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Investigation of Antibiotic Susceptibility Profiles of *Escherichia coli* Strains Grown in Urine Cultures

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Abstract

Objective: *Escherichia coli (E. coli)* is the most commonly isolated agent in urinary tract infections, and since antibiogram test results take a long time, empirical antibiotics are usually chosen when starting treatment. Since antibiotic susceptibilities show geographical differences, regional susceptibility results should be known. The aim of this study was to retrospectively determine the antibiotic susceptibilities of *E. coli* strains isolated from urine cultures between April 2021 and April 2024 in the Microbiology laboratory of Ordu University Medical Faculty Hospital.

Method: Urine samples were processed in the laboratory according to routine microbiological standards and examined with the BD Phoenix M50 automated bacterial identification and antibiotic susceptibility testing systems.

Results: During the study period, 38151 urine samples were sent to the laboratory and *E. coli* growth was detected in 4241 (31.7%) of them. The most sensitive antibiotics in *E. coli* were nitrofurantoin (2.8%), fosfomycin (4.3%), imipenem (4.4%) and amikacin (4.5%), while the most resistant antibiotics were ampicillin (60.4%), ceftazidime (36. 2%), levofloxacin (36.1%), trimethoprim/sulfamethoxazole (TMP-SXT) (35.1%), ciprofloxacin (32.1%) and amoxicillin-clavulanic acid (AMC) (31.5%). In addition, resistance rates have changed over the years.

Conclusion: As a result of increasing antibiotic resistance, treatment of urinary tract infections becomes more difficult. For this reason, determining regional antibiotic resistance profiles will help to ensure success in treatment by selecting appropriate antibiotics and to prevent unnecessary use of antibiotics.

Keyword: Antibiotic resistance, *E. coli*, urinary tract infection, fosfomycin.

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INTRODUCTION

Urinary tract infection (UTI) is defined as the presence of bacteriuria and/or pyuria with clinical findings including dysuria, pollakuria, fever, costovertebral angle tenderness and urinary incontinence. It is the second most common among all infectious diseases and peaks in sexually active women aged 15-24 years and postmenopausal women (1). It has been reported that an average of 5 million cases is diagnosed with UTI every year in our country (2,3). In UTI, mostly a single bacterium is the causative agent and the most frequently isolated agent is *Escherichia coli* (*E. coli*). Complicated UTI should be treated rapidly in patients with underlying diseases such as urinary tract stones, diabetes mellitus and prostatic hyperplasia. Since the antibiogram test takes a long time to result, antibiotics are usually started empirically in the treatment of UTI. Due to antibiotic resistance, the antibiotic used after the correct diagnosis affects the success of the treatment. For this reason, the resistance profile of the hospital should be monitored at certain intervals in order to make appropriate antibiotic selection in treatment (4).

Antibiotic resistance rates against urinary pathogens may vary geographically and even different resistance patterns may be observed in different hospitals in the same region. There are also changes in resistance rates in the same center over time. Therefore, resistance rates especially against urinary pathogens should be determined at certain times and empirical antibiotic treatment should be planned in line with these data (5).

This study aimed to guide empirical antibiotic selection by determining the resistance rates of *E. coli* strains grown in urine cultures against antibiotics.

METHODS

In this study, *E. coli* strains isolated from urine cultures obtained between April 2021 and April 2024 in Ordu University Medical Faculty Hospital Microbiology laboratory were retrospectively analyzed. Morning urine samples or urine that had been in the bladder for 4 hours or more were collected by midstream urine collection method. Pediatric bags were used in children who could not provide urine specimens and Foley catheter specimens were used in patients with catheters. Urine samples collected in sterile urine containers were inoculated on sheep blood and EMB agar by quantitative inoculation (colony counting) method with a 0.001 ml standard extract without waiting. The samples were incubated at 37°C for 24 hours. A growth of one species of bacteria at 104 or more colony-forming units (cfu)/mL in urine was considered suggestive of bacteriuria, or a growth of two species of bacteria at 105 cfu/mL was considered suggestive of UTI. Bacterial species identification, antibiotic resistance patterns and extended spectrum beta-lactamase (ESBL) production were determined using the BD

Phoenix™ M50 automated bacterial identification and antibiotic susceptibility testing system. European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations were used for bacterial identification and antibiotic susceptibility determination. The limitation of our study is that ESBL confirmation tests were not performed, and resistance results were reported according to the results obtained from the automated diagnosis system. Numbers and percentages were used for categorical variables in the statistical description of the data.

Information such as age, gender, growth agent and antibiotic resistance status of the patients were obtained and recorded on the laboratory information management system.

RESULTS

38151 urine culture specimens received by our laboratory were retrospectively analyzed. The causative microorganism growth was detected in 13368 of the urine culture samples, and *E. coli* was detected in 4241 (31.7%) of them. Of the samples with *E. coli* growth, 3260 were female, 981 were male and 33% of the patients were over 65 years of age. Of the samples with E. coli, 7.8% were from clinics, 3.4% from intensive care unit and the rest from outpatients.

Table 1. Antibacterial resistance rates of *E. coli* isolates by years

	2021-2022 (n=1404)		***2022-2023*** (n=1377)		***2023-2024*** (n=1460)		
	%	**n**	**%**	**n**	**%**	**n**	**%**
Nitrofurantoin	3.7	51	2.9	39	1.9	28	2.8
Fosfomycin	5.1	71	4.3	58	3.5	51	4.3
Imipenem	4.2	59	4.3	60	4.5	65	4.4
Amikacin	1.5	21	5.8	80	6.3	91	4.5
Meropenem	7.5	105	5.2	71	2.4	35	4.9
Piperacillin tazobactam	8.1	114	11.2	154	11.6	169	10.3
Gentamicin	19.7	277	12.2	168	12.5	182	14.8
GSBL	25.3	355	25.9	358	30.5	446	27.3
Ceftriaxone	31.8	447	30.3	416	31.8	461	31.4
Amoxicillin clavulanate	29.7	324	31	346	33.9	406	31.5
Ciprofloxacin	40.1	564	44.5	614	45.2	661	32.1
TMP-SXT	33.8	475	35.7	489	35.7	518	35.1
Levofloxacin	33.8	475	36.1	497	38.3	560	36.1
Ceftazidime	35.6	501	35	480	37.6	544	36.2
Ampicillin	57.1	801	61.5	846	62.5	912	60.4

TMP-SXT: Trimetoprim/sulfametoksazol. GSBL: Genişlemiş Spektrumlu Beta-laktamaz

Table 2: Distribution of *E.coli* strains according to clinics

Outpatient	*n*	*%*
Pediatrics	1382	32.6
Urology	911	21.5
Gynegology and obstetrics	427	10.1
Other clinics	1044	24.6
Inpatient		
Intensive Care Units	145	3.4
Wards	332	7.8
Total	4241	100

The most sensitive antibiotics in *E. coli* were nitrofurantoin (2.8%), fosfomycin (4.3%), imipenem (4.4%) and amikacin (4.5%), while the most resistant antibiotics were ampicillin (60.4%), ceftazidime (36. 2%), levofloxacin (36.1%), trimethoprim/sulfamethoxazole

(TMP-SXT) (35.1%), ciprofloxacin (32.1%) and amoxicillin-clavulanic acid (AMC) (31.5%). 1159 (27.3%) *E. coli* strains were positive for ESBL enzyme. The antibiotic resistance rates of *E. coli* according to years are given in Table 1. The distribution of urine samples with *E. coli* growth according to clinics is shown in Table 2.

DISCUSSION

UTI treatment should be initiated by evaluating guideline recommendations and local epidemiologic data (6). The gold standard diagnostic test in the diagnosis of UTI is urine culture. However, the process of determination of the causative pathogen in urine culture and antibiogram takes two days and therefore empirical treatment is initiated in most clinics. In this context, the antibiotic to be selected in empirical treatment should be chosen correctly. For this, the most common causative agents of the region or health center and the antibiotic resistance of the causative agents should be monitored and analyzed well (7,8). In order to start empirical antibiotic treatment in patients diagnosed with urinary tract infection, the resistance rate against the drug to be given should be below 20% (9).

The most common causative agent of urinary tract infections in our country and in the world is E. coli. Due to increasing resistance rates, the current antibiotic susceptibility profile should be taken into consideration for empirical treatment to be effective (10). Keskin et al. found the frequency of *E. coli* in urinary tract infections to be 73% (11). Similar to our study, Çakır and Acar found a prevalence of *E. coli* in urinary tract infections of 39.1% (12). In our study, *E. coli* was the most common causative agent (31.7%). According to our data, nitrofurantoin, fosfomycin, imipenem, amikacin, meropenem, piperacillin-tazobactam and gentamicin have low resistance rates.

Oral antibiotics are frequently preferred as the first choice in empirical treatment. In studies, the rate of resistance to ampicillin in *E. coli* strains was found to be more than 60% (13–16). In our country, AMC resistance is observed between 38.5-46% in *E. coli* strains (14,17,18). Due to high resistance rates, ampicillin and AMC are not recommended in the treatment of urinary infections in our country. In our study, a resistance rate of 60.4% to ampicillin and 31.5% to AMC was found. When we analyzed our data according to years, we observed an increase in resistance rates for both ampicillin and AMC. This is thought to be due to the fact that these antibiotics are still frequently preferred in our hospital.

The resistance rate of piperacillin/tazobactam, the other beta lactam/beta lactamase combination in our study, was found to be low (10.3%) as in other studies conducted in Türkiye (3,14,19). Especially in urinary tract infections caused by ESBL positive E. coli, piperacillin/tazobactam can be used effectively in treatment to prevent carbapenem resistance

(20). In our study, an increase in the resistance rate of piperacillin/tazobactam was found over the years.

Fluoroquinolones and TMP-SXT are among the most commonly used antimicrobial agents in empirical treatment due to their ease of oral administration. In the IDSA guidelines, TMP-SXT is recommended as the first choice, and quinolones are recommended as an alternative in regions with over 20% resistance to this antimicrobial agent. However, resistance to these antibiotics has increased in recent years (1,6,21). Avcıoğlu and Behçet found ciprofloxacin resistance in 41% and TMP-SXT resistance in 40% of *E. coli* strains isolated from urine (17). Duran et al. determined ciprofloxacin resistance as 42.9% and TMP-SXT resistance as 42.6% (14). Yüksek et al. found ciprofloxacin resistance to be 31.8% and resistance to TMP-SXT to be 38.9% (22). Çakır and Acar found 20.3% resistance to ciprofloxacin and 31.3% resistance to TMP-SXT (12). In our study, ciprofloxacin resistance rate was 32.1% and TMP-SXT resistance rate was 35.1%, which is lower than the resistance rates in Türkiye. However, due to the resistance rates detected, both fluoroquinolones and TMP-SXT are not an appropriate approach in the empirical treatment of urinary tract infections in our region. In our study, an increase in resistance to both ciprofloxacin and TMP-SXT was observed over the years.

In the Infectious Diseases Society of America (IDSA) guidelines, nitrofurantoin and fosfomycin with low resistance rates are recommended in the treatment of uncomplicated urinary tract infections due to their ease of oral use (23,24). In our country, resistance rates to these two agents are generally below 10% (3,14,17,18). In our study, resistance rates to fosfomycin and nitrofurantoin were 4.3% and 2.8%, respectively, and when we analyzed our data according to years, we observed a decrease in resistance rates. Our findings support that these two antibiotics may be appropriate empirical treatment options in our region.

Due to the widespread use of cephalosporins, especially third generation cephalosporins in urinary tract infections, resistance rates have increased in our country (25). In the study of Tuna et al., resistance to ceftriaxone was found to be 14.3% (8). In our study, ceftriaxone resistance rate was 31.4%. When we analyzed the resistance of *E. coli* to ceftriaxone over the years, no change was observed.

ESBL positivity in *E. coli* is increasing day by day and makes treatment difficult. In studies conducted in our country, ESBL positivity rate in *E. coli* strains isolated from urine samples varies between 8-42% (6,19,26). In our study, the rate of ESBL positive *E. coli* strains was 27.3%.

Aminoglycosides are successfully used in urinary infections because they can eradicate

bacteria in the urinary system at a high rate and reach high concentrations in urine. Although their use is limited especially in patients with renal failure due to their nephrotoxicity, they are preferred in the treatment of resistant infections due to their low resistance profiles (3,18,19,27). In our study, the low resistance rate to amikacin (4.5%) indicates that this agent is an important alternative for our region. However, when we look at the resistance profile of amikacin over the years, a significant increase is observed. Amikacin should be used more carefully due to this increase. Gentamicin, on the other hand, has shown a decrease in resistance over the years.

Carbapenems are frequently preferred in parenteral treatment of UTIs caused by resistant microorganisms. In many studies, the lowest resistance rates were reported against carbapenems in urinary tract infections caused by *E. coli* (19,27). Çaycı et al. found imipenem resistance to be 0.12% for *E. coli* and 0.15% for meropenem (13). Kömürlüoğlu et al. found imipenem resistance in *E. coli* isolates as 1.5% and meropenem resistance as 1.3% (27). In our study, imipenem resistance was 4.4% and meropenem resistance was 4.9%. When we analyzed the resistance rates of *E. coli* according to the years, imipenem resistance did not change, while meropenem resistance decreased. We think that this is due to the addition of amikacin to the treatment protocol instead of meropenem in inpatients.

In other studies, *E. coli* was isolated in 60.4%-72.8% of outpatients and 39-46% of ward patients (28–30). In our study, *E. coli* was isolated in 88.8% of the samples obtained from outpatients, while it was isolated in 11.2% of the ward patients.

CONCLUSION

In conclusion, our study shows that nitrofurantoin may be a good treatment alternative with a low resistance rate in the treatment of urinary tract infections caused by *E. coli*. Our data will guide clinicians in choosing the appropriate antibiotic and preventing unnecessary antibiotic use. Therefore, it is also important for each center to create its own data and follow it regularly.

Ethics Committee Approval: Approval for this study was obtained from the Ordu University Non-Interventional Research Ethics Committee (Date: 11/10/2024 Number: 146).

We state that the parents have given their written informed consent to be involved in the study, in accordance with the Declaration of Helsinki.

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Analysis and Interpretation: HKO, MKÇ, YEİ, Writing: HKO, MKÇ, YEİ

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