https://doi.org/10.31689/rmm.2023.30.3.181

ORIGINAL PAPERS

Colonization, Infection and Risk Factors for Death in an Infectious Disease ICU in Romania

Nicoleta-Dorina VLAD[1,2,3*], Andreea CAPILNA[4], Anca DUMITRESCU[1], Aurora CRACIUN[5], Sergiu CHIRILA[5], Tony HANGAN[2,5], Elena DUMEA[1,5], Septimiu VOIDAZAN[6], Sorin RUGINA[2,7,8], Claudia-Simona CAMBREA[1,2,5], Irina-Magdalena DUMITRU[1,2,5,7]

Abstract

Knowing the bacterial strains in the intensive care unit (ICU) is important for reducing the rate of bacterial transmission and the risk of healthcare-associated infections (HAIs), allowing for targeted interventions to reduce the risk of death by HAIs. We performed a retrospective case-control study in a single center that included 320 bacteriologically screened patients from the ICU of the Infectious Diseases Hospital in Constanta between September 2017 and March 2020. Sixty-five secondary bacterial infections were identified as the cause of hospital admission and 60 bacterial colonizations. There were 20 cases and 300 controls for the mortality rate and risk factors for death. Multivariate analysis identified that hospitalization of patients for HIV infection (OR 11.82, 95% CI: 1.69-83.62, P ≤0.05) and Clostridioides difficile infection (OR 7.38, 95% CI: 1.39 -39.22, P ≤ 0.05) were independent risk factors associated with death. We observed that the number of colonizations or secondary infections in the ICU was similar, and the mortality rate in the ICU was influenced by HIV infection or *Clostridioides difficile* infection.

Keywords: mortality, risk factors; colonization; infection.

Rezumat

Cunoașterea tulpinilor bacteriene din unitatea de terapie intensivă este importantă pentru reducerea ratei de transmitere a bacteriilor și a riscului de infecții asociate asistenței medicale (IAAM), permițând intervenții direcționate pentru a reduce riscul de deces prin IAAM. Am efectuat un studiu retrospectiv, de tip caz-control, într-un singur centru care a inclus 320 de pacienți screenați bacteriologic din unitatea de terapie intensivă a Spitalului Clinic de Boli Infecțioase din Constanța, în perioada septembrie 2017 – martie 2020. Au fost identificate 65 de infecții bacteriene secundare cauzei admisiei și 60 de colonizări bacteriene. Au fost 20 de cazuri și 300 de controale pentru determinarea ratei mortalității și a factorilor de risc pentru deces. Analiza multivariată a identificat că spitalizarea pacienților pentru infecție cu HIV (OR 11,82, IC 95%: 1,69-83,62, P ≤0,05) și infecția cu Clostridioides difficile (OR 7,38, IC 95%: 1,39 -39,22, P ≤ 0,05) au fost factori de risc independenți asociați cu deces. Am observat că numărul de colonizări sau infecții secundare în unitatea de terapie intensivă a fost similar, iar rata mortalității în terapie intensivă a fost influențată de infecția HIV sau infecția cu *Clostridioides difficile*..

Cuvinte cheie: mortalitate, factori de risc; colonizare; infecție.

[1]Clinical Infectious Diseases Hospital, 100 Ferdinand Str, 900709 Constanța, Romania;
[2]Doctoral School of Medicine, Ovidius University of Constanța, Aleea Universitații nr.1,
900470 Constanta, Romania
[3]Military Emergency Hospital Constanta, 96 Mamaia Str, 900228 Constanța, Romania
[4]Military Hospital Regina Maria Brasov, 9 Pieții Str, 500007 Brasov, Romania
[5]Faculty of Medicine, Ovidius University of Constanța, Aleea Universitații, nr.1, 900470 Constanța, Romania
[6]George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, 38 Gheorghe Marinescu Str, 540142, Târgu Mureș, Romania
[7]Romanian Academy of Scientist, 125, Calea Victoriei, sector 1, 010071 Bucharest, Romania
[8]Romanian Academy of Medical Sciences, Spl Independentei, nr. 54, 50085, Bucharest, Romania

Corresponding author:
Vlad Nicoleta-Dorina, Aleea Universitații nr.1, 900470 Constanta, Romania
E-mail: nicoleta.lalescu@yahoo.com

INTRODUCTION

Globally, multidrug-resistant bacteria (MDRB) infections are a major public health problem[1]. In the Extended Prevalence of Infection in Intensive Care (EPIC II) study, in which 75 countries and 1.265 intensive care units (ICUs) were involved, 35% of the isolated bacteria were MDRB[1]. According to the European Centre for Disease Prevention and Control (ECDC), patients admitted to ICUs are at a high risk of infection because of their underlying disease and frequent exposure to invasive devices[2]. Regarding ICU-acquired infections, in the ECDC, six countries, including Romania, provided only data based on units, and three countries reported patient and unit-based data[3].

In a Polish study that evaluated the risk factors for death in ICU patients in 347 ICUs, Weigl et al. observed that variables associated with survival in the ICU were the tertiary level of hospital care, the high annual volume of patients admitted to the ICU, younger patient age, female sex, and a lower number of comorbidities[4]. In another study conducted in Canada, Detsky et al. reported that among patients who spend at least three days in an ICU and who require even short periods of life support therapy, almost half will die and less than a third will return to baseline after six months, and of those who survive, most patients will return home at six months[5]. During the coronavirus disease 2019 (COVID-19) pandemic, numerous studies have been conducted to identify the risk factors associated with ICU admission. A large-scale study conducted in Brazil on a sample of 1,048,575 patients infected with SARS-CoV-2 argued that obesity is the main risk factor for intensive care unit admission and death[6]. Regarding the study of risk factors for the death of patients in the ICU before the COVID-19 pandemic, no studies with data related to the situation in Romania were found in the research conducted.

The study aimed to identify the bacterial strains and risk factors for death in patients who were bacteriologically screened in the ICU.

MATERIAL AND METHODS

Study design

This retrospective case-control study was conducted in a single center between September 2017 and March 2020, in which 320 patients hospitalized in the ICU were included. Sixty bacterial colonizations with resistance mechanisms and 65 bacterial strains that caused secondary infections were detected, of which 24 had resistance mechanisms.

The inclusion criteria were hospitalization for a minimum of 24 hours in the ICU and the performance of at least one bacteriological screening during hospitalization in the ICU.

Clinical and microbiological data

Data were collected from the electronic medical records. The microbiological laboratory tests used to perform bacteriological screening in the ICU were performed using the phenotypic methods of bacterial identification. Chromogenic agar medium, double disc synergy, and modified Hodge tests were used. Bacterial strains were identified using VITEK 2-Compact 15 and MALDI-TOF MS 1000, according to the European Committee for Antimicrobial Susceptibility Testing (EUCAST) guidelines[7]. Antibiotic resistance was confirmed by ATB either by microdilution (VITEK) or diffusimetry. No antibiogram was performed for the bacterial strains detected by screening. Colonization was detected during bacteriological screening according to ICU guidelines. Evidence of the symptoms and signs of infection was based on organ-specific diseases (e.g., urinary tract infection, pneumonia, and invasive bloodstream infection). These data were associated with suggestive paraclinical data such as increased levels of inflammatory markers.

Statistical analysis and ethical review

This study was conducted in accordance with the principles of the Declaration of Helsinki. This study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[8].

Statistical analysis was performed using IBM SPSS Statistics, Version 20.0, and Microsoft Excel. This study was paired with cases (patients who died in the ICU) and controls (patients who survived. The variables associated with death were $p<0.05$, in the univariate and multivariate analyses. Univariate analysis was performed using a $\chi 2$-test model and multivariate analysis using logistic regression.

RESULTS

Detected bacterial strains

Of the 320 patients included in the study, 105 (33%) were found to have bacterial strains in the ICU and 215

(67%) patients did not have bacterial strains detected (Figure 1). In 65 (20%) patients, bacterial strains that produced infections secondary to the cause of admission to the ICU, of which only 24 (37%) were detected strains with resistance mechanisms (ESBL, carbapenemases, MRSA, VRE) and 41 (63%) bacterial strains without resistance mechanisms were detected. Regarding the bacterial strains identified in the ICU, bacteriological screening revealed that 60 patients (19%) had bacterial strains with resistance mechanisms (Figure 1). In total, only five (5%) patients acquired infection and colonization with the same bacterial strain and the same resistance mechanism, and in 15 (14%) patients, bacterial colonization and infection were detected, (Figure 1).

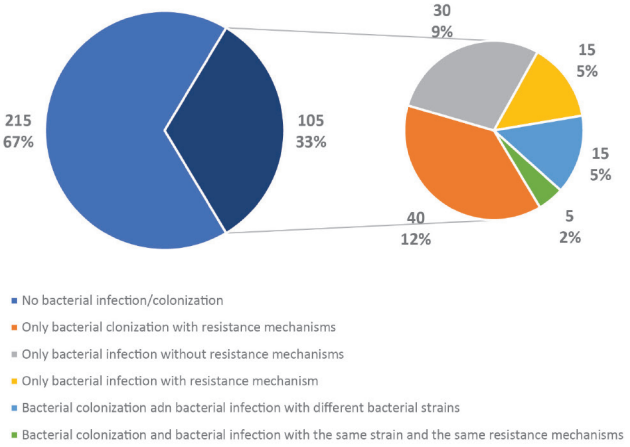

Figure 1. Strains circulation in the ICU, period September 2017-March 2020

Location of bacterial strains

Regarding the number of isolated bacterial strains, 6 strains were detected in blood, 13 strains in sputum, 33 in urine, 53 in the rectal swab, 12 in the nasal swab, 3 in conjunctival secretion, 14 in purulent discharge, and one strain each in the pharyngeal swab, one in otic secretion, one in vaginal secretions and one strain in feces. Table 1 (next page) also shows the common location of bacterial infections and colonization.

Risk factors for death in patients hospitalized in ICU

Regarding the demographic data of the patients who died, the female sex predominated, with nine (45%) male patients and 11 (55%) female patients. Fifteen (75%) urban and 221 (73.7%) rural patients were included in the study. According to Table 2, 20 patients died.

Regarding age, 13 (65%) patients who were >65 years old died and 105 (35%) patients >65 years old survived. According to the univariate analysis performed in Table 2, male gender is not a risk factor for death if the patient is colonized.

Table 2. Demographic characteristics - the mortality rate

Characteristics of colonized patients-mortality rate N (%)	Cases (Death) (N=20)	Control (Survival) (N=300)	Univariate analysis	
			OR (CI 95%)[a]	P Value
Sex				
Males	9 (45%)	151 (50.3%)	0.80 (0.32-1.99)	0.63
Females	11 (55%)	149 (49.7%)		
Environment				
Urban	15 (75%)	221 (73.7%)	1.07 (0.37-3.06)	0.88
Rural	5 (25%)	79 (26.3%)		
Average age	58.14	57.74	-	0.60
Age >65 years	13 (65%)	105 (35%)	2.25 (0.87-5.81)	0.08

% = percentage; the test was performed with Chi-Square, the P value in bold is statistically significant ($p \leq 0.05$). General characteristics of patients admitted to the ICU - mortality rate - September 2017-March 2020

Regarding the death of patients hospitalized in the ICU, 18 (90%) patients had a Carmeli score > 1 point, 10 (50%) had a Carmeli score > 3 points, 17 (85%) had a Charlson Comorbidity Index score > 1 point, and 9 (45%) had a Charlson Comorbidity index > 4 points. Among patients who did not die, 218 (73%) had a Carmeli score > 1 point, 94 (31%) had a Carmeli score > 3 points, 211 (70%) had a Charlson Comorbidity index > 1 point, and 86 (29%) had a Charlson Comorbidity index > 4 points. (Table 3). In the univariate analysis, we observed no association between the two categories.

Table 1. Bacterial strains in ICU

Location of bacterial strains N (%)	Bacterial colonization and infections N=105 (%)	Bacterial infection with resistance mechanisms and without resistance mechanisms N=65 (%)	Bacterial infections with resistance mechanisms N=24 (%)	Bacterial infections without resistance mechanisms = N =41 (%)	Bacterial colonization N=60 (%)
Blood	2 (1.9%)	2 (3.1%)	1 (4.2%)	1 (2.4%)	0 (0%)
Conjunctival discharge	2 (1.9%)	2 (3.1%)	2 (8.3%)	2 (4.9%)	0 (0%)
Otic discharge	1 (1%)	1 (1.5%)	0 (0%)	1 (2.4%)	0 (0%)
Purulent discharge	8 (7.6%)	8 (12.3%)	0 (0%)	8 (19.5%)	0 (0%)
Sputum	6 (5.7%)	6 (9.2%)	1 (4.2%)	8 (19.5%)	0 (0%)
Urine	19 (18.1%)	19 (29.2%)	15 (62.5%)	14 (34.14%)	0 (0%)
Rectal swab/nasal swab/ urine	1 (1%)	1 (1.5%)	0 (0%)	0 (0%)	1 (1.7%)
Rectal swab/urine	6 (5.7%)	6 (9.2%)	0 (0%)	0 (0%)	6 (10%)
Rectal swab/blood	2 (1.9%)	2 (3.1%)	2 (8.3%)	0 (0%)	2 (3.3%)
Nasal swab/urine	2 (1.9%)	2 (3.1%)	0 (0%)	0 (0%)	2 (3.3%)
Rectal swab/sputum	5 (4.8%)	5 (7.7%)	0 (0%)	0 (0%)	5 (8.3%)
Rectal swab/conjunctival discharge	1 (1%)	1 (1.5%)	0 (0%)	0 (0%)	1 (1.7%)
Rectal swab/purulent discharge	3 (2.9%)	3 (4.6%)	1 (4.2%)	0 (0%)	3 (5%)
Blood /vaginal secretions	1 (1%)	1 (1.5%)	1 (4.2%)	0 (0%)	0 (0%)
Blood /purulent discharge	1 (1%)	1 (1.5%)	0 (0%)	0 (0%)	0 (0%)
Purulent discharge/urine	2 (1.9%)	2 (3.1%)	0 (0%)	1 (2.4%)	0 (0%)
Sputum/urine	2 (1.9%)	2 (3.1%)	0 (0%)	1 (2.4%)	0 (0%)
Urine /faecal	1 (1%)	1 (1.5%)	0 (0%)	1 (2.4%)	0 (0%)
Rectal swab	31 (29.5%)	0 (0%)	0 (0%)	0 (0%)	31 (51.7%)
Nasal swab	4 (3.8%)	0 (0%)	0 (0%)	0 (0%)	4 (6.7%)
Pharyngeal swab	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rectal and nasal swab	4 (3.8%)	0 (0%)	0 (0%)	0 (0%)	4 (6.7%)
Nasal and pharyngeal swab	1 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (1.7%)

N=number; (%) = percent; Site of detection of bacterial infections and bacterial colonization, in ICU, September 2017-March 2020

Table 3. Risk factors for death

Risk factors for death N (%)	Cases (Death) (N=20)	Control (Survival) (N=300)	Univariate analysis	
			OR (CI 95%)	P
Carmeli score > 1 point	18 (90%)	218 (73%)	2.68 (0.77-14.98)	0.08
Carmeli score 3 points	10 (50%)	94 (31%)	2.18 (0.87-5.41)	0.08
Median of the Carmeli score Carmeli	2.1	2.05	-	-
Charlson Comorbidity Index (CCI) ≥1	17 (85%)	211 (70%)	2.40 (0.68-8.40)	0.15
Charlson Comorbidity Index (CCI) ≥4	9 (45%)	86 (29%)	2.06 (0.82-5.14)	0.11
Median Charlson Comorbidity Index	2.54	2.47	-	-

N= number; % = percentage; the test was performed with Chi-Square, the P value in bold is statistically significant (p ≤ 0.05).
Death risk factors, ICU, September 2017-March 2020;

Of the 20 patients who died, 11 (55%) had a bacterial infection on admission, 14 (70%) had a 6-month previous exposure to hospitalization or antibiotics and 1 (2%) patient was mechanically ventilated, (Figure 2).

Of the 300 patients who survived, 95 (32%) had a bacterial infection on admission, 144 (48%) had a 6-month prior exposure to hospitalization or antibiotics and 1 (2%) was mechanically ventilated (Figure 2).

From the total number of patients, there were a number of 33 (10%) patients in whom data on bacterial admission at hospitalization were missing and 11 (3%) patients missing data on 6 months prior to hospitalization or antibiotic exposure.

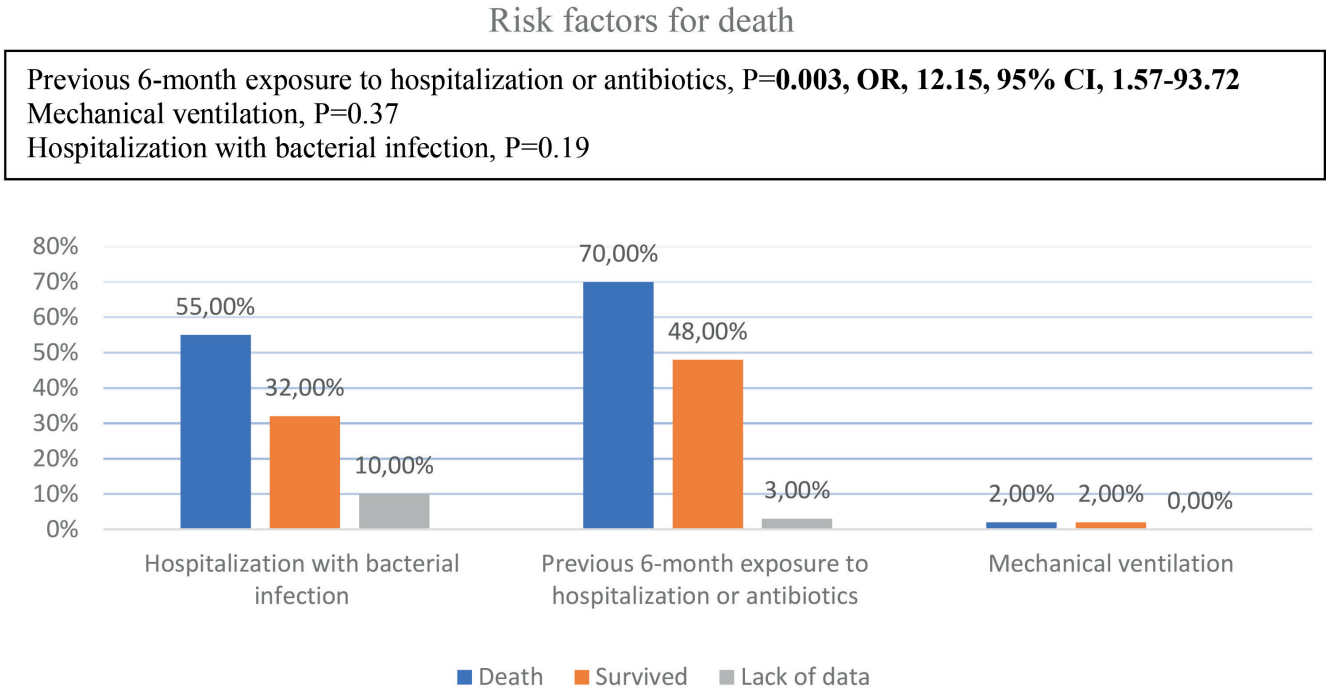

Figure 2. % = percentage; the test was performed with Chi-Square, the P value in bold is statistically significant (p ≤ 0.05). Hospitalization with bacterial infection, previous hospitalization or previous antibiotic therapy-death risk factors, in the ICU, September 2017-March 2020.

Regarding the length of stay (LOS) in the ICU, in Figure 3, we note that among the patients who died during hospitalization, 13 patients (65%) had more than 3 days of hospitalization in the ICU, of which 12 (60%) had more than 7 days of ICU admission and 11 (55%) had more than 10 days of admission. Among the patients who survived, 230 (77%) had more than 3 days of hospitalization, 137 (46%) had more than 7 days of hospitalization, and 88 (29%) had > 10 days of hospitalization. We observed in a univariate analysis, a positive association between death and patients who had more than 10 days of hospitalization, with a 2.93 times higher risk of dying.

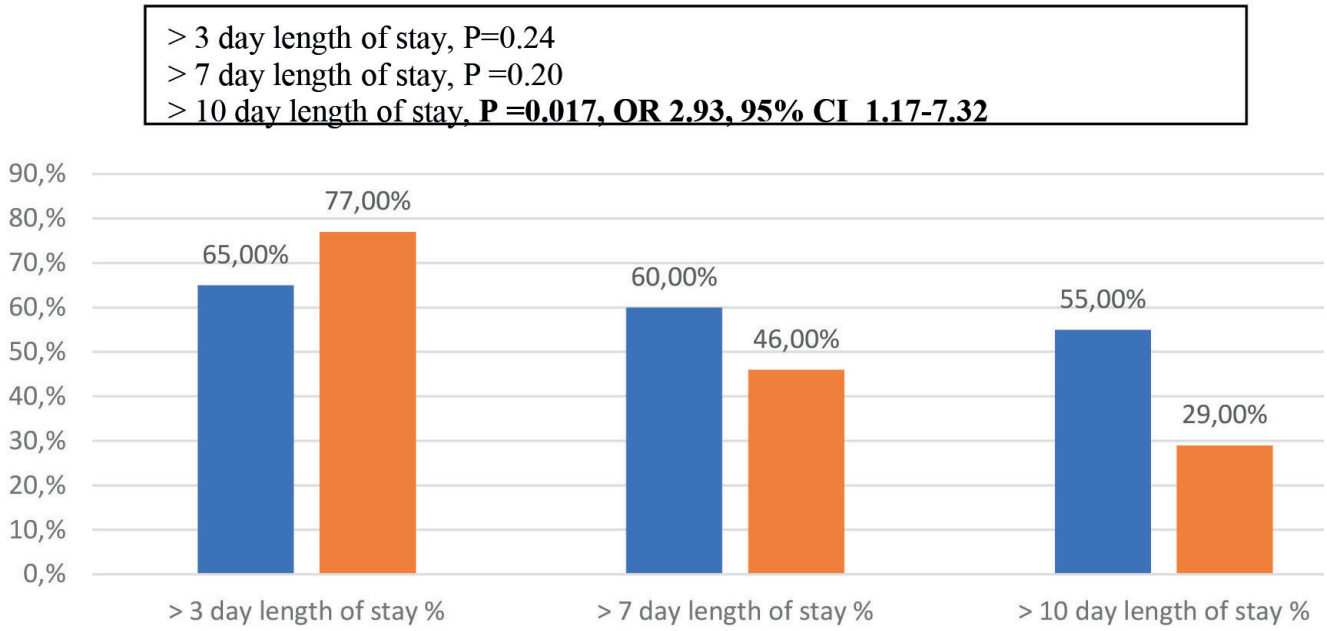

Figure 3. % = percentage; the test was performed with Chi-Square, the P value in bold is statistically significant (p ≤ 0.05). Hospitalization with bacterial infection, previous hospitalization, previous antibiotic therapy - risk factors, in the ICU, September 2017-March 2020

Other risk factors evaluated in the study for mortality rate were patients with bacterial infection, those without bacterial infection, those with bacterial colonization, those without bacterial colonization, and those with bacterial infection or bacterial colonization. There were 5 (25%) patients who had bacterial infection and died, 7 (35%) who had bacterial colonization and died, 11 (55%) who had bacterial infection secondary to the cause of ICU admission or bacterial colonization, and 9 (45%) who had neither bacterial infection nor bacterial colonization and died (Table 4). Patients who survived and had bacterial infections numbered 60 (20%). Among the survivors, 53 (17.7%) had bacterial colonization, 94 (31.3%) had bacterial infection or colonization, and 206 (68.7%) did not have bacterial infection or colonization (Table 4). We noted that there was a statistically significant positive association between patients who had a bacterial infection or bacterial colonization and death, with a 2.6-fold higher risk of death (Table 4).

Table 4. Bacterial infection, bacterial colonization-risk factors for death

Risk factors for death N (%)	Cases (Death) (N=20)	Control (Survival) (N=300)	Univariate analysis	
			OR (CI 95%)	P
Bacterial infection	5 (25%)	60 (20%).	1.32 (0.46-3.79)	0.59
Bacterial colonization	7 (35%)	53 (17.7%)	2.49 (0.95-6.56)	0.056
Bacterial infection secondary to the cause of admission or bacterial colonization	11 (55%)	94 (31.3%)	**2.66 (1.06-6.64)**	**0.030**
No bacterial infection and no bacterial colonization	9 (45%)	206 (68.7%)	0.37 (0.15-0.93)	**0.030**

N= number; % = percentage; the test was performed with Chi-Square, and the p value in bold is statistically significant (p ≤ 0.05). Bacterial infection, bacterial colonization-death risk factors, in the ICU, September 2017-March 2020

The causes of ICU admission in patients who died varied. There were 10 (50%) with digestive disorders who died. Of the total number of deceased patients, four (20%) were hospitalized for HIV infection, two (10%) for neurological conditions or systemic inflammatory response syndrome (SIRS), and one patient each for influenza or hepatitis (Figure 4). Among the patients who had a digestive condition as the reason for admission, nine were diagnosed with *Clostridioides difficile* infection. Additionally, *Clostridioides difficile* infection was detected as the cause of SIRS in one SIRS patient, but no germs were detected in the second SIRS patient. On univariate analysis, it was found that patients with HIV infection had a 5.5 times greater risk of dying compared to other patients during hospitalization, (Figure 4).

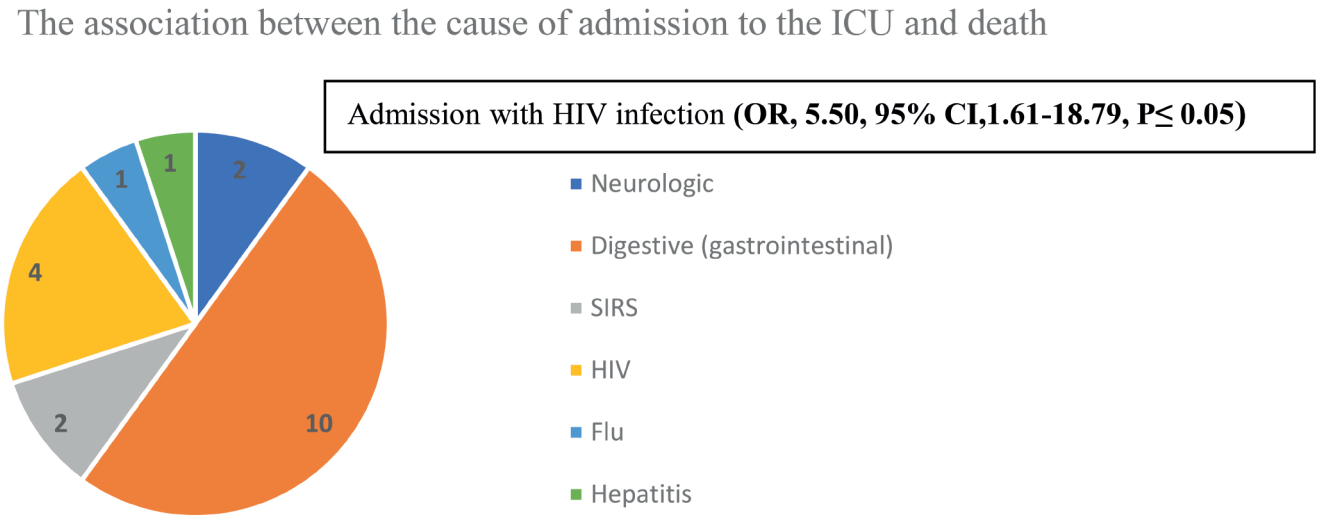

Figure 4. N = number; the test was performed with Chi-Square, and the p value in bold is statistically significant ($p \leq 0.05$). Causes of ICU admission and death, September 2017-March 2020.

The bacterial strains detected as the cause of admission to the ICU in the deceased patients were *Clostridioides difficile* in 10 (50%) patients, HIV infection in 4 (20%), influenza virus in 1 (5%), and *Mycobacterium tuberculosis* in another patient. Regarding survival, there were 53 (17.67%) patients with Clostridioides difficile, 13 (4.3%) with HIV infection, 33 (11%) with influenza virus and only 2 (0.7%) with Mycobacterium tuberculosis who survived. Data on bacterial strains were missing for 106 (33.1%) hospitalized patients. Patients who had *Clostridioides difficile* had a 5.97 times higher risk of death, and those who had HIV infection had a 4.7 times higher risk of death (Figure 5).

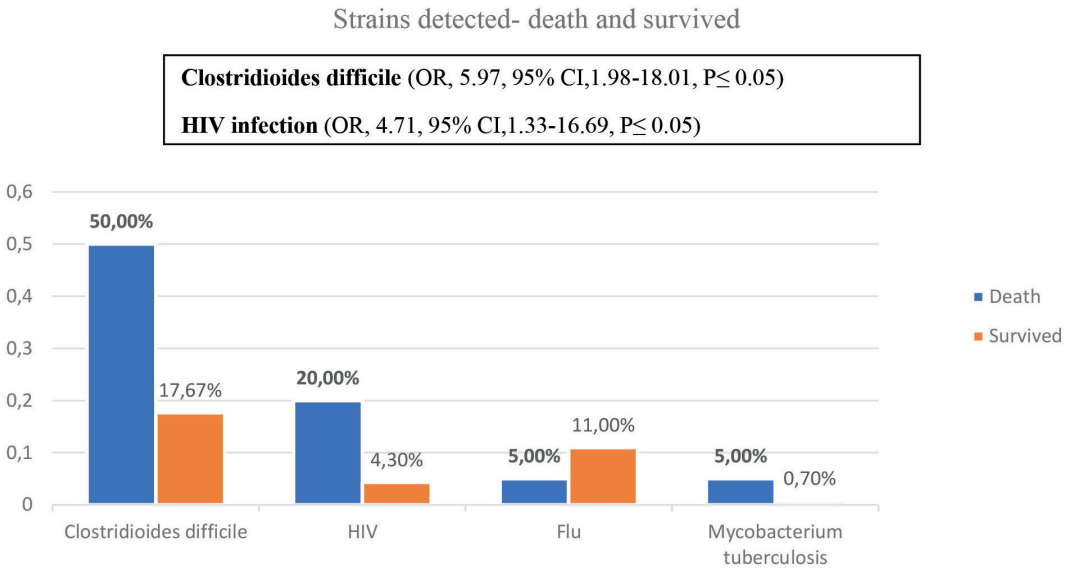

Figure 5. % = percentage; the test was performed with Chi-Square, the P value in bold is statistically significant (p ≤ 0.05). causes of admission, death and survival, ICU, September 2017-March 2020

Comorbidities in patients who died during hospitalization were present in 18 (90%) of the 20 patients. Ten (50%) patients had a single comorbidity, and eight (40%) had two comorbidities. Numerical data, percentages and univariate statistical analysis are presented in Table 5.

Table 5. Comorbidities and death

Patients' comorbidities and the risk of death N (%)	**Cases (Death) (N=20)**	**Control (Survival) (N=300)**	**Univariate analysis**	
			OR (CI 95%)	**P**
Comorbidities	18 (90%)	225 (75%)	3.01 (0.68-13.29)	0.12
A single comorbidity	10 (50%)	129 (43%)	1.33 (0.54-3.30)	0.53
Two comorbidities	8 (40%)	91 (30.3%)	1.52 (0.60-3.85)	0.37
Three comorbidities	0 (0%)	5 (1.7%)	-	-

N=number; (%) = percentage; the test was performed with Chi-Square, and the p value in bold is statistically significant (p ≤ 0.05). Patient comorbidities and risk of death in patients admitted to the ICU, September 2017-March 2020.

In the multivariate analysis, we observed that the independent risk factors associated with death were HIV infection (OR 11.82, 95% CI: 1.69-83.62, P ≤0.05) and *Clostridioides difficile* infection (OR 7.38, 95% CI: 1.39 -39.22, P ≤ 0.05), (Table 6).

Table 6. Risk factors for death- multivariate analysis

Risk factors detected in univariate analysis	**Multivariate analysis**	
	OR (CI 95%)	**P**
Previous 6-month exposure to hospitalization or antibiotics	3.05 (0.30-30.43)	0.34
>10 days of thlength of stay in the ICU	2.57 (0.75-8.82)	0.13
Bacterial infection or bacterial colonization	0.56 (0.16-1.99)	0.37
HIV infection	**11.82 (1.69-82.62)**	**0.013**
Clostridioides difficile infection	**7.38 (1.39-39.22)**	**0.019**

OR= Odds ratio; CI= Confidence interval, the test was performed with logistic regression, and the p value in bold is statistically significant (p ≤ 0.05). Multivariate analysis of the risk of death in the ICU, September 2017-March 2020.

DISCUSSION

The prevalence of bacterial strains according to the data obtained from September 2017 to March 2020 was 33% out of 320 patients, of which 7.5% had resistance mechanisms detected. The prevalence of bacterial strains that were considered to cause infections was 20.3% of the 320 patients included in the study, and the prevalence of bacterial colonization detected in the ICU was 18.7%.

Of the total bacterial strains, only 9 (2.8%) had bacterial infection and colonization, of which only 5 (1.6%) had the same bacterial strain and the same resistance mechanism. Therefore, the percentage of healthcare-associated infections (HAIs) due to bacterial infections acquired from bacterial colonization was small.

In a study conducted in seven wards of five university hospitals in Italy, during the period beginning in January 2006, it was observed that during 30 days, 4 (9%) of 42 patients newly colonized with antibiotic-resistant bacteria suffered from an infection due to the same bacteria as those isolated in a previous screening sample. Colonizing and infecting strains from the patients were genotypically identical. One conclusion of this study was that early identification of colonization with antibiotic-resistant bacteria during antibiotic therapy could target a high-risk hospitalized population that may benefit from intervention to decrease the subsequent risk of HAIs[9].

Analyzing international statistical data from published studies, in the article "Antibiotic Usage and Risk of Colonization and Infection with Antibiotic-Resistant Bacteria: a Hospital Population-Based Study" 6,245 swabs from 864 hospitalized patients were processed. Acquisition rates were 3% and 2% for MRSA and VRE, respectively. Four risk factors were observed in this study that was independently associated with the acquisition of antibiotic-resistant bacteria: carbapenem use, age >70 years, hospitalization >16 days, and human immunodeficiency virus infection[9].

Another study conducted in tertiary intensive and intermediate neonatal care units examined 584 patients, of which 48.3% (N=282) were colonized with at least one of the bacteria included in the screening, and 26.2% (N=74) had multidrug-resistant strains. A total of 534 bacterial isolates were identified. In conclusion, colonization surveillance provides a comprehensive overview of species and antibiotic resistance patterns. This allowed for the early detection of a colonization cluster. Knowledge of colonization and sepsis surveillance is useful in guiding infection control measures and antibiotic treatment[10].

In this study, we observe that 5 risk factors increase the death rate in the ICU of the Constanța Clinical Hospital for Infectious Diseases, of which only 2 are independent risk factors. Looking at the situation of deaths and the independent risk factors associated with them at the international level, we noticed that the situation is slightly different; the risk factors detected in our study are also found in other international studies, but not all of them are independent risk factors [9.11.12]. In studies of surgical intensive care unit patients, death was independently associated with the need for mechanical ventilation, Simplified Acute Physiology Score (SAPS II), community-acquired infection, HAIs and intensive care unit-acquired infection[10]. In the same study, for patients in the medical ICU, death was independently associated with the prognostic score and the need for mechanical ventilation [10]. Other independent risk factors found in studies associated with mortality were age 50-64, 65-74, 75-84 and ≥ 85 years versus 18-39 years, male sex, immunosuppression, renal disease, chronic lung disease, neurological disorders, cardiovascular disease and diabetes[12]. Screening and reporting bacterial strains are important as part of an antimicrobial stewardship plan[13]. Antimicrobial stewardship programs influence mortality from HAIs, patient outcomes, and hospital revenue[14].

CONCLUSION

We note that the detected bacterial colonizations that acquired bacterial infections were in a small percentage, below 2%. HIV infection, which is a universal risk factor known to increase the risk of death, and *Clostridioides difficile* infection were confirmed in this study as independent risk factors for death.

Author Contributions: Conceptualization, N.D.V; methodology, E.D.; A.C.; formal analysis, N.D.V.; S.V. and S.C; investigation, A.D. and C.S.C; resources, A.D. and T.H.; data curation, N.D.V. and S.R; original draft preparation, N.D.V.; review and editing, N.D.V.; supervision, I.M.D. All authors have read and agreed to the published version of the manuscript.

Acknowledgements
Not applicable.
Funding: This study did not receive any external funding.

Institutional Review Board Statement: Ethical review and approval were waived for this study because of the requirement of the Ethics Committee of the Clinical Infectious Diseases Hospital.

Informed Consent Statement: Patients provided written consent to use their personal data upon admission to the hospital. Patient anonymity was guaranteed during the whole process of data analysis and the reporting of results.

Data Availability Statement: Restrictions apply to data availability. Data are available from the authors with permission from the Clinical Infection Diseases Hospital of Constanta. NR 23/26/05.2023. CODE F.05.PO.17.00-ACFOCG.
Conflicts of Interest: The authors declare no conflict of interest.

References

1. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, Moreno R, Lipman J, Gomersall C, Sakr Y, Reinhart K; EPIC II Group of Investigators. International study of the prevalence and outcomes of infection in intensive care units. JAMA. 2009 Dec 2;302(21):2323-9. doi: 10.1001/jama.2009.1754. PMID: 19952319.
2. European Centre for Disease Prevention and Control. Incidence and attributable mortality of healthcare-associated infections in intensive care units in Europe, 2008-2012. Stockholm: ECDC; 2018.
3. European Centre for Disease Prevention and Control. SURVEILLANCE REPORT. Incidence and attributable mortality of healthcare-associated infections in intensive care units in Europe. 2008-2012. https://www.ecdc.europa.eu/sites/default/files/documents/surveillance-report-HAI-Net-ICU-mortality-2008-2012.pdf. [Accessed 15.05.2023].
4. Weigl W, Adamski J, Goryński P, Kański A, Hultström M. ICU mortality and variables associated with ICU survival in Poland: A nationwide database study. Eur J Anaesthesiol. 2018 Dec;35(12):949-954. doi: 10.1097/EJA.0000000000000889. PMID: 30234666.
5. Detsky ME, Harhay MO, Bayard DF, Delman AM, Buehler AE, Kent SA, Ciuffetelli IV, Cooney E, Gabler NB, Ratcliffe SJ, Mikkelsen ME, Halpern SD. Six-Month Morbidity and Mortality among Intensive Care Unit Patients Receiving Life-Sustaining Therapy. A Prospective Cohort Study. Ann Am Thorac Soc. 2017 Oct;14(10):1562-1570. doi: 10.1513/AnnalsATS.201611-875OC. PMID: 28622004; PMCID: PMC5718567.
6. Silva I, Faria NC, Ferreira ÁRS, Anastácio LR, Ferreira LG. Risk factors for critical illness and death among adult Brazilians with COVID-19. Rev Soc Bras Med Trop. 2021 Apr 28;54:e0014 2021. doi: 10.1590/0037-8682-0014-2021. PMID: 33950121; PMCID: PMC8083890
7. European Committee on Antimicrobial Susceptibility Testing. Antimicrobial susceptibility testing. https://www.eucast.org/ast_of_bacteria [Accessed 16.05.2023].
8. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med 2007; 147: 573–577
9. Tacconelli E, De Angelis G, Cataldo MA, Mantengoli E, Spanu T, Pan A, Corti G, Radice A, Stolzuoli L, Antinori S, Paradisi F, Carosi G, Bernabei R, Antonelli M, Fadda G, Rossolini GM, Cauda R. Antibiotic usage and risk of colonization and infection with antibiotic-resistant bacteria: a hospital population-based study. Antimicrob Agents Chemother. 2009 Oct;53(10):4264-9. doi: 10.1128/AAC.00431-09. Epub 2009 Aug 10. PMID: 19667289; PMCID: PMC2764223
10. Baier, C. et al., Prospective surveillance of bacterial colonization and primary sepsis: findings of a tertiary neonatal intensive and intermediate care unit. Journal of Hospital Infection Vol. 102, Issue 3, p 325–331, Published online: February 1, 2019
11. Toufen C Jr, Franca SA, Okamoto VN, Salge JM, Carvalho CR. Infection as an independent risk factor for mortality in the surgical intensive care unit. Clinics (Sao Paulo). 2013;68(8):1103-8. doi: 10.6061/clinics/2013(08)07. PMID: 24037005; PMCID: PMC3752640.
12. Kim L, Garg S, O'Halloran A, Whitaker M, Pham H, Anderson EJ, Armistead I, Bennett NM, Billing L, Como-Sabetti K, Hill M, Kim S, Monroe ML, Muse A, Reingold AL, Schaffner W, Sutton M, Talbot HK, Torres SM, Yousey-Hindes K, Holstein R, Cummings C, Brammer L, Hall AJ, Fry AM, Langley GE. Risk Factors for Intensive Care Unit Admission and In-hospital Mortality Among Hospitalized Adults Identified through the US Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET). Clin Infect Dis. 2021 May 4;72(9):e206-e214. doi: 10.1093/cid/ciaa1012. PMID: 32674114; PMCID: PMC7454425.
13. Doron S, Davidson LE. Antimicrobial stewardship. Mayo Clin Proc. 2011 Nov;86(11):1113-23. doi: 10.4065/mcp.2011.0358. PMID: 22033257; PMCID: PMC3203003.
14. Vadala R, Princess I. Antimicrobial Stewardship Program in Critical Care-Need of the Hour. Indian J Crit Care Med. 2020 Sep;24(9):847-854. doi: 10.5005/jp-journals-10071-23557. PMID: 33132571; PMCID: PMC7584847.