Annals of Biomedical and Clinical Research

Original article

ABCR Vol 4; No 2; 2025;51-57

The Antimicrobial Resistance of Bacterial Uropathogens Before and During the Coronavirus Pandemic

Robert Nikolić, Svjetlana Grgić, Linda Soldo, Marjana Jerković Raguž, Sanja Jakovac

School of Medicine, University of Mostar, Bosnia and Herzegovina

ABSTRACT

Background: This study aimed to define the most common bacterial isolates of urinary tract infections and the differences in antibiotic resistance before and during the coronavirus pandemic.

Methods: The study included 213 patients with a diagnosis of urinary tract infection treated at the Clinic for Infectious Diseases in Mostar in a two-year period, 2019 and 2021. We analyzed the incidence of urinary infections and uropathogens, as well as antibiotic resistance.

Main findings: This study included a total of 213 patients, with a greater number of female patients, an average age of 66 and over, and the most frequent clinical diagnosis being acute cystitis. The most common bacterial isolates were *E. coli*, *K. pneumoniae*, and *Enterococcus* spp. We showed a decrease in the incidence of *E. coli* in 2019 and an increase in *K. pneumoniae* in 2021. Antibiogram results revealed a rise in antibiotic resistance in 2021 for all bacterial isolates except for *K. pneumoniae*.

Principal conclusion: The frequency of urinary tract infections was highest in older women, with the most frequent diagnosis being acute cystitis. The most common bacterial pathogens in urinary tract infections are *E. coli*, *K. pneumoniae*, and *Enterococcus* spp., representing the main cause. In general, there has been an increase in the antibiotic resistance of uropathogens.

Key words: antibiotic resistance, *E. coli*, urinary tract infections, *K. pneumoniae*

Article processing history:
Received March 10, 2025
Revised May 11, 2025
Accepted September 8, 2025

ORCID IDs of the authors:
R.N. 0009-0009-4554-4873
S.G. 0000-0003-2543-9987
M.J.R. 0000-0002-1158-7965
S.J. 0000-0003-0676-8179

Corresponding author:
Robert Nikolić
School of Medicine, University of Mostar, Bosnia and Herzegovina
E-mail: robert.nikolic453@gmail.com

Cite this article as: Nikolić R, Grgić S, Soldo L, Jerković Raguž M, Jakovac S. The Antimicrobial Resistance of Bacterial Uropathogens Before and During the Coronavirus Pandemic. Annals of Biomedical and Clinical Research. 2025;4:51-57.

https://doi.org/10.47960/2744-2470.2025.2.4.51

INTRODUCTION

Antimicrobial resistance has been a significant problem in medicine for several years due to the increasing number of resistant bacteria that cause various infections in the human body, especially urinary tract infections (1). Insight into the patterns of antimicrobial resistance enables more rational and accurate empiric prescribing of antibiotics in the treatment of urinary tract infections according to various guidelines for treatment (1). The most common uropathogens are from the Enterobacteriaceae family, especially *Escherichia coli* of different sensitivities (2, 3). Multiple resistant Enterobacteriaceae are present mainly in immunocompromised patients in hospital conditions and are connected with urinary catheters (CAUTI) and invasive procedures, as well as overuse of antibiotics. Due to all these factors, there is a significant increase in morbidity and mortality as well as higher costs due to prolonged medical treatment. Therefore, antimicrobial resistance monitoring in hospitals is crucial to provide adequate empirical therapy, which varies in different hospital environments.

According to the ECO•SENS study analyzing the antibiotic susceptibility of *Escherichia coli* in several European countries, the uropathogenic *Escherichia coli* continues to show a high resistance to ampicillin (28%), sulfamethoxazole (24.8%), trimethoprim (16.7%), and trimethoprim/sulfamethoxazole (16.1%), while the resistance of *E. coli* to cefadroxil (as a representative of oral cephalosporins), nitrofurantoin, fosfomycin trometamol, gentamicin, cefotaxime, and ceftazidime is less than 2%. An increase in resistance to fluoroquinolones and trimethoprim/sulfamethoxazole has been observed (4). Similar results with a significant rise in resistance for *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are also reported by Polish authors (5). Non-European studies emphasize the dominance of these pathogens, with 37.7% *Escherichia coli*, 11.4% *Klebsiella pneumoniae*, and 9.1% *Staphylococcus aureus* demonstrating a resistance of over 70% to cefuroxime, trimethoprim/sulfamethoxazole, and beta-lactams, while the lowest resistance was observed for amikacin and carbapenems (6, 7).

The antimicrobial resistance pattern in Bosnia and Herzegovina and neighboring countries is similar to that worldwide. According to the data from the Clinical Center in Tuzla, the most common bacterial isolate is *Escherichia coli* (73.5%), followed by *Klebsiella* spp. (8.5%), *Proteus mirabilis* (5.5%), and *Pseudomonas aeruginosa* (4%), with a high resistance to ampicillin, amoxicillin, and trimethoprim/sulfamethoxazole, and good sensitivity to carbapenems (8). Similar results in Serbia show an average resistance for *E. coli* under 20% for the three antibiotics amikacin, meropenem, and imipenem. Because of the high resistance of uropathogens, empirical therapy with trimethoprim/sulfamethoxazole, gentamicin, ciprofloxacin, and cephalosporins is not recommended (9). Croatian authors reported an increase in carbapenem resistance for *Pseudomonas aeruginosa* up to 20% and for *Acinetobacter baumannii* up to 87%, representing the biggest challenge in the application of antimicrobial therapy in Croatia (10). One of the problems in monitoring antimicrobial resistance in our country is the lack of national guidelines for the treatment of hospital pathogens. The aim of this study is to define the antimicrobial resistance of uropathogens and highlight the rise in multidrug-resistant uropathogens during the coronavirus pandemic as a consequence of antibiotic overuse, compared to the period before it.

PARTICIPANTS AND METHODS

Participants

This research is structured as a retrospective cross-sectional study that includes all patients treated for urinary tract infection at the Clinic for Infectious Diseases of the Mostar University Clinical Hospital during 2019 and 2021.

The main inclusion criteria for the participants were the presence of a bacterial pathogen in the first urine culture with an antibiotic susceptibility test and a diagnosis of urinary tract infection. The study included patients who, in addition to the two aforementioned criteria, had complete medical documentation.

Methods

The data were collected from the medical charts at the Clinic for Infectious Diseases of the Mostar University Clinical Hospital. The following parameters were considered from the patients' medical history: demographic (age and sex), diagnosis of urinary infection (cystitis, pyelonephritis, or urosepsis), and the first urine culture with an antibiotic susceptibility test. MacConkey agar (package: 500 g, product code: DM141D), manufactured by Mast Group Ltd., was used for the isolation of bacterial pathogens from urine. The antibiotic susceptibility testing was performed by utilizing the disk diffusion method according to Kirby-Bauer on Mueller-Hinton agar plates. Disks for selected antibiotics were utilized (Mast Group Ltd) to test the antibiotic resistance, which required:

1. Mueller-Hinton agar (packaging: 500 g, product code: DM170D, manufacturer: Mast Group Ltd.) used for cultivation of the bacterial pathogen that we were observing.
2. Antibiotic tablets – MASTDISCS AST (packaging: 5x50 tablets of the appropriate antibiotic, manufacturer: Mast Group Ltd.).

Statistical analysis

The IBM SPSS Statistics v.26 statistical software package was used. The results were expressed as numbers and percentages. The Chi-square test for independent samples and Fisher's exact test were utilized for the data analysis. The limits of statistical significance were set at p <0.05. P-values that could not be expressed to three decimal places were expressed as p<0.001.

RESULTS

In the overall sample of the participants (213), there were significantly more female (69.01%) than male ones (30.99%), while the gender structure between the samples in 2019 and 2021 was statistically insignificant (Table 1).

Table 1. The structure of participants by gender, age, and diagnosis in 2019 and 2021 (Fisher's exact test)

	Year					
	2019		2021		χ^2	p
	n	%	n	%		
Gender					0.640	0.424
F	99	71.2	48	64.9		
M	40	28.8	26	35.1		
Age					3.764	0.447*
18–30	5	3.6	1	1.4		
31–45	11	7.9	3	4.1		
46–55	7	5.0	1	1.4		
56–65	14	10.1	9	12.2		
66+	102	73.4	60	81.1		
Diagnosis					3.017	0.221
Acute cystitis	58	41.7	40	54.1		
Acute pyelonephritis	16	11.5	6	8.1		
Urosepsis	65	46.8	28	37.8		
Causative agents					24.205	**<0.001***
Escherichia coli	61	43.9	12	16.2		
Klebsiella pneumoniae	23	16.5	29	39.2		
Proteus mirabilis	15	10.8	7	9.5		
Enterococcus spp.	26	18.7	14	18.9		
Pseudomonas aeruginosa	7	5.0	5	6.8		
Acinetobacter spp.	3	2.2	4	5.4		
Morganella morganii	2	1.4	1	1.4		
Serratia spp.	2	1.4	2	2.7		

*Fisher's exact test

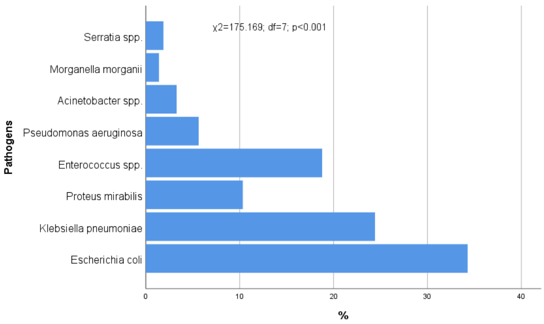

Image 1. The structure of the sample according to causes

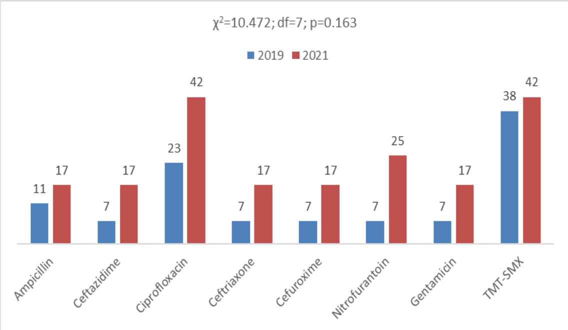

Image 2. Antimicrobial resistance profile of *Escherichia coli* in 2019 and 2021 at the Clinic for Infectious Diseases

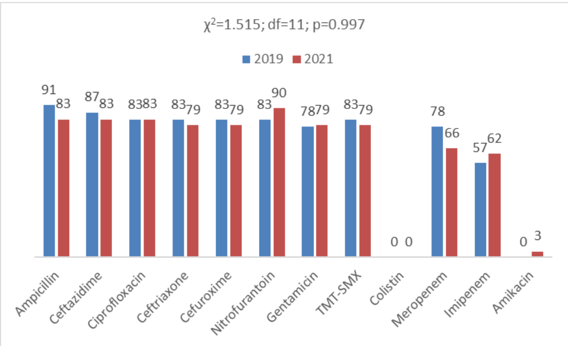

Image 3. Antimicrobial resistance profile of *Klebsiella pneumoniae* in 2019 and 2021 at the Clinic for Infectious Diseases

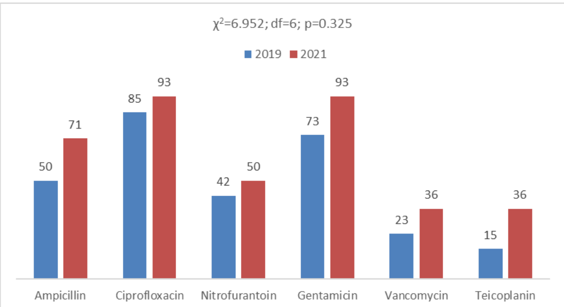

Image 4. Antimicrobial resistance profile of *Enterococcus* spp. in 2019 and 2021 at the Clinic for Infectious Diseases

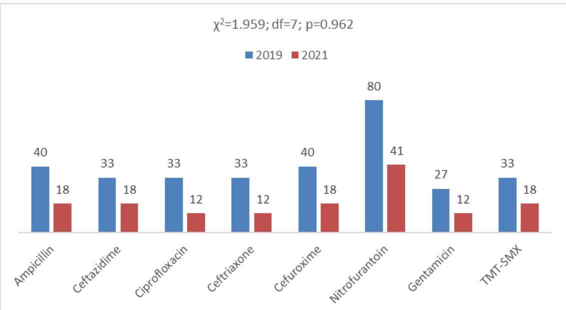

Image 5. Antimicrobial resistance profile of *Proteus mirabilis* in 2019 and 2021 at the Clinic for Infectious Diseases

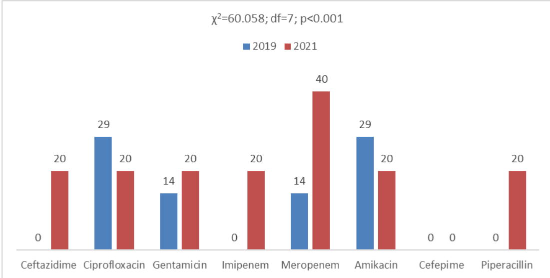

Image 6. Antimicrobial resistance profile of *Pseudomonas aeruginosa in* 2019 and 2021 at the Clinic for Infectious Diseases

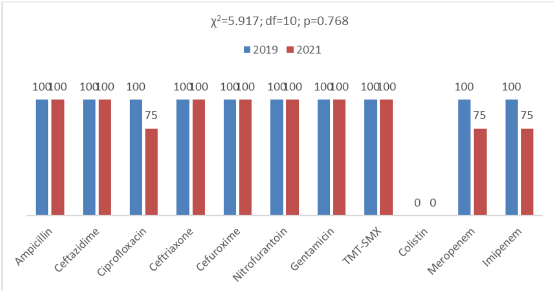

Image 7. Antimicrobial resistance profile of *Acinetobacter* spp. in 2019 and 2021 at the Clinic for Infectious Diseases

Significantly more participants were 66 years and older (χ^2=422.423; df=1; p<0.001). The most common diagnosis was acute cystitis with 46.01%, followed by urosepsis with 43.66%, and acute pyelonephritis with only 10.33% (χ^2=50.901; df=2; p<0.001). Among the total sample of participants (213), the most common causative pathogen of urinary tract infections was *E. coli*, which was statistically significant (Image 1).

In 2019, the most common causative pathogen of urinary tract infections was *E. coli* (43.09%), while in 2021 *Klebsiella pneumoniae* (39.2%) was statistically significant (Table 1.).

There was no statistically significant difference in the resistance of *E. coli* in the two observed periods, but there was an increased resistance to antibiotics during the coronavirus pandemic in 2021. The highest resistance of *Escherichia coli* during 2019 and 2021 was to the antibiotic trimethoprim/sulfamethoxazole, and the greatest resistance was shown by ciprofloxacin in 2021 (Image 2).

The highest resistance of *E. coli* during 2019 and 2021 was to trimethoprim. The resistance of *Klebsiella pneumoniae* increased in both periods. During the coronavirus pandemic, an increased resistance to nitrofurantoin was noticeable. Unexpectedly, there was lower resistance to meropenem and ceftazidime (Image 3).

The antimicrobial resistance of *Enterococcus* spp. in the two different periods was not statistically significant, although the increase in resistance to all antibiotics during the pandemic year, especially to gentamicin and ciprofloxacin, was significant (Image 4).

There was no statistically significant difference in the antimicrobial resistance of *Proteus mirabilis* between the two periods. Notably, during the pandemic year, there was a decrease in the antimicrobial resistance of *Proteus mirabilis* to all antibiotics (Image 5).

During the same year, *Pseudomonas aeruginosa* showed statistically significant higher resistance to meropenem, ceftazidime, and piperacillin/tazobactam, but resistance to ciprofloxacin and amikacin was lower (Image 6).

There was no statistically significant difference in *Acinetobacter* spp. resistance between the two periods. The results show the high resistance of *Acinetobacter* spp. to antibiotics, but good sensitivity to colistin (Image 7).

DISCUSSION

The results of this research, in accordance with the literature and similar studies worldwide, confirm that urinary tract infections are more common in females, particularly among those over 66 years of age (5, 7, 11). The degree of antimicrobial resistance rises with the higher age of the participant (12).

In our research, the most common causative pathogen of urinary tract infections is *Escherichia coli* followed by *Klebsiella pneumoniae*, which is similar to the results worldwide (2, 6–8). There was an increase in UTIs caused by *Klebsiella pneumoniae* during the pandemic period and a significant decrease of those due to *Escherichia coli*, which can be explained by overuse and irrational antibiotic use during the coronavirus pandemic. Similar results by other authors highlight a significant rise in the incidence of *Klebsiella pneumoniae* over the last few years in Bosnia and Herzegovina (13).

Escherichia coli shows a high resistance to trimethoprim/sulfamethoxazole and ciprofloxacin before the pandemic and a significant rise in the resistance of *E. coli* to all antibiotics during the pandemic year. Similar results are provided by an 11-year-long Irish survey in which the most common pathogen was *E. coli* with an incidence increase from 50% to 60%, and a significant rise in resistance to ampicillin, trimethoprim, gentamicin, ciprofloxacin, and cefuroxime (14). It is concerning that before and during the pandemic, *Klebsiella pneumoniae* demonstrated high resistance (over 80%) to a great number of antibiotics with the exception of carbapenems and amikacin. No resistance to colistin was recorded. This is not surprising considering that *Klebsiella pneumoniae* causes a wide range of infections including severe pneumonias, urinary infections, sepsis, and liver abscesses. In particular, it causes severe infections in immunocompromised individuals, diabetics, patients with carcinomas, and those with alcohol use disorders. *Klebsiella pneumoniae* strains have become more resistant to antibiotics, making the infections caused by these strains very difficult to treat, often with poor outcomes (15).

Enterococcus spp. showed an increase in resistance to gentamicin and ciprofloxacin during the pandemic year which can be explained by the rise in patients with complicated urinary tract infections who also have risk factors. The prevalence of multiple resistant *Enterococcus* spp., especially *E. faecium* and *E. faecalis*, which are resistant to vancomycin, has been rising worldwide. This is associated with increased morbidity, as well as limited treatment options and higher health care costs (16). *Proteus mirabilis*, which usually causes complicated urinary tract infections, was recorded in half of the cases in our participants during the pandemic year. A significantly lower resistance rate was recorded for all antibiotics, fewer than 40%, with particular sensitivity to nitrofurantoin during both periods. In a similar study that included two periods, before and during the pandemic, Brazilian authors recorded a rise in the resistance of *Proteus mirabilis* during the pandemic period (17). *Acinetobacter baumannii* is a causative pathogen of nosocomial infections, especially in intensive care units (ICUs). A high rate of antimicrobial resistance was observed in patients with a severe coronavirus infection treated in the ICU due to bacterial complications, multiple comorbidities, prolonged hospitalizations, and immune dysfunction (18). *Acinetobacter* spp. demonstrated high resistance to all antibiotics in both observed periods, including over 75% to carbapenems and ciprofloxacin with the exception of colistin. The synergistic use of colistin with the other antibiotics was the only treatment option for these patients.

Pseudomonas aeruginosa is an opportunistic pathogen in the hospital environment and a causative agent of different infections. It can cause hospital pneumonias due to mechanic ventilation (ventilator-assisted pneumonia, VAP), as well as urinary tract infections due to urinary catheters in use with immunocompromised patients. Therefore, a high resistance to carbapenems, as well as a rate of over 40% and 20% to piperacillin/tazobactam and ceftazidime during the pandemic year, does not surprise us. Overuse of these antibiotics during the pandemic with critically ill patients in the ICU has led to an increase in multiple resistant isolates of *Pseudomonas* spp.

This result is similar worldwide and indicates a high rise in the resistance of *Pseudomonas aeruginosa* to carbapenems and piperacillin/tazobactam, which represents a great problem in antibiotic use (19, 20). Antimicrobial resistance to cefepime was not recorded in our research, which ensures empirical treatment for immunocompromised patients.

CONCLUSION

During the two observed periods, the most common urinary tract infections involved females aged 66 and older, with the most common diagnosis being acute complicated urinary tract infection.

The most common uropathogens were from the Enterobacteriaceae family (*E. coli*), following *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterococcus*, and *Acinetobacter*. All of these have shown an increase in resistance to antibiotics during the pandemic period, with *Proteus mirabilis* as an exception.

Antimicrobial treatment is still inadequate and irrational in clinical use, especially during the coronavirus pandemic, with the consequence of developing multiple resistance and higher costs of treatment. Therefore, it is important to follow guidelines for the treatment of UTIs with a tendency towards the rational usage of antibiotics, both locally and globally.

Our research found an increase in the antimicrobial resistance of uropathogens, but there are still possibilities for antimicrobial treatment. These findings recommend the proper selection of an effective empirical therapy which can contribute to a better treatment outcome and cheaper and shorter treatments, as well as a decrease in resistance.

ACKNOWLEDGMENTS

None.

FUNDING

The authors did not receive any financial support for the research authorship and/or publication of this study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTIONS

RN: contribution to study conception and design, literature review, supervision, writing of the paper, interpretation of data, critical revision of the paper; SG: acquisition of data, contribution to study conception and design, literature review, critical revision of the paper, assistance in writing the paper; LS, MJR, and SJ: acquisition of data, contribution to study conception and design, literature review.

ETHICAL BACKGROUND

Institutional review board statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the School of Medicine, University of Mostar (Reg. No. 1185/22)

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Data availability statement: We deny any restrictions on the availability of data, materials, and associated protocols.

REFERENCES

1. Malmros K, Huttner BD, McNulty C, Rodríguez-Baño J, Pulcini C, Tängdén T; ESGAP UTI Working Group. Comparison of antibiotic treatment guidelines for urinary tract infections in 15 European countries: results of an online survey. Int J Antimicrob Agents. 2019;54:478-86.
2. Yang Q, Zhang H, Wang Y, Xu Z, Zhang G, Chen X, et al. Antimicrobial susceptibilities of aerobic and facultative gram-negative bacilli isolated from Chinese patients with urinary tract infections between 2010 and 2014. BMC Infect Dis. 2017;17:192.
3. Cullen IM, Manecksha RP, McCullagh E, Ahmad S, O'Kelly F, Flynn RJ, et al. The changing pattern of antimicrobial resistance within 42,033 Escherichia coli isolates from nosocomial, community and urology patient-specific urinary tract infections, Dublin, 1999-2009. BJU Int. 2012;109:1198-206.
4. Kahlmeter G, Poulsen HO. Antimicrobial susceptibility of Escherichia coli from community-acquired urinary tract infections in Europe: the ECO•SENS study revisited. Int J Antimicrob Agents. 2012;39:45-51.
5. Kot B, Grużewska A, Szweda P, Wicha J, Parulska U. Antibiotic resistance of uropathogens isolated from patients hospitalized in District Hospital in Central Poland in 2020. Antibiotics (Basel). 2021;10:447.
6. Kasew D, Desalegn B, Aynalem M, Tila S, Diriba D, Afework B, et al. Antimicrobial resistance trend of bacterial uropathogens at the university of Gondar comprehensive specialized hospital, northwest Ethiopia: a 10 years retrospective study. PLoS One. 2022;17:0266878.
7. Farajnia S, Alikhani MY, Ghotaslou R, Naghili B, Nakhlband A. Causative agents and antimicrobial susceptibilities of urinary tract infections in the northwest of Iran. Int J Infect Dis. 2009;13:140-4.
8. Piljić D, Ahmetagić S, Piljić D, Stojić V, Petrović J. Antimikrobna rezistencija uzročnika izvanbolničkih infekcija mokraćnog sustava u odraslih bolesnika hospitaliziranih u Klinici za infektivne bolesti Tuzla. Infektološki Glasnik. 2009;29.
9. Zec S, Despotovic A, Spurnic-Radovanovic A, Milosevic I, Jovanovic M, Pelemis M, Stevanovic G. Antimicrobial resistance in patients with urinary tract infections and the impact on empiric therapy in Serbia. J Infect Dev Ctries. 2016;10:1065-72.
10. Tambić Andrašević A, Lucić S, Tambić T. Antibiotic resistance in Croatia. Medicina Fluminensis. 2018;54:312-21.
11. Damjanov I, Seiwerth S, Jukić S, Nola M, eds. Patologija. Peto izdanje. Zagreb: Medicinska naklada; 2018:552-8.
12. Sahuquillo-Arce JM, Selva M, Perpiñán H, Gobernado M, Armero C, López-Quílez A, et al. Antimicrobial resistance in more than 100,000 Escherichia coli isolates according to culture site and patient age, gender, and location. Antimicrob Agents Chemother. 2011;55:1222-8.
13. Czaja CA, Scholes D, Hooton TM, Stamm WE. Population based epidemiologic analysis of acute pyelonephritis. Clin Infect Dis 2007;45:273-80.
14. Wagenlehner FM, Pilatz A, Weidner W. Urosepsis – from the view of the urologist. Int J Antimicrob Agents 2011;38:51-7.
15. Michelle KP, Joan M. Klebsiella pneumoniae: going on the offense with a strong defense. Microbiol Mol Biol Rev. 2016.;80:629-61.
16. Xenofon G, Hercules S, Vasileios R, Evangelos T, Petros B, Angelos M. Impact of enterococcal urinary tract infections in immunocompromised – neoplastic patients. J BUON. 2019:24:1768-75.
17. de Almeida LKS, Silva LC, Migliorini Guidone GH, de Oliva DBH, do Nascimento AB. Impact of COVID-19 pandemic on antimicrobial resistance of Proteus mirabilis in a Brazilian hospital. Braz J Microbiol. 2024;56:499-510.
18. Karyne R, Thiago Pavoni Gomes CH, Giovanni De-Simone S. Acinetobacter baumannii Infections in Times of COVID-19 Pandemic. Pathogens 2021;10:1006.
19. WHO Regional Office for Europe/European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2022 – 2020 data. Copenhagen: WHO Regional Office for Europe; 2022.
20. Heidari R, Farajzadeh Sheikh A, Hashemzadeh M, Farshadzadeh Z, Salmanzadeh S, et al. Antibiotic resistance, biofilm production ability and genetic diversity of carbapenem-resistant Pseudomonas aeruginosa strains isolated from nosocomial infections in southwestern Iran. Mol Biol Rep. 2022;49:3811-22.