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ORIGINAL ARTICLE

Evaluation of Urinary Tract Infections in Pediatric Patients Admitted to the Emergency Department

Çocuk Acile Başvuran Hastalarda İdrar Yolu Enfeksiyonlarının Değerlendirilmesi

[1]Aysun Tekeli, [2]Bedriye Nuray Alpman, [3]Merve Tırıs, [3]Hilal Işık, [2]Cengiz Zeybek

[1]Department of Pediatric Emergency Medicine, University of Health Sciences Gulhane Training and Research Hospital in Ankara, Türkiye
[2]Department of Pediatric Nephrology, University of Health Sciences Gulhane Training and Research Hospital in Ankara, Türkiye
[3]Department of Pediatric Health and Diseases University of Health Sciences Gulhane Training and Research Hospital in Ankara, Türkiye

Correspondence

Aysun Tekeli, Department of Pediatric Emergency Medicine, University of Health Sciences Gulhane Training and Research Hospital in Ankara, Türkiye

E-Mail: aysunnakay@yahoo.com.tr

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ABSTRACT

Background/Aim: Urinary tract infections (UTIs) are among the most common infections in children and one of the important reasons for admission to the pediatric emergency department. This study aimed to determine demographic characteristics, complaints, microorganisms isolated in urine culture analysis, and antibiotic resistance rates in pediatric patients diagnosed with UTIs.
Material and Method: The data of patients aged 1 month to 18 years, who presented to our hospital from January 1, 2020, through December 31, 2020 with a preliminary diagnosis of UTIs and underwent urine culture analysis, were retrospectively screened from the computer registry system. The patients' demographic characteristics, complaints, microorganisms isolated in urine culture analysis, and antibiotic resistance were evaluated.
Results: The mean age of the 286 patients included in the study was 76.95±8.64 months, and 238 (83.2%) were girls. The most common complaint at admission was dysuria (39.9%), followed by fever (35.3%) and abdominal pain (26.9%). In urine culture analysis, the most frequently detected microorganisms were Escherichia coli (n=242, 84.6%), Proteus spp. (n=21, 7.3%), and Klebsiella spp. (n=16, 5.6%). The highest antibiotic resistance was observed in ampicillin (54.9%) and the lowest in amikacin (5.6%).
Conclusion: Inappropriate treatment choices in UTIs are important in terms of complications that may occur in future. Therefore, healthcare centers should evaluate their own infectious agents and antibiotic susceptibility at certain intervals and determine appropriate empirical treatment choices. Empirically initiated treatments should be re-evaluated according to urine culture and sensitivity results.

Keyword: Children, emergency department, treatment, urinary tract infections

ÖZ

Giriş: İdrar yolu enfeksiyonları çocuklarda en sık görülen enfeksiyonlardandır ve çocuk acil servisine başvuruların önemli nedenlerinden biridir. Çalışmamızda, idrar yolu enfeksiyon tanısı alan hastaların demografik özellikleri, yakınmaları, idrar kültüründe izole edilen mikroorganizmalar ve antibiyotik direnç oranlarının belirlenmesi amaçlanmıştır.
Materyal metod: 01.01.2020 – 31.12.2020 tarihlerinde hastanemize başvuran İYE ön tanısıyla tam idrar tetkiki ve idrar kültürü alınan 1ay-18 yaş arası hastaların verileri retrospektif olarak bilgisayar kayıt sisteminden tarandı. Hastaların demografik özellikleri, yakınmaları, idrar kültüründe izole edilen mikroorganizmalar ve antibiyotik dirençleri değerlendirildi.
Bulgular: Çalışmaya dahil edilen toplam 286 hastanın yaş ortalaması 76.95±8.64 ay ve 238'i (%83,2) kız idi. En sık başvuru yakınması %39,9 dizüri, %35,3 ateş ve %26,9 karın ağrısıydı. İdrar kültüründe en sık tespit edilen mikroorganizmalar; 242 (%84,6) hastada E. coli, 21 (%7,3) hastada Proteus spp. ve 16 (%5,6) hastada Klebsiella spp. idi. En yüksek direnç ampisiline %54,9 ve en düşük direnç amikasine %5,6 tespit edilmiştir.
Sonuç: İdrar yolu enfeksiyonlarında uygunsuz tedavi seçimleri ilerleyen dönemlerde ortaya çıkabilecek komplikasyonlar açısından önemlidir. Bu nedenle merkezler belirli aralıklar ile kendi enfeksiyon etkenlerini ve antibiyotik duyarlılıklarını takip ederek ampirik tedavi seçimlerini oluşturmalıdır. Ampirik başlanan tedavilerin idrar kültür ve duyarlılık sonucuna göre yeniden değerlendirilmesi gereklidir.

Anahtar Kelimeler: Acil servis, çocuk, idrar yolu enfeksiyonu, tedavi

Introduction

Urinary tract infections (UTI) are one of the most common infections in childhood (1). The incidence of UTIs in children varies according to age and gender, with these infections being more commonly seen in boys in the first months of life and in girls in later periods. They most frequently occur in the infantile period and second most frequently during the periods of toilet training and adolescence (2). UTIs may have a mild course presenting with simple cystitis or progress to pyelonephritis and even sepsis. In UTIs, the most frequently isolated uropathogen is Escherichia coli, followed by Proteus, Klebsiella, Pseudomonas, and Enterobacter species. The early diagnosis and appropriate treatment of UTIs are important for the prevention of morbidities, such as renal scarring, chronic renal failure, and hypertension (3,4). Most patients with UTIs, especially those under the age of one year, present with non-specific complaints to the pediatric emergency department, where their examinations are planned and empirical treatment is initiated before the results of culture analysis are obtained.

In this study, it was aimed to determine effective treatment methods by evaluating the demographic characteristics, complaints, microorganisms isolated in urine culture analysis and antibiotic resistance rates of pediatric patients diagnosed with UTI in our center.

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Complaints: geneltip@selcuk.edu.tr

Material and Method

This study included patients aged one month to 18 years who presented to the pediatric emergency outpatient clinic of Gulhane Training and Research Hospital between January 1, 2020, and December 31, 2020. Complete urinalysis and urine culture data of pediatric patients who were considered to have UTIs based on anamnesis, complaints, and physical examination findings were retrospectively scanned from the hospital computer system. The patients' clinical histories, demographic characteristics, complete urinalysis and urine culture analysis results, and antibiotic susceptibility/resistance status were evaluated.

Pyuria was defined as the presence of five or more leukocytes in an objective area of 40 in the light microscopic examination of the urine sediment underlying after the centrifugation of the urine sample in complete urinalysis (5). Urine samples were taken using the mid-stream urine or catheterization method according to the patient's age, clinical condition, and international guidelines and cultured in the microbiology laboratory. Urine samples obtained with a bag were not included in the study. The antimicrobial susceptibility test results of the urine samples were generally available within 48-72 hours. The growth of a single microorganism of ≥ 50.000 colonies/ml in a sample collected by sterile bladder catheterization and 100.000 colonies/ml in midstream urine was considered as urine culture positivity (6,7).

Patients younger than one month and older than 18 years of age, those with a history of antibiotic use, and cases whose samples were suspected to have been contaminated were excluded from the study.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) software (version 23.0; SPSS, Inc. Chicago, IL, USA) was used to analyze the data obtained from the sample. Data obtained by measurements were expressed as mean ± standard deviation and median (minimum-maximum) values, and grouped data were expressed as numbers (percentages). Categorical data were examined using the χ^2 test or the Pearson chi-square test probability test. Statistical significance was considered as $p < 0.05$.

Ethical approval

To collect data, approval (2021/342) was obtained from the Clinical Research Ethics Committee of Gulhane Training and Research Hospital and official permission from the Turkish Medical Specialization Education Board.

Results

The mean age of the 286 patients included in the study was 76.95±8.64 months [the median age: 54 months (IQR, minimum-maximum) (111, 2-204 months)], and 238 (83.2%) were girls. Seventy-three patients (25.5%) were aged one to 24 months and 46 (63.1%) were girls, with 47 being younger than 12 months. There were 103 (36%) patients in the 25-84-months group and 92 (89.3%) were girls. The remaining 110 (38.5%) patients were 84 months and older and 100 (90.9%) were girls. A statistically significant difference was found between age groups and gender (p<0.001).

The most common complaints of the patients were dysuria (n = 114, 39.9%), fever (n = 101, 35.3%), abdominal pain (n = 77, 26.9%), and vomiting (n = 46, 16.1%). Table 1 shows the distribution of clinical presentation by age group. Twenty-two patients had upper respiratory tract infections, and 10 of these patients were younger than two years.

Table 1: Clinical presentation by age group

Age group (n, %)	Dysuria (n, %)	Abdominal pain (n, %)	Vomiting (n, %)	Fever (n, %)	Irritability (n, %)	Flank pain (n, %)	Pollakiuria (n, %)
1-24 months (n: 73; 25.5%)	11 (15.1)	4 (5.5)	7 (9.6)	41 (56.2)	21 (28.8)	-	1 (1.4)
25-84 months (n: 103; 36%)	58 (56.3)	30 (29.1)	20 (19.4)	38 (36.9)	1 (0.9)	2 (1.9)	4 (3.9)
≥84 months (n: 110; 38.5%)	45 (40.9)	43 (39.1)	19 (17.2)	22 (20)	-	9 (8.2)	4 (3.6)
Total (n:286)	114 (39.9)	77 (26.9)	46 (16.1)	101 (35.3)	22 (7.6)	11 (3.8)	9 (3.1)

Urinalysis revealed pyuria in 243 (84.9%) patients and nitrite positivity in 84 (29.4%). Leukocyte esterase positivity could not be evaluated because it is not assayed in the laboratory of our hospital. The most frequently detected microorganism was E. coli (n = 242, 84.6%), followed by Proteus spp. (n = 21, 7.3%), and Klebsiella spp. (n = 16, 5.6%). The frequency distribution of bacteria by age groups is presented in Table 2. There was no statistically significant difference between age groups and bacteria isolated in urine culture (p>0.05).

Antibiotic resistance of bacteria isolated from urine culture is presented in Table 3.

Sixty-three patients (22%) had a history of recurrent UTIs, 33 were older than 84 months and 55 were girls. In recurrent urinary tract infections, E. coli in 47 patients Klebsiella spp. in 7 patients, Proteus spp. in 5 patients, and 4 other bacteria (Enterobacter spp., Staphylococcus saprophyticus, Serratia marcescens, Acinetobacter pittii) were detected most frequently. The resistance rates were respectively ampicillin in 37 patients (58.7%), ACA in 26 patients (41.3%), Ceftriaxone in 20 patients (31.7%), TMP-SMX in 18 patients (28.6%), nitrofurantoin in 11 patients (17.5%), and amikacin in 3 patients (4.8%). Table 4 presents the recurrent UTI antibiotic resistance of bacteria that grew in urine culture samples. A significant difference was found in the rate of resistance to nitrofurantoin in urine culture in patients with recurrent urinary tract infections (p=0,026).

Ten patients were followed up in the inpatient ward. Eight of these patients were infants under two years of age and had a fever. The treatment and follow-up of all the remaining patients were planned in the outpatient setting.

Table 2: Distribution and frequency of bacteria according to age group

Uropathogens	Age group			p value	Total n:286
	0-24 months (n:73)	25-84 months (n:103)	≥84 months (n:110)		
	n %	n %	n %		n %
E. coli	57 (23.6)	92 (38)	93 (38.4)	0.126	242 (84.6)
Proteus spp.	10 (47.6)	6 (28.6)	5 (23.8)	0.051	21 (7.3)
Klebsiella spp	6 (37.5)	3 (18.8)	7 (43.7)	0.290	16 (5.6)
Other	-	2 (28.6)	5 (71.4)	0.137	7 (2.5)

Other: *Enterobacter spp. (n = 3), Staphylococcus saprophyticus (n = 2), Acinetobacter pittii (n = 1), Serratia marcescens (n = 1)*

Table 3: Antibiotic resistance of bacteria isolated from urine culture

Antibiotic	Susceptibility	*E. coli*	*Proteus* spp.	*Klebsiella* spp.	Other	Total
		(n: 242, 84.6%)	(n: 21, 7.3%)	(n: 16, 5.6%)	(n: 7, 2.5%)	(n: 286)
Ampicillin	Resistant	130 (53.7%)	8 (38.1%)	15 (93.7%)	4 (57.1%)	157 (54.9%)
	Susceptible	112 (46.3%)	13 (61.9%)	1 (6.3%)	3 (42.9%)	129 (45.1%)
Amoxicillin-clavulanate	Resistant	94 (38.8%)	3 (14.3%)	4 (25%)	4 (57.1%)	105 (36.7%)
	Susceptible	148 (61.2%)	18 (85.7%)	12 (75%)	3 (42.9%)	181 (63.3%)
TMP-SMX	Resistant	79 (32.6%)	6 (28.6%)	4 (25%)	1 (14.3%)	90 (31.5%)
	Susceptible	163 (67.4%)	15 (71.4%)	12 (75%)	6 (85.7%)	196 (68.5%)
Nitrofurantoin	Resistant	3 (1.2%)	19 (90.5%)	4 (25%)	1 (14.3%)	27 (9.4%)
	Susceptible	239 (98.8%)	2 (9.5%)	12 (75%)	6 (85.7%)	259 (90.6%)
Ceftriaxone	Resistant	64 (26.4%)	3 (14.3%)	5 (31.2%)	2 (28.6%)	74 (25.9%)
	Susceptible	178 (73.6%)	18 (85.7%)	11 (68.8%)	5 (71.4%)	212 (74.1%)
Amikacin	Resistant	13 (5.4%)	2 (9.5%)	1 (6.3%)	0 (0%)	16 (5.6%)
	Susceptible	229 (94.6%)	19 (90.5%)	15 (93.7%)	7 (100%)	270 (94.4%)

TMP-SMX: trimethoprim/sulfamethoxazole; Other: *Enterobacter spp. (n = 3), Staphylococcus saprophyticus (n = 2), Acinetobacter pittii (n = 1), Serratia marcescens (n = 1)*

Table 4: Antibiotic resistance of bacteria isolated from urine culture in recurrent urinary tract infection

Antibiotic	Susceptibility	Reccurent UTI	Non-recurrent UTI	p value
		(n: 63, %)	(n: 223, %)	
Ampicillin	Resistant	37 (58.7)	120 (53.8)	0.488
	Susceptible	26 (41.3)	103 (46.2)	
Amoxicillin- clavulanate	Resistant	26 (41.3)	79 (35.4)	0.483
	Susceptible	37 (58.7)	144 (64.6)	
TMP-SMX	Resistant	18 (28.6)	72 (32.3)	0.684
	Susceptible	45 (71.4)	151 (67.7)	
Nitrofurantoin	Resistant	11 (17.5)	16 (7.2)	**0.026**
	Susceptible	52 (82.5)	207 (92.8)	
Ceftriaxone	Resistant	20 (31.7)	54 (24.2)	0.297
	Susceptible	43 (68.3)	169 (75.8)	
Amikacin	Resistant	3 (4.8)	13 (5.8)	1.000
	Susceptible	60 (95.2)	210 (93.7)	
Gender				
Female	Resistant	55 (87.3)	183 (82.1)	0,429
Male	Susceptible	8 (12.7)	40 (17.9)	

TMP-SMX: trimethoprim/sulfamethoxazole; UTI: urinary tract infection

Discussion

UTIs rank second after upper respiratory tract infections in children and are one of the important reasons for pediatric admission to the emergency department (8,9). The frequency of UTIs varies according to age and gender. They can cause morbidities, such as renal scarring, growth retardation, chronic renal failure, and hypertension, as well as mortality by leading to the development of urosepsis. Therefore, the early diagnosis and appropriate treatment of UTIs are important, especially in younger children.

While UTIs are more common in boys in the first six months of life, their frequency increases significantly in girls in the following periods (10,11). In our study, 46 children aged under two years were girls and 27 were boys. In the group older than two years, the rate of girls with UTIs increased with age (girl/boy ratio: 8.4/1 for 25-84 months and 10/1 for 85 months and older. In our study, a statistically significant difference was found between age groups and gender. ($p<0.001$). We consider that we may have detected a lower rate of boys with UTIs in the first few years due to the exclusion of neonatal cases.

Children with UTIs may present to the pediatric emergency department with various complaints. Non-specific complaints, such as fever, restlessness, vomiting, and decreased feeding are observed in infancy, and specific complaints, e.g., abdominal pain, frequent urination, and dysuria become more prominent as age increases (12-14). In our study, similar to the literature, the most common complaints under the age of two years were fever and restlessness, while in advanced ages, complaints such as dysuria, abdominal pain, and flank pain were more frequent.

Increased presence of leukocytes (pyuria) in urine during the microscopic examination of the complete urinalysis is an indicator of inflammation associated with UTIs. Pyuria may sometimes not be seen in cases of early infection, insufficiency, or suppression of the immune system (4). In our study, 243 (84.9%) patients had pyuria.

The nitrite test is a method based on the conversion of nitrate to nitrite by bacteria belonging to the Enterobacteriaceae family. When the nitrite test is positive, it supports the diagnosis of UTIs, but its negativity does not exclude these infections (6). In our samples, nitrite positivity was detected in 84 (29.4%) patients. Considering that nitrite test positivity is observed in urine evaluated in the morning or in urine that has remained in the bladder for four hours, the positivity rate we obtained from the nitrite test may have been low in young children without bladder control since it was not possible to collect their morning urine or urine that had been in the bladder for four hours.

Urine culture analysis is the gold standard in the diagnosis of UTIs. However, the method used to collect urine may affect the validity of results and treatment. The collection of urine in a sterile plastic bag attached to the cleaned genital area is a technique frequently used in many centers. Although the culture-negative bladder specimen is reliable, this technique results in a high rate of false positive cultures due to contamination with the periurethral flora (15). If UTIs are suspected in patients aged under two years without toilet training, the recommended methods to reduce the risk of contamination are suprapubic aspiration (SPA) and transurethral catheterization (6,16). However, due to the invasive and painful nature of SPA, families and doctors are usually not willing to apply it and prefer transurethral bladder catheterization. In patients aged over two years with toilet training, the main recommended method for urinalysis is to collect midstream urine (17). In our study, urine samples were taken with the transurethral catheter method in the patients younger than two years and the midstream method in those older than two years.

Gram-negative enteric bacteria are the most common agents in UTIs in all age groups, with E. coli being responsible for 80-90% of cases (18-20). Other common agents after E. coli include Klebsiella spp., Proteus spp., Staphylococcus saprophyticus, and Enterobacter spp. Among rarely seen pathogens are Pseudomonas aeruginosa, Enterococcus spp., Staphylococcus, and Group B streptococci (21,22). In our study, similar to the literature, E. coli growth was detected in the urine culture analysis of 242 (84.6%) patients. This was followed by Proteus spp. 21 (7.3%), and Klebsiella spp. 16 (5.6%) (6,23). In studies conducted in Turkiye, E. coli, Klebsiella spp., and Enterobacter spp. are reported to be the most common pathogens with growth in culture (24-26). Similar to our study, Bozkurt et al. also found that Proteus spp. had the second highest frequency in urine culture analysis (27).

In the empirical treatment of UTIs, narrow-spectrum antibiotics are preferred first, considering the most common microorganism and the lowest resistance to this agent. However, the patient's clinical findings and the possible side effects of antibiotics should also be taken into account when making this decision (28-30). The increase in the widespread and inappropriate use of antibiotics in recent years has led to an increase in antibiotic resistance among urinary tract pathogens across the world (31). In our study, the highest resistance rate among antibiotics was observed in ampicillin (54.9%), followed by amoxicillin-clavulanate (ACA) (36.7%). Gökçe et al. reported that the resistance rate was 71% for ampicillin, 43% for ACA, 31% for trimethoprim/sulfamethoxazole (TMP-SMX), 14% for ceftriaxone, and 4% for amikacin (32). In another study, İdil et al. determined the resistance rate as 70.2% for ampicillin, 49% for ACA, and 37.1% for TMP-SMX, 34.2% for ceftriaxone, and 1.3% for amikacin resistance (26). In our study, the resistance rates of ceftriaxone and amikacin were determined as 25.9% and 5.6%, respectively.

In studies conducted in Turkiye in recent years, the TMP-SMX resistance of E. coli has been reported to vary from 34% to 57.2%, and resistance to ceftriaxone from 24.4% to 36.7% (24-27). Similarly, in our study, the resistance rates of E. coli for TMP-SMX and ceftriaxone

were 32.6% and 26.4%, respectively. For this pathogen, the lowest resistance rates were observed in amikacin (5.4%) and nitrofurantoin (1.2%). In the literature, the rate of amikacin resistance was reported as 1.11% by Çaycı et al. (33) and 0.41% by İdil et al. (26), while this rate was much higher in a study by Çağ et al. (24) (12.1%). We found the amikacin resistance rate for E.coli as 5.4%. These data suggest that amikacin and nitrofurantoin can be preferred in the empirical treatment of UTIs according to age.

In our hospital, the antibiotic resistance of Proteus spp. was determined as 38.1% for ampicillin, 14.3% for ACA, and 28.6% for TMP-SMX. Proteus spp. strains have intrinsic resistance to nitrofurantoin; therefore, this antibiotic has no place in the treatment of UTI cases associated with these bacteria. In our study, this pathogen had the lowest resistance to amikacin at 9.5%. Similarly, Çoban et al. (34) detected ampicillin resistance at a rate of 46.7%; ACA resistance at 17.7%, and TMP-SMX resistance at 35.3%. Bozkurt et al. found the resistance rates as 44% for ampicillin, 12.2% for ACA, 54.8% for TMP-SMX, and 6.1% for amikacin (27).

In our study, Klebsiella spp. were resistant to ampicillin at a rate of 93.7% and ceftriaxone at 31.2%. In addition, 75% susceptibility was detected for nitrofurantoin and TMP-SMX. In the literature, İdil et al. (26) reported 97% resistance to ampicillin and 97% susceptibility to amikacin. In this study, the susceptibility of amikacin was found as 93.7%. The rate of resistance to TMP-SMX in Klebsiella strains was determined as 25.2% by Çağ et al. (24) and 55.97% by Çaycı et al. (33). In contrast, we determined the resistance rate to TMP-SMX as 25%.

Sixty-three patients (22%) had a history of recurrent UTIs. The lowest resistance in recurrent UTIs was 4.8% amikacin. It was followed by nitrofurantoin with a 17.5% resistance rate. However, nitrofurantoin resistance was significantly higher in recurrent UTIs (p=0.026). Patients should be questioned in terms of recurrent UTI in the treatment decision.

Conclusion

This study, E. coli was the most frequently isolated agent in urine culture analysis. Resistance rates against ampicillin were found high, and therefore we consider that it would not be suitable for use in the empirical treatment of pediatric patients with UTIs. Amikacin presents as an alternative treatment option. Inappropriate treatment choices in UTIs can cause renal scarring, which may lead to proteinuria, hypertension, and chronic renal failure in advanced cases. Therefore, healthcare centers should monitor their own infectious agents and antibiotic susceptibility at regular intervals and establish appropriate empirical treatment choices. It is important to re-evaluate empirically initiated treatments according to the results of urine culture and susceptibility analyses and revise treatment if necessary.

Our study has some limitations. The limited number of our cases is due to the fact that the recent antibiotic use history of the patients is not known and it is a retrospective study. We think that prospective, multicenter studies with a large number of patients will contribute to the literature.

Conflict of Interest

None declared by the authors.

Financial Disclosure

None declared by the authors.

Authorship Contributions

Concept: A.T.; Design: A.T., B.N.A., C.Z. ; Supervision: A.T., B.N.A., C.Z.; Fundings: A.T., B.N.A., C.Z., Materials: A.T., M.T.,H.I.; Data: A.T., M.T.,H.I.; Analysis: A.T., C.Z.; Literature search: A.T., B.N.A.; Writing: .A.T.; Critical revision: A.T., B.N.A., C.Z.

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