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Community-acquired urinary tract infections in children: pathogens, antibiotic susceptibility and seasonal changes

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Abstract. – AIM: Urinary tract infections (UTIs) are common infections affecting children. The aim of our study is to determine microorganisms that cause community-acquired urinary tract infections and their antibiotic susceptibility in children.

MATERIALS AND METHODS: Our investigation includes 150 cases which has positive urine culture. The cases are detected at Pediatric Polyclinics of Dicle University between June 2010 and June 2011.

RESULTS: The study included 118 (78.7%) female and 32 (21.3%) male children. Urinary tract infections were seen in autumn 10.7% (n = 16), summer 35.3% (n = 53), winter 30.7% (n = 46) and spring 23.3% (n = 35). The culture results indicated 75.3% (n = 113) *Escherichia coli*; 20.7% (n = 31) *Klebsiella*; 2.7% (n = 4) *Proteus* and % 1.3 (n = 2) *Pseudomonas*. The antibiotic resistance against *Escherichia coli* was found out is amikacin (3%), ertapenem (7%), imipenem (0%), meropenem (0%), nitrofurantoin (9%), trimethoprim/sulfamethoxazole (58%), piperacillin (83%), amoxicillin/clavulanate (50%), ampicillin/sulbactam (65%), cefazolin (54%), cefotaxime (51%), cefuroxime sodium (51%) and tetracycline (68%). The resistance ratios of *Klebsiella* are amikacin (0%), imipenem (0%), levofloxacin (0%), meropenem (0%), amoxicillin/clavulanate (57%), ampicillin/sulbactam (79%), ceftriaxone (68%), cefuroxime sodium (74%) and trimethoprim/sulfamethoxazole (61%).

CONCLUSIONS: The results represent the increasing antibiotic resistance against microorganisms among the community-acquired UTI patients in a developing country such as Turkey. So, the physicians should consider resistance status of the infectious agent and choose effective antibiotics which are nitrofurantoin and cefoxitin for their empirical antibiotic treatment. Furthermore, they should be trained about selection of more effective antibiotics and check the regional studies regularly.

Key Words:
Urinary tract infections, Children, Season, Antibiotics resistance.

Introduction

Urinary tract infections (UTIs) are common infections that affect organs of the urinary system such as urethra, bladder, ureter or renal parenchyma. It is the most common group of infection seen in childhood[1]. The prevalence of UTIs varies according to age, gender, seasons and living region. It is reported that the prevalence of UTIs is 8.4% for females under seven years old and 1.7% for males under seven years old[2]. Nowadays still *Escherichia coli* is the most frequently isolated pathogen followed by *Klebsiella spp*, *Proteus*, *Enterococcus* and *Enterobacter spp*[3,4]. If UTIs do not treat by appropriate antibiotics, they may transformed into chronic urinary tract infections and cause important states like formation of scar tissues in the kidneys, hypertension and chronic renal failure. Moreover, they constitute a serious economic cost for countries[5,6].

Especially, in the underdeveloped and developing countries, due to inappropriate use of antibiotics, antibiotic resistance is increasing and treatment of UTIs becomes more difficult by time. Physicians should mind the regional antibiotic resistance for determining empirical therapy until they get culture results or they have no culture tests.

In our work, we aim to investigate pathogen microorganisms, status of their antibiotic susceptibility, seasonal changes and risk factors.

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Materials and Methods

Our report includes 150 cases which has positive urine culture. The cases are detected at Pediatric Polyclinics of Dicle University between June 2010 and June 2011. Hospitalized patients were excluded. The files of patients were retrospectively scanned and age, gender, date of application, culture and antibiogram results were recorded.

Urine samples were collected after the standard cleaning from small age patients without urine control by sterile urine bag and from patients with urine control from mid-stream urine. Urine samples were planted to Eosin Methylen Blue (EMB) and 5% sheep blood agar by 4-mm caliber loop in the Laboratory and were incubated at 37°C average of 18-24 hours. Clinical findings and addition to a single type multiplication of bacteria more than 100.000 colonies/ml in cultures were based for diagnosis of urinary tract infections. Conventional methods (colony morphology, Gram stain, MV C reactions) and Phoenix TM 100 (Becton Dickinson, Franklin Lake, NJ, USA) fully automatic identification system was used for the definition of isolates. All of the antimicrobial susceptibility of isolated and identified strains were studied according to recommendations of Clinical and Laboratory Standards Institute (CLSI) with the automatic identification system against to amikacin, amoxicillin/clavulanate, ampicillin, ampicillin/sulbactam, aztreonam, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, cefuroxime sodium, ciprofloxacin, ertapenem, gentamicin, imipenem, levofloxacin, meropenem, nitrofurantoin, norfloxacin, piperacillin, piperacillin/tazobactam, tetracycline, tobramycin, trimethoprim/sulfamethoxazole.

Statistical Analysis

Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) for Windows 16 statistical package program was used for statistical analysis of the data. The data were mean ± standard deviation and the percentages. For statistical analysis of normal distribution quantitative data, one-ANOVA test and Student's *t*-test and for statistical analysis of anormal distribution quantitative data or qualitative data chi-square test were used. $p < 0.05$ was considered statistically significant.

Results

Gender and Age

Our case load consisted a total of 150 pediatric cases, 118 (78.7%) female and 32 (21.3%) male. Female/male ratio was 3.7. The statistic rate of females was significantly higher than the rate of males ($p < 0.001$). Their ages ranged from 1 month to 15 years and the mean age of cases were 6.58 ± 4.24 years. 75% (n = 24) of male cases were 3 years old or younger and only 23.7% (n = 28) of female were 3 years old or younger. The mean age of females were 7.36 ± 3.99 years and the mean age of males were 3.69 ± 3.93 years. The difference was statistically significant ($p < 0.001$).

The Isolated Pathogens

From the cultures, most often 75.3% (n = 113) *Escherichia coli* and 20.7% (n = 31) *Klebsiella spp* were isolated. Less often 2.7% (n = 4) *Proteus spp* and % 1.3 (n = 2), *Pseudomonas spp* were isolated. The percentage of *Escherichia coli* was 86.7% (n = 98) in the females and 46.9% (n = 15) in the males; the prevalence of *Klebsiella spp* was 12.7% (n=15) in the females and 50% (n=16) in the males. The difference was statistically significant ($p < 0.001$, Figure 1).

Seasonal Changes

UTIs were most oftenly seen 35.3% (n = 53) in summer, 30.7% (n = 46) in winter and less of-

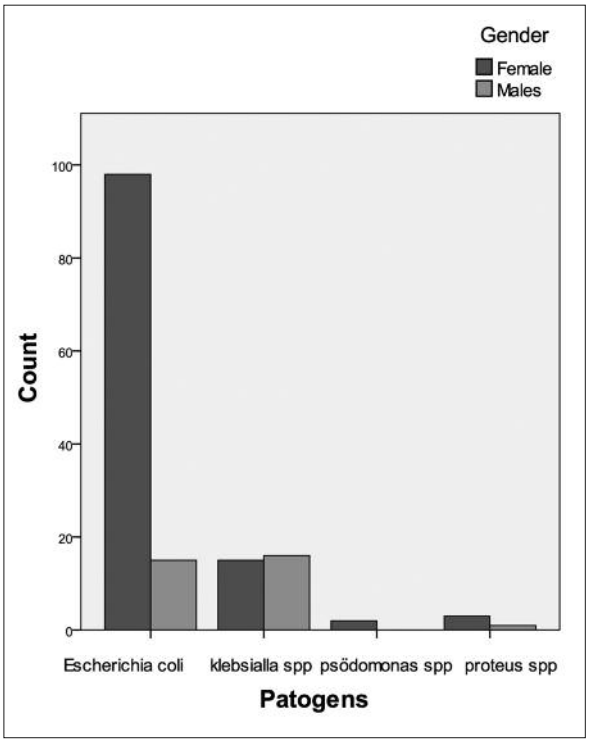

Figure 1. The distributions of isolated pathogens according to gender.

tenly seen 23.3% (n = 35) in spring and % 10.7 (n = 16) in autumn. UTIs seen in females were most often 43.8% (n = 14) in summer and least often 15.6% (n = 5) in spring, in males most often 33.9% (n = 14) in winter and least often 7.6% (n = 9) in autumn (p = 0.036, Figure 2). *Escherichia coli* infections were seen most often 35.4% (n = 40) in summer and least often % 9.7 (n = 11) in spring. *Klebsiella spp* coli infections were seen most often 38.7% (n = 12) in summer and less often % 12.9 (n = 4) in spring.

Antibiotic Susceptibilities

In the *Escherichia coli* the major sensitivity was against to amikacin, ertapenem, imipenem, meropenem and nitrofurantoin and the major resistance was against to ampicillin, trimethoprim/sulfamethoxazole, piperacillin, amoxicillin/clavulanate, ampicillin/sulbactam, cefazolin, cefotaxime, cefuroxime sodium and tetracycline (Table I). In the *Klebsiella spp* the major sensitivity was against to Imipenem, levofloxacin, meropenem and the major resistance

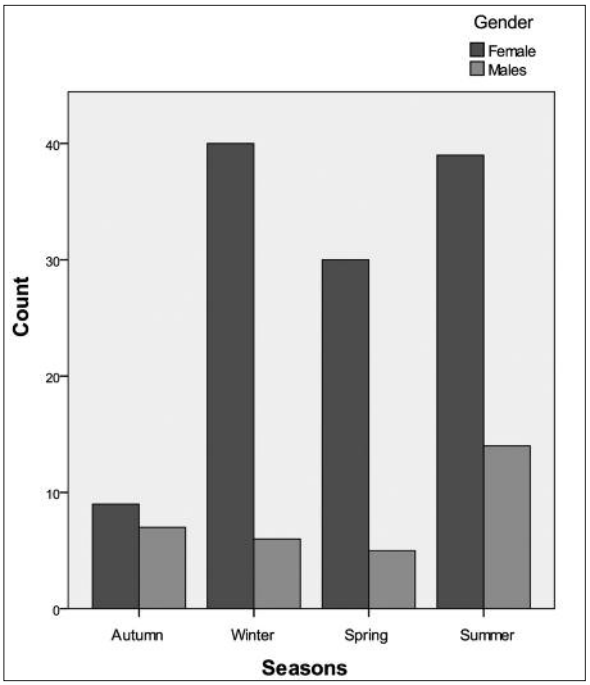

Figure 2. The distributions of cases according to seasons and gender.

Table I. Antibiotic susceptibility against *Escherichia coli*.

	Escherichia coli						
	Sensitive		Middle-sensitive		Resistance		
Antibiotic	n	%	n	%	n	%	Total n
Amicasin	110	(97)	–	–	3	(3)	113
Amoxicillin/clavulanate	33	(34)	16	(16)	49	(50)	98
Ampicillin	8	(16)	–	–	43	(84)	51
Ampicillin/sulbactam	20	(32)	2	(3)	40	(65)	62
Aztreonam	59	(53)	4	(4)	49	(44)	112
Cefazolin	50	(46)	2	(2)	60	(54)	112
Cefepime	58	(52)	4	(4)	48	(44)	110
Cefotaxime	18	(44)	2	(5)	21	(51)	41
Cefoxitin	90	(81)	10	(9)	11	(10)	111
Ceftazidime	69	(61)	3	(3)	42	(37)	114
Ceftriaxone	34	(49)	3	(4)	32	(46)	69
Cefuroxime sodium	31	(45)	3	(4)	35	(51)	69
Ciprofloxacin	86	(76)	3	(3)	24	(21)	113
Ertapenem	56	(93)	–	–	4	(7)	60
Gentamicin	74	(65)	1	(1)	38	(34)	113
Imipenem	113	(100)	–	–	–	–	113
Levofloxacin	29	(71)	–	–	12	(29)	41
Meropenem	113	(100)	–	–	–	–	113
Nitrofurantoin	62	(90)	1	(1)	6	(9)	69
Norfloxacin	59	(83)	–		12	(17)	71
Piperacillin	2	(9)	2	(9)	19	(83)	23
Piperacillin/tazobactam	67	(71)	6	(6)	22	(23)	95
Tetracycline	13	(32)	–		28	(68)	41
Tobramycin	14	(56)	3	(12)	8	(32)	25
Trimethoprim/sulfamethoxazole	47	(42)	–		66	(58)	113

was against amoxicillin/clavulanate, ampicillin, ampicillin/sulbactam, ceftriaxone, cefuroxime sodium, trimethoprim/sulfamethoxazole (Table II).

Discussion

UTIs continue to be a huge health problem over the world due to complications such as chronic renal failure and hypertension and also cause high economic cost. UTIs may demonstrate different epidemiological and etiologic features due to gender, age and region. So the regional studies from different times are of great importance for better understanding of the disease, effective treatment and prevention of complications.

The appearance of UTIs due to gender may change by age. However, especially in male infants according to the presence of tissue prepisium, the incidence of UTIs is high and it significantly decrease by age. The incidence of UTIs shows a similar percentage in all ages of female groups[7]. Irem et al[8] reported the incidence of UTIs in females as 84.3% in their study. A study[9] made in our Hospital between the years 2003-2005 reported UTIs' rate of females 87.4% and males 12.6%. In this very investigation, 78.7% of cases were female; the majority of male cases were 3 years old or younger and there was no correlation between the incidence and age in the females.

The studies about the incidence and rate of pathogens taking part in etiology of UTIs according to the seasons are scarce. In a report about UTIs caused by *Escherichia coli* was referred that there was a positive correlation between the air temperature and UTIs, a negative correlation between the air humidity and UTIs[10]. In our study, UTIs were seen most often in summer and less often in autumn. Also, UTIs caused by *Escherichia coli* or *Klebsiella spp* were seen most often in summer and less often in spring.

Type of UTIs pathogens may vary according to gender and age. To know the causal pathogens is very important for appropriate treatment. The most common pathogens for UTIs are *Es-*

Table II. Antibiotic susceptibility against *Klebsiella spp.*

	Klebsialla spp						
	Sensitive		Middle-sensitive		Resistance		
Antibiyotikler	n	%	n	%	n	%	Total n
Amicacin	28	(100)	–	–	–	–	28
Amoxicillin/clavulanate	9	(3)	4	(13)	17	(57)	30
Ampicillin	–	–	–	–	17	(100)	17
Ampicillin/sulbactam	2	(14)	1	(7)	11	(79)	14
Aztreonam	11	(35)	5	(16)	15	(48)	31
Cefazolin	9	(29)	–	–	22	(71)	31
Cefepime	13	(42)	2	(6)	16	(52)	31
Cefotaxime	6	(50)	1	(8)	5	(42)	12
Cefoxitin	20	(67)	2	(7)	8	(27)	30
Ceftazidime	13	(42)	2	(6)	16	(52)	31
Ceftriaxone	5	(26)	1	(5)	13	(68)	19
Cefuroxime sodium	4	(21)	1	(5)	14	(74)	19
Ciprofloxacin	24	(89)	–	–	3	(11)	27
Ertapenem	12	(86)	–	–	2	(14)	14
Gentamicin	16	(52)	–	–	15	(48v	31
Imipenem	31	(100)	–	–	–	–	31
Levofloxacin	12	(100)	–	–	–	–	12
Meropenem	25	(100)	–	–	–	–	25
Nitrofurantoin	9	(47)	3	(16)	7	(37)	19
Norfloxacin	15	(79)	1	(5)	3	(16)	19
Piperacillin	4	(36)	1	(9)	6	(55)	11
Piperacillin/tazobactam	17	(55)	2	(6)	12	(39)	31
Tetracycline	7	(58)	–	–	5	(42)	12
Tobramycin	3	(50)	–	–	3	(50)	6
Trimethoprim/sulfamethoxazole	12	(39)	–	–	19	(61)	31

cherichia coli followed by *Klebsiella spp*. in the world. A previous research reported the rate of *Escherichia coli* as 84.8% and the rate of *Enterobacter spp*. as 6.1%[8]. A study that was made in our Hospital between the years 2003-2005 reported the rate of patogens as *Escherichia coli* (75.7%), *Klebsiella spp* (7.2%), *Proteus spp* (6.3%) and *Enterobacter spp* (1.8%)[9]. Our findings similar to other study results, represented 75.3% *Escherichia coli*, 20.7% *Klebsiella spp*, 2.7% *Proteus spp* and 1.3% of *Pseudomonas spp*. Addition to that, the frequency of *Escherichia coli* was 86.7% in females and 46.9%in males; the frequency of *Klebsiella spp* was 12.7% in females and 50% in males. Therefore, in light of these findings before starting an empirical treatment, gender and factors involved in the etiology should be considered.

Antibiotic resistance of the living area should be known well for the selection of appropriate empirical antibiotic treatment of UTIs. However, rates of antibiotic resistance may change over time by the region. Especially in the underdeveloped and developing countries, rates of antibiotics resistance is quite high due to using unsuitable antibiotics. In a study that was made between 2007-2009 in Italy which is a developed country, the antibiotic resistance for *Escherichia coli* was found out that cotrimoxazole (inpatients: 22%, outpatients: 15%), coamoksilav (inpatients: 6%, outpatients: 10%) and for ceftazidime, ceftriaxone, nitrofurantoin and gentamycine resistance ratio was below 1%[11]. Savas et al[12] found the rates of antibiotic resistance against *Escherichia coli* as ampicillin (7%), aztreonam (40%), gentamicin (17%), amikacin (10%), ampicillin-sulbactam (42%), cefuroxime (18%), ceftriaxone (13%), ceftazidime (13%), ciprofloxacin (25%), trimethoprim-sulfamethoxazole (59%), imipenem (0%) and against *Klebsiella* spp ampicillin (79%), aztreonam (45%), gentamicin (20%), amikacin (19%), ampicillin-sulbactam (60%), cefuroxime (42%), ceftriaxone (35%), ceftazidime (25%), ciprofloxacin (18%), trimethoprim-sulfamethoxazole (48%), imipenem (0%) in the community-acquired UTIs. An investigation made in our Hospital between the years 2003-2005 reported the final rates of antibiotic resistance against *Escherichia coli* to ampicillin (82.4%), aztreonam (37.3%), gentamicin (26.8%), amikacin (8.1%), cefuroxime (38.2%), ceftriaxone (16%), ceftazidime (22.4%), ciprofloxacin (1.1%), trimetoprim-sulfamethoxazole (71.3%) (8). And also, rates of antibiotic resistance against *Escherichia coli* to amikacin (3%), ertapenem (7%), imipenem (0%), meropenem (0%), nitrofurantoin (9%), ampicillin (84%), trimethoprim/sulfamethoxazole (58%), piperacillin (83%), amoxicillin/clavulanate (5%), ampicillin/sulbactam (65%), cefazolin (5%), cefotaxime (51%), ceftazidime (37%), cefuroxime sodium (51%) and tetracycline (68%) and the resistance against *klebsiella* spp to amikacin (0%), imipenem (0%), levofloxacin (0%), meropenem (0%), ceftazidime (5%), nitrofurantoin (37%), amoxicillin/clavulanate (57%), ampicillin (100%), ampicillin/sulbactam (79%), ceftriaxone (68%), cefuroxime sodium (74%), trimethoprim/sulfamethoxazole (61%).

In light of these findings, in our country, cause of *Escherichia coli* strains' high antibiotic resistance against ampicillin, trimethoprim/sulfamethoxazole, piperacillin, amoxicillin/clavulanate, ampicillin/sulbactam, cefazolin, cefotaxime, cefuroxime sodium and tetracycline, more effective antibiotics which are amikacin, ertapenem, imipenem, meropenem and nitrofurantoin should be used for empirical antibiotic treatment of *Escherichia coli* strains. Also, because of *Klebsiella spp* strains' high antibiotic resistance against ampicillin, trimethoprim/sulfamethoxazole, piperacillin, amoxicillin/clavulanate, ampicillin/sulbactam, cefazolin, cefotaxime, cefuroxime sodium, nitrofurantoin and tetracycline, more effective antibiotics for example amikacin, ertapenem,imipenem or meropenem should be used for empirical antibiotic treatment.

Conclusions

Developing countries like Turkey, there is a quite high antibiotic resistance among the patients with UTI. Therefore, because the majority of UTIs seen in females caused by *Escherichia coli*, amoxicillin/clavulanate, ceftazidime and trimethoprim/sulfamethoxazole should not be preferred for empirical antibiotic treatment of outpatients anymore. Conversely, nitrofurantoin and Cefoxitin should be preferred. Also, because of the same ratio was seen in UTIs in males caused by *Escherichia coli* and *Klebsiella spp*, amoxicillin/clavulanate, ceftazidime, trimethoprim/sulfamethoxazole and nitrofurantoin should not be preferred for empirical antibiotic treatment of outpatients anymore. Effective antibiotics against both *Escherichia coli* and *Klebsiella spp* such as ciprofloxacin and cefoxitin should be

preferred. We think that the physicians who work in the primary health care facility should be trained for the selection of more appropriate antibiotics and regional studies about UTIs should be repeated more frequently.

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