The Pattern of Urinary Tract Infection, Antimicrobial Resistance and Associated Factors in Gölcük of Kocaeli Region

Kocaeli İli Gölcük Bölgesinde İdrar Yolu Enfeksiyonu, Antibiyotik Direnci ve İlişkili Faktörler

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ABSTRACT

INTRODUCTION: This study aimed to evaluate antibiotic susceptibility patterns of bacterial microorganisms isolated from patients with community-acquired urinary tract infections (UTIs) in our region.

METHODS: Between November 2019 and November 2020, 294 patients whose urine culture was positive in the Nephrology outpatient clinic of Gölcük Necati Çelik State Hospital were included in the study. Patient information was recorded from medical files retrospectively.

RESULTS: Escherichia coli (E. coli) was the most common isolated pathogen in culture (76.2%) with Klebsiella spp. ranking second, (10.5%), followed by Pseudomonas and Enterococcus. The incidence of diabetes mellitus (DM) among the 294 patients was 41.5%; the incidence of hypertension was 53%; 3.1% had urinary catheters, and 9.5% (28) of the woman patients were pregnant.

DISCUSSION AND CONCLUSION: This study determined that E.coli was the predominant bacterial pathogen of community-acquired UTIs in our region. We have found that resistance against ceftriaxone, ceftazidime, cefixime, amoxycillin-clavulanic acid, and trimethoprim-sulfamethoxazole was most frequently observed both in the general population as well as in patients with diabetes mellitus. However, resistance against nitrofurantoin and fosfomycin was found to be very low. We believe that the evaluation of antibiotic resistance by the district against microorganisms should be done periodically, and the information obtained from these evaluations should be used when initiating the proper empirical treatment.

Keywords: urinary tract infection, bacterıuria, antibiotic resistance

ÖZ

GİRİŞ ve AMAÇ: Bu çalışmanın amacı bölgemizde toplum kökenli idrar yolu enfeksiyonu (İYE) olan hastalardan izole edilen bakteriyel mikroorganizmaların sıklığını ve antibiyotik duyarlılık paternlerini değerlendirmektir.

YÖNTEM ve GEREÇLER: Kasım 2019-Kasım 2020 tarihleri arasında Gölcük Necati Çelik Devlet Hastanesi Nefroloji polikliniğinde idrar kültüründe üreme saptanan 294 hasta çalışmaya dahil edildi. Hasta bilgileri geriye dönük olarak hastane otomasyon sisteminden kaydedildi.

BULGULAR: En sık izole edilen patojenin E.coli (%76,2) olduğu ikinci sırada Klebsiella spp. (%10,5) olduğu ve bunu Pseudomonas ve Enterococcus suşlarının izlediği saptandı. Diabetes mellitus insidansı %41,5, hipertansiyon insidansı %53 idi. Hastaların %3,1'inde üriner kateter mevcuttu ve kadın hastaların %9,5'i (28) gebe idi.

TARTIŞMA ve SONUÇ: Bölgemizde toplum kökenli İYE'lerde baskın bakteriyel patojeninin E.coli olduğu belirlendi. Seftriakson, seftazidim, sefiksim, amoksisilin-klavulanik asit, trimetoprim-sülfametoksazole karşı direncin hem genel popülasyonda hem de diabetes mellitus'lu hastalarda en sık gözlendiği, nitrofurantoin ve fosfomisine karşı ise direnç oranının oldukça düşük olduğu gözlendi. Bölgelere göre antibiyotik direnç oranlarının periyodik değerlendirilmesi ve bu değerlendirmelerden elde edilen bilgilerin doğru ampirik tedavi seçiminde kullanılması gerektiğine inanıyoruz.

Anahtar Kelimeler: idrar yolu enfeksiyonu, bakteriüri, antibiyotik direnci

INTRODUCTION

The infection of urine and the urinary tract by bacteria, viruses, and other microorganisms is defined as a urinary tract infection (UTI). UTI is one of the most common infections, and it is known that 10% of people will experience UTI at least once in their lives. It can present in different clinical conditions ranging from asymptomatic bacteriuria to sepsis and acute pyelonephritis. In young women that are not pregnant, the prevalence of bacteriuria is very high (1-3%) compared to adult men (0.1% or less). Structural abnormalities of the urinary tract increase this rate in old males. In individuals without anatomical or functional abnormalities, UTIs are generally self-limiting but tend to recur (1,2).

Gram-negative bacilli of Escherichia coli (E. coli) is the most common microorganism leading to 80-90% of the community-acquired and 30-50% of hospital-acquired UTIs in all age groups (2).

UTI is diagnosed using a combination of urinary symptoms and urine culture demonstrating numbers of a known uropathogenic above a given threshold (usually defined as >1,000 colony forming units/mililiter (CFU/ml) of urine, but thresholds as low as 100 CFU/ml and as high as 100,000 CFU/ml are also used (3).

UTI is one of the diseases for which antibiotics are most often prescribed (4). Ineffective antibiotic use can result in failure of treatment. In various studies, different antibiotic resistance rates have been reported. Reasons for this are; the differences between studied patient populations and commonly used antibiotics in different regions. This manuscript highlights the problem of antimicrobial resistance in uncomplicated community-acquired UTIs, focusing on antibiotic resistance (4-6).

The aim of this study was to determine the causative pathogens of UTIs, their susceptibility patterns to commonly used antibiotics, and the underlying risk factors.

MATERIAL and METHODS

This retrospective, cross-sectional study was carried out with results from urine samples obtained from outpatients at the Nephrology department of Gölcük Necati Çelik Statement Hospital in Kocaeli, Turkey, from November 2019 to November 2020.

For a total of 294 participants suspected of UTI, clean catch mid-stream urine samples were collected using a sterile wide-mouth container from enrolled patients. All the samples were analyzed to ensure that the pathogenic organisms present in the urine were isolated and to avoid overpopulation of the pathogenic organism. The patient's urine analysis was positive for pyuria (>10 leukocytes) and leukocyte esterase. Positive urine culture was considered as bacillus isolation >10^5 CFU/ml in urine culture according to European guidelines.

We excluded in-significant cultures (the growth of more than one bacterium, the growth of lower than standard quantity CFU/ml, and the growth of bacteria considered contaminants).

Samples were analyzed in the Gölcük Necati Çelik Hospital's Microbiology laboratory. Isolated bacteria and antibiotic susceptibility were identified by standard laboratory techniques (7).

Uropathogens were classified using traditional phenotypic methods, with antibiotic resistance determined by Vitek N257 cards (bioMérieux, France). Categorical susceptibility breakpoints followed current guidelines from the Clinical and Laboratory Standards Institute (8,9). Antibiotic susceptibility analysis was carried out using the Kirby-Bauer disc diffusion technique on Muller-Hinton agar, and commercial antibiotic plaques (United Kingdom) were used for antimicrobial testing. The antibiotic disc-impregnated culture plates were incubated at 37°C overnight. The diameter of the zone of inhibition was measured and recorded as resistant or susceptible according to the National Committee for Clinical Laboratory Standards (NCCLS) interpretative criteria (8,9).

Approval of the local ethics committee (Bahçeşehir University Clinical Research Ethics Committee, 16/02/2022 date and 2022-03/06 number) for the study protocol in accordance with Helsinki Declaration agreements, written informed consent of the patients, and legal guardians were obtained.

Statistics

We used to Mann-Whitney U-test and Kruskal-Wallis test to compare median variables between groups and independent samples. Also, t-test and one-way ANOVA tests were used for comparing parametric variables. For investigated the risk factors for the development of UTIs were used Cox regression analysis. Comparing categorical data were analyzed, and Chi-square and Fisher's exact test was used. For all statistical analyses, a p-value <0.05 was considered significant. All data are analyzed with SPSS (version 20.0; SPSS Inc, Chicago, IL) statistical package. The characteristics of the study patients were expressed as mean or median, as appropriate for categorical variables, percentages, and variables with continuity.

RESULTS

This cross-sectional study was conducted with the objective of describing prevalence, microbiological profile, and resistance to antibiotics in UTIs. A total of 294 UC were collected. Of these samples, 233 (79.3%) were women, and 61 (20.3%) were men. The mean age was 58.41 ± 20.174 years (18-94). Mean glomerular filtration rate (GFR) was %67.23 ± 25.69 ml/min (10-121 ml/min). Demographics and clinical data of male/female patients are in Table 1.

Table 1. Demographics and Clinical Data of Patients

	Male (n)	Female (n)	Total (n)
Age (years)	60.42	50.4	58.41
GFR (ml/min)	55.9	72.81	67.23
Diabetes mellitus (n)	25	97	122
Hypertension (n)	33	125	158
Recurrent UTI (n)	8	16	24

UTI: urinary tract infection, GFR: glomerular filtration rate

Isolated of the bacteria were: E. coli 224 (76.2%), Klebsiella spp. 31 (10.5%), Proteus spp. 10 (3.4%), Pseudomonas spp. 10 (3.4%), Staphylococcus spp. 7 (2.4%), and Streptococcus spp. 8 (2.8%). Of 18 Fungi isolated (6.12%) from the patient's urinary cultures. Fifteen of those patients were women, and they had a history of antibiotic use at the time. Figure 1 reveals the distribution and percentage of isolated etiologic microorganisms according to gender.

The rate of resistance of E. coli and Klebsiella spp. to a panel of antibiotics, including penicillins, cephalosporins, quinolones, aminoglycosides, and trimethoprim-sulfamethoxazole which are routinely used to treat UTI is shown in Figure 2.

E. coli, as the most dominant cause of UTI, detected the highest percentage of resistance to ampicillin (53.6%) and lowest resistance to levofloxacin (1.3%). Klebsiella spp., the second most prevalent pathogen of UTI, described a similar resistance pattern (Figure 2)

Analysis of the results according to patient's gender indicated that although E. coli is the most common isolated pathogen from both genders. The prevalence of UTI due to Klebsiella spp. and Pseudomonas spp. were lower in females than males, respectively (8.6% and 18%), but there was no statistically significant (p=0.10).

In our study group, 41.5% of the patients had diabetes mellitus (DM). Furthermore, 53% of the patients had hypertension, 12.2% had a history of the cerebrovascular event, 3.1% of the patients had urinary catheters placed at the time, 9.5% (28 patients) of the women patients had a history of pregnancy, and 3 of them had a history of malignancy.

In diabetic patients, E. coli was the most commonly isolated pathogen (75.4%), followed by Klebsiella spp. (8.2%) and Pseudomonas spp. (5.7%) respectively. Of 28 patients who had a history of pregnancy, E. coli was also the most common pathogen identified in this group. Also, in hypertensive patients, the most common pathogen was E. coli.

We examined the patterns of antibiotic resistance to E. coli in diabetic patients and found the following antibiotics patterns; penicillin 40.7%, cephalosporines

42.8%, quinolone 61.1%, trimethoprim-sulfamethoxazole 43.5%, and nitrofurantoin 6.5%.

In recurrent UTI episodes, the primary pathogen was E. coli isolated in patients 25 (69.4%), and the second pathogen was Klebsiella pneumonia in 8 (22.2%). Fungal agents were found as causative agents in 3 (8.33%) UTI episodes.

According to multivariable analysis, factors independently associated with cefixime, ciprofloxacin resistance were female sex (adjusted odds ratio [AOR] 3.09; 95% CI, 1.48 to 10.89; p: 0.02) and DM (AOR 2.24; 95% CI, 1.12 to 6.99; p: 0.03). Factors independently associated with trimethoprim-sulfamethoxazole, ceftriaxone, and amoxicillin-clavulanate resistance were recent UTI (all three) as well as age, obesity, and urinary abnormalities. The most frequent agents causing UTIs were E. coli and Klebsiella pneumonia for isolated recurrent UTIs.
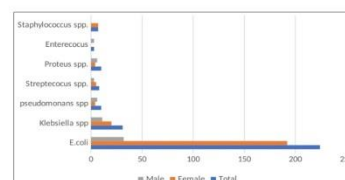

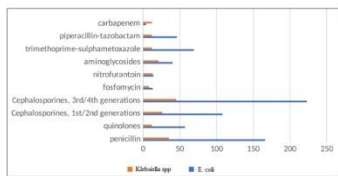Figure 1. Frequency Isolated Bacteria from Urine Samples according to Gender

Figure 2. Resistance of *E. coli* and *Klebsiella spp.* to Antibiotics

DISCUSSION

We aimed to determine antibiotic resistance and sensitivity of the isolated bacteria in UTI cases in our region. E. coli is the most common uropathogen causing complicated and uncomplicated UTIs in accordance with the literature (1,10). Our study results showed that E. coli is the most common microorganism too. Unfortunately, antibiotic resistance is increasing among microorganisms that cause UTIs.

The purpose of using standard treatment protocols both in our country and all over the world is to increase treatment consistency while decreasing the cost of diagnosis and treatment of UTIs (11).

It is known that there are numerous factors and co-existent diseases that increase the possibility of UTI. Risk factors for developing UTI include; being a woman, pregnancy, hydronephrosis, ureteropelvic stenosis, prostate disease, history of kidney stones, urinary catheter placement, and constipation (12,13).

Khawcharoenporn et al. reported that 34% of the patients that had community-acquired UTIs had a history of prior UTI infections (14). A similar study by Martinez et al. reported that in patients with community-acquired UTIs, recurrent UTI infections were present in 11.4%, while urolithiasis was present in 9.6%, 5.7% had immunosuppression, and 5.6% had placed urinary catheters while 3% of their patients were pregnant at the time of the study (15). In another study by Yilmaz et al., it was found that urolithiasis was present in 17.8% of UTI patients, while 9.5% of these UTI patients were pregnant (16). Upon investigation of our patients based on their risk factors, 9.5% of our patients were pregnant, 4% had prostate diseases, 5% had urolithiasis, 8.16% had recurrent UTI history, and 3.1% had placed urinary

catheters. Our results showed a significant increase in the amoxicillin-clavulanate resistance rate in recurrent UTIs (26.5%, 13.4% p: 0.04).

DM rates in UTI patients were (41.5%) in our study groups. After reviewing the literature for similar topics, only 13% of these patients had DM in one of the studies, and 9.1% had DM in a study by Martinez et al. (15). In a study that took place in our country by Yilmaz et al., 26% of UTI patients had accompanying DM (14).

Kabugo et al. showed that UTI infection rates were higher in diabetic groups. They have proposed that the reasons for these high rates were weakened immune systems, dysfunctional polymorphonuclear leukocytes, functional impairments in adherence, chemotaxis, and phagocytosis of leukocytes in UTI patients. Neurologic complications, neurogenic bladder, and high urine glucose have also been identified as risk factors (17,18).

In several studies that have evaluated antibiotic resistance in UTIs, it is observed that resistance of E. coli to ampicillin, amoxycillin-clavulanic acid, trimethoprim-sulfamethoxazole, and ciprofloxacin due to their common use in daily practice (19).

Resistance rates to E. coli in patients in our study were as follows; amoxycillin 20.5%, trimethoprim-sulfamethoxazole 30.8%, cefuroxime 37.9%, cefoxitin 10.3%, cefixime 31.7%, ceftazidime 32.6%, ceftriaxone 31.3%, amikacin 31.3%, gentamicin 9.4%, levofloxacin 1.3%, ciprofloxacin 24.1%, fosfomycin 5.8%, nitrofurantoin 6.3%, and ampicillin 53.6%.

Among the studies in our country, Pullukçu et al. reported this resistance to E. coli; ampicillin 76.1%, amoxycillin-clavulanic acid 21.6%, trimethoprim-sulfamethoxazole 58.4%, ciprofloxacin 4% (20). In another study by Gazi (21) et al., they reported resistance rates of 65.2% to ampicillin, 14.6% to amoxycillin-clavulanic acid, and 38.8% to trimethoprim-sulfamethoxazole. Uslu et al. reported 59% resistance rates to ampicillin, 16.4% to amoxicillin-clavulanic acid, and 22.1% to ciprofloxacin (22). These findings were similar to our study. However, they have found that resistance to levofloxacin was substantially higher (22.3%) when compared to our results.

Also, from the world literature, different resistance rates have been reported. Garza-Monufor et al. revealed 9.5% resistance rates to ceftazidime, 65% to quinolones, and 58% to trimethoprim-sulfamethoxazole (23). In a study by Sierra Diaz et al., resistance rates were found to be 77% for ampicillin and 72.8% for moxifloxacin (24). In another study, Wong et al. reported that the resistance of E. coli to trimethoprim-sulfamethoxazole was 28.6%, while it was 7.9% against ciprofloxacin and 0.4% for nitrofurantoin (25).

We found that the resistance rate to nitrofurantoin and fosfomycin was the lowest. We believe that the reason for this is because of the limited prescription of these drugs in patients applying to clinics and emergency

departments.

Twenty-eight (9.5%) of female patients were pregnant, and 26 of them had UTIs caused by E. coli. E. coli resistance rates in pregnant patients were as follows; 8.7% for amoxycillin, 7.2% for trimethoprim-sulfamethoxazole, 7% for cefixime, and 8.6% for ceftriaxone. Resistance to levofloxacin, ciprofloxacin, fosfomycin, nitrofurantoin, meropenem, and imipenem was not present.

In conclusion, antibiotic resistance rates of E. coli change depending on the region. However, numerous studies showed that resistance against routinely used drugs such as ampicillin, ampicillin-sulbactam, amoxycillin-clavulanic acid, trimethoprim-sulfamethoxazole, ceftriaxone, cefixime, and ciprofloxacin are high everywhere due to their routine prescription. These rates continue to rise every year. Therefore, regional antibiotic resistance should be evaluated periodically, and the results of these evaluations should be used while selecting correct empiric antibiotic treatments. Accordingly, this will result in increased treatment success while decreasing unnecessary antibiotic use. Most importantly, this will result in a decreased speed of resistance development. Periodic briefing on rational antibiotic use and antibiotic resistance will be beneficial for this to become a reality.

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