

EVALUATION OF ANTIMICROBIAL RESISTANCE OF UROPATHOGENES INVOLVED IN URINARY TRACT INFECTIONS IN ICU PATIENTS

M.E. IDOMIR^{1,2*} C.S. COSTINAŞ²

Abstract: *The aim of the retrospective study was the analysis of antibiotic resistance patterns of bacteria involved in urinary tract infections in patients hospitalized during 2019 in the Intensive Care Unit of the Clinical County Emergency Hospital Brasov. The main bacteria involved were Escherichia coli (38,68%), Klebsiella species (23,69%) and Enterococcus species (15,68%). Various degrees of resistance to the tested antibiotics were observed. ESBL strains were detected at Escherichia coli (20,72.%) and Klebsiella species (10,29%). Carbapenem resistant strains were detected at Klebsiella spp. (48,48%), P. aeruginosa (56,25%) and Acinetobacter spp. (85,71%). MRSA, VRE and HLAR strains were also detected in the studied group.*

Key words: *urinary infections, antimicrobial resistance, intensive care unit*

1. Introduction

Nosocomial infections represent currently a very important public health problem, with an incidence of 5-10% in developed countries and 25% or more in developing countries [2], [4], [15].

The favoring factors for the occurrence of nosocomial infections can be the patient age (the children and elderly are more susceptible), diseases associated with immunodeficiency, failure in organs, surgery, malnutrition, using of various

medical devices, injuries, immuno-suppressive drugs [14].

These infections are also associated with significant rates of morbidity and mortality and are the cause of the prolongation of hospitalization and of the high increase in costs associated with health care.

There have been reported increases by up to 33% in the mortality rate due to these infections, the main cause of death being nosocomial pneumonia (especially ventilator-associated pneumonia), as well

¹Transilvania University of Brasov, Faculty of Medicine

²Clinical County Emergency Hospital Brasov

*corresponding author: mihaela.idomir@unitbv.ro

as extending the hospitalization period by 7 to 10 days and additional costs of about 10 billion dollars annually [2], [15].

The incidence of nosocomial infections in the Intensive Care Unit (ICU) is 2-5 times higher than the general incidence in the hospitalized patients, these infections having profound social, economic and even legal implications. The most common infections are pneumonia, urinary tract infections (UTI) and bloodstream infections [1], [4], [5], [9], [10], [15].

Other studies also report other localizations such as soft tissue infections, gastroenteritis, hepatitis, meningitis, otitis [2], [3], [5].

Urinary infections represent an important category of nosocomial infections in ICU, various studies reporting incidences up to 40% varied depending on the geographical region, hospital and department. The majority (60-80%) are detected in patients with urinary catheterization. Studies do not report age, sex, disease severity or comorbidities as being significant favorable factors, but the average length of stay in ICU, the duration of catheter use (increased risk by 5% daily) and the conditions of catheter use (there is higher frequency of symptomatic UTIs when urinary catheters were placed in an emergency or in the operating room) [2], [5], [11], [12], [13], [15], [16].

The main bacteria involved in UTI in ICU are *Escherichia coli*, *Klebsiella species*, *Pseudomonas aeruginosa*, *Acinetobacter sp.*, *Proteus sp.*, *Citrobacter sp.* [2], [3], [4], [5], [7], [9], [12], [15], [18].

The involvement of anaerobic germs in UTIs from the ICUs was also reported [17].

The results reported in various studies on the antibiotic resistance profiles of isolated germs and the share of multidrug-resistant strains vary from one ICU to

another. Resistance to beta-lactams is most commonly reported in *Enterobacteriaceae P. aeruginosa* and *Acinetobacter baumannii* have high resistance to most antibiotics tested [1], [13].

The involvement of resistance phenotypes has often been reported in both gram negative bacilli (ESBL = Extended Spectrum Beta-lactamases producing strains and carbapenem resistant strains) and gram positive cocci (MRSA = Methicillin Resistant Staphylococcus aureus, VRE = Vancomycin Resistant Enterococci, HLAR = High Level Amino-glycosides Resistance) [7], [14].

2. Material and Methods

The study was retrospective and aimed to analyse the antibiotic resistance of bacteria isolated from the urine specimens collected from patients hospitalized in the Intensive Care Unit (ICU) of the Clinical County Emergency Hospital Brasov in the period 1.01.2019-31.12.2019.

The urine culture was made by calibrated loops method using the 10 µl bacteriological loop. The culture media used for the in vitro cultivation of the bacteria was Columbia Blood Agar (non-selective medium), Mac Conkey Agar (selective medium) and UTI Agar (Urinary Tract Infections).

Usually, for the genre identification of the bacteria, biochemical tests were made by manual methods. VITEK 2 COMPACT automated system was also used during the study for the identification of species or for confirmation on results.

Antibiograms were performed according to CLSI guide (Clinical Laboratory Standard Institute) from 2019.

The detection of ESBL strains (Extended

Spectrum Beta Lactamases) was made by the synergy test. For the detection of MRSA (Methicillin Resistant Staphylococcus aureus) 30 µg cefoxitin discs were used, for VRE (Vancomycin Resistant Enterococci) 30 µg vancomycin discs and for HLAR (High Level Aminoglycoside Resistance) 120 µg gentamicin discs were used. The automated system was used to confirm the resistance profiles or expand the list of antibiotics.

3. Results and Discussions

The first aim of the study was to analyse the categories of germs involved in urinary tract infections in patients admitted to the ICU as well as the analysis of the bacterial genre isolated from urine samples.

The collected data are presented in Table 1 and illustrated in Figure 1.

Table 1
Germs isolated from urine samples from ICU patients

Germs	Number of strains
Escherichia coli	111
Klebsiella spp.	68
Proteus spp.	26
Serratia spp.	1
Providencia spp.	14
Pseudomonas aeruginosa	16
Acinetobacter spp.	7
Enterococcus spp.	45
Staphylococcus aureus	3
Coagulase negative staphylococci	2
Streptococcus spp.	1
Total	294

Figure 1 illustrates the etiological spectrum of UTI in ICU dominated by Gram-negative bacilli (Enterobacteriaceae), especially E. coli (38.68%) and Klebsiella spp. (23, 69%). Enterococcus spp. had also a relatively high share (15.68%).

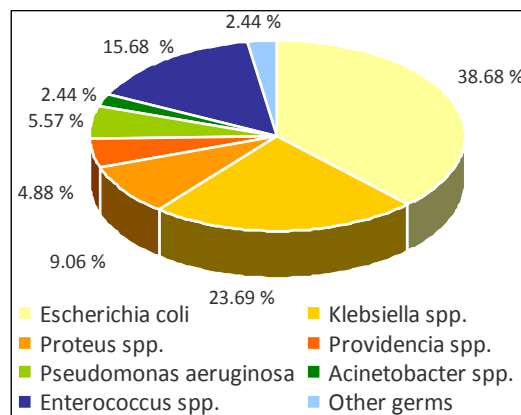


Fig. 1. *The etiological spectrum of urinary infections in ICU*

The antibiotic resistance patterns of the analyzed, as shown in Figures 2 to 8. germs isolated from urine have been also

Table 2
Share of germs isolated from urine from total germs isolated from ICU patients

Germs	Number of isolated strains fom ICU	Percentage of strains from urine (%)
<i>Escherichia coli</i>	205	54.15
<i>Klebsiella spp.</i>	226	30.09
<i>Proteus spp.</i>	71	36.62
<i>Serratia spp.</i>	7	14.29
<i>Providencia spp.</i>	84	16.67
<i>Citrobacter spp.</i>	2	0
<i>Pseudomonas aeruginosa</i>	92	17.39
<i>Acinetobacter spp.</i>	157	4.46
<i>Enterococcus spp.</i>	105	42.86
<i>Staphylococcus spp.</i>	23	21.74
<i>Streptococcus spp.</i>	3	33.33
Total	749	39,25%

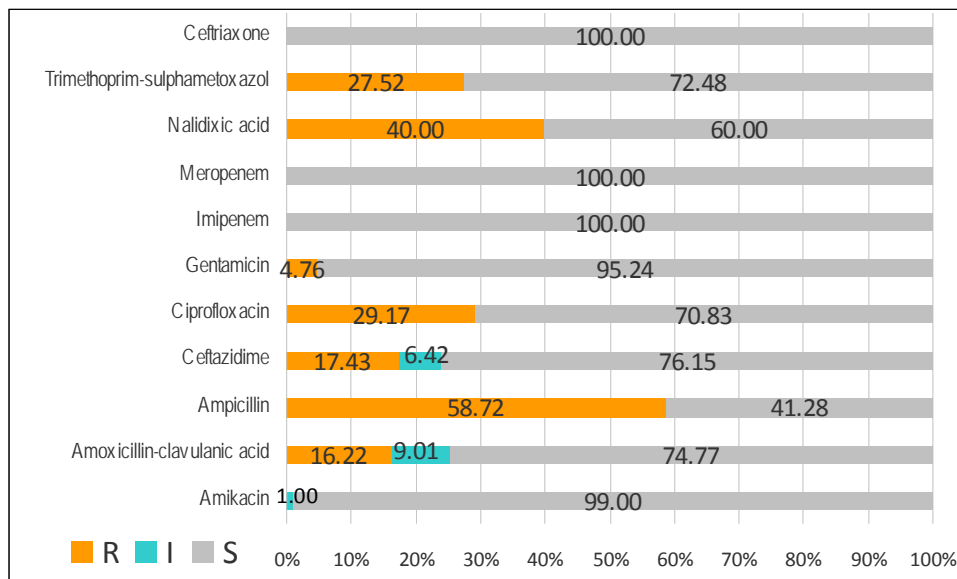


Fig. 2. *The resistance to antibiotics of Escherichia coli*

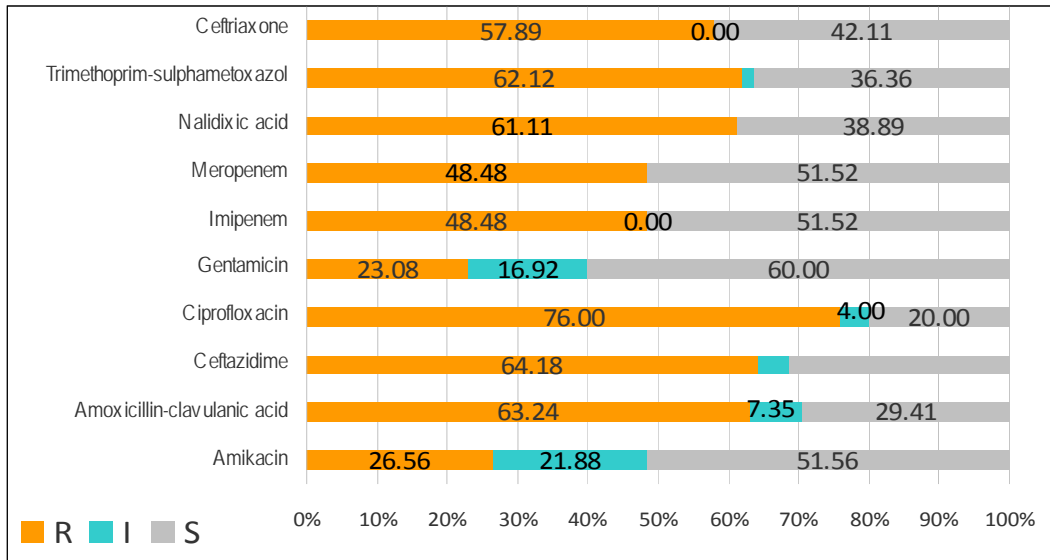


Fig. 3. *The resistance to antibiotics of Klebsiella spp.*

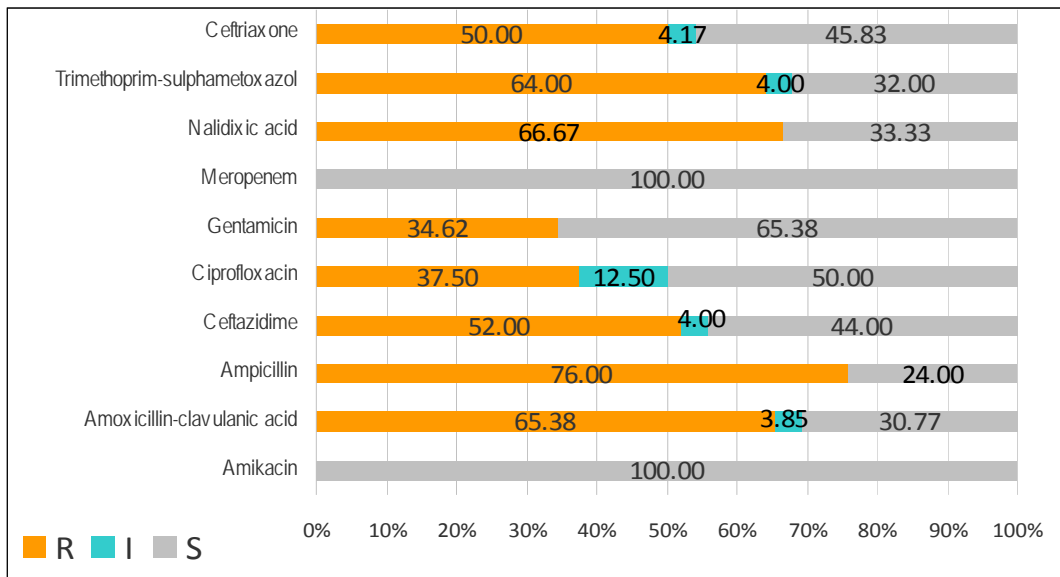


Fig. 4. *The resistance to antibiotics of Proteus spp.*

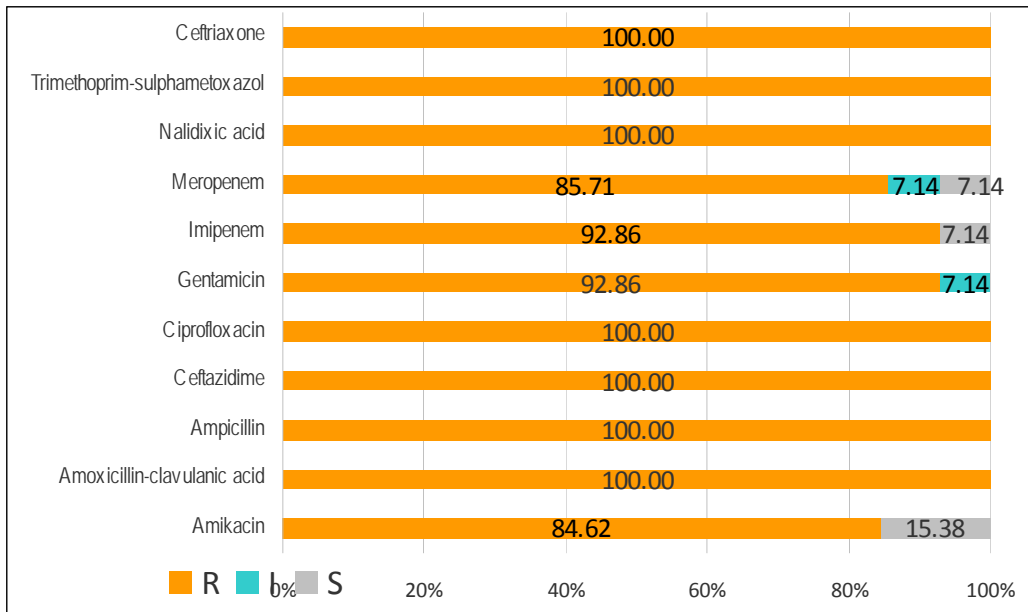


Fig. 5. *The resistance to antibiotics of Providencia spp.*

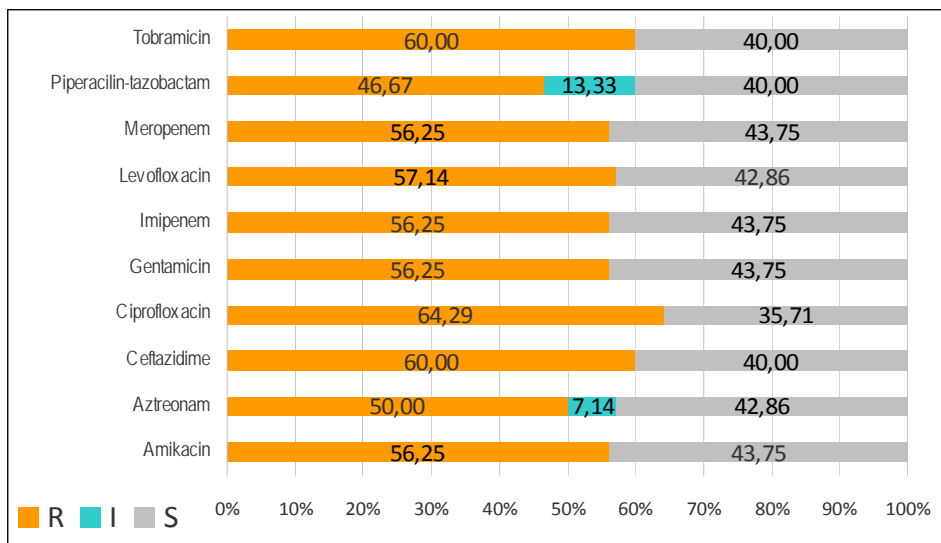


Fig. 6. *The resistance to antibiotics of Pseudomonas aeruginosa*

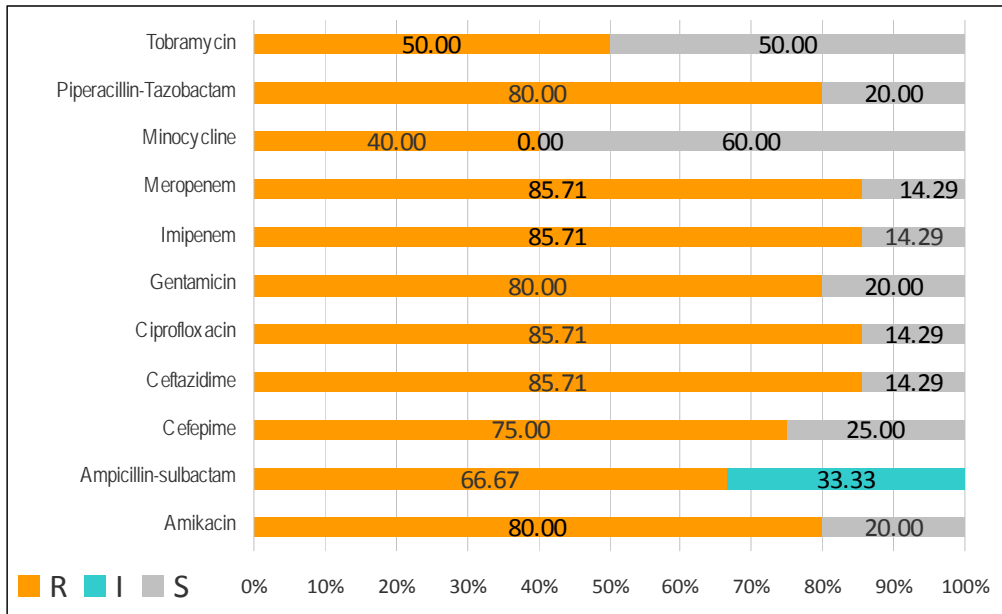


Fig. 7. The resistance to antibiotics of *Acinetobacter* spp.

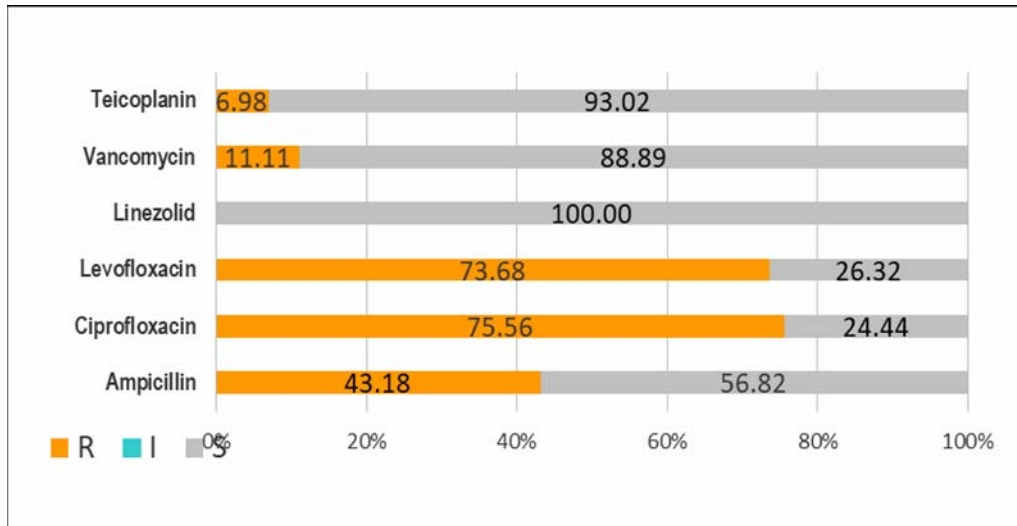


Fig. 8. The resistance to antibiotics of *Enterococcus* spp.

In the study it was also analysed the etiological therapy problems, as shown in resistance phenotypes that raise Tables 3 ÷ 5.

Table 3
Evaluation of ESBL producing strains

Enterobacteriaceae	ESBL	nonESBL
E. coli	23	88
Klebsiella spp.	7	61
Proteus spp.	0	26
Providencia spp.	0	14
Serratia spp.	0	1

Table 4
Evaluation of MRSA strains

Staphylococcus genre	MRSA	Non MRSA
S. aureus	2	1

Table 5
Evaluation of VRE and HLAR strains

Enterococcus genre	Specific phenotype	Other strains
VRE	5	40
HLAR	23	22

The results of the study show that the bacterial strains identified in the urine accounted for 39.25% of the strains identified in the pathological products in patients admitted to the ICU, which shows the important place of these infections in this category of patients.

The spectrum of germs was wide being dominated by *Escherichia coli* (38.68%) but in a lower percentage than in community urinary tract infections or in other hospital wards.

The high share of *Enterococcus spp.* (15.68%) is also noteworthy.

In the case of *Enterobacteriaceae* strains, very high resistance to all tested antibiotics was observed for *Providencia spp.*, but the percentages are also worrying in *Klebsiella spp.*

The share of ESBL strains was higher in *Escherichia coli* (20.72%) compared to *Klebsiella spp.* (10.29%).

Non-fermentative gram-negative bacilli from the *Pseudomonas* and *Acinetobacter* genere were also highly resistant to antibiotics of various classes, which raises therapy problems.

Enterococcus species had the highest resistance to fluoroquinolones but the involvement of VRE strains is worrying.

The results of the study are consistent with other studies and sustain the importance of monitoring antibiotic resistance especially in Gram-negative bacilli, included by WHO (World Health Organisation), since 2017, in the category Critical level, on the list of multi-resistant germs for which new therapies are required with priority. Although colistin, meropenem, amikacin, gentamicin can still be used to treat these infections, the high percentages of resistance are worrying. Data collected by EARS-Net (European Anti-microbial Resistance Surveillance Network) showed, in many countries, especially in south-eastern Europe, high levels of resistance of Gram negative bacteria. Reports from CDC (Center for Disease Control and Prevention) and WHO sustain the need for the correct prescriptions of existing antibiotics, modern equipment of laboratories for testing the resistance phenotypes and concentrate efforts to develop new antibiotics and evaluate new therapies (adjuvants, nanoparticles, peptides, bacteriophages, photon light) [8], [19].

4. Conclusions

In ICU, the etiological spectrum of urinary infections was broadly dominated by gram

negative bacilli, especially *E. coli* (38.68%), *Klebsiella* species (23.69%).

Among the gram positive cocci were isolated with higher frequency *Enterococcus* species (15.68%).

E. coli strains had higher resistance to ampicillin (58.72%), nalidixic acid (40%) and trimethoprim-sulphamethoxazole (27.52%).

Klebsiella spp. recorded relatively high percentages of resistance to all antibiotics currently tested, including carbapenems (48.48%).

Proteus spp. had varying degrees of resistance to the tested antibiotics with the exception of meropenem and amikacin to which the sensitivity was 100%.

Providencia spp. had high resistance to all tested antibiotics, the involvement in the pathology of these strains being very worrying due to the high risk of therapeutic failure.

High levels of antibiotic resistance have also been observed in gram-negative non-fermentative bacilli, including carbapenems.

Enterococcus spp. had higher resistance to fluoroquinolones (75.56% to ciprofloxacin, 73.68% to levofloxacin) and VRE strains were isolated (11.11%).

The results of the study support the need for uroculture monitoring of urinary catheterized ICU patients and the importance of knowing the bacterial etiological spectrum and antibiotic resistance patterns in each ICU in order to optimize therapy, especially empirical therapy.

References

1. Agaba, P., Tumukunde, J. et al.: *Nosocomial bacterial infections and their antimicrobial susceptibility patterns among patients in Ugandan intensive care units: a cross sectional study*. In: BMC Research Notes (2017), 10(349), p. 1-12.
2. Baviskar, A. S., Khatib, K.I., et al.: *Nosocomial infections in surgical intensive care unit: A retrospective single-center study*. In: International Journal of Critical Illness&Injury Science (2019), 9(1), p. 16-20.
3. Choudhuri, A.H., Chakravarty, M., et al.: *Epidemiology and characteristics of nosocomial infections in critically ill patients in a tertiary care intensive care unit of Northern India*. In: Saudi Journal of Anesthesia (2017), 11(4), p. 412-407.
4. Dasgupta, S., Das, S., et al.: *Nosocomial infections in the intensive care unit: Incidence, risk factors, outcome and associated pathogens in a public tertiary teaching hospital of Eastern India*. In: Indian J Crit Care Med. (2015), 19(1), p. 14–20.
5. Despotovic, A., Milosevic, B., et al: *Hospital-acquired infections in the adult intensive care unit - Epidemiology, antimicrobial resistance patterns, and risk factors for acquisition and mortality*. In: American Journal of Infection Control (2020), 48(10), p. 1211-1215.
6. Duszyńska, W., Rosenthal, V., et al.: *Urinary tract infections in intensive care unit patients — a single-centre, 3-year observational study according to the INICC project*. In: Anaesthesiology Intensive Therapy (2016), 48(1), p. 1–6.
7. ECDC: *Healthcare-associated infections acquired in intensive care units*. In: Annual Epidemiological Report, 2016.
8. ECDC: *Surveillance of antimicrobial resistance in Europe 2017*. In: Annual report of the EARS-Net., 2018.

9. Esfahani, B.N., Basiri, R., et al.: *Nosocomial Infections in Intensive Care Unit: Pattern of Antibiotic-resistance in Iranian Community*. In: *Adv Biomed Res.* (2017), 6(1), p. 54.
10. Hamishehkar, H., Shadmehr, P., et al.: *Antimicrobial susceptibility patterns among bacteria isolated from intensive care units of the largest teaching hospital at the northwest of Iran*. In: *Brazilian Journal of Pharmaceutical Sciences* (2016), 52(3), p.403-412.
11. Lee, E., Teo, A., et al.: *Risk factors associated with urinary tract infections in intensive care patients*. In: *Original Research* (2016), 21(2), p. 62-66.
12. Liu, Y., Xiao, D., et al.: *Urinary tract infection control in intensive care patients*. In: *Medicine (Baltimore)*, (2018), 97(38), p. 1-3.
13. Mishra, D., Rao, K.B.: *Catheter associated urinary tract infection in an acute care setting of a tertiary care center in South India*. In: *International journal of research in medical sciences* (2019), 7(6), p. 2182-2186.
14. Nouri, F., Karami, P., et. al.: *Prevalence of Common Nosocomial Infections and Evaluation of Antibiotic Resistance Patterns in Patients with Secondary Infections in Hamadan, Iran* In: *Infect Drug Resist.* (2020), 13, p. 2365–2374.
15. Özdemir, K., Dizbav, M.: *Nosocomial infection and risk factors in elderly patients in intensive care units*. In: *Journal of Microbiology and Infectious Diseases* (2015), 5 (1), p. 38-43.
16. Podkovik, S., Toor, H., et al.: *Prevalence of Catheter-Associated Urinary Tract Infections in Neurosurgical Intensive Care Patients – The Overdiagnosis of Urinary Tract Infections*. In: *Cureus* (2019), 11(8), p. 1-9.
17. Rozenfeld, K. L., Nitzan, O., et al.: *Presence of anaerobic bacteria in the urinary tract of catheterized ICU patients*. In: *European Journal of Clinical Microbiology & Infectious Diseases* (2018), 37, p. 2131–2136.
18. Savanur, S., Gururaj, H.: *Study of Antibiotic Sensitivity and Resistance Pattern of Bacterial Isolates in Intensive Care Unit Setup of a Tertiary Care Hospital*. In: *Indian J Crit Care Med.* (2019), 23(12), p. 547–555.
19. WHO: *Global priority list of antibiotic-resistant bacteria to guide research, discovery and development of new antibiotics*. In: WHO Publications, 2017.