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ORIGINAL ARTICLE

# Bacteria That Cause Community-Acquired Urinary Tract Infections and Their Antibiotic Resistance Profiles

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## Abstract

Introduction: Urinary tract infections (UTIs) are one of the most common community-acquired infectious diseases globally. This study was conducted to contribute to the data of our country by examining the distribution of UTI agents isolated from outpatients and their antibiotic susceptibility results.

Methods: The positive urine cultures of 24,917 outpatients aged 18 years and older, which were sent to the Istanbul Public Hospitals Services Presidency-2 Central Laboratory between January 2016 and December 2019, and their antibiotic susceptibility results were retrospectively evaluated.

Results: Of the 24,917 uropathogens, 87% were Gram-negative bacteria and 13% were Gram-positive bacteria. The most commonly isolated organisms were *Escherichia coli* (57%), *Klebsiella pneumoniae* (15%), and *Enterococcus spp* (12%). *E. coli* showed high resistance to all antibiotics tested except for aminoglycoside group, carbapenem group, nitrofurantoin, and fosfomycin, while *K. pneumoniae* showed high resistance to all antibiotics except for aminoglycoside group and carbapenem group. In enterococci, high-level resistance was determined only to gentamicin and ciprofloxacin.

Discussion and Conclusion: In our study, it was determined that most of the antibiotics used for the treatment of community-acquired UTIs had a higher resistance rate than the recommended 10–20% value for empirical treatment. We think that it is very important to follow region-specific epidemiological data, take the necessary measures, and use antibiotics rationally.

Keywords: Antibiotic resistance; community-acquired urinary tract infection; empirical treatment.

Urinary tract infections (UTIs) rank at the list of the most common infections, and their associated health-care costs are quite high[1]. About 15% of the antibiotics are prescribed for UTIs annually in the USA, which costs approximately 1.6 billion USD[2]. UTIs can be treated with antibiotics; however, urine culture and antibiotic sensitivity results are needed to apply the correct antibiotic therapy due to increasing antibiotic resistance. Rapid identification of pathogens is often delayed due to the nature of conventional microbiological methods available. This poses a challenge in daily practice, and physicians prescribe a considerable percentage of antibiotics empirically, which means that they are prescribed with no culture findings that will help choose antibiotics. This can also occur even before a bacterial infection is confirmed[3]. The Centers for Disease Control and Prevention reports an approximate rate of 50%

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for inappropriate antibiotic administration across in all infectious diseases[4]. The knowledge of the organism that most probably causes infection and the local antibiogram-based resistance profiles usually determines the success of empirical antibiotic treatment[5].

In our study, it was aimed to contribute to the data of our country by examining the distribution of urinary system infection agents isolated from polyclinic patients and antibiotic susceptibility results in a central laboratory that has a high test capacity and receives samples of patients with different demographic characteristics from different hospitals.

## Materials and Methods

This retrospective and descriptive study was carried out by collecting usage data in compliance with the principles outlined in the Declaration of Helsinki. University of Health Sciences, Haydarpasa Numune Education and Research Hospital provided ethical approval for this study (Approval number: HNEAH-KAEK 2021/131, Approval date: April 12, 2021).

The positive urine cultures of 24,917 outpatients aged ≥18 years, which were sent to the Istanbul Public Hospitals Services Presidency-2 Central Laboratory between January 2016 and December 2019, and their antibiotic susceptibility results were retrospectively evaluated. Only the initial sample results of the patients, whose samples were submitted to the laboratory multiple times, were utilized. Urine samples that were accepted to the laboratory were inoculated with PREVI Isola (Biomerieux, France) fully automatic seeding device on chrome agar (CPSE/Biomerieux, France) and sheep blood agar (COS/Biomerieux France) and incubated at 35–37°C for 18–24 h. Colony morphologies and colony numbers in incubated Petri dishes were evaluated based on internationally defined urine culture evaluation criteria[6]. "Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF)" (Biomerieux, France) was employed to identify microorganisms and antibiotic susceptibility was studied on the VITEK 2 Compact (Biomerieux, France).

### Statistical Analysis

Statistical analyses were performed on the IBM Statistical Package for the Social Sciences (SPSS) version 21 software. Study data were presented as numbers and percentages. The Chi-square test was employed to examine the trend of change in antibiotic susceptibilities over the years for each bacterial species included in the report. Cases where the p value was below 0.05 were considered statistically significant results.

## Results

Of the 24,917 outpatients that were recorded over 4 years and involved in the current research, 31% were men, 69% were women, and their mean age was 53.41±22.18 years. The distribution of the factors causing community-acquired UTIs by years is summarized in Figure 1.

Of these factors, 87% (n:21.802) were Gram-negative bacteria (GNB), and 13% (n:3115) were Gram-positive bacteria. As shown in Figure 1, the most frequently isolated organisms and their rates were *Escherichia coli* (57%) (n=14,287), *Klebsiella pneumoniae* (15%) (n=3622), and *Pseudomonas aeruginosa* (4%) (n=839) among GNBs and *Enterococcus spp* (12%) (n=3075) and Coagulase-negative staphylococci (1.5%) (n=394) among Gram-positive cocci.

The antibiotic resistance rates of *E. coli, K. pneumoniae*, and *Enterococcus spp*, which were found to be the most common agents in the research period, were evaluated. Antibiotic resistance rates of these bacteria are summarized in Tables 1 and 2.

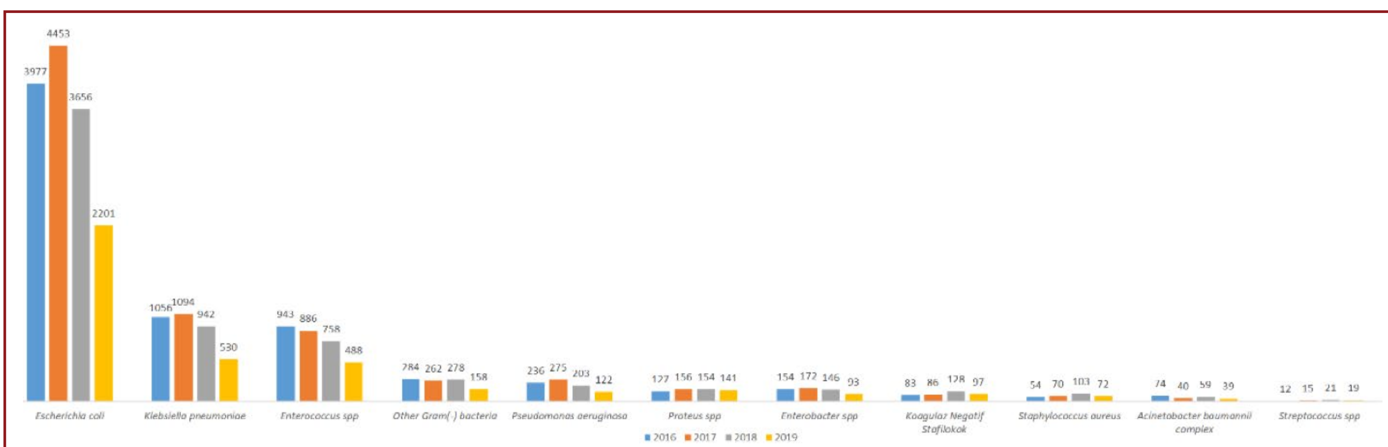


**Figure 1.** Distribution of Factors causing community-acquired urinary system infection by years.

**Table 1.** Antibiotic resistance rates of E. coli and K. pneumoniae strains by years (%)

| | Ampicilin | Amoxicillin-clavulanate | Amikacin | Gentamicin | Cefixime | Ceftazidime | Ceftriaxone | Cefuroxime-axetil | Ciprofloxacin | Imipenem | Meropenem | Ertapenem | Trimethoprim/ sulfamethoxazole | Fosfomycin | Nitrofurantion |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Escherichia coli* 2016 | 54 | 29 | 6 | 11 | 29 | 29 | 25 | 32 | 38 | 0.08 | 0.05 | 0.2 | 26 | 0.7 | 2 |
| *Escherichia coli* 2017 | 61 | 31 | 7 | 14 | 37 | 35 | 35 | 35 | 40 | 0,2 | 0,1 | 0,4 | 32 | 2 | 2 |
| p | <0.005 | >0.005 | >0.005 | >0.005 | <0.005 | <0.005 | <0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | <0.005 | >0.005 | >0.005 |
| *Escherichia coli* 2017 | 61 | 31 | 7 | 14 | 37 | 35 | 35 | 35 | 40 | 0,2 | 0,1 | 0,4 | 32 | 2 | 2 |
| *Escherichia coli* 2018 | 60 | 34 | 8 | 14 | 38 | 35 | 35 | 40 | 43 | 0,1 | 0,3 | 0,7 | 32 | 2 | 2 |
| p | | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | <0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 |
| *Escherichia coli* 2018 | 60 | 34 | 8 | 14 | 38 | 35 | 35 | 40 | 43 | 0,1 | 0,3 | 0,7 | 32 | 2 | 2 |
| *Escherichia coli* 2019 | 62 | 34 | 16 | 16 | 36 | 34 | 34 | 41 | 43 | 0,2 | 0,2 | 0,4 | 34 | 2 | 6 |
| p | | >0.005 | <0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | <0.005 |
| *Klebsiella pneumoniae* 2016 | | 35 | 8 | 13 | 33 | 37 | 37 | 41 | 39 | 5 | 5 | 9 | 30 | | 36 |
| *Klebsiella pneumoniae* 2017 | | 33 | 7 | 15 | 36 | 41 | 43 | 45 | 43 | 6 | 6 | 8 | 33 | | 52 |
| p | | >0.005 | >0.005 | >0.005 | <0.005 | <0.005 | <0.005 | <0.005 | <0.005 | >0.005 | >0.005 | >0.005 | >0.005 | | <0.005 |
| *Klebsiella pneumoniae* 2017 | | 33 | 7 | 15 | 36 | 41 | 43 | 45 | 43 | 6 | 6 | 8 | 33 | | 52 |
| *Klebsiella pneumoniae* 2018 | | 39 | 11 | 18 | 36 | 45 | 45 | 49 | 44 | 10 | 10 | 14 | 37 | | 65 |
| p | | <0.005 | <0.005 | <0.005 | >0.005 | <0.005 | >0.005 | <0.005 | >0.005 | <0.005 | <0.005 | <0.005 | >0.005 | | <0.005 |
| *Klebsiella pneumoniae* 2018 | | 39 | 11 | 18 | 36 | 45 | 45 | 49 | 44 | 10 | 10 | 14 | 37 | | 65 |
| *Klebsiella pneumoniae* 2019 | | 35 | 12 | 19 | 38 | 43 | 43 | 45 | 44 | 8 | 8 | 10 | 39 | | 65 |
| p | | <0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | <0.005 | >0.005 | >0.005 | >0.005 | <0.005 | >0.005 | | >0.005 |

**Table 2.** Antibiotic resistance rates of *Enterococcus spp* strains by years (%)

| | Ampicilin | Amoxicillin-clavulanate | Gentamicin | Ciprofloxacin | Linezolid | Teicoplanin | Vankomycin |
|---|---|---|---|---|---|---|---|
| *Enterococcus spp* 2016 | 5 | 10 | 7 | 25 | 0,9 | 0,4 | 1 |
| *Enterococcus spp* 2017 | 6 | 8 | 19 | 30 | 1,7 | 0,9 | 2 |
| p | >0.005 | >0.005 | <0.005 | <0.005 | <0.005 | >0.005 | >0.005 |
| *Enterococcus spp* 2017 | 6 | 8 | 19 | 30 | 1,7 | 0,9 | 2 |
| Enterococcus spp 2018 | 9 | 9 | 20 | 30 | 1,4 | 1 | 2 |
| p | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 | >0.005 |
| *Enterococcus spp* 2018 | 9 | 9 | 20 | 30 | 1,4 | 1 | 2 |
| *Enterococcus spp* 2019 | 11 | 10 | 23 | 35 | 0,9 | 2 | 5 |
| p | >0.005 | >0.005 | >0.005 | <0.005 | >0.005 | >0.005 | >0.005 |

The analysis of the years 2016–2017 revealed a statistically significant increase in the resistance rates of ampicillin, ceftazidime, ceftriaxone, cefixime, and trimethoprim/sulfamethoxazole, all of which were tested against *E. coli*. According to the comparison of the years 2017–2018, a meaningful increase was found in the rates of resistance to only cefuroxime-axetil, while the increase in the rates of resistance to amikacin, and nitrofurantoin was found to be significant when the years 2018–2019 were compared. The changes in the rates of resistance to other antibiotics examined were not statistically significant (p<0.005).

When consecutive years were examined for *K. pneumoniae*, the comparison of the years 2016–2017 indicated a statistically meaningful rise in the rates of resistance to cefixime, ceftazidime, ceftriaxone, cefuroxime-axetil, ciprofloxacin, and nitrofurantoin, and to amoxicillin/clavulanic acid, amikacin, gentamicin, ceftazidime, cefuroxime-axetil, carbapenem group antibiotics, and nitrofurantion according to the comparison of the years 2017–2018. Contrary to these data, when the resistance rates in 2018–2019 were compared, although the antibiotic resistance rates tended to remain the same or decreased in general, the decrease in the resistance rates only in amoxicillin/clavulanic acid, cefuroxime-axetil, and ertapenem was statistically significant (p<0.005).

While carbapenem resistance in *E.coli* was observed at 0.4%, the highest rate over the years, this rate increased to 14% in *K. pneumoniae*.

When we look at *Enterococcus spp*, we see that high-level gentamicin ciprofloxacin and linezolid resistance showed a rapid increase in 2017 compared to 2016 data. The change in the ciprofloxacin resistance rate between 2018 and 2019 was found to be statistically significant (p<0.005). Changes over the years in other antibiotics did not yield statistically meaningful results.

## Discussion

According to the World Health Organization, antibiotic resistance is a public health problem that requires urgent action, especially drawing attention to the multiple drug resistance in GNB, and classified *Enterbacteriacaea, Acinetobacter baumannii, and Pseudomonas aeruginosa* as a high priority pathogen that requires urgent new antibiotic development[7]. The organization has recommended that health authorities and health institutions should establish and distribute regional standard treatment guidelines for antibiotic use to prevent the development of antibiotic resistance[8]. In our country, numerous studies have been conducted regarding antibiotic resistance/sensitivity in UTIs. It has been mentioned that the resistance to antibiotics utilized in these studies is progressively on the rise. Consequently, researchers are advised to appropriate certain antibiotics that are suitable for their respective service areas[9]. According to our literature review, our study, in which only community-acquired UTI agents and antibiotic susceptibility results were evaluated in Türkiye, has the largest data to date.

In the guidelines and literature, it has been reported that the ampirical treatment can be initiated in case, the local resistance rate of the relevant antibiotic has not exceeded 10–20%[10-12]. Considering the findings of the present study and the studies that were carried out in our country between 2013 and 2023, the resistance rate of only aminoglycosides and carbapenems was under 20% for both of the bacteria. In addition, fosfomycin and nitrofurantoin resistance rates of *E. coli* strains were under 20%[9,10,13-16]. Studies are summarized in Table 3.

As seen in our study, community UTIs are mainly caused by GNBs, especially *E. coli* and *K. pneumonia*[14,17]. Therefore, the primary option for the treatment of these infections should include antibiotics with Gram-negative activity. The

**Table 3.** Studies showing the rates of antibiotic resistance to community-acquired UTIs in Turkey(%)

| | Years | Bakteri | Ampicilin | Amoxicillin-clavulanate | Amikacin | Gentamicin | Cefixime | Ceftazidime | Ceftriaxone | Cefuroxime -axetil | Ciprofloxacin | Imipenem | Meropenem | Ertapenem | Trimethoprim/ sulfamethoxazole | Fosfomycin | Nitrofurantion | Linezolid | Teicoplanin | Vankomycin |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Kalyoncu et al.[13] | 2023 | | | | | | | | | | | | | | | | | | | |
| *Escherichia coli* | | 61 | 63 | 38 | | 12 | | | 33 | | 33 | 0.1 | 0.1 | | 32 | 6 | 3 | | | |
| *Klebsiella pneumoniae* | | 13 | | 36 | | 14 | | | 41 | | 35 | 3 | 3 | 7 | 34 | | 41 | | | |
| Keskin et al [14] | 2021 | | | | | | | | | | | | | | | | | | | |
| *Enterobactericaea* | | 51/12* | 69 | 33 | 3 | 15 | 36 | | | 38 | 23 | 1 | 2 | 5 | | 1** | 2** | | | |
| Öztürk et al [15] | 2021 | | | | | | | | | | | | | | | | | | | |
| *Escherichia coli* | | 72 | 51 | 19 | | 10 | | 84 | | 35 | 23 | 15 | 10 | | 24 | 5 | 5 | | | |
| *Klebsiella pneumoniae* | | 11 | | 12 | | 7 | | 100 | | | 54 | 0 | 0 | | 52 | 24 | 32 | | | |
| *Enterococcus spp* | | 9 | 25 | | | 17 | | | | | 43 | | | | | | | 0 | 50*** | 50*** |
| Yılmaz et al [10] | 2016 | | | | | | | | | | | | | | | | | | | |
| *Escherichia coli* | | 67 | 67 | 37 | 0,3 | 24 | | 15 | 28 | | 50 | 0 | 0 | | 20 | 4 | 0,9 | | | |
| Çoşkun et al [16] | 2022 | | | | | | | | | | | | | | | | | | | |
| *Escherichia coli* | | 64 | | 54 | 9 | | | | 50 | | 53 | | | 2 | 37 | 4 | 6 | | | |
| *Klebsiella pneumoniae* | | 11 | | 55 | | | | | 55 | | 50 | | | | 40 | | 20 | | | |
| Aykan et al [9] | 2013 | | | | | | | | | | | | | | | | | | | |
| *Escherichia coli* | | | 62 | 34 | 6 | 16 | | 14 | | | 21 | 4 | | | 49 | | 11 | | | |

* *E.coli/K. pneumoniae*; **Only *E.coli*; ***Data of only two patients.

Infectious Diseases Society of America proposes that fosfomycin, nitrofurantoin, or TMP-SMX should be used for uncomplicated cystitis in women. Furthermore, beta-lactams or fluoroquinolones should be used in acute pyelonephritis in cases where local resistance rates are not over 20%[12].

According to our evaluations in terms of *K. pneumoniae* and *E.coli*, as shown in Tables 1 and 3, only gentamicin and amikacin showed resistance rates below 20% among the antibiotic groups preferred in empirical treatment. In addition to gentamicin and amikacin, fosfomycin and nitrofurantoin still remained preferable options in the empirical management of *E. coli* contaminations. High nitrofurantoin resistance (65%) held particular significance within *K. pneumoniae* isolates.

Ampicillin and amoxicillin/clavulanic acid yielded the highest antibiotic resistance rates, which showed similarity to the results reported from different countries (resistance rates: 50–75%)[18].

In a study conducted in 2012, second or third-generation oral cephalosporins were also recommended for the management of uncomplicated UTIs in cases where resistance to employed empirical antibiotics was observed. Nevertheless, our resistance rate to cephalosporin group antibiotics increased to approximately 45% over the years, and such a possibility disappeared[19].

In a meta-analysis study that consisted of 101 studies carried out in Türkiye from 1996 to 2012, ciprofloxacin resistance in *E. coli* in patients with community-acquired UTI was 21%, while this rate increased to 43% in our study. We think that this increase in the resistance rate to ciprofloxacin was due to the fact that it was the most preferred antibiotic for the management of UTI, especially for the empirical treatment of uncomplicated acute cystitis in women. As a result of the study, consumption of fluoroquinolones in the previous 6 months was found to be an important determinant contributing to the emergence of resistance[20]. In the French Infectious Diseases Society guidelines published in 2017, it was reported that fluoroquinolones should not be used in ampirical treatment but be prescribed according to the antibotic susceptibility testing results[11].

Although carbapenem resistance is rare in the *Enterobacteriaceae* family, infections with carbapenem-resistant or carbapenemase-producing *Enterobacteriaceae* have gained importance in recent years. As seen in our study, while carbapenem resistance to *E. coli* was at minimum levels, resistance to *K. pneumoniae* tended to increase.

The limited oral antibiotic options due to the resistance in community-acquired UTIs will increase the need for parenteral treatment regimens and will constitute an indication for hospitalization in these patients. This situation brings along a social and economic burden[21].

When we evaluated the 4-year period, it was seen that the patient data of 2019 decreased by 38%. When we compared the resistance in 2019 with that in 2018 in our study, the antibiotic resistance rates tended to remain the same or decreased in general. In addition, the change in resistance rates in amoxicillin/clavulanic acid, cefuroxime-axetil, and ertapenem was statistically significant ($p<0.005$). We think that the COVID-19 pandemic, which started in our country in the second half of 2019, had an effect. The change in the antibiotic resistance profile was due to multifactorial causes, such as the decline in the number of hospital admissions during the pandemic, increased isolation measures, and the difficulty in reaching the antibiotic prescription[22].

When we look at *Enterococcus spp*, we see that gentamicin and ciprofloxacin cannot be used in the empirical treatment of community-acquired UTIs. Since the resistance to ampicillin and amoxicillin/clavulanic acid was detected at a rate of 10–11% in our study, they can be used as the first choice in empirical treatment. Keskin et al.[14] found ampicillin resistance in community-acquired UTIs at 19% and high gentamicin and ciprofloxacin levels at 33%. It has been stated that resistance rates to this antibiotic are high due to the frequency of use of ciprofloxacin and the frequent prescription of gentamicin to outpatients because it can be administered intramuscularly. It has been specifically reported that these antibiotics should not be used unnecessarily due to increasing resistance rates.

As a result, increasing resistance rates of ampicillin, amoxicillin/clavulanic acid, cephalosporins, trimethoprim-sulfamethoxazole, and quinolones among *E. coli* and *K. pneumoniae* strains which are the most two frequently detected causes of UTIs in the catchment area of our laboratory have limited the use of the antibiotics in the treatment. However, low resistance rates of aminoglycosides, fosfomycin, and nitrofurantoin among *E. coli* isolates, and aminoglycosides among *K. pneumoniae* strains may highlight that these antibiotics may be suitable options for the empirical treatment of UTIs. Ampicillin remains a good option for empirical treatment of in community-acquired UTIs due to *Enterococcus spp*.

Antibiotic resistance is no longer a problem only in hospitalized patients but also emerges as a problem in community-acquired infections. We think that it is very important to follow-up country and region-specific epidemiological data, take the necessary precautions, and support the rational use of antibiotics.

**Ethics Committee Approval:** University of Health Sciences, Haydarpasa Numune Education and Research Hospital provided ethical approval for this study (Approval number: HNEAH-KAEK 2021/131, Approval date: April 12, 2021).

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**Authorship Contributions:** Concept: Ş.D.D., C.Y.; Design: Ş.D.D., C.Y., A.S., S.A.; Supervision: S.A.; Fundings: Ş.D.D., C.Y., A.S.; Materials: Ş.D.D, C.Y, A.S.; Data Collection or Processing: C.Y., A.S.; Analysis or Interpretation: Ş.D.D., S.A.; Literature Search: Ş.D.D., A.S.; Writing: Ş.D.D., C,Y.; Critical Review: S.A.

**Conflict of Interest:** None declared.

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