and *Klebsiella spp.* Infections [24]. In our study, bacteriuria was observed in the majority of patients with infections caused by *E. coli*, *Klebsiella spp.*, and *Enterococcus spp.* The antibiotic resistance has been increasing in UTIs in recent decades [25]. Especially ampicillin and TMP-SMX resistance is quite high [26]. Morover, ceftriaxone and cefixime resistance were also observed at high rates. Antibiotic resistances were higher in patients with CIC or prophylactic antibiotics compared to those without. In last years, ESBL-positivity for *E. coli* and *Klebsiella spp.* have been increasing. For example, ESBL positivity was 69% in *E. coli* and 50% in *Klebsiella spp*. in a study [27]. In our study, *E. coli* and *Klebsiella spp.* were the most common microorganisms. Therefore, it may be wise not to use a beta-lactam antibiotic such as ceftriaxone in empirical treatment in a patient with UTI. However, the empirical use of antibiotics with lower resistance rates such as amikacin and carbapenem in first-line treatment will increase resistance rates in the following years.

Conclusion

Urinary tract infection is a common condition in childhood with high morbidity. It is essential to assess each patient's risk factors for UTI and to start appropriate treatment. However, any treatment administered might contribute to an increase in existing resistance rates or potentially lead to the emergence of new resistance in the future.

Acknowledgment

The preliminary version of this study was presented as an oral presentation at the 12th International Gevher Nesibe Health Sciences Congress, Ankara, Türkiye on 19/02/2024.

Funding

The authors received no financial support for the research, authorship, and/or publication

of this study.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this study.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. Korbel L, Howell M, Spencer JD. The clinical diagnosis and management of urinary tract infections in children and adolescents. Paediatr Int Child Health. 2017;37:273-9. doi: 10.1080/20469047.2017.1382046.
2. Millner R, Becknell B. Urinary tract infections. Pediatr Clin North Am. 2019;66:1-13. doi: 10.1016/j.pcl.2018.08.002.
3. Autore G, Bernardi L, La Scola C, Ghidini F, Marchetti F, Pasini A, et al. Management of pediatric urinary tract infections: A Delphi study. Antibiotics (Basel). 2022;11:1122. doi: 10.3390/antibiotics11081122.
4. Montini G, Tullus K, Hewitt I. Febrile urinary tract infections in children. N Engl J Med 2011;365:239-50. doi: 10.1056/NEJMra1007755.
5. Balighian E, Burke M. Urinary tract infections in children. Pediatr Rev. 2018;39:3-12. doi: 10.1542/pir.2017-0007.
6. Williams GJ, Macaskill P, Chan SF, Turner RM, Hodson E, Craig JC. Absolute and relative accuracy of rapid urine tests for urinary tract infection in children: A Meta-analysis. Lancet Infect Dis. 2010;10:240-50. doi: 10.1016/S1473-3099(10)70031-1.
7. Strohmeier Y, Hodson EM, Willis NS, Webster AC, Craig JC. Antibiotics for acute pyelonephritis in children. Cochrane Database Syst Rev. 2014;CD003772. doi: 10.1002/14651858.CD003772.pub4.
8. Mattoo TK, Shaikh N, Nelson CP. Contemporary management of urinary tract infection in children. Pediatrics. 2021;147:2020012138. doi: 10.1542/peds.2020-012138.
9. Montini G, Spencer JD, Hewitt IK. Urinary Tract Infections in Children. In: Emma F, Goldstein SL, Bagga A, Bates CM, Shroff R (eds). Pediatric Nephrology. 8th ed. Switzerland: Springer Nature, 2022: 1323-42.
10. Buettcher M, Trueck J, Niederer-Loher A, Heininger U, Agyeman P, Asner S, et al. Swiss Consensus recommendations on urinary tract infections in children. Eur J Pediatr. 2021;180:663-74. doi: 10.1007/s00431-020-03714-4.
11. Stein R, Dogan HS, Hoebeke P, Kočvara R, Nijman RJ, Radmayr C, et al. Urinary tract infections in children: EAU/ESPU guidelines. Eur Urol. 2015;67:546-58. doi: 10.1016/j.eururo.2014.11.007.
12. Su RR, Palta M, Lim A, Wald ER. Pyuria as a marker of urinary tract infection in neurogenic bladder: Is it reliable? Pediatr Infect Dis J. 2019;38:804-7. doi: 10.1097/INF.0000000000002370.
13. Sherkatolabbasieh H, Firouzi M, Shafizadeh S. Evaluation of platelet count, erythrocyte sedimentation rate and C-Reactive protein levels in paediatric patients with inflammatory and infectious disease. New Microbes New Infect. 2020;37:100725. doi: 10.1016/j.nmni.2020.100725.
14. Brandström P, Hansson S. Urinary tract infection in children. Pediatr Clin North Am. 2022;69:1099-114. doi: 10.1016/j.pcl.2022.07.003.
15. S Shaikh N, Shope TR, Hoberman A, Vigliotti A, Kurs-Lasky M, Martin JM. Association between uropathogen and pyuria. Pediatrics. 2016;138:20160087. doi: 10.1542/peds.2016-0087.
16. Kenosi M, Whitla L, Khan N, Carty E, Coghlan D, Nadeem M. Interpretation of pyuria in children with urinary tract infection. Acta Paediatr. 2018;107:358. doi: 10.1111/apa.14133.
17. Koçak M, Büyükkaragöz B, Çelebi Tayfur A, Çaltik A, Köksoy AY, Çizmeci Z, et al. Causative pathogens and antibiotic resistance in children hospitalized for urinary tract infection. Pediatr Int. 2016;58:467-71. doi: 10.1111/ped.12842.
18. Yilmaz Y, Tekkanat Tazegun Z, Aydin E, Dulger M. Bacterial uropathogens causing urinary tract infection and their resistance patterns among children in Turkey. Iran Red Crescent Med J. 2016;18:26610. doi: 10.5812/ircmj.26610.
19. Erol B, Culpan M, Caskurlu H, Sari U, Cag Y, Vahaboglu H, et al. Changes in antimicrobial resistance and demographics of utis in pediatric patients in a single institution over a 6-year period. J Pediatr Urol. 2018;14:176.e1-176.e5. doi: 10.1016/j.jpurol.2017.12.002.
20. Shaikh N, Liu H, Kurs-Lasky M, Forster CS. Biomarkers for febrile urinary tract infection in children. Pediatr Nephrol. 2022;37:171-7. doi: 10.1007/s00467-021-05173-x.
21. Foxman B. Urinary tract infection syndromes:

Occurrence, recurrence, bacteriology, risk factors, and disease burden. Infect Dis Clin North Am. 2014;28:1-13. doi: 10.1016/j.idc.2013.09.003.

22. Darogha SN, Azeez SH, Abdullah ZG. Evaluation of procalcitonin and interleukin-6 as a marker of bacterial urinary tract infection. Cell Mol Biol (Noisy-le-grand). 2022;67:203-13. doi: 10.14715/cmb/2021.67.4.23.

23. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, Roberts KB. Urinary Tract Infection: Clinical Practice Guideline for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months. Pediatrics. 2011;128:595-610. doi: 10.1542/peds.2011-1330.

24. Forster CS, Shaikh N, Hoberman A, Jackson E. Uropathogens and pyuria in children with neurogenic bladders. Pediatrics. 2018;141:20173006. doi: 10.1542/peds.2017-3006.

25. Ünsal H, Kaman A, Tanır G. Relationship between urinalysis findings and responsible pathogens in children with urinary tract infections. J Pediatr Urol. 2019;15:606.e1-606.e6. doi: 10.1016/j.jpurol.2019.09.017.

26. Esposito S, Biasucci G, Pasini A, Predieri B, Vergine G, Crisafi A, et al. Antibiotic resistance in paediatric febrile urinary tract infections. J Glob Antimicrob Resist. 2022;29:499-506. doi: 10.1016/j.jgar.2021.11.003.

27. Pouladfar G, Basiratnia M, Anvarinejad M, Abbasi P, Amirmoezi F, Zare S. The antibiotic susceptibility patterns of uropathogens among children with urinary tract infection in Shiraz. Medicine (Baltimore). 2017;96:7834. doi: 10.1097/MD.0000000000007834.