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Bacterial Uropathogens Causing Urinary Tract Infection and Their Resistance Patterns Among Children in Turkey

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Abstract

Background: Urinary tract infection (UTI) is a common problem in infants and children, as well as adults.
Objectives: The aim of this study was to assess the most common bacterial uropathogens, their susceptibility, and resistance to antibiotics in children with UTI.
Materials and Methods: This study included 7,365 urine samples sent from various departments to the Kars state hospital microbiology laboratory between January 2012 and May 2014. Bacterial isolation from clinical samples was made using standard microbiological methods. Antibiotic susceptibilities were determined by disk diffusion, according to CLSI recommendations.
Results: Bacterial growth was obtained in 1,373 samples (18.5%). The percentage distributions of the isolates were as follows: *Escherichia coli*, 940 (68.5%); *Proteus* spp, 183 (13.3%); *Staphylococcus* spp, 85 (6.2%); *Enterococcus* spp, 65 (4.7%); *Klebsiella*, 62 (4.5%); *Pseudomonas aeruginosa*, 21 (1.5%); and other Gram-negative bacteria and Gram-positive bacteria, 17 (1.2%). UTIs were more prevalent, after two years of age, among females than males ($P < 0.001$).
Conclusions: The identification of the most common microorganisms causing infectious diseases and regional resistance patterns is important in order to determine the antimicrobial policies and infection control guidelines of hospitals.

Keywords: Uropathogens, Antibiotic, Resistance, Children

1. Background

Urinary tract infections (UTIs) are the second most common bacterial infection, after respiratory tract infections, and can result in chronic kidney disease in children (1, 2). Therefore, the diagnosis of UTI is important to preserve renal function of the growing kidney (3). *E. coli* is the most common causative agent isolated from uncomplicated UTI (3). Treatment of UTI begins before the culture results are available and then changed to culture-specific therapy (4). Antimicrobial resistance of urinary pathogens is increasing worldwide and patients with risk factors for resistance may especially benefit from urine culture (5). Sensitivity and resistance of microorganisms to antibiotics have geographical variation and knowledge of these factors is important in determining the antimicrobial policies of hospitals.

2. Objectives

In the present study, we aimed to assess the most common bacterial uropathogens, their antibiotic susceptibility, and resistance pattern in our region.

3. Materials and Methods

Before antibiotic use, 7,365 urine samples were obtained for this study from the departments of pediatrics, infectious diseases, and clinical microbiology between January 2012 and May 2014 at Kars state hospital. This study was approved by the ethics committee of Kars state hospital (02.10.2014-42288353/8213).

The inclusion criteria for this study were as follows: (1) children 0 - 18 years of age presenting with symptoms of UTI; (2) the use of urine culture as a diagnostic test; and (3) a positive urine culture of more than 105 colony forming units (CFU) of a single organism per milliliter of urine. The exclusion criteria were as follows: (1) duplicated samples; (2) samples that grew more than one type of microorganism; and (3) children with records that were not available.

Eosin methylene blue (EMB) agar and blood agar were used for urine culture. Identification of bacterial isolates was performed on the basis of their cultural and biochemical characteristics. Drug resistance evaluation was carried out using the disk diffusion method and the Kirby-Bauer method on Mueller-Hinton medium. Then, according to the size of the growth inhibition zone around the disks, and the international numbers of the Clinical and laboratory standards institute (CLSI), the results were categorized and reported as sensitive (S) and resistant (R). Amoxicillin-clavulanate, Ampicillin-sulbactam, cefazolin, cefotaxime, ceftriaxone, ceftazidime, cefepimee, piperacillin tazobactam, trimethoprim–sulfamethoxazole, ofloxacin, netilmicin, nitrofurantoin, ciprofloxacin, levofloxacin, fosfomycin, gentamicin, amikacin, imipenem, and meropenem were tested against *Enterobacteriaceae*. Carbenicillin, tobramycin, cephoperazone, cefotaxime, cefepimee, ofloxacin, netilmicin, aztreonam, ciprofloxacin, levofloxacin, gentamicin, amikacin, imipenem, and meropenem were tested against *P. aeruginosa*. Erythromycin, clarithromycin, clindamycin, trimethoprim-sulfamethoxazole, ciprofloxacin, ofloxacin, chloramphenicol, rifampicin, azithromycin, linezolid, vancomycin, tetracycline, teicoplanin were tested against Coagulase negative staphylococcus (CNS). Erythromycin, ampicillin, fosfomycin, gentamicin, ciprofloxacin, levofloxacin, linezolid, vancomycin, tetracycline, teicoplanin were used against *Enterococcus* spp. Standard strains of *E. coli* (ATCC 25922), *S. aureus* (ATCC 25923), and *P. aeruginosa* (ATCC 27853), *Enterococcus faecalis* (ATCC 29212) were used routinely in this study as controls.

3.1. Statistical Analysis

Statistical analysis was performed using SPSS software version 11.5. P values of less than 0.05 were regarded as statistically significant. Statistical analysis was performed with the Pearson's Chi-Square test.

4. Results

Out of 7,365 cultured urine specimens, significant bacteriuria were detected only on 1,373 (18.5%) of the samples. Among the positive cases, 884 (64.4%) were female and 489 (35.6%) were male. The ages of the positive cases were between 0 and 18 years.

The age and sex distribution of the positive cases is shown in Table 1. There were almost equal numbers of positive cases in both male and female patients under two years old; however, in patients over two years old, females had a higher rate than males ($P < 0.001$).

The most commonly discovered microorganism was *Escherichia coli* (68.5%). The second most prevalent isolate was *Proteus* spp. (13.3%) followed by CNS (6.2%), *Enterococcus* spp. (4.7%), *Klebsiella* spp. (4.5%), *Pseudomonas* spp. (1.5%), and others (1.3%).

In this study, the highest resistance rates of *E. coli* and *Proteus* spp. were to trimethoprim-sulfamethoxazole (37% and 45%, respectively) and the highest resistance rate of *Klebsiella* spp. was to ampicillin-sulbactam (39%) followed by trimethoprim-sulfamethoxazole (38%). The highest sensitivity of these germs was to carbapenems (MRP and IMP) (Table 2). The highest resistance of *Pseudomonas aeruginosa* was to cephotaxime (83%) followed by cephoperazone (75%). Amikacin, netilmicin and carbenicillin showed 100% sensitivity against *P. aeruginosa* isolates (Table 2). CNS showed 71% were resistant to erythromycin, and 98% were sensitive to linezolid and vancomycin (Table 2). *Enterococci* was resistant to ampicillin (61%) and erythromycin (55%) (Table 2). The sensitivity of vancomycin against both *enterococci* and CNS was 98% (Table 2).

5. Discussion

UTI is the most common infection encountered by clinicians (6, 7). It is important that area-specific monitoring studies be performed that may help the clinician to choose the correct empirical treatment. In our study, only 1,373 (18.5%) of 7,365 patients with clinically suspected UTI had a urinary tract infection, possibly because UTI symptoms are not a dependable indicator of infection, particularly in children. This condition shows that urine culture is very important for the accurate diagnosis of UTI (8). The incidence of UTI varies according to the age and sex of children (9). This study found that there are almost equal numbers of cases of UTI for the first two years of life in male and female patients, and then a marginally higher rate of UTI is found among female children older than two years. This is possibly because females have a longer urethra than males (10) (Table 1). Although the prevalence of pathogens in different regions of the world is quite similar, antimicrobial resistance patterns are considerably different, which may be explained in part by varying local antibiotic practices.

Our results showed that *E. coli* was the most common bacterium that caused urinary tract infections (68.5%), and this result agrees with previous studies both in Turkey and in other countries (11-16).

In our study, the highest resistance rates of *E. coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, *Proteus* spp., CNS, and *Enterococcus* were to trimethoprim-sulfamethoxazole, ampicillin-sulbactam, cephotaxime, trimethoprim-sulfamethoxazole, erythromycin, and ampicillin, respectively.

It has been suggested that the excessive and inappropriate use of antibiotics results in an increased risk of antibiotic resistance (17). Bacteria with a biofilm forming ability are thought to be more resistant to antibiotics (18). Transmission of resistant isolates between people,

Table 1. Distribution Pattern of Positive Cases According to Age and Sex[a]

Age, y	Male	Female	Total	Chi-Square
< 2	354 (49.8)	357 (50.2)	711	51.78
2 - 6	102 (33.6)	202 (66.4)	304	22.15
> 6	33 (9.2)	325 (90.8)	358	26.07
Total	489 (35.6)	884 (64.4)	1373	100.0

[a] $P < 0.001$ df = 2, $x^2 = 171.6$.

Table 2. Antibiotic Resistance Pattern in Uropathogens[a]

	AMC	SAM	CZ	CXT	CRO	CAZ	FEP	TZP	SXP	OFX	NET	F	CIP	LEV	FF	CN	AK	IMP	MEM
E. coli	33	33	20	23	23	14	15	5	37	11	4	7	10	10	6	18	2	0.8	0.4
Proteus spp	22	19	26	8	7	6	4	1.5	45	6	1	7	3	4	28	17	3	1.5	0
Klebsiella spp	29	9	33	27	27	21	26	11	38	6	7	22	6	6	10	16	9	7	10
	CB	**TOB**	**CFP**	**CXT**	**CAZ**	**FEP**	**TZP**	**OFX**	**NET**	**ATM**	**CIP**	**LEV**	**CN**	**AK**	**IMP**	**MEM**			
P. aeruginosa	0	25	75	83	33	17	0	8	0	15	6	8	24	0	7	7			
	E	**CLT**	**DA**	**SXT**	**CN**	**CIP**	**OFX**	**C**	**RIF**	**AZM**	**LNZ**	**VA**	**TE**	**TEC**					
CNS	71	53	27	25	24	25	30	10	6	25	2	2	56	10					
	E	**AMP**	**FF**	**CN**	**CIP**	**LEV**	**LNZ**	**VA**	**TE**	**TEC**									
Enterococcus spp	55	61	19	27	25	28	19	2	56	10									

Abbreviations: AK, Amikacin; AMC, Amoxicillin-clavulanate; AMP, Ampicillin; ATM, Aztreonam; AZM, Azithromycin; C, Chloramphenicol; CAZ, Ceftazidime; CB, Carbenicillin; CFP, Cephoperozone; CIP, Ciprofloxacin; CLT, Clarithromycin; CN, Gentamycin; CRO, Ceftriaxone; CXT, Cefotaxime; CZ, Cephozolin; DA, Clindamycin; E, Erythromycin; FEP, Cefepimee; F, Nitrofurantoin; FF, Fosfomycin; IMP, Imipenem; LEV, Levofloxacin; LNZ, Linezolid; MEM, Meropenem; NET, Netilmicin; OFX, Ofloxacin; RIF, Rifampicin; SAM, Ampicillin sulbactam; SXT, Trimethoprim-sulfamethoxazole; TE, Tetracycline; TEC, Teicoplanin; TOB, Tobramycin; TZP, Piperacillin-tazobactam; VA, Vancomycin.
[a] Values are expressed as %.

the consumption of animals that have received antibiotics, and the mobility of individuals worldwide have also contributed to the expansion of antibiotic resistance (19, 20). Togan et al. showed that (21) antibiotic use in the previous two weeks or three months, hospitalization during the previous one-year period, and a previous diagnosis of urinary tract ınfection were the risk factors identified for the development of infections with multi-drug resistant isolates. In addition, studies show the consumption of probiotics in addition to antibiotics in children with UTI is safe and more effective in reducing the incidence of UTI in comparison to prophylactic antibiotics alone (22).

Mirzarazi et al. (23) recently reported that among *E. coli* isolates the highest antibiotic resistance was related to nalidixic acid and trimethoprim-sulfamethoxazole, and *Klebsiella* spp. isolates were the most antibiotic resistant to trimethoprim-sulfamethoxazole, ciprofloxacin, and nalidixic acid. In another study, it was determined that *E. coli* was the most frequent isolate with resistance to ampicillin, with 69.5%, and that a high or increasing resistance to trimethoprim-sulfamethoxazole was characterized by all uropathogens (24). Among children hospitalized for urinary tract infection in northwest Iran, Ghorashi et al. (25) showed that isolated pathogens were highly resistant to ampicillin, cotrimoxazole, and cephalexin.

In conclusion, antibiotic treatment should be based on areal observation of antibiotic resistance, because the bacterial pattern of resistance to antibiotics significantly varies by region. This study is the first research to evaluate the prevalence and susceptibility patterns of bacteria isolated from children with UTI in Kars, Turkey. This important knowledge contributes to the determination of regional antimicrobial policies.

Footnote

Authors' Contribution: Study concept and design: Yunus Yilmaz; acquisition of data: Yunus Yilmaz, Zuhal Tekkanat Tazegun, Emsal Aydin, Mahmut Dulger; analysis and interpretation of data: Yunus Yilmaz; drafting of the manuscript: Yunus Yilmaz; critical revision of the manuscript for important intellectual content: Yunus Yilmaz, Zuhal Tekkanat Tazegun, Emsal Aydin; statistical analysis: Yunus Yilmaz; administrative, technical, and material support: Yunus Yilmaz; study supervision: Yunus Yilmaz, Zuhal Tekkanat Tazegun, Emsal Aydin, Mahmut Dulger.

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