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Infections in a surgical intensive care unit of a university hospital in Greece

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Summary
Objectives: We aimed to evaluate the clinical and microbiological characteristics of the patients who developed an infection in our surgical intensive care unit (SICU).
Methods: This was a prospective study of all patients who sustained an ICU-acquired infection from 2002 to 2004.
Results: Among 683 consecutive SICU patients, 123 (18.0%) developed 241 infections (48.3 infections per 1000 patient-days). The mean age of patients was 66.7 ± 3.8 years, the mean APACHE II score (acute physiology and chronic health evaluation) on SICU admission was 18.2 ± 2.4, and the mean SOFA score (sepsis-related organ failure assessment) at the onset of infection was 8.8 ± 2. Of the study patients, 51.2% were women. Infections were: bloodstream (36.1%), ventilator-associated pneumonia (VAP; 25.3%, 20.3/1000 ventilator-days), surgical site (18.7%), central venous catheter (10.4%, 7.1/1000 central venous catheter-days), and urinary tract infection (9.5%, 4.6/1000 urinary catheter-days). The most frequent microorganisms found were: *Acinetobacter baumannii* (20.3%), *Pseudomonas aeruginosa* (15.7%), *Candida albicans* (13.2%), *Enterococcus faecalis* (10.4%), *Klebsiella pneumoniae* (9.2%), *Enterococcus faecium* (7.9%), and *Staphylococcus aureus* (6.7%). High resistance to the majority of antibiotics was identified. The complication and mortality rates were 58.5% and 39.0%, respectively. Multivariate analysis identified APACHE II score on admission (odds ratio (OR) 4.63, 95% confidence interval (CI) 2.69—5.26, $p = 0.01$), peritonitis (OR 1.85, 95% CI 1.03—3.25, $p = 0.03$), acute pancreatitis (OR 2.27, 95% CI 1.05—3.75, $p = 0.02$), previous aminoglycoside use (OR 2.84, 95% CI 1.06—5.14, $p = 0.03$), and mechanical ventilation (OR 3.26, 95% CI: 2.43—6.15, $p = 0.01$) as risk factors for infection development. Age (OR 1.16, 95% CI 1.01—1.33, $p = 0.03$), APACHE II score on admission

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(OR 2.53, 95% CI 1.77—3.41, $p = 0.02$), SOFA score at the onset of infection (OR 2.88, 95% CI 1.85—4.02, $p = 0.02$), and VAP (OR 1.32, 95% CI 1.04—1.85, $p = 0.03$) were associated with mortality. *Conclusions:* Infections are an important problem in SICUs due to high incidence, multi-drug resistance, complications, and mortality rate. In our study, APACHE II score on admission, peritonitis, acute pancreatitis, previous aminoglycoside use, and mechanical ventilation were identified as risk factors for infection development, whereas age, APACHE II score on admission, SOFA score at the onset of infection, and VAP were associated with mortality.

Introduction

Nosocomial infections are a common, severe problem worldwide, associated with significant morbidity and mortality as well as rapidly increasing multi-drug resistance of the responsible microorganisms to antibiotics.[1—6] Intensive care unit (ICU) patients are at greater risk of developing a hospital infection and, moreover, resistance rates of pathogens isolated in ICU infections to antimicrobial agents are substantially higher than those in community and other hospital ward infections.[1,5—9] The high incidence of infection and multi-drug resistance in ICU patients is attributable to severe underlying medical condition, frequent and, sometimes, unnecessary use of broad-spectrum antibiotics, mechanical ventilation, utilization of several devices placed with interventional techniques, prolonged hospital stay, and greater risk of cross-transmission of resistant microorganisms.[1,5—7,9—12]

Significant differences with regard to infection rates, the rates of occurrence of organisms, infection sites incidence, and antimicrobial resistance profiles have been identified among different countries, among centers in the same country, and even among the departments of a hospital.[1—4,7,9—12] Such discrepancies emphasize the importance of local surveillance in the prevention, control, and treatment of infections. The objective of the present prospective observational study was the identification and analysis of the demographic, clinical, and microbiological characteristics of the patients who developed an ICU-acquired infection during their hospitalization in the surgical intensive care unit (SICU) of our hospital. In particular, we evaluated the incidence and associated morbidity and mortality of infections along with the occurrence rates of the pathogens and their susceptibility to antibiotics. Furthermore, we investigated potential risk factors for infection as well as for infection-related mortality.

Materials and methods

Study patients

This prospective study was conducted in the SICU of the 1st Department of Propaedeutic Surgery, Hippokrateion Hospital, University of Athens. All adult patients (aged over 14 years) who developed an ICU-acquired infection, according to the standard Centers for Disease Control and Prevention (CDC) criteria[13,14] (National Healthcare Safety Network (NHSN) criteria) and International Sepsis Forum (ISF) criteria,[15] regardless of infection site, from January 1, 2002 to December 31, 2004 were included in our study. Colonizations, defined as any positive culture without clinical signs of infection, were excluded. Infections occurring prior to patient SICU admission or in the first 48 hours of SICU hospitalization and after the first 48 hours following discharge from the SICU to the ward were also excluded. Patients under 14 years are not hospitalized in our unit since there is no pediatric or pediatric surgical department in our hospital. Institutional review board approval was obtained before study initiation.

Data collection and microbiological analysis

Complete data of all patients hospitalized in our SICU (including information prior to SICU admission, during SICU hospitalization until discharge or death, and after discharge from the SICU until discharge from the hospital) are collected on a daily basis through our unit's computerized registry, starting immediately from patient SICU admission.

Patients with ICU-acquired infection were identified and followed prospectively from the date of infection to hospital discharge or death. Isolates were considered duplicates and excluded from the database if they were collected over a 7-day period from the same patient and were of the same bacterial species and had identical antibiograms. Identical isolates from different specimen sources collected within the same 7-day period were also excluded.

Isolates were identified by conventional methods. Antimicrobial resistance was determined according to the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS).[16] Intermediate susceptibility was regarded as resistance.

Cultures were performed based on the clinical picture of the patient. All patients with clinical signs of infection received empirical antimicrobial therapy. After culture results were known, administered antibiotics were maintained or adapted on the basis of standard sensitivity testing. Regarding diagnosis of ventilator-associated pneumonia (VAP), diagnosis required a radiographic image of a new, progressive and persistent pulmonary infiltrate not otherwise explained on chest X-ray and at least two of the following criteria: temperature $>38\ ^\circ C$ or $<35.5\ ^\circ C$, white blood cell count $>12 \times 10^9/l$ or $<4 \times 10^9/l$, $PaO_2/FiO_2 <240$, and purulent bronchial secretions. Moreover, a positive quantitative culture of a bronchoalveolar lavage (BAL) specimen was required. Fiberoptic bronchoscopic examination using BAL was performed on all these patients. The diagnosis of VAP was made only if quantitative cultures of BAL specimens yielded $>10^4$ cfu/ml. Finally, a pneumonia was considered VAP when its onset occurred at >48 hours following initiation of mechanical ventilation and was judged not to have been incubated before starting mechanical ventilation.

Data recorded and analyzed were: age, sex, medical history, underlying surgical pathology (hospital admission diagnosis), APACHE II score (acute physiology and chronic health evaluation)[17] on the day of SICU admission, SOFA score (sepsis-related organ failure assessment)[18] on the day of infection diagnosis, type of management (conservative or operative), days in hospital before SICU admission, antibiotics prior to the day of the onset of infection (exposure, type and duration), presence and duration of invasive procedures (ventilator, arterial, central and peripheral venous lines, urinary catheters), days of SICU hospitalization and postoperative days until infection, infection site, microorganisms and their susceptibility to antibiotics, complications (such as organ/system failure, peritonitis, and hemorrhage), length of SICU and hospital stay, and final outcome.

Prior exposure to antimicrobial agents was defined as at least 48 hours of therapy during the 14 days before the day of the onset of infection, i.e., before the day that the patients presented clinical signs of infection. Antibiotics administered on the day of the onset of infection until the culture results became available, given as empiric therapy, were not considered as antibiotics prior to infection and were, thus, not included in the analysis. Organ/system failure was defined according to the American College of Chest Physicians (ACCP)

Table 1 Univariate comparison of demographic and clinical data of the patients with and without infection

Variable	Infection (N = 123)	No infection (N = 560)	p-Value
Age (years)[a]	66.7 ± 3.8 (25–86)	64.9 ± 2.6 (23–80)	NS
Female gender[b]	63 (51.2%)	297 (53.0%)	NS
APACHE II score on admission[a]	18.2 ± 2.4 (8–30)	8.3 ± 3.1 (5–14)	0.001
SOFA score on the day of infection[a]	8.8 ± 2 (0–16)		
Medical history[b]			NS
Cardiovascular disease	55 (44.7%)	252 (45%)	
Respiratory disease	26 (21.1%)	112 (20%)	
Diabetes mellitus	19 (15.4%)	78 (13.9%)	
Cancer	11 (8.9%)	45 (8.0%)	
Renal disease	5 (4.1%)	23 (4.1%)	
Corticosteroid use	3 (2.4%)	12 (2.1%)	
Surgical pathology[b]			
Gastrointestinal cancer	46 (37.4%)	251 (44.8%)	NS
Peritonitis	20 (16.3%)	60 (10.7%)	0.04
Intestinal obstruction	15 (12.2%)	85 (15.2%)	NS
Acute pancreatitis	12 (9.8%)	26 (4.6%)	0.02
Gastrointestinal hemorrhage	9 (7.3%)	50 (8.9%)	NS
Superior mesentery artery infarction	6 (4.9%)	10 (1.8%)	0.03
Acute cholangitis	6 (4.9%)	30 (5.4%)	NS
Acute cholecystitis	5 (4.1%)	33 (5.9%)	NS
Abdominal trauma	4 (3.3%)	15 (2.7%)	NS
Operation[b]	109 (88.6%)	476 (85%)	NS
Reoperation[b]	20 (16.3%)	60 (10.7%)	0.04
Days in hospital before SICU[c]	2 (1–3)	2 (1–3)	NS
Days in SICU before infection[c]	7 (3–13)		
Postoperative days before infection[c]	6 (4–11)		
Prior aminoglycoside administration[b]	42 (34.1%)	39 (7.0%)	0.01
Prior carbapenem administration[b]	27 (22.0%)	11 (2.0%)	0.02
Days of previous aminoglycoside use[c]	4 (3–6)	0 (0–2)	0.01
Days of previous carbapenem use[c]	4 (3–7)	0 (0–2)	0.01
Mechanical ventilation[b]	76 (61.8%)	80 (14.3%)	0.001
Mechanical ventilation days[c]	11 (4–22)	1 (0–3)	0.001
Central venous catheter days[c]	12 (6–20)	2 (1–3)	0.01
Urinary catheter days[c]	13 (10–24)	3 (1–4)	0.01
Complications[b]	72 (58.5%)	72 (12.9%)	0.001
SICU mortality[b]	48 (39.0%)	21 (3.8%)	0.001
Total ICU stay (days)[c]	14 (7–28)	4 (2–7)	0.02
Total hospital stay (days)[c]	25 (18–36)	10 (8–14)	0.02

NS, not statistically significant; APACHE, acute physiology and chronic health evaluation; SOFA, sepsis-related organ failure assessment; SICU, surgical intensive care unit.

[a] Values are presented as mean ± SE (standard error of the mean) and range (in parenthesis).

[b] Values are presented as number of patients and percentage (in parenthesis).

[c] Values are presented as median and interquartile range (in parenthesis).

and Society of Critical Care Medicine (SCCM) criteria[19] as well as the SCCM/European Society of Intensive Care Medicine (ESICM)/ACCP/American Thoracic Society (ATS)/Surgical Infection Society (SIS) criteria.[20]

Statistical analysis

Data regarding the demographic and clinical features of the patients, the incidence and associated complications and mortality of infections, infection sites, microorganism occurrence rates in the total of infections and per infection type, and antimicrobial susceptibility were analyzed. Moreover, potential risk factors for the development of infection and for infection-related mortality were investigated. Particularly, patients with ICU-acquired infection were compared with patients who did not sustain an infection, using univariate and multivariate analysis, in order to identify predisposing factors for infection in the patients hospitalized in our SICU during the study period. Additionally, comparison between patients with infection who survived and those who died was performed, using both univariate and multivariate analysis, in order to identify risk factors for mortality in the patients who sustained infection.

Univariate analysis was conducted using the Student's *t*-test and Mann–Whitney test for numeric variables and Chi-square and Fisher's exact test for categorical variables. Multivariate analysis was performed with a logistic regression model in order to identify independent risk factors for infection development and mortality, respectively. Only variables occurring prior to infection were analyzed as possible predisposing factors for infection development whereas all variables were used for mortality. Data are presented as mean $\pm$ SE (standard error of the mean) and number of patients or infections and percentage unless otherwise specified. Length of utilization of invasive devices, antibiotic use, and SICU and hospital stay are presented as median with interquartile range. Statistical significance was set to $p < 0.05$. Results in multivariate analyses are also presented with odds ratios (OR) and 95% confidence intervals (95% CI).

Results

During the 3-year study period, 683 consecutive patients were hospitalized in our SICU; 123 patients (18.0%) developed an infection and formed the study group. The mean age of the patients was 66.7 $\pm$ 3.8 years, the mean APACHE II score on the day of SICU admission was 18.2 $\pm$ 2.4, and the mean SOFA score on the day of infection diagnosis was 8.8 $\pm$ 2. Fifty-three patients (43.1%) developed one infection, 50 (40.6%) two, and 20 (16.3%) more than two infections.

Demographic and clinical features of the patients with infection and those who did not develop an infection are presented in Table 1. Comparison of these two groups of patients using univariate analysis revealed significant differences in APACHE II score on admission ($p = 0.001$), peritonitis ($p = 0.04$), acute pancreatitis ($p = 0.02$), and superior mesentery artery infarction ($p = 0.03$) as the underlying surgical pathology, reoperation ($p = 0.04$), previous use of an aminoglycoside or carbapenem ($p = 0.01$ and $p = 0.02$, respectively), duration of previous aminoglycoside or carbapenem administration ($p = 0.01$), mechanical ventilatory support and days in ventilator ($p = 0.001$), length of central venous and urinary catheter utilization ($p = 0.01$), complications ($p = 0.001$), SICU mortality ($p = 0.001$), and length of total SICU and hospital stay ($p = 0.02$) (Table 1). Furthermore, multivariate analysis identified APACHE II score on admission (OR 4.63, 95% CI 2.69–5.26, $p = 0.01$), peritonitis (OR 1.85, 95% CI 1.03–3.25, $p = 0.03$), acute pancreatitis (OR 2.27, 95% CI 1.05–3.75, $p = 0.02$), previous aminoglycoside administration (OR 2.84, 95% CI 1.06–5.14, $p = 0.03$), and mechanical ventilation (OR 3.26, 95% CI 2.43–6.15, $p = 0.01$) as independent risk factors for infection development.

The study group sustained 241 infections (48.3 infections per 1000 patient-days). Infections and incidence of each infection among study patients and the total of SICU patients as well as per 1000 patient-days and 1000 device-days are described in Table 2. Bloodstream infections and VAP were the most common infections.

Acinetobacter baumannii (20.3%), *Pseudomonas aeruginosa* (15.7%), *Candida albicans* (13.2%), *Enterococcus faecalis* (10.4%), *Klebsiella pneumoniae* (9.2%), *Enterococcus faecium* (7.9%), and *Staphylococcus aureus* (6.7%) were the most frequent organisms identified. The rates of pathogen groups are presented in Table 3 and antimicrobial susceptibility of Gram-positive and Gram-negative organisms in Table 4. High resistance to the majority of antibiotics was found.

The overall complication rate for the study patients was 58.5% ($n = 72$). Particularly, the most common complication after the diagnosis of infection was septic shock ($n = 48$,

Table 2 Incidence of infections

Infections	Number of infections ($N = 241$) [a]	Per 1000 patient-days	Per 1000 device-days [b]	Infected patients ($N = 123$) [c]	All SICU patients ($N = 683$) [d]
Bloodstream	87 (36.1%)	17.4		73 (59.3%)	73 (10.6%)
VAP	61 (25.3%)	12.2	20.3	45 (36.6%)	45 (6.6%)
Surgical site	45 (18.7%)	9		31 (25.2%)	31 (4.5%)
CV catheter	25 (10.4%)	5.1	7.1	20 (16.3%)	20 (2.9%)
Urinary tract	23 (9.5%)	4.6	4.6	22 (17.9%)	22 (3.2%)

SICU, surgical intensive care unit; VAP, ventilator-associated pneumonia; CV, central venous.
[a] Values in this column are presented as number of infections and percentage (in parenthesis).
[b] Ventilator-associated pneumonias are expressed per 1000 ventilator-days, central venous catheter infections per 1000 central venous catheter-days, and urinary tract infections per 1000 urinary catheter-days.
[c] Values are presented as number of study patients who developed each infection and percentage (in parenthesis).
[d] Values are presented as number of patients hospitalized in the SICU who developed each infection and percentage (in parenthesis).

Table 3 Rates of microorganism groups in the total infections, per infection, and per 1000 patient- and device-days

Microorganism group	Bloodstream	VAP	Surgical site	CV catheter	Urinary tract	Total
Gram-positive	49 (56.3%)[a] [65.3%][b] 9.8[c]	2 (3.3%)[a] [2.7%][b] 0.4[c] 0.7[d]	17 (37.8%)[a] [22.7%][b] 3.4[c]	6 (24%)[a] [8%][b] 1.2[c] 1.8[e]	1 (4.4%)[a] [1.3%][b] 0.2[c] 0.2[f]	75 (31.1%)[a] [100%][b] 15[c]
Gram-negative	35 (40.2%)[a] [26.5%][b] 7[c]	49 (80.3%)[a] [37.1%][b] 9.8[c] 16.3[d]	20 (44.4%)[a] [15.2%][b] 4.2[c]	17 (68%)[a] [12.9%][b] 3.5[c] 4.7[e]	11 (47.8%)[a] [8.3%][b] 2.2[c] 2.2[f]	132 (54.8%)[a] [100%][b] 26.7[c]
Fungi	3 (3.5%)[a] [8.8%][b] 0.6[c]	10 (16.4%)[a] [29.4%][b] 2[c] 3.3[d]	8 (17.8%)[a] [23.5%][b] 1.4[c]	2 (8%)[a] [5.9%][b] 0.4[c] 0.6[e]	11 (47.8%)[a] [32.4%][b] 2.2[c] 2.2[f]	34 (14.1%)[a] [100%][b] 6.6[c]
Total	87 (100%)[a] [36.1%][b] 17.4[c]	61 (100%)[a] [25.3%][b] 12.2[c] 20.3[d]	45 (100%)[a] [18.7%][b] 9[c]	25 (100%)[a] [10.4%][b] 5.1[c] 7.1[e]	23 (100%)[a] [9.5%][b] 4.6[c] 4.6[f]	241 (100%)[a] [100%][b] 48.3[c]

VAP, ventilator-associated pneumonia; CV, central venous.
[a] Values are presented as number of infections and percentage (percentages in parenthesis refer to each column, i.e., per each infection).
[b] Values are presented as number of infections and percentage (percentages in brackets refer to each row, i.e., per each microorganism group).
[c] Values are presented as number of infections/1000 patient-days.
[d] Values are presented as number of infections/1000 ventilator-days.
[e] Values are presented as number of infections/1000 central venous catheter-days.
[f] Values are presented as number of infections/1000 urinary catheter-days.

39.0%), followed by respiratory failure (n = 40, 32.5%) and renal failure (n = 35, 28.5%), while 20 patients (16.3%) developed heart failure, 20 (16.3%) thrombocytopenia, 13 (10.6%) coagulopathy, and 13 (10.6%) hepatic failure. In addition, postoperative complications were peritonitis (n = 7, 5.7%) and hemorrhage (n = 2, 1.6%).

Moreover, SICU mortality of the study group was high (39.0%, n = 48). Univariate comparison of the patients with infection who survived and those with infection who died revealed statistically significant differences in age (p = 0.04), APACHE II score on the day of SICU admission (p = 0.001) and SOFA score on the day of infection diagnosis (p = 0.001), acute pancreatitis (p = 0.03) and superior mesentery artery infarction (p = 0.02), VAP (p = 0.001), *E. faecium* infection (p = 0.001), mechanical ventilation prior to infection (p = 0.01), complications (p = 0.001), and length of total SICU and hospital stay (p = 0.02) (Table 5). Finally, multivariate analysis identified age (OR 1.16, 95% CI 1.01—1.33, p = 0.03), APACHE II score on admission (OR 2.53, 95% CI 1.77—3.41, p = 0.02), SOFA score on the day of infection (OR 2.88, 95% CI 1.85—4.02, p = 0.02), and VAP (OR 1.32, 95% CI 1.04—1.85, p = 0.03) as independent risk factors for mortality of patients with infection.

Discussion

The search for the means to understand, control, and prevent the emergence and spread of infections and antimicrobial resistance has become a public health priority.[1,5,6,21] The prevention, control, and treatment of ICU infections demand thorough knowledge of the infection incidence and infection sites rates, the occurrence rates of organisms and their antimicrobial resistance profiles, and potential risk factors for infection and infection-associated mortality. The objective of this study was to identify and analyze the clinical and microbiological features of the patients who developed an ICU-acquired infection in our SICU, and to evaluate risk factors associated with infection development and infection-related mortality.

In agreement with the literature, the incidence of total infections in our patients was quite high (18.0% of the total of SICU hospitalized patients or 48.3 infections per 1000 patient-days).[1,4,9,12,22] Recorded infections were bloodstream, VAP, surgical site, central venous catheter, and urinary tract infections, with bloodstream and VAP representing the majority of them. The higher incidence of bloodstream infections than VAP and, also, than that usually reported in other series, may be explained by the fact that only cases with underlying surgical pathology, mostly of general surgery, are admitted to our unit and, moreover, approximately 90% of the study patients underwent abdominal surgery, particularly gastrointestinal surgical procedures. Surgery and especially gastrointestinal operations have been shown to increase intestinal permeability resulting in bacterial translocation. Therefore, some of these bloodstream infections may have an intestinal origin due to bacterial translocation. This may also be implied by our finding that *A. baumannii*, *E. faecium*, and *E. faecalis* caused 46% of such infections.

Regarding the microbiological profile of the total of infections, *A. baumannii*, *P. aeruginosa*, *C. albicans*, *E. faecalis*, *K. pneumoniae*, *E. faecium*, and *S. aureus* were more frequently isolated; similar results have also been found in other studies.[1,3,4,7,8,11,12,22,23] *A. baumannii* was the most common,

Table 4 Susceptibility of the most frequent Gram-negative and Gram-positive microorganisms to antibiotics

Antibiotic	Microorganism					
	Acinetobacter baumannii	*Pseudomonas aeruginosa*	*Klebsiella pneumoniae*	*Enterococcus faecalis*	*Enterococcus faecium*	*Staphylococcus aureus*
Methicillin				12%	10.5%	12.5%
Amoxicillin—clavulanate	4%	7.9%	9.1%	8%	0%	6.2%
Ampicillin—sulbactam	26.5%	7.9%	13.6%	16%	5.2%	6.2%
Piperacillin—tazobactam	4%	57.9%	13.6%	20%	15.8%	12.5%
Ticarcillin—clavulanate	2%	39.5%	9.1%	16%	5.2%	6.2%
Ceftazidime	8.1%	60.5%	18.2%			
Cefepime	6.1%	47.3%	27.2%			
Gentamicin	10.2%	60.5%	40.9%	32%	26.3%	25%
Tobramycin	30.6%	55.2%	13.6%	16%	21%	25%
Netilmycin	24.5%	63.1%	31.8%	16%	26.3%	18.7%
Amikacin	24.5%	55.2%	31.8%	16%	21%	18.7%
Imipenem	24.5%	65.8%	72.7%			
Meropenem	14.3%	50%	63.6%			
Aztreonam	2%	55.2%	36.3%			
Ciprofloxacin	4%	55.2%	27.2%	16%	15.8%	25%
Levofloxacin	4%	55.2%	27.2%	16%	15.8%	25%
Clindamycin				0%	15.8%	12.5%
Tetracycline				12%	15.8%	18.7%
Erythromycin				4%	0%	12.5%
Rifampin				24%	26.3%	37.5%
Vancomycin				76%	63.1%	93.7%
Teicoplanin				80%	63.1%	93.7%
Linezolid				100%	100%	100%
Colistin	100%	100%	100%			

while *P. aeruginosa* and *C. albicans* were the second and third most frequently identified pathogen in our study population, respectively.

The major pathogens causing bloodstream infections were *A. baumannii*, *E. faecium*, *E. faecalis*, *S. aureus*, and *Staphylococcus epidermidis*, whereas for VAP they were *A. baumannii*, *P. aeruginosa*, *C. albicans*, and *K. pneumoniae*. These findings are in accordance with the literature.[1,10–12,22,23] The predominant microorganisms in surgical site infections were *E. faecalis*, *C. albicans*, *A. baumannii*, and *E. faecium* and in central venous catheter infections *P. aeruginosa* and *A. baumannii*.[11,12] Finally, *C. albicans* and *Escherichia coli* were over-represented in urinary tract infections as also reported in other studies.[11,12,23,24]

Regarding isolation sites of the microorganisms, similarly to several studies in the literature, the most frequent infections by *A. baumannii* and *P. aeruginosa* in our patients were VAP and bloodstream infections,[12,22,23,25,26] while *C. albicans* was more often identified in urinary tract infections and VAP.[24] Bloodstream and surgical site infections were the predominant infections by *E. faecalis* and *E. faecium*, *K. pneumoniae* was more frequently isolated from bloodstream and VAP, whereas the majority of *S. aureus* infections were bacteremias. These results are also in accordance with those observed in other series.[10–12,23]

However, unlike several studies in the literature, VAP due to *C. albicans* in our study was quite high. The incidence of Candida pneumonia varies among different studies with data from several studies showing an incidence varying from 0% to 4.5%.[27,28] In a study by Palabiyikoğlu et al., Candida colonization incidence in endotracheal aspirates was 12% and Candida pneumonia incidence 2%.[27] However, el-Ebiary et al., in a study of 25 non-neutropenic, mechanically ventilated (>72 hours) patients, found an incidence of Candida isolation from lung biopsies of 40% with definite Candida pneumonia in 8%.[28] The criteria for diagnosis of pulmonary candidiasis are controversial.[27,28] Moreover, the value of quantitative cultures of respiratory samples in the diagnosis of Candida pneumonia has not been thoroughly evaluated.[27,28] Despite the debate about the diagnosis of pulmonary candidiasis, the definite diagnosis of pulmonary candidiasis still rests on histologic demonstration of Candida in lung tissue with associated inflammation.[27,28] In our study, however, such histologic demonstration was not performed, but positive quantitative culture results of BAL specimens together with the described radiologic and clinical criteria were required for VAP diagnosis. Furthermore, we believe that the number of patients with VAP ($n = 61$) and, particularly, the number of patients with VAP due to *C. albicans* ($n = 10$) in the presented study are very small in order to draw any conclusions or to evaluate this result. This specific finding should, therefore, be interpreted with great caution.

Prolonged SICU and hospital stay, significant resistance of the pathogens to the majority of antibiotics, as well as high complication and SICU mortality rates of our patients were found. More importantly, comparison of hospitalized patients in our SICU developing infection with those without an infection revealed that patients with infection had significantly longer SICU and hospital stays along with higher complication and mortality rates. These findings indicate

Table 5 Comparison between patients with infection who survived and those who died (univariate analysis)

Variable	Non-survivors ($N = 48$)	Survivors ($N = 75$)	p-Value
Age (years)[a]	71.3 ± 8.7 (25–80)	62.4 ± 10.3 (30–86)	0.04
Female gender[b]	24 (50%)	39 (52%)	NS
APACHE II score on admission[a]	25.2 ± 6.5 (10–30)	10.7 ± 5.6 (8–14)	0.001
SOFA score on the day of infection[a]	10.9 ± 2 (4–16)	4 ± 1 (0–6)	0.001
Medical history[b]			NS
Cardiovascular disease	23 (47.9%)	32 (42.7%)	
Respiratory disease	10 (20.8%)	16 (21.3%)	
Diabetes mellitus	8 (16.7%)	11 (14.7%)	
Cancer	4 (8.3%)	7 (9.3%)	
Renal disease	2 (4.2%)	3 (4%)	
Corticosteroid use	1 (2.1%)	2 (2.7%)	
Surgical pathology[b]			
Gastrointestinal cancer	16 (33.3%)	30 (40%)	NS
Peritonitis	7 (14.6%)	13 (17.3%)	NS
Intestinal obstruction	5 (10.4%)	10 (13.3%)	NS
Acute pancreatitis	7 (14.6%)	5 (6.7%)	0.03
Gastrointestinal hemorrhage	3 (6.3%)	6 (8%)	NS
Superior mesentery artery infarction	4 (8.3%)	2 (2.7%)	0.02
Acute cholangitis	2 (4.2%)	4 (5.3%)	NS
Acute cholecystitis	2 (4.2%)	3 (4%)	NS
Abdominal trauma	2 (4.2%)	2 (2.7%)	NS
Infection[b]			
Bloodstream	34 (70.8%)	39 (52%)	NS
Ventilator-associated pneumonia	33 (68.8%)	12 (16%)	0.001
Surgical site	17 (35.4%)	14 (18.7%)	NS
Central venous catheter	8 (16.7%)	12 (16%)	NS
Urinary tract	8 (16.7%)	14 (18.7%)	NS
Microorganism[b]			
Acinetobacter baumannii	10 (20.8%)	12 (16%)	NS
Pseudomonas aeruginosa	7 (14.6%)	11 (14.7%)	NS
Candida albicans	7 (14.6%)	10 (13.3%)	NS
Enterococcus faecalis	7 (14.6%)	10 (13.3%)	NS
Klebsiella pneumoniae	4 (8.3%)	8 (10.7%)	NS
Enterococcus faecium	10 (20.8%)	2 (2.7%)	0.001
Staphylococcus aureus	3 (6.3%)	5 (6.7%)	NS
Staphylococcus epidermidis	3 (6.3%)	4 (5.3%)	NS
Operation[b]	42 (87.5%)	67 (89.3%)	NS
Reoperation[b]	7 (14.6%)	13 (17.3%)	NS
Days in hospital before SICU[c]	2 (1–3)	2 (1–3)	NS
Days in SICU before infection[c]	7 (5–14)	7 (3–12)	NS
Aminoglycoside before infection[b]	16 (33.3%)	26 (34.7%)	NS
Carbapenem before infection[b]	10 (20.8%)	17 (22.7%)	NS
Aminoglycoside days before infection[c]	4 (3–6)	4 (3–7)	NS
Carbapenem days before infection[c]	4 (3–7)	4 (3–6)	NS
Mechanical ventilation before infection[b]	40 (83.3%)	36 (48%)	0.01
Mechanical ventilation days before infection[c]	11 (4–20)	10 (3–16)	NS
Central venous catheter days before infection[c]	10 (6–15)	11 (5–17)	NS
Urinary catheter days before infection[c]	11 (8–14)	12 (6–18)	NS
Complications[b]	41 (85.4%)	31 (41.3%)	0.001
Total ICU stay (days)[c]	19 (9–28)	11 (5–19)	0.02
Total hospital stay (days)[c]	29 (14–36)	17 (9–24)	0.02

NS, not statistically significant; APACHE, acute physiology and chronic health evaluation; SOFA, sepsis-related organ failure assessment; SICU, surgical intensive care unit.

[a] Values are presented as mean ± SE (standard error of the mean) and range (in parenthesis).

[b] Values are presented as number of patients and percentage (in parenthesis).

[c] Values are presented as median and interquartile range (in parenthesis).

the importance of effective prevention and treatment of infections in ICU patients. Several studies also suggest that ICU infections are associated with prolongation of hospitalization time and high multi-drug resistance, morbidity and mortality.[1,2,4–6,9,22,25]

Univariate analysis for infection development risk factors in our patients showed a significant association with APACHE II score on admission, underlying surgical pathology (namely, peritonitis, acute pancreatitis, and superior mesentery artery infarction), reoperation, previous exposure to and duration of aminoglycoside or carbapenem administration, and utilization of invasive devices such as ventilator and central venous and urinary catheters. Moreover, multivariate analysis identified APACHE II score on the day of SICU admission, peritonitis, acute pancreatitis, prior aminoglycoside administration, and mechanical ventilation as independent predisposing factors for infection.

ICU infections and multi-resistance are attributed to several causes such as decreased host resistance, poor compliance with hygiene regimes, inadequate disinfection or sterilization of devices and equipment, prolonged use of invasive devices and hospitalization, overcrowding and inefficient isolation of infected patients, and inappropriate antibiotic use.[1,4,6,7,10–12,21–23] A combination of effective infection control measures is, thus, required.[21]

In our study, univariate analysis for risk factors for mortality of patients with infection revealed a significant association with age, APACHE II score on the day of SICU admission, SOFA score on the day of infection diagnosis, acute pancreatitis, superior mesentery artery infarction, VAP, *E. faecium* infection, and mechanical ventilation prior to infection. Furthermore, multivariate analysis identified age, APACHE II score on admission, SOFA score on the day of infection diagnosis, and VAP as independent risk factors for mortality of patients with infection. Since VAP is the only parameter potentially amenable to interventions among these factors, our results highlight the significance of implementation of effective VAP prevention measures in ICUs.

The most effective antimicrobial agents for Gram-positive organisms were linezolid, teicoplanin, and vancomycin. High resistance of *S. aureus* and *S. epidermidis* to methicillin was observed, whereas few isolates were resistant to vancomycin and teicoplanin; in contrast, all isolates were susceptible to linezolid. All isolates of enterococci were susceptible to linezolid, while high resistance to all other antibiotics was noted. High methicillin-resistant *S. aureus* (MRSA)[1,3,7] and vancomycin-resistant enterococci (VRE) or glycopeptide-resistant enterococci (GRE)[3,29] incidence along with resistance of *S. aureus* to vancomycin[29,30] have also been noted in other studies. This high prevalence of GRE is an endemic phenomenon in our unit that highlights the urgent need for prompt implementation of rigorous and effective measures for prevention, control, and treatment of GRE infections in our patients, and of strategies to prevent and control the selection and spread of these organisms. A combination of several such measures has been implemented in our unit in the last years. Even though detailed analysis of more recent data has not been completed, our progress so far has been good, and we believe that our results are encouraging. Though considerable improvements have been made, we still have a long way to go.

Colistin was the only particularly effective antibiotic for Gram-negative bacteria in our study. Although differences regarding the antimicrobial resistance patterns of *A. baumannii*, *P. aeruginosa*, and *K. pneumoniae* infections have been identified, high resistance to most commonly used antibiotics has been found in several studies.[9,21,25,26] A substantial portion of these strains are susceptible only to colistin. In our study, no strains resistant to colistin were identified. In accordance with our results, resistance to colistin appears to be rare.[25,26] Moreover, the safety and efficacy of colistin treatment in multi-resistant nonfermenting Gram-negative bacillus infections has been reported in other studies.[25,26] In an era of continuously increasing rates of infections with multi-resistant pathogens, the development of newer therapeutic alternatives to address the problem of such multi-drug resistance is, therefore, of the utmost importance.

The high incidence of multi-resistant ICU infections suggests that more effective strategies are needed to control the selection and spread of resistant organisms.[9,21] Organization of infection prevention and control programs, pathogen and antibiotic surveillance, and antibiotic use optimization are crucial to reduce infection incidence, prevent multi-resistance, reduce hospital costs, and improve patient prognosis.[9,12,21] Empiric treatment should be based on unit-specific data.[2,12,21] Since each hospital unit has a distinct bacteriological profile and antibiotic resistance pattern, knowledge of these differences is critical for planning effective therapy and reducing infection-related costs, morbidity, and mortality.[7,12,21]

In conclusion, infections are a very important problem in our SICU, associated with high incidence, complication rate, mortality, and multi-drug resistance of the responsible microorganisms. Eradication requires implementation of rigorous infection control measures, prudent antibiotic use, and effective antimicrobial therapy. Recognition of clinical and microbiological characteristics of these patients is essential for prevention and treatment of infections. In our study, APACHE II score on admission, peritonitis, acute pancreatitis, previous aminoglycoside use, and mechanical ventilation were identified as risk factors for infection development, whereas age, APACHE II score on admission, SOFA score at the onset of infection, and VAP were associated with mortality.

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