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Research article

Bacterial etiology and antimicrobial susceptibility profiles of 7741 urine cultures in outpatients: A 5-year single-center experience in Turkey

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ABSTRACT

Aim: To determine the epidemiological and antibiotic **s**usceptibility profile of bacterial uropathogens in outpatients.

Methods: This study analyzed data taken from outpatients with urinary tract infection (UTI) collected from January 2013 to January 2018 in the laboratory of Maltepe Medical Center in İstanbul. Species of uropathogens were made using routine laboratory methods. Antibiotic resistance profile of uropathogens was determined using disk diffusion method.

Results: There were 7741 urine cultures and 1563 of them were positive for bacterial uropathogens. The identified major organisms were Gram-negative bacteria (1376/1563; 88.0%), while Gram-positive bacteria only 5.4% (187/1563) were representing. The patients with positive samples, 84.8% (1326/1563) were female and 15.1% (237/1563) were male. The main isolated uropathogen was *E. coli* (58.1%), followed by *Enterobacter spp* (10.1%), *P. mirabilis* (8.6%), *K. pneumoniae* (7.8%), *Enterococcus* (4.7%) *and P. aeruginosa* (3.1%). *E. coli* was more prevalent in all age groups. A total of 74.8% of *E. coli* isolates were resistant to ampicillin and the lowest resistance rate was to imipenem (0.3%). *Enterobacter species* were found to have higher resistance to ampicillin (87.3%), lower resistance to carbapenem (1.8%) and amikacin (6.9%).

Conclusion: Due to the emergence of various antibiotics resistant bacterias, it was concluded that empirical antibiotic treatment should be reviewed periodically according to the regions. Empirical therapy must be based on local epidemiological data, which should be constantly updated. Therefore, the results of our study may help physicians to select an appropriate antimicrobial therapy.

Keywords: Urinary tract infection, antibiotic resistance, uropathogens, outpatients.

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Introduction

Urinary tract infections are a serious public health problem with urinary symptoms accompanied by bacteriuria. It is one of the most common bacterial infections seen with a high rate of financial cost and morbidity [1,2].

The agents that cause urinary tract infection vary by region and besides that, antibiotic susceptibility and resistance profiles also vary [2]. Antibiotic resistance rates of uropathogenic bacteria are increasing day by day worldwide. [1,2,3]. The treatment of the cases is usually done empirically considering the antibiotic susceptibility and resistance profiles of uropathogens. These treatments can result in long-term alteration of the normal microbiota and development of resistant microorganisms [3-5]. The most common bacterial uropathogens of UTI are *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Enterococcus faecalis* and *Staphylococcus saprophyticus* [2-4]. Today in the treatment of urinary tract infections most commonly used chemotherapeutics are amoxicillin, cotrimoxazole, aminoglycosides, cephalosporins, nitrofurantoin, and quinolone group antibiotics. As a result of widespread and misuse, there is increasing resistance to these antibiotics [1].

In order to enhance patient health outcomes and reduce the emergence of resistance to antibiotics, coordinated strategies are needed. It is essential to carry out surveillance of the bacterial spectrum. Resistance to antibiotics of locally occurring uropathogens that could serve as a basis for empirical treatment of UTIs and surgical prophylaxis [6,7].

Antibiotic resistance rates can vary geographically and include significant differences between countries and regions. Accurate bacteriological recordings of culture results provide guidance to empirical treatment before sensitivity patterns are found. Because many of the urinary tract infections are empirically treated, the choice of antibiotics should be determined according to the most likely pathogen and expected resistance profile in a geographic area [1,7,8].

The purpose of this retrospective study was to determine the isolation frequency and antimicrobial resistance patterns of uropathogens through 5 years of results in outpatients in a single center in Turkey.

Methods

The study was ethically approved by the local ethical committee of İstanbul Memorial Hospital (Protocol number: 2018/7-4). This retrospective study involved all urine samples analyzed during the period from January 2013 to January 2018 in the medical microbiology laboratory of Maltepe Medical Center in İstanbul. Patients received any antimicrobial treatment before sampling were excluded. All of the outpatients, all of the age and gender, all departments of the Medical Center were included.

Urine samples were collected from outpatients. Urine culture results were analyzed using the ‘’Laboratory Information System’’ database. Identification codes were used for data and results were used solely for scientific purposes. Age, gender, growing bacterial species and antibiotic resistance rates were recorded in the excel file. Age groups; between 0-17 pediatric age, 18-64 adult age, and 65 years old and older were accepted as geriatrics age groups. All of the data were entered by Microsoft Excel 2007.

Sample Collection

While medium flow urine is taken in outpatients, urinary aspiration method was used in patients with urinary catheters. Pediatric urine samples were collected by special plastic bags produced differently for girls and boys. After routine cleaning procedures in male and female patients, medium flow urine was collected. The patients were guided to pass urine sample of at least 20 *mL* by un-touched, sterile technique in a wide-mouth screwcapped sterile container. Samples were analyzed in the laboratory within 1 hour after collection.

Isolation and identification of uropathogens

All samples were inoculated on blood agar EMB agar (Bioanalyse /Turkey) and incubated at 35±2°C for 24 h. Following incubation, the bacterial colonies were counted and counts of ≥10^5colony-forming units (CFUs)/mL were included in the study. Isolated uropathogens were identified to species level using routine laboratory methods.

Antibiotic susceptibility test

Antibiotic susceptibility patterns of the bacterial isolates were determined using the Kirby-Bauer disc diffusion method on Mueller-Hinton (MHA) agar (Ekbak/Turkey). The antibiotic disc (Bioanalysis/Turkey) containing the following antibiotics: Ampicillin 10 μg, ampicillin/sulbactam 30 μg, cefuroxime 30 μg, cefprozil 30 μg, cefixime 30 μg, ceftrıaxone 30μg, imipenem 10μg, ciprofloxacin10μg, Levofloxacın 5 μg, gentamicin 30 μg, amikacin 30 μg, trimethoprim/sulfamethoxazole (TMX) 25 μg and nitrofurantoin 200 μg.

Standardized overnight culture of each isolate was used MHA. The antibiotic disks were aseptically placed on the surface of the culture media. After incubated, the inhibition zones were measured and isolates were classified as susceptible, intermediate and resistant according to the National Committee for Clinical Laboratory Standards [8].

Statistical analysis

Data from the study was entered in Microsoft Excel 2007 and analyzed in SPSS 13.0 was used to analyze general data (SPSS, Chicago, IL, USA). Chi-square test was used to compare the relationship between age and sex with uropathogens and antibiotic susceptibility ratio. For statistical evaluations, frequency, percentage and mean ± standard deviations were calculated and the study variables presented in the form of tables.

Results

Characteristics of the patients

A total of 7741 urine samples were analyzed during the five years period, among which 1563 samples (20.1%) were positive, whereas 6178 (79.8%) sample were negative for UTI. All of the total urine samples came from the outpatient department. Patients with positive samples 1326 (84.8%) were female and 237 (15.1%) were male. The age of our patients ranged from 0 to 96 years, with a mean of 31.9 ± 28.9 years and a median of 27 years.

Microbiological profile

When uropathogens were evaluated according to culture results, Gram-negative isolates were more dominant than Gram-positive isolates. (Table 1). While 1376 (88.0%) of all isolated pathogens were Gram-negative bacteria and 187 (11.9%) were Gram-positive bacteria. The main isolated pathogen was *E. coli* (58.1%), followed by *Enterobacter spp* (10.1%), *P. mirabilis* (8.6%), *K. pneumoniae* (7.8%), *Enterococcus* (4.7%), *P. aeruginosa* (3.1%), *Group B streptococcus* (3.0%), *Coagulase-negative staphylococci* (2.2%), *Staphylococcus aureus,* (1.8%). The most common bacteria observed in women were *Escherichia coli* (88.6%) *Enterobacter species* (88.0%), *Group B streptococcus* (88.0%) while the men were *Pseudomonas aeruginosa* (38.0%), *Proteus mirabilis* (30.8%), *Coagulase-negative staphylococci* (25.7%) (Table 2).

E. coli was more prevalent in all age groups. (pediatric 57.7%, adult 58.7% and elderly 57.4%). *Proteus mirabilis* and *Enterobacter* *species* were the most common agents isolated from pediatric patients, while *Enterobacter species* and *K. Pneumoniae* were in adult and geriatric patients. (Table 3).

Table 1. Distribution of the Gram-negative and Gram-positive bacterial isolates from urine samples.

Microorganism	**N**	**%**
Gram-negative	**1376**	**88.0**
Escherichia coli	909	58.1
Enterobacter species	159	10.1
Proteus mirabilis	136	8,6
Klebsiella pneumoniae	122	7.8
Pseudomonas aeruginosa	50	3.1
Gram-positive	**187**	**12.0**
Enterococcus	75	4.7
Group B streptococcus	48	3.0
Coagulase-negative staphylococci	35	2.2
Staphylococcus aureus	29	1.8
Total	**1563**	**100**

Antibiotic susceptibility

Among the isolated microorganisms, the antibiotic resistance of Gram-negative and Gram-positive bacteria groups were analyzed. The antibiotic resistance profile of uropathogens is shown in the table (Table 4-5). A total of 74.8% of *E. coli* isolates were resistant to ampicillin, resistance to cephalosporins were ranged from 21.3% to 35.5% and, 35.4% were resistant to trimethoprim-sulfamethoxazole. Resistance to fluoroquinolones were lower (18.9% ciprofloxacin and 17.7% levofloxacin), as well as the resistance to aminoglycosides (25.6% for gentamicin, and 6.2% for amikacin). The lowest resistance rate was to carbapenem (0.3%). *Enterobacter species* showed higher resistance to ampicillin (87.3%), lower resistance to carbapenem (1.8%) and amikacin (6.9%). *Proteus spp.* were showed higher resistance to amoxicillin (61.7%) nitrofurantoin (48.1%) and trimethoprim-sulfamethoxazole (43.7%).

Table 2. Distribution of the bacterial isolates from urine samples by gender of the patient.

Uropathogens	**Isolates (N / %)**			
	Male	**Female**	**Total**	***P values***
Escherichia coli	103 (11.4)	806 (88.6)	909 (58,1)	0.000
Enterobacter species	19 (11.9)	140 (88.0)	159 (10.1)	0.000
Proteus mirabilis	42 (30.8)	94 (69.1)	136 (8,6)	0.000
Klebsiella pneumoniae	27 (22.1)	95 (77.8)	122 (7.8)	0.000
Enterococcus	12 (16.0)	63 (84.0)	75 (4.79)	0.000
Pseudomonas aeruginosa	19 (38.0)	31 (62.0)	50 (3.19)	0.001
Group B streptococcus	1 (2.0)	47 (88.0)	48 (3.07)	0.000
Coagulase-negative staphylococci	9 (25.7)	26 (74.2)	35 (2.23)	0.000
Staphylococcus aureus	5 (17.2)	24 (82.7)	29 (1.8)	0.000
Total	**237 (15.1)**	**1326 (84.8)**	**1563 (100)**	0.000

Table 3. Frequency among patients with urinary tract infection according age category.

Uropathogens	Pediatric (N / %)	Adult (N / %)	Elderly (N / %)	Total (N)
Escherichia coli	378 (41.5)	343 (37.7)	188 (9.2)	909
Enterobacter species	75 (47.1)	53 (33.3)	31 (19.4)	159
Proteus mirabilis	93 (68.3)	20 (14.7)	23 (16.9)	136
Klebsiella pneumoniae	42 (34.4)	53 (43.4)	27 (22.1)	122
Enterococcus	17 (22.6)	39 (52.0)	19 (25.3)	75
Pseudomonas aeruginosa	16 (32.0)	8 (16.0)	26 (52.0)	50
Group B streptococcus	11 (22.9)	33 (68.7)	4 (8.3)	48
Coagulase-negative staphylococci	12 (34.2)	19 (54.2)	4 (11.4)	35
Staphylococcus aureus	8 (27.5)	16 (55.1)	5 (17.2)	29
Total	**654(41.8)**	**584(37.3)**	**327(20.9)**	**1563**

Klebsiella pneumoniae showed high degree of resistance to ampicillin (97.5%), trimethoprim-sulfamethoxazole (44.2%) cefprozil (43.4%). *Pseudomonas aeruginosa* was showed lower resistance rates to carbapenem, Quinolones and Aminoglycosides while it was resistant to all of the other groups. *Enterococcus spp.*, the most commonly isolated Gram-positive uropathogen, showed a low grade of resistance to ampıcıllın (13.3%), amoxicillin-clavulanic acid (10.6%) and carbapenem (6.6%), but a high grade of resistance to all of the other groups of antibiotic. The other Gram-positive bacterial resistance to antibiotics is summarized in the table-4 and table-5.

Discussion

UTI is one of the most common infectious diseases diagnosed in outpatients. It is the most common problem throughout the world, particularly in developing countries and associated with substantial morbidity and recurrent infections. Importantly, the epidemiology of UTI varies among countries due to geography variation and antibiotic use [2]. Unfortunately, antibiotic resistance has become an increasingly pressing problem in many countries [1-3]. In our study, the positive rate of urinary cultures was found to be 20.1% (1563 out of 1741 samples) and nearly 85% (1326 (out of 1563 samples) of all isolates were obtained from women. Women are more likely to experience UTIs than men. It is well documented that UTI is more common in females than in males due to the anatomical differences of urogenital organs between the two sexes. Our study finding is in agreement with other studies [6,9 -12]. UTI is prevalent in the study area and the most frequently isolated uropathogens were Gram- negative bacteria. Among the isolated pathogens 88.0 % (n=1376) were Gram- negative bacteria and 11.9% (n=187) were Gram-positive bacteria in our study. Gram-negative bacteria were the most commonly isolated organisms in the present study, and previous studies have reported similar findings [1-3].

In our study, Escherichia coli was the most frequently isolated microorganism. Our finding was consistent with similar studies conducted locally [13–17] and internationally [10-12]. The main isolated pathogen was *E. coli* followed by *Enterobacter spp*, *P Mirabilis, K. pneumoniae* respectively. Our findings are different from the literature. Because *Klebsiella pneumonia* was the second most frequent bacteria in the national and international literature [10-17].

Table 4. Resistance of bacterial species to antibiotics containing β-lactam group.

Species (N[a])	Penicillins		Cefalosporins				Carbapenem
	Ampicillin N (%R)	AMC N	Cefuroxime N (%R)	Cefprozil N (%R)	Cefixime N (%R)	Ceftriaxone N (%R)	Imipenem N (%R)
Escherichia coli (909)	680 (74.8)	293 (32.2)	210 (23.1)	322 (35.5)	226 (24.9)	194 (21.3)	3 (0.3)
Enterobacter species (159)	138 (87.3)	69 (43.3)	67 (42.1)	88 (55.3)	65 (40.8)	60 (37.7)	3 (1.8)
Proteus mirabilis (136)	84 (61.7)	40 (29.4)	35 (25.7)	56 (41.1)	38 (27.9)	34 (25.0)	6 (4.4)
Klebsiella pneumoniae (122)	119 (97.5)	45 (36.8)	42 (34.4)	53 (43.4)	34 (30.3)	38 (33.9)	1 (0.8)
Enterococcus (75)	10 (13.3)	8 (10.6)	72 (96.0)	73 (97.3)	72 (96.0)	74 (98.6)	5 (6.6)
Pseudomonas aeruginosa (50)	50 (100)	44 (88.0)	42 (84)	43 (86.0)	43 (86.0)	28 (56.0)	1 (2.0)
Group B streptococcus (48)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Coagulase-negative staphylococci (35)	35 (100)	nt	24 (68.5)	nt	nt	18 (51.4)	10 (25.7)
Staphylococcus aureus (29)	29 (100)	16 (55.1)	13 (44.8)	nt	nt	10 (34.4)	12 (41.3)

N[a]: Total bacterial isolates from urine samples; R: Resistance; nt: non tested.

Table 5. Resistance of bacterial species to quinolones, aminoglycosides, trimethoprim/sulfamethoxazole and nitrofurantoin.

Species (N[a])	Quinolones		Aminoglycosides		Others	
	Ciprofloxacin N (%R)	Levofloxacin N (%R)	Gentamicin N (%R)	Amikacin N (%R)	TMX N (%R)	Nitrofurantoin N (%R)
Escherichia coli (909)	181 (19.9)	161 (17.7)	233 (25.6)	57 (6.2)	322 (35.4)	82 (9.0)
Enterobacter species (159)	46 (28.9)	35 (22.0)	46 (28.5)	11 (6.9)	62 (38.9)	28 (17.6)
Proteus mirabilis (136)	11 (8.0)	13 (9.5)	28 (20.5)	9 (6.6)	59 (43.7)	65 (48.1)
Klebsiella pneumoniae (122)	20 (17.8)	21 (17.2)	35 (31.2)	9 (7.37)	54 (44.2)	52 (42.6)
Enterococcus (75)	64 (85.3)	59 (78.6)	nt	71 (94.6)	68 (90.6)	nt
Pseudomonas aeruginosa (50)	9 (18.0)	10 (20.0)	9 (18.0)	3 (6.0)	43 (86.0)	39 (78.0)
Group B streptococcus (48)	2 (4.1)	0 (0.0)	nt	36 (75.0)	46 (95.8)	nt
Coagulase-negative staphylococci (35)	24 (68.5)	18 (51.4)	8 (22.8)	nt	27 (77.1)	nt
Staphylococcus aureus (29)	24 (68.5)	24 (68.5)	9 (25.7)	nt	30 (85.7)	2 (6.8)

TMX: Trimethoprim/Sulfamethoxazole; N[a] : Total bacterial isolates from urine samples; R: Resistance; nt: non tested.

The prevalence of the bacterial uropathogens varies from region to region and from one study to another study [3,5,9]. In our study, significant difference was also found in frequency of certain uropathogens in relation to gender. E. coli was the most predominant in both genders; however, its incidence was significantly higher in women (60.7%) than in men (43.4%), which was also observed in other similar studies [1,6,10-12]. The highest difference between female and male patients was observed for *P. Mirabilis* and *P. Aeruginosa.* Due to biofilm production capacity, *P. mirabilis* is a serious medical problem in catheter-associated UTI [1,18,19]. *Pseudomonas aeruginosa*, were strongly associated with particular host characteristics, including male gender, previous history of using antimicrobials, prior undergoing interventions in the urinary and neurogenic bladder [19-21]. In our study, *E. coli* was more prevalent in all age groups (Pediatric, 57.7%, Adult 58.7%, and Elderly 57.4%). Similar to previous studies that, *E. coli* remains the majority of pathogen which isolated from urine culture in pediatric, adult, and elderly [1, 22, 23]. The second most common causative agents isolated from pediatric patients were *Proteus mirabilis, Enterobacter species* while adult and geriatric patients were *Enterobacter species, K. Pneumoniae.* Our finding was consistent with similar studies [1, 17,24]. Antibiotic resistance because of inappropriate antibiotic use has become increasingly encountered health problems [3,6,15]. In our study, resistance to antibiotics of uropathogens were investigated (Table-3, 4). The most effective antibiotics for *E. coli* were carbapenem (98.7%), amikacin (94.8%) and nitrofurantoin (91.0%), whereas resistance to ampicillin, cefprozil and trimethoprim / sulfamethoxazole was 74.8%, 35.5% and 35.4%, respectively. *Enterobacter species* showed higher resistance to ampicillin (87.3%), lower resistance to carbapenem (1.8%) and Amikacin (6.9%). Our study finding is in agreement with other local and international studies [1,6,15,23]. The resistance rate of uropathogens *Proteus mirabilis* isolates to TMX 43.7%, to ampicillin, 61.7% to nitrofurantoın 48.1% to carbapenem 4.4%, which was similar rates shown in other studies. [15,19] The isolates of *Klebsiella spp*. showed a high degree of resistance to ampicillin (97.5%) while sensitivity rates of carbapenem (99.0%) and amikacin (92.7%) were observed similar *E. coli.* Our results were found to be consistent with the results of other studies [14,25]. *Pseudomonas Aeruginosa* was the least resistant to carbapenem (2.0%) and amikacin (6.0%) but showed a high degree of resistance to all other antibiotics. Previous studies also reported that amikacin and imipenem were the most effective drugs against *P. Aeruginosa* [26,27]. *Enterococcus*, which is the most commonly isolated Gram-positive bacteria, were resistant to cephalosporins (96.0-98.6%), quinolones (85.3-78.6%), amikacin (94.6%), TMX (90.6%), carbapenem (6.6%) and penicillins (13.3-10.6%). Unlike other studies, cephalosporin and quinolone resistance were found to be high, while penicillin resistance was lower [14,28]. Gram-positive and Gram-negative bacterial resistance to antibiotics is summarized in the table (4-5). Unlike Dordevic et al. [18**]** in Group B streptococcus, resistance to b-lactam antibiotics was not observed while 95% TMX resistance and 75% amikacin resistance were found. The antibiotic resistance profiles of *Staphylococcus aureus* and *Coagulase-negative staphylococci* were consistent with other studies [14,28-30].

Here, we also want to specify some limitations of our study. As the presented data are a laboratory-based on the analysis of microbiological samples without clinical background information, the rate of asymptomatic bacteriuria or symptomatic UTI could not be calculated. It includes urine samples taken from patients with catheters that may be biased to the interpretation of the results. Some antibiotics have not been routinely tested by the microbiology laboratory; therefore, they were not included in our analysis. Moreover, since our study is a single-center study, there is no generalizability of the results to the whole society.

As a result, as these infections are very common, adequate treatment has an important role in regard to the patients' health, development of antibiotic resistance and health care costs. This study determined the prevalence of urinary tract infection and antibiotic susceptibility patterns of the bacteria in outpatients. The most prevalent bacteria responsible for UTI were Gram- negative *Enterobacteriaceae* being that *E. coli* proved to be responsible for more than half of these infections. *Enterococcus*, which is the most commonly isolated Gram-positive bacteria responsible for UTI. These pathogens that cause UTIs have increased resistance to antibiotics in recent years. The emergence of bacteria resistant to various antimicrobials has revealed the necessity of periodic review of empirical antibiotic therapy at regional level. Therefore, the results of our retrospective study may help physicians to select an appropriate antimicrobial therapy. In conclusion, we suggest that antibiotic selection in the treatment of bacterial uropathogens should be based on the local prevalence and antibiotic resistance of bacterial organisms.

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Informed consent: *This was a retrospective study and all patient data were anonymized; informed consent was therefore not required under country-specific regulations.*

Ethical approval: *The study was ethically approved by the local ethical committee of İstanbul Memorial Hospital (Protocol number: 2018/7-4)***.**

References

[1]Alanazi MQ, Alqahtani FY, Aleanizy FS. An evaluation of E. coli in urinary tract infection in emergency department at KAMC in Riyadh, Saudi Arabia: retrospective study. Ann Clin Microbiol Antimicrob. 2018; 17(3):2-7.

[2]Yang B, Yang F, Wang S, Wang Q, Liu Z, Feng W, Sun F, et al. Analysis of the spectrum and antibiotic resistance of uropathogens in outpatients at a tertiary hospital. J Chemother. 2018;30(3):145-149.

[3]Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nat Rev Microbiol. 2015;13(5):269–84.

[4]Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med. 2002;113(1):5-13.

[5]Stefaniuk E, Suchocka U, Bosacka K. Hryniewicz W. Etiology and antibiotic susceptibility of bacterial pathogens responsible for community-acquired urinary tract infections in Poland. Eur J Clin Microbiol Infect Dis. 2016;35(8):1363–69.

[6]Magyar A, Köves B, Nagy K, Dobák A, Arthanareeswaran VKA, Bálint P, et al. Spectrum and antibiotic resistance of uropathogens between 2004 and 2015 in a

tertiary care hospital in Hungary. J Med Microbiol. 2017;66(6):788-97.

[7] Yüksel S, Öztürk B, Kavaz A, Özçakar ZB, Acar B, Güriz H et al. Antibiotic resistance of urinary tract pathogens and evaluation of empirical treatment in Turkish children with urinary tract infections. Int J Antimicrob Agents. 2006;28:(5):413–416.

[8] Clinical and laboratory standarts institute. Performance standards for antimicrobial testing. 7th International. CLSI Document. 2007: M100- S16.

[9] Lu PL, Liu YC, Toh HS, Lee YL, LiuYM, Ho CM et al. Epidemiology and antimicrobial susceptibility profiles of Gram-negative bacteria causing urinary tract infections in the Asia-Pacific region: 2009–2010 results from the Study for Monitoring Antimicrobial Resistance Trends (SMART). Int J Antimicrob Agents. 2012;40 (Suppl):37-43.

[10] Bitew A, Molalign T, Chanie M. Species distribution and antibiotic susceptibility profile of bacterial uropathogens among patients complaining urinary tract infections. BMC Infect Dis. 2017;17(1):654.

[11] Guermazi-Toumi S, Boujlel S, Assoudi M, Issaoui R, Tlili S, Hlaiem ME. Susceptibility profiles of bacteria causing urinary tract infections in Southern Tunisia. J Glob Antimicrob Resist. 2018;12:48-52.

[12] Nzalie RNT, Gonsu H K, Koulla-Shiro S. Bacterial etiology and antibiotic resistance profile of community-acquired urinary tract infections in a Cameroonian city. Int J Microbiol. 2016;2016: 3240268.

[13] Aykan SB, Ciftci IH. Antibiotic resistance patterns of Escherichia coli strains isolated from urine cultures in Turkey: a meta-analysis. Mikrobiyol Bul. 2013;47(4):603-618.

[14] Tandogdu Z, Cek M, Wagenlehner F, Naber K, Tenke P, Ostrum E, et al. Resistance patterns of nosocomial urinary tract infections in urology departments: 8-year results of the global prevalence of infections in urology study. World J Urol. 2014;32(3):791-801.

[15] Abuhandan M, Güzel B, Oymak Y, Çiftçi H. Antibiotic sensitivity and resistance in children with urinary tract infection in Sanliurfa. Turk J Urol. 2013;39(2):106-110.

[16] Doğru A, Karatoka B, Ergen P, Aydın ÖŞ, Tigen ET. The resistance rates of urinary tract infections: Our data from year 2010. Turk J Urol. 2013;39(4):237-243.

[17] Çoban B, Ülkü N, Kaplan H, Topal B, Erdoğan H, Baskın E. Five-year assessment of causative agents and antibiotic resistances in urinary tract infections. Turk Pediatri Ars. 2014;49(2):124-129.

[18] Đorđević Z, Folić M,Janković S. Community-acquired urinary tract infections: causative agents and their resistance to antimicrobial drugs. Vojnosanit Pregl. 2016;73(12):1109–1115.

[19] Linhares I, Raposo T, Rodrigues A, Almeida A. Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: a ten-year surveillance study (2000–2009). BMC Infect Dis. 2013;13(19):1-14.

[20] Tabibian JH, Gornbein J, Heidari A, Dien SL, Lau V H, Chahal P, et al. Uropathogens and host characteristics. J Clin Microbiol. 2008;46(12), 3980-3986.

[21] Costa T, Linhares I, Ferreira R, Neves J, Almeida A. Frequency and Antibiotic Resistance of Bacteria Implicated in Community Urinary Tract Infections in North Aveiro Between 2011 and 2014. Microb Drug Resist. 2018;24(4):493-504.

[22] Chu C.M, Lowder JL Diagnosis and treatment of urinary tract infections across age groups. Am J Obstet Gynecol. 2018;219(1):40-51.

[23] Erdem HA, Uysal S, Tasbakan MI, Pullukcu H, Sipahi OR, Yamazhan T, Ulusoy S. Is Urinary Tract Infection Different in Elderly and Adults Aged Under 65 Years? Ege University Experience. Mediterr J Infect Microb Antimicrob. 2016; 5:10.

[24] Kahlmeter G. The ECO.SENS Project: a prospective, multinational, multicenter epidemiological survey of the prevalence and antimicrobial susceptibility of urinary tract pathogens--interim report. J Antimicrob Chemother. 2000;46 Suppl 1:15-22.

[25] Daglar D, Demirbakan H, Yıldırım Ç, Öztürk F, Özcan A, Sipen N et al. Microorganisms Isolated from Urine Samples and Their Antimicrobial Susceptibilities. Türk Mikrobiyol Cem Derg. 2005;35(3):189-194.

[26] Abbas HA, El-Ganiny AM, Kamel HA. Phenotypic and genotypic detection of antibiotic resistance of Pseudomonas aeruginosa isolated from urinary tract infections. Afr Health Sci. 2018;18(1):11-21.

[27] Etiz P, Kibar F, Ekenoğlu Y,Yaman A. Evaluation of the Antibiotic Resistance Profiles of Enterococcus Species Isolated from Urine Cultures. Türk Mikrobiyol Cem Derg. 2014; 44(3):107-113.

[28] Altoparlak Ü, Özbek A , Aktaş F.Antibiotic Susceptibilities of Gram negative Bacteria Isolated from Urinary Tract Infections. Turk Mikrobiyol Cem Derg. 2001;32(3-4): 167-173.

[29] Hashmi A, Abdullah FE, Abdullah NE, Kazmi SU. Species identification and antibiotic susceptibilities of coagulase-negative staphylococci isolated from urinary tract infection specimens. J Coll Physicians Surg Pak. 2016;26(7):581-4.

[30] Sina H, Semassa JA, TamÃ V, AdjilÃ AA, Baba-Moussa F, Baba-Moussa L. Antibiotics Resistance Profile of Staphylococci Isolated from Urogenital Infections and Toxins Production of Staphylococcus aureus Strains. Ann Med Health Sci Res. 2018;8(Suppli 1): 29-34.