ORIGINAL RESEARCH

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Evaluation of the Antimicrobial Resistance Rates in Urine Samples of the Elderly

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Abstract

Objective: Urinary tract infections (UTIs) are common in the community. The prevalence of UTIs rises in the elderly as a result of age-related changes and comorbidities. In treating the elderly, it is important to choose antibiotics carefully and avoid unnecessary ones. The goal of this study was to analyze the bacteria isolated from geriatric urine samples and their resistance patterns.

Materials and Methods: Urine culture results in geriatric patients (>65 years old) were analyzed between January 1, 2016 and February 1, 2020. Antibiotic resistance was evaluated in frequently isolated bacteria. In terms of antibiotic resistance, antibiotics that can be used in outpatient therapy and do not require the approval of an infectious disease specialist were investigated.

Results: The records of 37735 urinary samples were screened. In 31.3% (11840/37735) of the urine culture microorganisms were isolated. *Escherichia coli* was the most common microorganism with a rate of 40.1% (4758/11840), followed by *Klebsiella* spp. with 15.5% (1844/11840), *Enterococcus* spp. with 10.3% (1222/11840), and *Pseudomonas aeruginosa* with 3.4% (406/11840). Ceftriaxone resistance of 37.6% was found in *Escherichia coli*; ciprofloxacin resistance was 41.5%, trimethoprim-sulfamethoxazole (TMP-SMX) resistance was 43.4%, and nitrofurantoin resistance was 1%. There was no resistance to fosfomycin. The antibiotic resistance of *Klebsiella* spp. gave a result of 41.6% ceftriaxone resistance, while ciprofloxacin resistance was 32.6%, and TMP-SMX resistance was 39.6%. The antibiotic resistance of *Pseudomonas aeruginosa* was 19.04% ciprofloxacin resistance, and 5.1% amikacin resistance. In *Enterococcus* spp. ampicillin resistance was found to be 42.9%.

Conclusion: Infections in geriatric patients can quickly prove fatal. Antibiotic selection is critical in regard to elderly patients, and knowing regional antimicrobial resistance patterns is important. But balancing efficacy, safety, and tolerability with the development of antimicrobial resistance in this patient population is difficult.

Keywords: Urine sample, antimicrobial resistance, antibiotics, clinical geriatrics, geriatric care management

Introduction

Due to advances in technology and medicine, the population of older adults is steadily increasing. The World Health Organization predicts that the number of people over 60 years will increase from 12% to 22% of the total global population between 2015-2050, and advises countries to adjust their policies accordingly (1). According to the United Nations, Turkey will be among the countries with an elderly community of more than 10% (2). Advances in disease treatment and public health over the last century have resulted in increased life expectancy, a lower birth rate, changes in age pyramids, and a prognostic increase in the proportion of the world's elderly population. Aging causes a progressive and general decline in functional reserve capacity, followed by a loss in all functions. Although aging is not a disease, it does increase the risk of people contracting several diseases, as well as the overall mortality rate (3).

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Urinary tract infections (UTIs) are common in the elderly and have a significant health impact. UTIs are responsible for 15.5% of hospitalizations due to infectious diseases in adults aged over 65, second only to pneumonia. It is responsible for 6.2% of deaths from infectious (4). In UTIs, isolation of the causative agent, determination of antibiotic susceptibility, and appropriate antimicrobial therapy will prevent treatment failure.

Because of the variability of symptoms and laboratory values in elderly patients, empirical treatment is frequently initiated in UTIs. Antibiotic resistance rates rise when antibiotics are misused. Antibiotic resistance is still a major concern all over the world. Knowing and following regional changes in the antibiotic susceptibility of isolated bacteria is critical for treatment efficacy. As a result, the topic is still relevant. Resistance to quinolones, one of the first treatment options for UTIs, has been reported to be as high as 30-42% in studies conducted in our country (5).

The purpose of this study was to determine the distribution of microorganisms and the antibiotic resistance rates isolated from urine samples of geriatric patients.

Materials and Methods

Our study, which was designed as a retrospective cross-sectional descriptive study, examined urine cultures sent to the microbiology laboratory between January 1, 2016, and February 1, 2020. Outpatient and inpatient outcomes with positive urine culture from people over the age of 65 were included. Only one sample of each patient was included. Samples were from the urethral, urinary catheter, nephrostomy, or cystostomy catheter. Detection of 10^5 cfu/mL of one species or two types of microorganisms in cultures, or detection of 104 cfu/mL of one type of microorganism were considered positive. The results were analyzed from laboratory records. Urine samples were evaluated for the presence of *Escherichia coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, and *Enterococcus* spp., as well as the rate of antimicrobial resistance. Other microorganisms that are rarely isolated were not included. In this study, we examined the rates of resistance to antibiotics that can be administered orally or intramuscularly and do not require the approval of an infectious disease specialist. The results were evaluated in terms of antibiotic resistance to such as penicillin, cephalosporin, aminoglycoside, fosfomycin, nitrofurantoin, and trimethoprim-sulfamethoxazole.

Urine samples carried to our hospital's microbiology laboratory are inoculated on 5% sheep blood agar and eosin methylene blue agar using a quantitative method involving a 0.01 mL standard loop. Urine samples are incubated at 35-37 °C for 24-48 hours according to standard procedures. Bacterial identification and antibiotic susceptibility tests are carried out using both conventional and automated systems (Phoenix BD, USA). Antibiogram data are evaluated in accordance with the recommendations of EUCAST (European Committee on Antimicrobial Susceptibility Testing).

Statistics

The data were taken from the hospital information management system and analyzed with the Excel program. Number (n) and % age (%) will be used to define categorical variables.

This study was approved by Başkent University Institutional Review Board (project no: KA21/476).

In organizing the study, Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) rules were followed.

Results

The geriatric patient group was screened, as were the urine culture samples sent during the study period. This group contained 37735 records. In 68.6% (25895/37735) of the urine culture results, there was no growth (Figure 1). The isolated microorganisms were distributed as follows: *Escherichia coli* was isolated in 40.1% (4758/11840), *Klebsiella* spp. in 15.5% (1844/11840), *Enterococcus* spp. in 10.3% (1222/11840), and *Pseudomonas aeruginosa* in 3.4% (406/11840). Other microorganisms (such as *Staphylococci, Candida,* proteus) accounted for 30.4% (3610/11840). The mean age was 77.9±7.9 years, and 59.1% (7004/11840) of the patients were women.

When we evaluated the antibiotic resistance pattern in *Escherichia coli*, ceftriaxone resistance was 37.6%, ciprofloxacin resistance was 41.5%, trimethoprim-sulfamethoxazole (TMP-SMX) resistance was 43.4%, gentamicin resistance was 15.2%, amikacin resistance was 1.7%, and nitrofurantoin resistance was 1%. There was no evidence of resistance to fosfomycin. The antimicrobial resistance rates are shown in Table 1. In the subgroup analysis, antimicrobial resistance in *E. coli* was higher in the male gender in both categories (inpatient and outpatient) (Table 2).

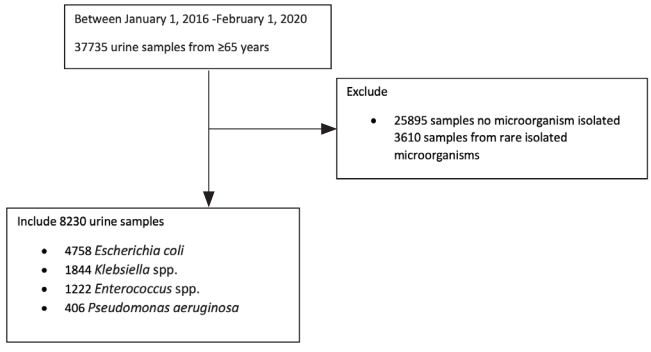

Figure 1. Study flowchart

In *Klebsiella* spp., ceftriaxone resistance was found to be 41.6%, ciprofloxacin resistance was 32.6%, TMP-SMX resistance was 39.6%, gentamicin resistance was 17.2%, and amikacin resistance was 3.5%. In the subgroup analysis, ceftriaxone resistance in *Klebsiella* spp. was over 50% in the inpatient group. TMP-SMX resistance was higher in males, while ciprofloxacin resistance was higher in females (Table 3).

The antibiotic resistance pattern in *Pseudomonas aeruginosa* showed ciprofloxacin resistance to be 19.04%, amikacin resistance was 5.1%, and gentamicin resistance of 8.7%. In the subgroup analysis, in males ciprofloxacin and gentamicin resistance was higher than in females. Antibiotic resistance rates were high in inpatients (Table 4).

In *Enterococcus* spp. ampicillin resistance was found to be 42.9%, and nitrofurantoin resistance was 6.06%. In the subgroup analysis, antimicrobial resistances were higher in females in all categories (Table 5).

Discussion

Atypical infection findings and increasing incidence of asymptomatic bacteriuria (ASB) in the elderly population make it difficult for the clinician to diagnose urinary tract infection.

Table 1. Antibiotic resistance rates of microorganisms

Antibiotic	Microorganisms			
	E. coli	*Klebsiella* spp.	*Enterococcus* spp.	*P. aeruginosa*
Ampicillin	70.5%	71.8%	42.9%	NE
Ceftriaxone	37.6%	41.6%	NE	NE
Ciprofloxacin	41.5%	32.6%	NE	19.04%
Amikacin	1.7%	3.5%	NE	5.1%
Gentamicin	15.2%	17.2%	NE	8.7%
Fosfomycin	0	NE	NE	NE
Nitrofurantoin	1.0%	NE	6.06%	NE
TMP-SMX	43.4%	39.6%	NE	NE

NE: Not effective, TMP-SMX: Trimethoprim-sulfamethoxazole

Table 2. Antibiotic resistance rates of *Escherichia coli*

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Male	Female	Male
Ampicillin	65.8%	75.7%	74.5%	79.7%	68.6%	76.9%
Ceftriaxone	29.7%	39%	46.6%	53.8%	35.1%	43.6%
Ciprofloxacin	35.6%	46.9%	45.7%	58.1%	38.9%	50.3%
Amikacin	1.4%	1.9%	1.3%	2.1%	1.4%	1.9%
Gentamicin	12.1%	20.5%	16.2%	24.1%	13.4%	21.6%
Fosfomycin	0	0	0	0	0	0
Nitrofurantoin	0.5%	1.5%	1.3%	3.4%	0.8%	2.1%
TMP-SMX	40.2%	49.4%	43.6%	53.8%	41.3%	50.7%

TMP-SMX: Trimethoprim-sulfamethoxazole

Table 3. Antibiotic resistance rates of *Klebsiella* species

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Male	Female	Male
Ampicillin	65.8%	75.7%	74.5%	79.7%	68.6%	76.9%
Ceftriaxone	32.2%	33.8%	55.9%	58.4%	41.2%	42.6%
Ciprofloxacin	24.3%	22.4%	48.2%	46.1%	33.4%	30.8%
Amikacin	2.1%	3.8%	0.9%	3.8%	1.7%	3.8%
Gentamicin	10.6%	13.5%	27.9%	23.8%	17.1%	17.2%
TMP-SMX	33.5%	37.2%	46.6%	58.4%	38.5%	44.8%

TMP-SMX: Trimethoprim-sulfamethoxazole

Table 4. Antibiotic resistance rates of *Pseudomonas aeruginosa*

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Female	Female	Male
Ciprofloxacin	11.2%	19.2%	19.7%	25.3%	16.3%	22.5%
Amikacin	0	1.7%	8.7%	7.9%	5.2%	5%
Gentamicin	1.6%	7%	7%	10.9%	7.1%	10.8%

Table 5. Antibiotic resistance rates of *Enteroccoccus species*

Antibiotics	Outpatient		Inpatient		All	
	Female	Male	Female	Male	Female	Male
Ampicillin	45.5%	35.2%	54.9%	32%	50.7%	33.8%
Nitrofurantoin	3.5%	2.4%	12.1%	7.3%	7.7%	3.1%

There is still no consensus for the definition of UTIs in the elderly. UTIs are a common and a serious reason for hospitalization in the older population (6). In our study, we determined the antibiotic resistance in the urinary isolates of patients admitted to our hospital, which is a common factor for admissions. While we found low resistance rates for aminoglycosides (amikacin and gentamicin), and nitrofurantoin, we found no resistance to fosfomycin.

When aminoglycosides are considered among these agents, their Gram-negative activities are good, and urine concentrations reach peak plasma levels within one hour of drug administration (7). However, their use in treating the elderly is avoided due to their nephrotoxic and ototoxic side effects. Chinzowu et al. (8) reported the use of aminoglycosides caused acute kidney injury in the elderly. While it is recommended not to exceed 48 hours in empirical treatment, the duration may be extended in targeted therapy, but caution should be exercised (9). Raveh et al. (10) reported that nephrotoxicity was rare in the use of aminoglycosides for over 11 days in the elderly. Meanwhile their only parenteral use is another challenge. The patient must apply to a healthcare provider for parenteral use. This situation also includes risk factors such as the formation of a regional abscess, hematoma, and thrombophlebitis in intravenous use. However, elderly patients diagnosed with urinary system infections sometimes do not want to be treated in a hospital. On the other hand, aminoglycosides are an appropriate antibacterial agent when patients do not have an oral treatment option or have resistant microorganisms. It is comfortable to use in a single daily dose. Based on these results, it is important to inform the patients and their relatives of its short-term use and closely monitor for side effects.

According to our findings, nitrofurantoin appears to be a viable option with a low rate of resistance. Nitrofurantoin is only approved for the treatment and prevention of lower UTIs (11). It is preferred from a medical perspective when the patient has urinary complaints (dysuria, urgency, frequency) but no systemic findings (fever or hypothermia, anorexia, loss of appetite, regression in cognitive and physical functions). Beers Criteria should be avoided in people with creatinine clearance of less than 30 mL/min or for long-term use, according to the 2015 American Geriatrics Society. The society advises using a safer alternative because there is a risk of pulmonary toxicity, hepatotoxicity, and peripheral neuropathy side effects, particularly with long-term use (12).

In our study, we determined a resistance rate of approximately 40% for ciprofloxacin, ceftriaxone and TMP/SMX. For an appropriate empirical treatment, resistance should be less than 20% (13). Based on our findings, quinolones, third-generation cephalosporins, and TMP/SMX do not appear to be viable options for empirical treatment. On the other hand, nitrofurantoin and TMP/SMX are recommended as first-line empirical treatments of UTIs (14). Quinolones have recently been associated with a higher risk of aortic aneurysm and dissection (15). However, this risk has not been related to age. During quinolone therapy, a high incidence of tendon rupture was noted (16).

In the elderly, metabolic side effects, such as hypoglycemia or hypokalemia, can occur as a result of antibiotic use. Although antibiotic-induced neurotoxicity is uncommon, it is unpredictable. However, different symptoms can be encountered, ranging from delirium to convulsions. Higher risk classes include fluoroquinolones, macrolides, sulfonamides, nitrofurans, and some β-lactams (17).

The Infectious Diseases Society of America lists fosfomycin as a first-line treatment for cystitis because of its ease of administration, but cautions that it may be slightly less effective than other agents (13). Due to its long half-life, studies show that it can be effective in uncomplicated lower UTIs with a single dose or 3 g doses repeated every 48 to 72 hours (18).

Enterococci are microorganisms of the gastrointestinal tract and are common in patients with urinary instrumentation or anatomical anomalies of the urinary tract (19). It is more frequently encountered as a causative agent in catheter-related UTIs and UTIs in those with incontinence or who are diapered.

We reported higher antimicrobial resistance in females than in males, and ampicillin resistance was found to be 42.9%. Vancomycin is avoided in the elderly due to nephrotoxicity, and teicoplanin requires the approval of an infectious disease specialist. Vancomycin-resistant enterococcal (VRE) strains are another threat. In our country, there is an oral form of linezolid available, but it is not approved for use in the treatment of VRE-associated UTIs.

Study Limitations

Our study includes data from a single center, and may not reflect the antimicrobial resistance rate of other regions. More wide-ranging research on this topic is required.

We only screened at the laboratory database. The patients' symptoms, and comorbidities were not investigated, and no differentiation was made between complicated urinary tract infection and asymptomatic bacteriuria (ASB). There was no distinction between agent and colonization. ASB is common in the elderly, although screening or treatment in community and long-term care units is not advised. ASB therapy, according to research, is ineffective in terms of morbidity and mortality in the elderly, and also causes an increase in antimicrobial resistance (20).

Conclusion

It becomes easier for infections to emerge with the decrease of immune responses in old age. Infections in the elderly can quickly prove fatal if the appropriate treatment is not started in time. On the other hand, antibiotics are among the most commonly prescribed new medications in elderly patients. In addition to the difficulty of diagnosing infections, multiple comorbidities, drug side effects, drug-drug or drug-disease interactions, and changes in drug pharmacokinetics and pharmacodynamics further complicate the selection of appropriate antibiotics for elderly patients. Appropriate antibiotic prescription is critical in elderly patients, but balancing efficacy, safety, and tolerability with the development of antimicrobial resistance in this patient population is difficult.

Information: This study was presented at the 3rd International & 13th Academic Geriatrics Congress.

Ethics

Ethics Committee Approval: This study was approved by Başkent University Institutional Review Board (project no: KA21/476) and supported by Başkent University Research Fund.

Informed Consent: The study is retrospective and laboratory-based.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept and Design: T.Y.Y., Ö.K.A., Data Collection or Processing: T.Y.Y., F.S., N.S., Literature Search: T.Y.Y., F.S., Writing: T.Y.Y., F.S., N.S., Supervision: Ö.K.A, H.D.

Conflict of Interest: No conflict of interest was declared by the authors.

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