

Antimicrobial Susceptibility and Uropathogens Isolated From Children and Adults with Community-Acquired Urinary Tract Infections

Toplum Kökenli Üriner Sistem Enfeksiyonu Olan Çocuk ve Yetişkin Hastalardan İzole Edilen Üropatojenler ve Antimikrobik Duyarlılıkları

Mustafa YILDIRIM, MD,^a
İdris ŞAHİN, MD,^b
Aynur GÜLCAN, MD,^c
Davut ÖZDEMİR, MD^a
Abdulkadir KÜÇÜKBAYRAK, MD,^d
Hakan UZUN, MD,^e
Demet KAYA, MD^b

Departments of ^aClinical Microbiology and Infectious Diseases,
^bMicrobiology and Clinical Microbiology,
^cPediatrics,
Düzce University Faculty of Medicine, Düzce
^dDepartment of Microbiology and Clinical Microbiology,
Kütahya State Hospital, Kütahya
^eAtatürk Chest Diseases and Thoracic Training and Research Hospital, Ankara

Geliş Tarihi/Received: 23.09.2008
Kabul Tarihi/Accepted: 10.03.2009

The study was presented as a poster presentation in the first international congress of central Asia infectious diseases.

Yazışma Adresi/Correspondence:
Mustafa YILDIRIM, MD
Düzce University Faculty of Medicine,
Clinical Microbiology and Infectious Diseases Specialist,
Department of Clinical Microbiology and Infectious Diseases, Düzce,
TÜRKİYE/TURKEY
mustafayildirim4@yahoo.com

ABSTRACT Objective: The aim of this study was to determine the distribution of uropathogens causing community-acquired urinary tract infections in Düzce, and their antimicrobial susceptibility patterns. **Material and Methods:** The study was conducted prospectively in the Düzce University Medical Faculty between July 2004-June 2006 and included outpatients. Identification of microbial growth and determination of antimicrobial susceptibility by the Kirby-Bauer disk diffusion technique were performed according to the Clinical and Laboratory Standards Institute. **Results:** In total, 702 bacterial isolates were examined in the study. *E. coli* (64.1%) was the most common urinary pathogen identified. *Klebsiella spp.* (9.0%), *Proteus spp.* (5.8%), *Staphylococcus aureus* (4.7%), *Enterococcus spp.* (4.3%), coagulase-negative Staphylococci (2.6%), *S. agalactiae* (2.1%) and *P. aeruginosa* (1.9%) were the next most common species isolated. Community acquired uropathogens isolated in our region were highly resistant to trimethoprim/sulfamethoxazole, amoxicillin and amoxicillin clavulanate. However, ciprofloxacin was active against pathogens examined in this study with susceptibilities between 64.7% and 88.8% for the most prevalent pathogens (*E. coli*, 81.0% susceptible). The susceptibility of gram-negative pathogens to the parenteral antibiotics seemed to be higher than the oral agents. **Conclusion:** Many oral antimicrobial agents do not seem to be appropriate for the empirical treatment of community-acquired urinary tract infections in our region due to very high rates of resistance. Some oral antibiotics such as ciprofloxacin and ceftazidime should be used cautiously in adults.

Key Words: Urinary tract infections; outpatients

ÖZET Amaç: Bu çalışmanın amacı Düzce’de toplum kökenli üriner sistem enfeksiyonuna yol açan üropatojenlerin dağılımı ve antibiyotik duyarlılık paternlerinin belirlenmesidir. **Gereç ve Yöntemler:** Bu çalışma Temmuz 2004 – Haziran 2006’da Düzce Üniversitesi Tıp Fakültesinde prospektif olarak yapılmış ve çalışmaya poliklinik hastaları alınmıştır. Mikrobiyal üremelerin tiplendirilmesi ve antimikrobik duyarlılık testleri “Clinical and Laboratory Standards Institute” kriterlerine uygun olarak Kirby-Bauer disk difüzyon metodu ile yapılmıştır. **Bulgular:** Çalışmada toplam 702 bakteri izolatu elde edildi. *E. coli* (%64.1) en sık izole edilen üropatojendi. *Klebsiella spp.* (%9.0), *Proteus spp.* (%5.8), *Staphylococcus aureus* (%4.7), *Enterococcus spp.* (%4.3), koagülaz-negatif Stafilokoklar (%2.6), *S. agalactiae* (%2.1) ve *P. aeruginosa* (%1.9) diğer en sık izole edilen patojenlerdi. Bölgemizde izole edilen toplum kökenli üropatojenler trimetoprim/sulfametoksazol, amoksisilin ve amoksisilin klavulanat’a karşı yüksek oranda dirençlidir. Bununla beraber, siprofloksasin bu çalışmada en sık izole edilen patojenlere karşı %64.7-88.8 oranında etkiliydi (*E. coli*, için duyarlılık oranı %81.0). Gram-negatif patojenlerin parenteral antibiyotiklere duyarlılık oranları oral antibiyotiklerden daha yüksek görünmektedir. **Sonuç:** Direnç oranlarının yüksekliği nedeniyle, bölgemizde toplum kökenli üriner sistem enfeksiyonlarının tedavisinde bir çok oral antibiyotigin kullanımı uygun görünmemektedir. Siprofloksasin ve sefaklor gibi diğer oral antibiyotikler de yetişkinlerde dikkatli olarak kullanılmalıdır.

Anahtar Kelimeler: Üriner sistem enfeksiyonu; poliklinik hastaları

Urinary tract infections (UTIs) are one of the most common infectious diseases. Annually, they account for approximately seven million office visits, more than one million hospitalizations, and result in 1.6 billion dollars in medical expenditures in USA. *Escherichia coli* account for the majority of UTIs that occur in the community.¹ Other *Enterobacteriaceae*, *Pseudomonas spp.*, *Staphylococcus spp.* and *Enterococcus spp.* are infrequent causes of UTIs. Many of the patients had urinary tract infections in the childhood, and continue to have infections as adults.² Up to 20% of young women with acute cystitis develop recurrent UTIs. During these recurrent episodes, the causative organism should be identified by urine culture and then documented to help the differentiation between relapse and recurrence.³ In practice, antimicrobial treatment is usually started before the results of microbiological testing are available. Therefore, it is extremely important to obtain local and national data on antimicrobial resistance of common urinary tract pathogens from UTIs. The aim of this study was to obtain data on the susceptibility of common pathogens causing community-acquired UTIs (CA-UTIs) in Düzce against antimicrobial agents currently used in the treatment of CA-UTIs.

MATERIAL AND METHODS

The study was performed in the Düzce University Medical Faculty in Turkey, and was conducted prospectively between July 2004 to June 2006. It was approved by the institutional ethical review board.

We classified the patients as Group 1 (0-17 years), Group 2 (18-50 years) and, Group 3 (over 50 years). The study was included outpatients who had one or more symptoms of UTI (defined as dysuria, urgency, frequency, or costovertebral angle tenderness) and a positive urine culture (over 10⁵ CFUs) of a single pathogen obtained upon admission and a positive urinalysis (defined as >10 white blood cells/mm³ or presence of esterase).³ To include only community-acquired UTI, patients who developed UTI during hospitalization (>48 hours) or within 48 hours of hospital discharge were excluded.

Repeat isolates from the same patient were excluded from the study.

Urine cultures were performed by our Microbiology Laboratory Service according to standard techniques.⁴ Identification of microbial growth and determination of antimicrobial susceptibility by the Kirby-Bauer disk diffusion technique were performed according to the Clinical and Laboratory Standards Institute.⁵ Susceptibility was routinely tested for the following antimicrobial agents: amoxicillin, amoxicillin/clavulanate (AMC), cefaclor, ciprofloxacin, trimethoprim/sulfamethoxazole (TMP-SMZ), ceftriaxone, ceftazidime, imipenem, piperacillin, amikacin, gentamicin, oxacillin, and vancomycin.

All of the collected data were entered in a computer database for analysis. Pearson Chi-square test or Fisher's exact test was used to assess the statistical significance of differences. A statistically significant difference was defined as a P value of <0.05. Data analysis was performed using SPSS version 9.0 for Windows, statistical software package (SPSS Inc., Chicago, III., USA).

RESULTS

The overall female to male ratio was 2.0:1. This ratio was 1.3:1 in Group 1, 6.8:1 in Group 2, and 1.1:1 in Group 3. The mean age was 36.8 years (3.6 years in Group 1, 33.7 years in Group 2, and 66.2 years in Group 3) (Table 1).

In total, 702 bacterial isolates were examined in the study. *E. coli* (64.1%) was the most common urinary pathogen identified. *Klebsiella spp.*, *Proteus spp.*, *Staphylococcus aureus*, *Enterococcus spp.* and coagulase-negative Staphylococci (CNS) were the next most common species isolated with the rank order varying between age groups (Table 2).

TABLE 1: Gender and age distribution by group.

Age group (years)	Number of isolates	Female/male (ratio)	Mean age (years)
Group 1(0-17)	197	112/85 (1.3:1)	3.6
Group 2 (18-50)	257	224/33 (6.8:1)	33.7
Group 3 (>50)	248	129/119 (1.1:1)	66.2
All groups combined	702	465/237 (2:1)	36.8

TABLE 2: Relative frequency (% of total) of isolation of species causing various types of CA-UTIs

All groups combined (n=702)			Group 1 (n=197)			Group 2 (n=257)			Group 3 (n=248)		
Organism	n	%	Organism	n	%	Organism	n	%	Organism	n	%
<i>E. coli</i>	450	64.1	<i>E. coli</i>	109	55.3	<i>E. coli</i>	174	67.7	<i>E. coli</i>	167	67.3
<i>Klebsiella spp.</i>	63	9.0	<i>Proteus spp.</i>	27	13.7	<i>Klebsiella spp.</i>	19	7.4	<i>Klebsiella spp.</i>	30	12.1
<i>Proteus spp.</i>	41	5.8	<i>Klebsiella spp.</i>	14	7.1	<i>S. aureus</i>	14	5.4	<i>Enterococ. spp.</i>	11	4.4
<i>S. aureus</i>	33	4.7	<i>S. aureus</i>	13	6.6	CNS	10	3.9	<i>Proteus spp.</i>	7	2.8
<i>Enterococ. spp.</i>	30	4.3	<i>Enterococ. spp.</i>	10	5.1	<i>S. agactiae</i>	9	3.5	<i>Enterobac. spp.</i>	6	2.4
<i>Enterobac. spp.</i>	20	2.8	<i>Enterobac. spp.</i>	9	4.6	<i>Enterococ. spp.</i>	9	3.5	<i>P. aeruginosa</i>	6	2.4
CNS	18	2.6	CNS	5	2.5	<i>Proteus spp.</i>	7	2.7	<i>S. aureus</i>	6	2.4
<i>S. agactiae</i>	15	2.1	<i>P. aeruginosa</i>	3	1.5	<i>Enterobac. spp.</i>	5	1.9	<i>S. agactiae</i>	6	2.4
<i>P. aeruginosa</i>	13	1.9	Other species	7	3.5	<i>P. aeruginosa</i>	4	1.6	CNS	3	1.2
Other species	19	2.7				Other species	6	2.4	Other species	6	2.4

CNS: Coagulase-negative staphylococci

CA-UTIs: Community acquired urinary tract infections.

Other isolates of importance included *S. agalactiae* (responsible for 3.5% of bacterial isolates in 17-50 age group) and *P. aeruginosa* (2.4% of in patients more than 50 years). The frequency of *E. coli* isolates was found lower in Group 1 when compared to the other groups (P= 0.01) and the frequency of *Proteus spp.* isolates was higher than the other groups (P< 0.001). There were no differences between three groups with respect to frequencies of *Klebsiella spp.*, *S. aureus*, *Enterococcus spp.*, *Enterobacter spp.*, CNS and, *P. aeruginosa* (P > 0.05).

The activities of amoxicillin and AMC against *E. coli* were 30.8% and 60.3%, respectively. (Table 3). *Klebsiella spp.* isolates were fully resistant to amoxicillin *in vitro* (100% resistance). Cefaclor was active against the *E. coli* (72.3% susceptible) and it had low activity against *Klebsiella spp.*, *Proteus spp.* and *Enterobacter spp.* However it was inactive against *P. aeruginosa* (Table 3). The activity of TMP-SMZ was low against *E. coli* and this agent provided no or limited coverage against some of the other prevalent pathogens (Table 3). Ciprofloxacin was active against the UTI pathogens examined in this study with susceptibilities of between 64.7% and 88.8% for the most prevalent pathogens (*E. coli*, 81.0% susceptible). All oral antibiotics tested had insufficient activity against *P. aeruginosa*. Ciprofloxacin susceptibility among *E. coli* isolates was found higher in Group 1 than the other groups (P< 0.001); amoxicillin (P< 0.001) and TMP-SMZ (P<

TABLE 3: Percent susceptibility to oral antibiotics of gram-negative isolates from CA-UTIs.

Microorganism	TMP-SMZ	Amoxicillin	AMC	Cefaclor	Ciprofloxacin
<i>E. coli</i>					
All groups	59.9	30.8	60.3	72.3	81.0
Group 1	28.3	9.5	49.4	65.0	97.6
Group 2	69.4	50.0	63.8	80.8	78.4
Group 3	65.0	38.1	63.7	70.9	73.1
<i>Klebsiella spp.</i>					
All groups	51.2	0.0	38.1	49.0	67.2
Group 1	50.0	0.0	50.0	61.5	92.9
Group 2	66.6	0.0	52.6	69.2	78.9
Group 3	38.8	0.0	23.3	32.0	46.4
<i>Proteus spp.</i>					
All groups	64.0	25.0	56.8	50.0	88.8
Group 1	66.6	23.5	52.2	50.0	90.9
Group 2	66.6	20.0	71.4	57.1	100
Group 3	50.0	50.0	57.1	40.0	71.4
<i>Enterobacter spp.</i>					
All groups	53.3	7.7	10.5	35.7	64.7
Group 1	50.0	0.0	0.0	28.6	83.3
Group 2	40.0	25.0	40.0	60.0	100
Group 3	66.6	0.0	0.0	0.0	16.6
<i>P. aeruginosa</i>					
All groups	0.0	16.6	9.1	12.5	25.0

TMP-SMZ: Trimethoprim/Sulfamethoxazole

0.001) susceptibilities were lower than the other groups. Imipenem had excellent activity (91.9-100%) against to all of gram-negative pathogens. The susceptibility of gram-negative pathogens to all other parenteral antibiotics is shown in Table 4.

TABLE 4: Percent susceptibility to parenteral antibiotics of gram-negative isolates from CA-UTIs.

Mikroorganizm	Ceftriaxone	Ceftazidime	İmipenem	Piperacillin	Amikacin	Gentamycin
E. coli						
All groups	86.2	91.2	99.7	77.7	95.2	86.5
Group 1	81.5	95.6	100	54.5	90.5	82.3
Group 2	93.5	93.0	100	87.8	98.5	90.2
Group 3	81.4	87.7	99.2	78.8	94.7	85.6
Klebsiella spp.						
All groups	61.9	71.1	98.4	51.2	70.5	76.9
Group 1	78.6	87.5	100	62.5	76.9	66.6
Group 2	84.2	84.6	100	58.3	89.5	81.2
Group 3	40.0	52.9	96.6	42.9	55.2	77.7
Proteus spp.						
All groups	66.6	77.3	91.9	84.0	89.2	87.1
Group 1	72.7	83.3	91.3	80.0	87.0	85.0
Group 2	42.9	80.0	85.7	100	100	100
Group 3	71.4	60.0	100	85.7	85.7	80.0
Enterobacter spp.						
All groups	66.6	68.7	94.4	37.5	94.7	64.7
Group 1	71.4	83.3	85.7	33.3	100	33.3
Group 2	80.0	75.0	100	0.0	100	100
Group 3	50.0	50.0	100	40.0	83.3	66.6
P. aeruginosa						
All groups	50.0	70.0	100	77.7	69.2	66.6

CA-UTIs: Community acquired urinary tract infections.

Percent susceptibility of gram-positive isolates from CA-UTIs is shown in Table 5.

DISCUSSION

This study shows the distribution of microbial agents causing CA-UTIs in a Turkish hospital between July 2004 - June 2006, and their susceptibility patterns to the most commonly used oral and parenteral antimicrobial agents. Patients were divided to three groups according to their ages.

Overall, 16 different species of bacteria were identified in the 702 patients with UTI with between 11 and 13 species being found in each category. *E. coli* was the most frequent uropathogen in all of the age groups. The frequency of *E. coli* is 64.1% in total, category range 55.3-67.7%. *Klebsiella spp.* were the second most common isolates causing 9.0% of infections. This corresponds to the data obtained by other groups.⁶⁻⁸

Recent reports have found *Staphylococcus aureus* to be present in 2.0% (n= 103223), 3.6% (n=

TABLE 5: Percent susceptibility of gram-positive isolates from CA-UTIs.

Antibiotic	Enterococcus spp	S. aureus	CNS	S. agalactiae
Ampicillin	58.6	21.9	12.5	100
Oxacillin	-	62.5	52.9	-
Gentamycin	100	72.7	92.3	-
Ciprofloxacin	24.1	63.3	71.4	-
Vancomycin	100	100	100	-
TMP-SMZ	-	58.8	53.3	-

. Coagulase-negative staphylococci

. For Enterococcus spp, high-level gentamycin resistance was tested.

CA-UTIs: Community acquired urinary tract infections.

224), and 3.9% (n= 886) of patients with CA-UTIs.⁹⁻¹¹ In our study, the rate of *Staphylococcus aureus* infection was found as 4.7% (n= 702) in patients with CA-UTIs. This rate is higher in our study when compared to the previous reports.^{9,10,12}

The study of Kahlmeter reported an ampicillin susceptibility of 71.2% for *E. coli*.¹³ The rate of susceptibility to amoxicillin in our study (total 30.8%,

category range 9.5-50.0%) is lower than this percentage. The same study reported an AMC susceptibility of 96.6%.¹¹ This rate is vastly different from our rate (60.3%). Possible reason for this difference is geographical variation due to a higher prevalence of variants of beta-lactamase resistant *E. coli*.

The two oral antimicrobials (cefaclor and TMP-SMZ) did not have good in vitro coverage for many of the uropathogens isolated in this study. Because of this, they are of little use as empirical therapeutic options.

Although fluoroquinolones are widely used for treatment of UTIs in adults, few data are available regarding the use of fluoroquinolones in the pediatric population.¹³ Overall, ciprofloxacin demonstrated the greatest in vitro activity against the widest range of uropathogens for all of the oral agents tested (*E. coli*, 81.0% susceptibility). These results suggest that ciprofloxacin may be a proper drug for the treatment of UTIs.

Low susceptibility rates for amoxicillin and TMP-SMZ and high susceptibility rates for ciprofloxacin were reported in the agents of pediatric UTIs in some studies.¹⁴⁻¹⁶ In the present study, ciprofloxacin susceptibility among *E. coli* isolates was higher in Group 1 than other groups; amoxicillin and TMP-SMZ susceptibilities were lower than ot-

her groups. These results may be related to limited usage of ciprofloxacin in this age group.

In conclusion, in this study, the most common pathogen causing CA-UTIs was *E. coli*, accounting for 64.1% of the microorganisms recovered from these patients. Community acquired uropathogens isolated in the Düzce region were highly resistant to many oral antimicrobial agents. TMP-SMZ, amoxicillin and, AMC do not seem to be appropriate for the empirical treatment of CA-UTIs in all of the age groups in our region, because of very high rates of resistance. The other oral antibiotics such as ciprofloxacin and cefaclor should also be used cautiously in adults. Urine culture and antimicrobial susceptibility testing seem to be essential in our region for the patients with UTIs. On the contrary, the parenteral agents showed excellent in vitro coverage of the uropathogens isolated in this study. We suggest that they may be safely used for empiric therapy of patients with suspected urosepsis.

This prospective study should be followed by a multicentre study on antimicrobial resistance in Duzce and other regions in Turkey to obtain data on the susceptibilities of common pathogens causing CA-UTIs in Turkey to antimicrobial agents currently used in the treatment of UTI.

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