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Original Article

Antibiotic sensitivity and resistance in children with urinary tract infection in Sanliurfa

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ABSTRACT

Objective: This study aimed to evaluate antibiotic resistance in the province of Şanliurfa and to observe any difference between antibiotic resistance rates.

Material and methods: The study comprised 107 children who presented at the pediatric polyclinic with complaints of urinary tract infection with the diagnosis of urinary tract infection and whose urine cultures exhibited bacterial growth. The patients were analyzed with respect to the frequency of proliferating pathogens, sensitivity to the antibiotics used and the rates of developed resistance to the antibiotics.

Results: A total of 107 patients aged between 1 year and 15 years were included in the study, encompassing 14 (13.1%) males and 93 (86.9%) females. According to the urine culture results, proliferation of *Escherichia coli (E. coli)* was observed in 69 (64.5%), *Klebsiella* spp. in 13 (12.1%), Proteus mirabilis in 9 (8.4%), *Staphylococcus aureus* in 5 (4.7%), *Pseudomonas aeruginosa* in 5 (4.7%), *Acinetobacter* spp. in 3 (2.8%) and *Enterococcus* spp. in 3 (2.8%) patients. For proliferating *E. coli*, high resistance rates to ceftriaxone (39.5%), nitrofurantoin (19.7%), ampicillin-sulbactam (64.1%), co-trimoxazole (41.5%), amoxicillin-clavulanate (51.7%) and cefuroxime (38.1%) were observed. All of isolated microorganisms were resistant to ampicillin-sulbactam, amoxicillin-clavulanate, co-trimoxazole, ceftriaxone, cefuroxime and cefoxitin in decreasing frequencies. The most effective antimicrobial agents were determined to be imipenem, sulperazone, quinolone and aminoglycosides.

Conclusion: In our region, parenteral antibiotics that should be selected for the empirical treatment of UTIs in all age groups are the aminoglycosides and 3rd generation cephalosporines. In contrast to other studies, these results suggest that co-trimoxazole should be used for children aged 0-1, and 2nd generation cephalosporins should be used for the oral treatment of children aged 1-5 due to the low rate of resistance to nitrofurantoin in patients aged over 5 years.

Key words: Child; empirical treatment; development of resistance; urinary tract infections.

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Introduction

Urinary tract infections (UTIs) are among the frequently seen important infections in the pediatric age.[1] In the pediatric age group, incidence of morbidities of bacterial infections ranks second after that of upper respiratory tract infections.[2] In our country, among etiological factors of hypertension, and renal failure, UTI developed on the background of reflux nephropathy ranks on top in the pediatric age group.[3] As is the case in all age groups, also in children, gram-negative bacilli take the first place among microorganisms causing urinary tract infections. *E. coli* which is encountered most frequently among these gram-negative microorganisms is also responsible for 70-90% of episodes of urinary tract infections.[4-6] However in nosocomial infections, and in the presence of urinary system pathologies, gram-negative, and gram-positive microorganisms can cause urinary tract infections apart from *E. coli*.[7]

Because of the problem of resistance developing against the antibiotics used in the treatment of these most frequently seen community-acquired infections, knowledge about susceptibilities of these infection agents will be helpful in the planning of treatment protocols.[8-10]

In this study, microorganisms isolated from urine samples sent to microbiology laboratory were evaluated as their antibiotic sensitivities, and resistance patterns.

Material and methods

Medical files of 137 cases aged between one month, and 15 years who were referred to general pediatrics, and urology polyclinics between January 2011, and December 2011 with the diagnosis of UTI were reviewed. Thirty cases were excluded from the study because of incomplete data, growth of multiple microorganisms in the culture, and presence of complicated urinary tract infections,and so 107 cases were included in the study. Among patients with clinical symptoms of UTI (incontinence, dysuria, abdominal paain, and vomiting), those with a growth of more than 105 CFU/mL in urine cultures were accepted as patients with UTI.[11]

Polyclinic, and laboratory files of the cases were examined, and age, gender, clinical findings, and culture results of the patients, antibiotic sensitivities, and resistance patterns, and antibiotherapies applied were retrospectively evaluated.

Urine samples were collected following standard perineoscrotal hygiene, into sterile urine bags in incontinent patients and from continent patients midflow urine samples were obtained. Urine samples were sent to the laboratory where they were inoculated using a 4 mm caliber loop on culture medias containing eosin methylene blue (EMB) agar with 5% sheep blood, and incubated at 37°C for 18-24 hours.In urine cultures with significant growth, bacterial identification was performed using standard conventional methods. In compliance with NCCLS (National Committee for Clinical Laboratory Standards) criteria, disc diffusion method was used to perform *in vitro* antimicrobial susceptibility tests against trimetoprim-sulfometaxazole (TMP-SMX), cefotaxime, ceftriaxone, cefuroxime axetil, ciprofloxacine, amikacin, amoxycillin-clavulanate, and ampicilline-sulbactam, and identify extended spectrum beta lactamase (ESBL) producing *E. coli* strains.[12]

Statistical analysis

For the evaluation of the study data SPSS (Statistical Package for the Social Sciences, version 11.5 for Windows, SPSS® Inc, Chicago, IL, USA) statistical analysis program was used. Frequency, and mean±standard deviation (SD) of the data were provided.

Results

A total of 107 [14 (13.1%) male, and 93 (86.9%) female children] patients with a mean age of 8.8±3.6 years were included in the study. A significant difference was not found between female, and male patients ($p>0.05$).

Distribution of microorganisms isolated from urine cultures were *Escherichia coli* (n=69; 64.5%), *Klebsiella pneumoniae* (n=13; 12.1%), *Proteus mirabilis* (n=9; 8.4%), *Pseudomonas aeruginosa* (n=4; 3.7%), methicilline-sensitive coagulase-negative *Staphylococcus aureus* (MSCNS) (n=4; 3.7%), *Enterobacter faecalis* (n=3; 2.8%), and *Acinetobacter spp*. (n=3; 2.8%) (Table 1). *E. coli* demonstrated minimal resistance to imipenem (3.5%), however resistance rates gradually increased against sulperazone (5.9%), quinolone (5.9%), amikacin (8.5%) and nitrofurantoin (19.7%). Antimicrobial resistance of *K. pneumonia* to imipenem, amikacin, sulperazone, and quinolones was not observed, the highest resistance rates were detected against co-trimoxazole (28.6%). The most effective antibiotics against *P. mirabilis* were ceftriaxone, imipenem, nitrofurantoin, and amikacin, the highest microbial resistance rates (44.4%) were seen against ampicillin-sulbactam. In Table 2, antimicrobial resistance rates against various microorganisms grown in cultures are shown in Table 2.

Discussion

Urinary tract infections which are more often seen in in girls than boys are among frequently seen bacterial infections during pediatric age.[13] In our study 86.9% of the cases consisted of female children.In studies performed in various regions of the world mostly *E. coli* has been isolated in UTI.[13-19] Also in our country high rates of UTI with variations among regions have been reported.[20-26] Still, in our study as anticipated, gram-negative bacteria were the most frequently seen microbial agents, among this group mostly *E. coli* (64.5%) was isolated. *E. coli* was followed by *Proteus spp*.(12.1%) and *Klebsiella spp* (8.4%) in order of increasing frequency. In the medical medicine, higher resistance rates were detected against frequently used medications which are priorly preferred because of their oral intake.[27] Antimicrobial resistance of *E. coli* against ampicillin has bben indicated as 50% in European, 100% in African, and 82% in Asian countries, respectively.[14,18,27] In our country rates of antimicrobial resistance of *E. coli* differs between regions, and within years. Based on the reports of various studies, In a study reported from İzmir , rate of resistance of *E.coli* against ampicillin increased from 67 to 75% in İzmir, between the years 1999 to 2001, and from 57.1 to 79% between the years 1996 to 2006 in Isparta.[26,28] In the province of Sivas, *E. coli* was resistant to amoxicillin in 70.7% of the cases, respectively.[20] In our study the highest resistance was found against ampicillin-sulbactam (64.1%), followed by amoxicillin/clavulanate (57.1%). These higher resistance rates suggest that these antibiotics should not be selected for empirical treatment in our province. The reason for this higher resistance rates might be attributed to long-term preference of these antibiotics in general medical practice, and alteration in resistance rates with time.

In studies related to antimicrobial resistance of *E. coli* against increasingly prevalent 2., and 3. generation cephalosporins,

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resistance rates of *E. coli* against cefuroxime were 25% in Ankara, 21.9% in Isparta, 22.4% in Smyrna, 30% in Istanbul, 30.8% in Sivas. Resistance rates against 3. generation cephalosporins were 6.8% in Isparta, 16.4% in Smyrna, 7.5% in Ankara, and 12.8% in Sivas.[6,20,21,24,26] In compliance with literature findings, ın our study resistance rates of *E. coli* against increasingly prevalent cefuroxime axetil, and ceftriaxone were found to be 38.1, and 39.5%, respectively. These higher rates of resistance suggest that 3. generation cephalosporins should not be preferred for the empirical treatment of UTI. As is the case in the whole world, enhanced resistance rates of *E. coli* against co-trimoxazole (43.6%) were detected in our study.[6,14,18-22,26,29-33] In studies performed hitherto, *K. pneumonia* has been isolated as a responsible uropathogen in 10% of the cases with UTI. [17-19,21-26,28,32-34] In compliance with previous publications, antimicrobial resistance rate was detected as 12.1 percent. In a study reported from Tunisia, increased rates of antibiotic resistance of *K. pneumonia* were reported against amoxicillin/clavulanate, amoxicillin and cephalosporins in Tunisia, and and against nalidixic acid, and amoxicillin/clavulanate in Yemen.[14,18] Among our uropathogens *K. pneumonia* was rarely detected. Although we didn't detect significant rates of resistance of *K. pneumonia* against amoxicillin, amoxicillin/clavulanate, cephalosporins , and nitrofurantoin , we think that scarce number of cases preclude a satisfactory evaluation of antibiotic resistance for *K. pneumonia*.

Table 1. Distribution of microorganisms isolated from urine samples

	n (%)
Escherichia coli	69 (64.5)
Proteus mirabilis	9 (8.4)
Pseudomonas aeruginosa	5 (4.7)
Klebsiella pneumoniae	13 (12.1)
Staphylococcus aureus	5 (4.7)
Enterococcus faecalis	3 (3.8)
Acinetobacter	3 (2.8)

In studies performed in our country, various resistance rates against amikacin have been reported for *E. coli* (3-18%), and *P. aeruginosa* (0-9%).[35-42] In our study resistance of *E.coli* against amikacin was detected as 8.5 percent. Since amikacin maintains its efficacy against gram-negative bacteria without any decrease in its effectiveness with time, it can be preferred in the treatment of UTIs.

In a Hitit study conducted in six different centers, in the treatment of nosocomial urinary system infections resistance rates against imipenem-cilastatin were detected at a highest level for *P. aeruginosa* (27%) followed by *E. coli* (0.2%), and *K. pneumoniae* (0.5%).[43] In various publications of our country, antibiotic resistance rates of *E. coli* against imipenem-cilastatin ranged between 0%, and 8%, respectively. However in our study median antibiotic resistance rate was detected as 3.5%. [36,37,40,41,44] Since *E. coli* which is the most frequently isolated uropathogen in UTI has the lowest resistance rates against imipenem-cilastatin without any change in its resistance rates within years, this antibiotic combination is still a reliable alternative.

Table 2. Antimicrobial resistance rates of the microorganisms grown in urine culture

	E. coli	*Klebsiella*	*Proteus* spp.	*Pseudomonas*	*Staphylococcus*
Imipenem	3.5	0	0	0	0
Ceftriaxone	39.5	25	0	100	0
Nitrofurantoin	19.7	14.3	0	12.5	20
Amikacin	8.5	0	0	0	0
Gentamicin					
SAM	64.1	25	44.4	37.5	85.7
KAM	51.7				
TM-SM	41.5	28.6	20	37.5	75
Sulperazone	5.9	0	16.7	0	0
Quinolone	5.9	0	0	0	20
Cefuroxime	38.1	25	0	50	80
Cefoxitin	12.2	28.6	14.3	0	20

SAM: ampicillin-sulbactam; KAM: amoxycillin-clavulanate; TM-SM: Co-trimoxazole; *E.coli: Escherichia coli*

In conclusion, it is important that each country should have its own epidemiological data, and physicians should know antimicrobial resistance rates in their regions so as to arrange treatment, and prophylaxis accordingly. Antimicrobial resistance rates are increasing steadily against antibiotics expected to exert clinical efficacy in the treatment of UTI as a result of their widespread, and erroneous use. We think that at certain intervals centers should identify uropathogens prevalent in their regions, and aware of öantimicrobial susceptibilities of these pathogens which are very important for the economy of the country, and appropriate treatment.

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