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Research Article

Microbiological and Antimicrobial Profile of Urinary System Infections in Children in Uşak

Uşak İlinde Çocuklarda Üriner Sistem Enfeksiyonlarının Mikrobiyolojik ve Antimikrobiyal Profili

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Abstract

Aim: One of the most prevalent pediatric diseases is urinary tract infection (UTI), accounting for 3% of all infections among the pediatric population and affect 2% of males and 8% of females by age seven. Bacteria are the most prevalent cause of UTIs, accounting for more than 95 percent of cases. The most prevalent causal bacteria of UTI is Escherichia coli. Antibiotics are included in the treatment of these infections. As a result, determining the correct antibiotic susceptibility is critical in the therapeutic treatment of bacterial infections. This study aimed to analyse the aetiology and antimicrobial resistance characteristics of urinary tract infection among children presenting with symptoms in Uşak.

Material and Method: A total of 1250 urine culture results were retrospectively analyzed from pediatric patients aged 0–16 years who were admitted to Uşak Öztan Hospital as outpatients with symptoms and complaints of urinary tract infection and whose urine analysis and urine culture were taken between January 2018 and December 2020.

Result: Gram-negative microorganism growth was found in 238 (19%) of the 1250 pediatric patients evaluated in our study. There was no growth in the urine cultures of 877 (70%) patients. E. coli was the most isolated microorganism in our study, which was detected in 168 (70.5%) of the patients.

Conclusions: We present the first antimicrobial resistance data for the city of Uşak. Our study showed that amoxicillin/clavulanate is not the best option for the empirical therapy of community acquired UTIs, contrary to current local practice. In addition, ceftriaxone was found to be the second most resistant antibiotic in our study.

Keywords: Pediatrics, urinary tract infections, etiology, antibiotic resistance

Öz

Amaç: En yaygın pediatrik hastalıklardan biri, pediatrik popülasyondaki tüm enfeksiyonların %3'ünü oluşturan ve yedi yaşına kadar erkek çocukların %2'sini ve kız çocuklarının %8'ini etkileyen idrar yolu enfeksiyonudur (İYE). Bakteriler, vakaların yüzde 95'inden fazlasını oluşturan İYE'lerin en yaygın nedenidir. İYE'n de en sık izole eden bakteri Escherichia coli'dir. Antibiyotikler idrar yolu enfeksiyonların tedavisinin temelini oluşturur. Sonuç olarak, bakteriyel enfeksiyonların terapötik tedavisinde doğru antibiyotik duyarlılığının belirlenmesi kritik öneme sahiptir. Bu çalışmada Uşak'ta belirgin İYE semptomları ile başvuran çocuklarda idrar yolu enfeksiyonunun etiyolojisi ve antimikrobiyal direnç özelliklerinin incelenmesi amaçlanmıştır.

Materyal ve Metot: Uşak Öztan Hastanesi'ne ayaktan idrar yolu enfeksiyonu semptom ve şikayetleri ile başvuran, 2018 Ocak-2020 Aralık ayları arasında idrar tahlili ve idrar kültürü alınan 0-16 yaş arası çocuk hastalardan toplam 1250 idrar kültürü sonucu retrospektif olarak incelendi.

Bulgular: Çalışmamızda değerlendirilen 1250 pediyatrik hastanın 238'inde (%19) gram negatif mikroorganizma üremesi bulundu. 877 (%70) hastanın idrar kültüründe üreme olmadı. Çalışmamızda hastaların 168'inde (%70,5) E. coli en fazla izole edilen mikroorganizma E. coli idi.

Sonuçlar: Uşak ili için ilk antimikrobiyal direnç verilerini sunuyoruz. Çalışmamız, mevcut yerel uygulamanın aksine, toplum kökenli İYE'lerin ampirik tedavisi için amoksisilin/klavulanatın en iyi seçenek olmadığını göstermiştir. Ayrıca çalışmamızda seftriakson en dirençli ikinci antibiyotik olarak bulundu.

Anahtar Kelimeler: Pediatri, idrar yolu enfeksiyonu, İYE etiyoloji, antibiyotik direnci

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INTRODUCTION

One of the most prevalent pediatric diseases is urinary tract infection (UTI), accounting for 3% of all infections among the pediatric population. UTI is an infection that causes an inflammatory response in the urinary tract epithelium (1). Because females have a shorter urethra than males, UTIs are more common. (2). UTIs are frequent in children, affecting 2% of boys and 8% of girls by the age of seven. In febrile newborns with no other known cause, the incidence of UTI can reach 7% (3).

Bacteria are the most common cause of urinary tract infections (UTIs), accounting for more than 95 percent of all cases. Escherichia coli is the most prevalent causal bacteria of UTI, accounting for more than 80% of all UTIs; Klebsiella, Proteus, and Enterococci are other responsible pathogens (1). For as long as causative bacterium is antibiotic-resistant, antibiotics are included in the treatment of these infections. As a result, identifying antibiotic susceptibility is critical in the therapeutic management of bacterial infections. Bacteria that have the potential to develop resistance to antibiotics need to be monitored more closely. According to many physicians around the world, microbial resistance is increasing (4). Renal damage in children, such as kidney failure and chronic hypertension, recurrent infection, pyelonephritis, and sepsis, can be significantly reduced by early and effective antimicrobial therapy for UTIs in children (3).

Antimicrobial susceptibility tests of urine specimens are usually concluded in 48 to 72 hours after the specimens are delivered. According to clinical experience, the majority of antimicrobial treatment for UTIs in pediatric patients is given empirically before test results are available. Oral antibiotics for UTI include sulfonamides (trimethoprim-sulfamethoxazole or sulfisoxazole), amoxicillin-clavulanate and cephalosporins (cefuroxime axetil, cefixime, cefprozil, cefpodoxime or cephalexin) (5). Amoxicillin and ampicillin are effective against around half of E. coli germs. Furthermore, increasing rates of E. coli resistance to amoxicillin-clavulanic acid, ampicillin-sulbactam, first-generation cephalosporins (e.g., cephalexin) and trimethoprim-sulfamethoxazole have been seen in some populations. Resistance to extended spectrum cephalosporins (cefotaxime, ceftazidime, cefepime) has been found in children who have been given prophylactic antibiotics (6). In addition to long-term complications that may occur in patients, further diagnostic testing for structural urinary system problems within the scope of 2nd and 3rd level health care services after attending primary health care services before diagnosis and laboratory analysis, along with antibiotic resistance, cause significant economic impacts and indirect costs through loss of time in school for children and parent labor loss (7).

Unfortunately, apart from a few large cities in Turkey, there is limited data about patterns of antibacterial susceptibility of endemic uropathogens in small cities in Anatolia. This study aimed to analyse the aetiology and antimicrobial resistance characteristics of urinary tract infection among children presenting with symptoms in Usak

MATERIAL AND METHOD

The clinical research ethics committee of Usak University Faculty of Medicine approved the study on 02/12/2020 with decision number 102-07-11. A total of 1250 urine culture results were retrospectively analyzed from pediatric patients aged 0–16 years who were admitted to Usak Private Oztan Hospital as outpatients with symptoms and complaints of urinary tract infection and whose urine analysis and urine culture were taken between January 2018 and December 2020. The study included 238 culture growths that met the inclusion criteria. Pathogens and resistance patterns that were isolated from midstream urine culture were analyzed. The study population consisted of infants and pediatric patients under the age of 18 who sought hospital treatment for UTI symptoms. Symptoms included dysuria and lack of bladder control, as well as low back discomfort and cloudy or bad-smelling urine with fever. According to parents, newborns and younger children had fever and hazy or strong-smelling urine. Urine samples were taken in sterile containers after being captured cleanly. For clean pee collection, a plastic bag was affixed to the genital region of babies and non-potty-trained youngsters. From toilet-trained children, a cleanly captured voided midstream urine sample was taken. To reduce contamination, the vaginal region was cleansed first in both cases. Urine collecting methods that were invasive were avoided. Children who received antimicrobial treatment and had a bladder catheterization within 48 hours were excluded from the trial. Asymptomatic bacteriuria patients were also barred from participating in the trial. Antimicrobial susceptibility testing was used to determine empirical antibiotic treatment.

Laboratory analyses of samples

Urine color was assessed macroscopically immediately after collection for contamination signs. Urine samples accepted by the laboratory were taken for examination without waiting. Urine samples were incubated for 24–48 hours in an incubator at 35–37 °C under aerobic conditions with 0.01 ml of the calibrated standard loop on petri plates containing Eocene Methylene Blue (EMB) agar and blood agar base (8). Bacterial growth of 100000 cfu/ml and above was included in the study after incubation (9). The isolated bacteria were identified using conventional methods, and the API ID (BioMérieux, France) system was used for isolates that could not be identified with this method.

Testing for antimicrobial susceptibility

The sensitivity of the detected isolates to various antibiotics was investigated using the Kirby-Bauer disk diffusion technique on Muller-Hinton agar in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria. All detected E. coli and Klebsiella spp. isolates on Mueller-Hinton agar were interpreted using amikacin (30 g), ampicillin (10 g), cephalexin (30

g), cefixime (10 g), cefpodoxime (30 g), co-trimoxazole (1.25/23.75 g), nitrofurantoin (300 g), and ofloxacin (5 g) (HiMedia Pvt (HiMedia Pvt. Ltd., India). E. coli ATCC 25922 was used to check quality control. Multidrug-resistant isolates were those that were resistant to two or more antimicrobial drugs (MDR).

Statistical analysis

SPSS 21 (IBM SPSS, SPSS inc. an IBM Co., Somers, NY) statistical package program was used for statistical analysis. Descriptive statistics are presented as mean ± standard deviation (minimum-maximum) for continuous variables and the number of cases and percent for nominal variables.

RESULTS

Demographics

Gram-negative microorganism growth was found in 238 (19%) of the 1250 pediatric patients evaluated in our study. There was no growth in the urine cultures of 877 (70%) patients, non-gram negative microorganism growth was detected in 63 (5%) patients, and the urine culture results of 72 (6%) patients were evaluated as contamination. There were 145 (61%) females and 93 (74%) males among the 238 patients who were included in the study with gram-negative growth in their urine culture. The difference in mean age between men and women was not statistically significant (male: 2.94 2.19 years; female: 3.22 2.93 years; P>0.05).

Isolated pathogens

E. coli was the most frequently isolated microorganism in our study, which was detected in 168 (70.5%) of the patients. It was followed by Proteus spp. in 38 (16%) patients. These were followed by 23 (9.7%) Klebsiella spp. patients and 9 (3.8%) Pseudomonas spp. patients (Table 1). In male patients, the infection rate for E. coli was 68.8 percent, 14 percent for Klebsiella spp, 12.9 percent for Ptoteus spp., and 4.3 percent for Pseudomonas spp. In female patients, the infection rate for Ecoli was 71.8 percent, 17.9 percent for proteus, 6.9 percent for klebsiella, and 3.4 percent for pseudomonas.

Antibiotic susceptibility

The most commonly isolated E. coli had the highest detected antibiotic resistance for amoxicillin/clavulanate (46%), ceftriaxone (31%), trimethoprim/sulfamethoxazole (30%), fosfomycin and nitrofurantoin (17%). The resistance rates of isolated microorganisms to antibiotics are shown in Table 2.

Compared with susceptible patients in E. coli infections, resistance to Ceftriaxone was found to be 31% in 52 patients, 19 patients 11.3% in amikacin, amoxicillin in 45.8% in 77 patients, 17.3% in 29 patients on fosfomycin, 0 in imipenem, 16.7% in 28 patients on nitrofurantoin, there were 50 patients on Co-trimoxazole, and the rate was 29.8%.

Compared with susceptible patients in Klebsiella spp. infections, resistance to ceftriaxone was found to be 34.8% in 8 patients, 13% in amikacin in 3 patients, 52.2% in amoxicillin in 12 patients, 34.8% in fosfomycin 8 patients, 4.3% in imipenem in 1 patient, and 9 patients for nitrofurantoin 39.1%, Co-trimoxazole was seen in 7 patients as 30.4%.

Compared with susceptible patients in Proteus spp. infections, the rates of resistant patients were 1 patient on ceftriaxone, 2.6%, 1 patient on amikacin 2.6%, 4 patients on amoxicillin 10.5%, 4 patients on fosfomycin 10.5%, 6 patients on nitrofurantoin 15.8%, Co-trimoxazole, 9 patients were 23.7%.

In Pseudomonas spp. infections, resistance was seen only in 4 patients against Co-trimoxazole compared to susceptible patients, and its rate was 44.4%.

Table 1. Distributions of isolated pathogens from urine culture in 238 culture positive samples [n (%)]

Pathogens	n (%)
Escherichia coli	**168 (70.5)**
Proteus spp.	38 (16)
Klebsiella spp.	23 (9.7)
Pseudomonas spp.	9 (3.8)

Table 2. Antimicrobial susceptibility of isolated uropathogenic bacteria [n (%)]

Antibiotic Name	Escherichia coli	Proteus spp	Klebsiella spp	Pseudomonas spp
Amoksisilin-Klavulanat	**77 (44)**	4 (11)	12 (52)	-
Amikasin	19 (11)	1 (3)	3 (13)	0
Trimetoprim-Sülfametoksazol	50 (30)	9 (24)	7 (30)	4 (44)
Piperasilin/ tazobaktam	6 (4)	0	1 (4)	1 (11)
Seftriakson	52 (31)	1 (3)	8 (35)	-
Meropenem	1 (1)	0	0	0
Imipenem	0	0	1 (4)	0
Fosfomisin	29 (17)	4 (11)	8 (35)	-
Nitrofurantoin	28 (17)	6 (16)	9 (39)	-

DISCUSSION

Only 238 of 1250 urine samples tested positive in our study. The positive culture results were determined using a 100,000 CFU/ml threshold. A positivity rate of 19% was found. Lower bacterial counts may be missed as a result. A higher threshold could mean lower positive culture results. Childhood urinary tract infections (UTIs) can result in higher morbidity, hospitalization, and long-term clinical

implications such as renal scarring, hypertension, and chronic kidney disease (3). As a result, children who have UTI should be detected and treated as soon as feasible. Antimicrobial resistance patterns of isolated uropathogens that cause UTIs differ depending on region and race. Most microorganisms are unaffected by the use of ampicillin as an antibiotic for the empirical treatment of suspected UTI or the prevention of recurrent UTI, according to research done across the world. Amoxicillin-clavulanic acid (30%), trimethoprim-sulfamethoxazole (nearly 40%) and first generation cephalosporins all have high rates of resistance (6). Unfortunately, rising antibiotic resistance allows for ineffective empirical treatment. The formation of broad-spectrum lactamases is one of the mechanisms causing this resistance (ESBLs) (10). Therefore, a safe diagnosis of UTI in children is very significant.

In our hospital, E. coli was the most prevalent cause of pediatric UTI, and this genus accounted for 70.5% of all pathogens isolated. E. coli was identified in 71.4% of the 940 subjects with UTIs in a recent study conducted in Iran, which is consistent with previous studies as well as our study (11). The most common pathogens causing pediatric UTIs worldwide and in Turkey were reported to be E. coli and Klebsiella spp. (12-15). Klebsiella had a rate of 9.7% in our study, and it was placed 3rd after Proteus spp. The rate of Proteus was 16% and was higher than the rate in other studies.

The majority of children are treated empirically before test results are obtained both in our and similar clinics to avoid complications. Our antimicrobial resistance study is shown in Table 2. Both Klebsiella spp. and E. coli had high resistance to amikacin, with resistance rates of 45.8% for E. coli, 52.2% for Klebsiella spp., and 10.5% for Proteus spp. in our study. This is in line with the study by Miranda et al. (16). Co-trimoxazole is the oral antibiotic of choice for the treatment of pediatric UTI, but Proteus spp., Klebsiella spp. and E. coli were found to have resistance rates of 23.7%, 30.4% and 29.8% respectively, in our study. In terms of preference, these rates are high.

Low nitrofurantoin resistance was found in urine E. coli isolates from both children and adults throughout the world (17). In our study, nitrofurantoin was found to be effective against most Klebsiella spp. and Proteus spp. Resistance rates were 9% and 6%, respectively. However, this rate was 28% for E. coli. Moreover, studies evaluating childhood UTIs caused by ESBL-producing bacteria reported low rates of resistance to nitrofurantoin among these uropathogens as well. Because of the low tissue concentrations, it is not advised for use in acute pyelonephritis. Based on these data, nitrofurantoin may be suggested for the empirical treatment of lower-tract UTIs (18). Nitrofurans can also be chosen as a cost-effective alternative as they are relatively less expensive. Antimicrobial resistance is related to inappropriate antibiotic usage, poor diagnosis, self-medication, poor quality antibiotics, insufficient doses, males with uncircumcised penis, and bowel and bladder dysfunction (5). Treatment of childhood UTIs aims to eradicate the infection and prevent complications such as prevent recurrence, urosepsis and provide rapid relief for long-term clinical consequences and symptoms such as renal scarring, hypertension, and chronic kidney disease (3). To combat rising resistance rates, it is critical to do a urine culture and employ local antibiograms, treat only when required, and avoid broad-spectrum antibiotics as much as possible. Patients with severe vesicoureteral reflux and hydronephrosis should also be given selected antibiotic prophylaxis (19). Resistance to imipenem was found to be 4.3% in one case against Klebsiella spp., whereas resistance to meropenem was found to be 0.6% in one case against E. coli. Carbapenems should be preferred in the treatment of serious infections caused by ESBL-producing Enterobacteriaceae, as other studies reported low resistance to carbapenems (20). The prevalence of vancomycin-resistant enterococci (VRE) in pediatric patients has increased in recent years, posing a serious threat to children (21). Fortunately, no resistance was found in our study of pediatric urinary tract infections. Shortridge et al. showed that ceftolozane-tazobactam was the most effective cephalosporin against all Enterobacteriaceae, with only meropenem and colistin having greater susceptibility rates. Ceftolozane tazobactam was the most effective lactam against P. aeruginosa, with a susceptibility rate comparable to colistin (22).

Ampicillin and aminoglycoside combinations are also employed in the empirical treatment of acute pyelonephritis at our hospital, particularly in the early baby period. Because third generation cephalosporins are often inefficient in the treatment of UTIs caused by ESBL-producing bacteria, the combination of ampicillin and amikacin looks to be a practical alternative for avoiding unnecessary empirical therapy of patients with acute pyelonephritis. Furthermore, resistance against ESBL-producing bacteria and high costs associated with broad-spectrum antibiotics will be prevented. As a result, we agree with the usage of the combination of ampicillin plus amikacin for the treatment of patients with acute pyelonephritis who have ESBL-positive UTI risk vectors (23).

In a recent study by Kalaitzidou et al., E. coli was the most common uropathogen, followed by Klebsiella spp. and Proteus spp. In our study, E. Coli was the first at 71.4%, Proteus spp. was second at 16%, while Klebsiella spp. was third at 9.7%, and pseudomonas was fourth at 3% (24). According to the findings of Kalatitzidou et al., the most common antibiotic resistance in E. coli isolates was ampicillin, followed by piperacillin, amoxicillin-clavulanate, and trimethoprim-sulfamethoxazole. 4.21 percent of E. coli strains generated extended-spectrum beta-lactamases (ESBLs). Vesicoureteral reflux was discovered to be a substantial risk factor for multidrug resistance (24). The most prevalent antibiotic resistance of E. coli isolates in our study was for amoxicillin-clavulanate, ceftriaxone, and trimethoprim-sulfamethoxazole, in that order. Contrary to current local practice, both our investigation and the study by Kalatitzidou et al. demonstrated that amoxicillin/clavulanate is not the best option for empirical therapy of

community acquired UTIs. In addition, ceftriaxone was found to be the second most resistant antibiotic in our study. The most common reason for this, we think, is the use of ceftriaxone as a single or multiple-dose outpatient parenteral treatment agent in cases with fever of unknown origin and other infections without culture.

CONCLUSION

Our findings showed high antimicrobial resistance among common uropathogens. We present the first antimicrobial resistance data for the city of Usak. For this reason, these findings can be used as a reference for the treatment of UTI in children in the city of Usak. This study will help clinicians to choose proper antibiotics and identify trends in antimicrobial susceptibility, especially in our region.

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Author contribution: *SG designed the study, collected and analyzed the data, and drafted the manuscript reviewed and revised the manuscript and is the corresponding author. MU collected and analyzed the data and reviewed and revised the manuscript. All authors read and approved the final manuscript.*

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