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Research Article

Antimicrobial Resistance of E. coli Strains Isolated from Urine Cultures

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ABSTRACT: Urinary tract infections (UTIs) are among the most common infectious diseases. This study retrospectively analyzed the antimicrobial resistance rates of E. coli strains isolated from urine culture samples sent to the Pamukkale University Health Research and Application Hospital between July 12, 2023, and July 12, 2024. A total of 1,844 urine culture samples were analyzed. Of the isolates, 68.54% were from female patients, and 31.46% were from male patients. The highest resistance in antibiotic susceptibility tests was observed against drugs such as ampicillin (67.22%), cefazolin (51.62%), and cefuroxime (48.09%). The lowest resistance rates were found against tigecycline (1.12%), ceftazidime-avibactam (1.28%), imipenem, and meropenem (2.28%). Particularly, higher resistance rates to antibiotics were noted in intensive care units, which could be related to the more frequent use of antibiotics in these units. Antibiotics such as tigecycline and ceftazidime-avibactam exhibited relatively low resistance rates in intensive care.

Keywords: *antibiotic resistance, E. coli, urinary tract infections*

1 INTRODUCTION

Urinary tract infections (UTIs) are the most frequently occurring infectious diseases [1]. It is estimated that 10-12% of women experience at least one UTI annually [2]. Escherichia coli is the most common causative agent in the etiology of UTIs. Antibiotics are often initiated empirically in the treatment of UTIs. Trimethoprim-sulfamethoxazole, ciprofloxacin, and beta-lactam antibiotics are frequently used antibiotics in treatment [3]. There is an increasing trend of resistance to antibiotics that are initiated empirically [4].

The development of antimicrobial resistance in bacteria poses a significant problem in antibiotic selection and reduces treatment success rates [5].

The antibiotic resistance profiles of bacteria isolated in UTI cases can vary due to the rapid development of resistance. Therefore, it is essential to keep empirical treatment options updated in UTI cases [6].

Our study aims to evaluate the antimicrobial resistance of E. coli strains

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isolated from urine cultures.

2 MATERIAL AND METHOD

The antimicrobial resistance rates of *E. coli* strains isolated from urine culture samples sent to the Pamukkale University Health Research and Application Hospital Medical Microbiology Laboratory between July 12, 2023, and July 12, 2024, were retrospectively analyzed. Only the first isolate from multiple samples belonging to the same patient was included in the evaluation. Repeated samples were excluded from the study.

2.1 Identification of Bacteria and Antibiotic Susceptibility Testing

The urine culture samples sent to our laboratory were inoculated onto 5% sheep blood agar and "Eosine Methylene Blue" (EMB) agar (Becton Dickinson, USA). They were incubated at 37°C for 18-24 hours in an incubator. The growths in the cultures were evaluated according to guideline recommendations. Samples with uropathogenic growth of $\geq 10^3$ cfu/ml in invasive samples and $\geq 10^4$ cfu/ml in non-invasive samples ($\geq 10^3$ cfu/ml in women of reproductive age) were included in the evaluation. For the identification of bacteria growing in culture samples, traditional methods or the Bruker MALDI Biotyper (Bruker Daltonics, Bremen, Germany) automated identification system was used.

The Kirby Bauer disk diffusion method and the Phoenix™ (Becton Dickinson Diagnostics, USA) automated system were used to determine the antibiotic susceptibility of isolates identified as *E. coli*. The antimicrobial susceptibility of isolates to ampicillin, amoxicillin/clavulanic acid, piperacillin/tazobactam, cefazolin, cefotaxime, cefepime, ceftazidime, cefuroxime, ertapenem, imipenem, meropenem, gentamicin, amikacin, tobramycin, ciprofloxacin, trimethoprim/sulfamethoxazole, ceftazidime-avibactam, tigecycline, colistin, and fosfomycin was tested using the automated system and Kirby Bauer disk diffusion method. Antibiotic susceptibility results were evaluated according to "The European Committee on Antimicrobial Susceptibility Testing" (EUCAST) criteria [7].

This study was conducted with the approval of the Pamukkale University Non-Invasive Research Ethics Committee (Date: 06.08.2024 and Number: E-60116787-020-563968).

3 RESULT

A total of 1,844 urine culture samples sent to the Medical Microbiology Laboratory of the Health Research and Application Hospital between July 12,

2023, and July 12, 2024, were considered significant and subjected to bacterial identification and antimicrobial susceptibility testing. The age range of the patients was min. 0-max. 94 years. Of the *E. coli* isolates, 1264 (68.54%) were from female patient samples, and 580 (31.46%) were from male patient samples. Of the 1844 *E. coli* isolates included in the study, 1358 (73.64%) were from outpatient clinics, 430 (23.31%) from wards, and 56 (3.03%) from the intensive care unit. The antimicrobial agent with the highest resistance rate was ampicillin (67.22%), followed by cefazolin (51.62%), cefuroxime (48.09%), and cefotaxime (43.47%). The lowest resistance rates were observed against tigecycline (1.12%), ceftazidime-avibactam (1.28%), imipenem, and meropenem (2.28%).

The resistance rates for the carbapenems meropenem and imipenem were found to be the same (2.28%), while the resistance rate for ertapenem was higher (5.6%). The antimicrobial resistance percentages of the isolates are presented in Table 1.

Table 1. The antimicrobial resistance rates of *Escherichia coli* isolates (74 outpatient; 23 ward; 3 intensive care) isolated from 1,844 patients included in the study are [% (n)].

Antibiotic	Total (n=1844)	Outpatient Clinic (n=1358)	Inpatient (n=430)	Intensive Care Unit (n=56)
Amoxicillin/Clavulanic Acid	43.26 (764/1766)	40.32 (523/1297)	51.93 (215/414)	47.27 (26/55)
Ampicillin	67.22 (1124/1672)	62.84 (783/1246)	80.58 (303/376)	76 (38/50)
Ceftazidime-Avibactam	1.28 (15/1164)	0.69 (6/865)	2.29 (6/262)	8.10 (3/37)
Tigecycline	1.12(16/1418)	0.75 (8/1056)	1.88 (6/319)	4.65 (2/43)
Fosfomycin	9.18 (97/1056)	9.29 (74/796)	8.69 (20/230)	0.33 (3/30)
Ciprofloxacin	33.78 (595/1761)	28.33 (367/1295)	48.54 (200/412)	51.85 (28/54)
Imipenem	2.28 (42/1837)	1.70 (23/1352)	3.49 (15/429)	7.14 (4/56)
Ertapenem	5.6 (60/1070)	3.99 (32/801)	9.66 (23/238)	16.12 (5/31)

Meropenem	2.28 (42/1839)	1.47 (20/1356)	4.21 (18/427)	7.14 (4/56)
Gentamicin	17.23 (311/1804)	14.50 (193/1331)	23.44 (98/418)	36.36 (20/55)
Amikacin	3.15 (58/1839)	2.65 (36/1355)	4.43 (19/428)	5.35 (3/56)
Piperacillin/Tazobactam	14.36 (204/1420)	12.39 (130/1049)	19.03 (63/331)	27.5 (11/46)
Trimethoprim/Sulfamethoxazole	38.84 (677/1743)	36.22 (468/1292)	48.36 (192/397)	31.48 (17/54)
Cefazolin	51.62 (207/401)	46.55 (135/290)	62.88 (61/97)	78.57 (11/14)
Cefuroxime	48.09 (797/1657)	42.93 (532/1218)	62.21 (242/389)	64 (32/50)
Cefotaxime	43.47 (736/1693)	38.70 (483/1248)	56.85 (224/394)	56.86 (29/51)
Ceftazidime	42.44 (683/1609)	37.71 (445/1180)	55.52 (211/380)	55.10 (27/49)
Cefepime	28.48 (476/1671)	24.09 (300/1245)	41.37 (156/377)	40.81(20/49)

4 DISCUSSION

E. coli is among the most commonly isolated uropathogenic agents in urinary tract infections (UTIs), and fluoroquinolones, trimethoprim-sulfamethoxazole (TMP-SMX), or beta-lactam antibiotics are widely used as the first-line empirical treatment for UTIs. In recent years, a significant increase in resistance rates to commonly used antibiotics such as fluoroquinolones and TMP-SMX has been reported. The Infectious Diseases Society of America (IDSA) recommends that if the resistance rate to TMP-SMX in a region exceeds 20%, this agent should not be used as the empirical treatment for urinary infections [8]. Studies conducted in our country have reported resistance rates of 21% to 60% to TMP-SMX and 7% to 41% to fluoroquinolones in E. coli strains isolated from urine [9]. In our study, resistance rates of 39% to TMP-SMX and 34% to ciprofloxacin were observed, which are consistent with some studies conducted in our country. Considering the literature recommendations, the results of studies conducted in our country, and our findings, we conclude that the use of fluoroqinolones and TMP-SMX as empirical treatment for

UTIs may not be appropriate.

According to the IDSA guidelines, nitrofurantoin and fosfomycin are recommended for the treatment of uncomplicated urinary tract infections due to their oral convenience and low resistance rates [8]. In our country, data on fosfomycin resistance rates in E. coli strains have been analyzed in a limited number of studies. The analysis by Pullukçu et al. [10] reported an average fosfomycin resistance rate of 1.9% for a total of 6,439 isolates [10]. In a study conducted by Gündüz et al. [11], fosfomycin resistance was found to be 3.8% in 10,709 isolates. In our study, a resistance rate of 9.18% was observed. Resistance rates were 9.29% in outpatient clinics, 8.69% in wards, and considerably lower at 0.33% in the intensive care unit. The low fosfomycin resistance in the intensive care unit may be related to its less frequent use in these settings. Compared to other studies, our fosfomycin resistance rate is higher. However, since the resistance rate is below 20%, fosfomycin can still be considered a viable option for empirical treatment.

Carbapenems are frequently preferred antibiotics for the treatment of broad-spectrum beta-lactamase positive bacteria. However, inappropriate use of these agents has become a significant issue leading t o the development of resistance to carbapenems. An evaluation of our study and other literature reveals that carbapenem resistance rates, especially in intensive care units, have reached concerning levels. In a 2022 study by Aygar et al. [12], imipenem resistance was reported to be 7.3%. In our study, imipenem resistance was found to be 1.7% in outpatient clinic patients, 3.49% in ward patients, and 7.14% in intensive care unit patients. We believe that the higher resistance rate in intensive care unit patients may be associated with a greater use of imipenem for treatment in these units compared to other departments.

In our study, the resistance rate to tigecycline was found to be 1.12% overall, making it the antibiotic with the lowest resistance rate. We observed resistance rates of 0.75% in outpatient isolates, 1.88% in ward isolates, and 4.65% in intensive care unit isolates. We believe that the higher resistance rate in intensive care units compared to other departments may be attributed to the lack of an oral formulation of tigecycline, which prevents its frequent prescription for outpatient treatment. In a study by Alanli et al., the tigecycline resistance rate was determined to be 2% [13]. This finding is consistent with our results and indicates that there is still no high resistance rate to tigecycline.

Ceftazidime-avibactam is a combination of ceftazidime, a third-generation broad-spectrum cephalosporin, and avibactam, a β-lactamase inhibitor. Avibactam is a β-lactamase inhibitor with a diazabicyclooctane structure that does not have a β-lactam structure. This combination is effective against a broad spectrum of Gram-negative bacteria, including carbapenem-resistant Enterobacteriaceae and Pseudomonas aeruginosa [14]. In a study by Bilgin et al. [15], the resistance rate to ceftazidime-avibactam in E. coli isolates was found to be 5%. In our study, the overall resistance rate was 1.28%, with 0.69% in outpatient clinics and 2.29% in wards. However, in intensive care units, this rate reached a high value of 8.10%. We believe that the higher resistance rate in intensive care units may be related to the more frequent use of ceftazidime-avibactam in these units compared to other departments.

Since penicillins are not resistant to beta lactamases, their susceptibility has been increased by combining them with beta lactamase inhibitors. Yüksel G et al. reported piperacillin/tazobactam susceptibility as 90.95% in outpatients and 86.95% in ward patients [16]. It was compatible with the data of our study.

In intensive care units, resistance rates for most antibiotics are noticeably higher compared to other clinical settings. This may be a result of more frequent and intensive empirical use of antibiotics in intensive care patients or due to more severe infections. Antibiotics such as amoxicillin/clavulanic acid, ampicillin, fosfomycin, and trimethoprim/sulfamethoxazole exhibit low resistance rates in intensive care units. This situation may be due to the less frequent use of these oral medications in intensive care settings.

Conclusion: The findings from this study indicate that resistance rates are particularly higher in intensive care units and that increasing resistance rates to antibiotics can affect empirical treatment choices for urinary tract infections (UTIs). This underscores the necessity for careful use of antibiotics and regular monitoring of current resistance profiles.

AUTHOR CONTRIBUTIONS

Hypotesis: A.Ç., S.Z.Ö., M.D., Ç.E., E.M., İ.K.; Design: A.Ç., Ç.E; Literature review: A.Ç., S.Z.Ö., M.D., Ç.E., E.M., İ.K.; Data Collection: A.Ç., S.Z.Ö; Analysis and/or interpretation: A.Ç., S.Z.Ö., M.D., Ç.E.; Manuscript writing: A.Ç

CONFLICT OF INTEREST

In the conflict of interest section, if there is no conflict of interest, the "Authors declare that there is no conflict of interest." statement should be included.

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