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Assessment of bloodstream infections and risk factors in an intensive care unit

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Background/aim: Nosocomial bloodstream infection (BSI) increases mortality rates, duration of stay in hospital, and treatment costs. This study was conducted to determine the rate and the risk factors of BSIs among intensive care unit patients.

Materials and methods: Sixty-four patients with BSIs (patient group) and 79 patients without a nosocomial infection (control group) were enrolled in the study. Centers for Disease Control and Prevention criteria were used for diagnosing BSIs. Potential risk factors were evaluated by multivariate logistic regression model.

Results: The BSI development rate was 15.7% (64/407), with an incidence rate of 18.2/1000 patient days. Distribution of pathogens among BSI patients were as follows: gram-positive cocci, 42.18% (27/64); gram-negative cocci, 34.3% (22/64); and Candida spp., 23.4% (15/64). Risk factors were determined as intubation, arterial catheter, tracheostomy, duration of intubation, duration of catheter use, duration of nasogastric catheter, underlying diseases of chronic renal failure and diabetes mellitus, implemented treatments of sedation and enteral nutrition, and APACHE II score.

Conclusion: BSIs are the leading cause of mortality and morbidity in intensive care unit patients. Determination of the local risk factors is important and necessary for decreasing the rate of BSIs and the mortality rates.

Key words: Bloodstream infection, candidemia, intensive care unit

1. Introduction

Nosocomial infections are important public health problems in both developing and developed countries (1). The rate of nosocomial infections among intensive care unit (ICU) patients is 5- to 10-fold greater than in patients of other clinics (2). The most frequent types of nosocomial infections are urinary tract infection, surgical wound infection, pneumonia, and bloodstream infection (BSI) (3). Nosocomial BSI increases mortality rates, duration of stay in hospital, and treatment costs. Development of nosocomial BSI in ICUs leads to a duration of 24 additional days of stay in the hospital and an additional treatment cost of 40,000 US$ (2). The objective of this study was to determine the pathogenic agents causing nosocomial BSIs and the risk factors that play a role in the development of BSIs among patients followed in a central intensive care unit (CICU).

2. Materials and methods

This study was conducted in the Gaziantep University Medical Faculty's CICU during a 6-month period in 2011. It was approved by the Ethics Committee of the Gaziantep University Medical Faculty (05/20113). During the study period, patients hospitalized in CICU were followed on a daily basis and findings were recorded on a daily follow-up form specifically prepared for this study.

2.1. Subjects

Patients with a laboratory and clinical diagnosis of bloodstream infection followed in the CICU were enrolled in the study. Patients were not classified as primary or secondary BSI patients. If more than one BSI episode developed in same patient, only the first was included. Diagnosis of BSI was based on criteria issued by the Centers for Disease Control and Prevention and the International Sepsis Group (4,5). Patients hospitalized in the CICU without a diagnosis of nosocomial infection were designated as the control group.

Patients hospitalized for less than 48 h and those under 16 years of age were excluded. For all subjects, age, sex, underlying diseases, APACHE II score, duration of stay in CICU, duration of stay in hospital, invasive procedures and their durations (tracheostomy, central catheterization, urinary catheterization, arterial catheterization), and durations of any implemented treatments (steroid,

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antibiotics, sedation, gastroprotective agents) were recorded. Procalcitonin levels of all patients were noted and compared.

2.2. Sampling, microbiological evaluation, and identification

Blood cultures were assessed in a BacT/Alert automated blood culture system. Blood culture samples with positive signals were processed. Subcultures were prepared on eosin-methylene-blue and sheep blood agar 5% media. The identification and antibiograms of growing bacteria were determined with the VITEK 2 (BioMerieux, France) fully automated identification and antibiogram system. Production of expanded-spectrum beta lactamase (ESBL) by *E. coli* and *Klebsiella* spp. was assessed with the VITEK 2 ESBL test panels.

2.3. Statistical analysis

Statistical analysis was performed with SPSS 16.0 (SPSS Inc., USA). Correlation between categorical variables was evaluated by chi-square test and/or Fisher's exact test. For quantitative variables with normal distribution, significance of comparison of means in 2 groups was realized by Student's t-test. Means were assessed by standard deviation. In all tests, the minimum limit of significance was determined as 0.05 ($P < 0.05$). A further test of binary logistic regression analysis was implemented for independent risk factors. Based on findings of this analysis, odds ratios (ORs) were calculated.

3. Results

During the study period, a total of 407 patients were admitted to the CICU. Nosocomial infection developed in 165 (40.54%) of these patients. Among patients with nosocomial infections, 64 (15.7%) were diagnosed with BSI. The incidence rate of BSI was calculated as 18.2/1000.

3.1. Comparison of patients diagnosed with BSI

Patients with BSIs were compared with the control group by bivariate analysis. Total stay in CICU, duration of stay in hospital prior to admission to CICU, underlying diseases of chronic renal failure (CRF) and diabetes mellitus (DM), and, among invasive procedures, intubation, use of arterial catheter, and tracheostomy were observed to be significantly higher in patients with BSIs (Table 1). Mean durations of intubation, urinary catheter, nasogastric catheter, and central venous catheter (CVC) were longer in patients with BSIs and a statistically significant correlation was found between these parameters and development of BSIs. Sedation ($P = 0.039$) and enteral nutrition ($P = 0.016$) were found to be more common among the BSI group. Forty-seven of 64 patients with BSIs (73.4%) and 28 of 79 control patients (35.4%) died during their stays in the ICU. Mortality in the BSI group was determined to be significantly higher ($P = 0.000$) (Table 1).

Procalcitonin values were determined as 8.13 ± 17.48 ng/mL in the BSI group and 5.69 ± 16.62 ng/mL in the control group. The difference between the groups was not statistically significant ($P = 0.264$) (Table 1). The mean procalcitonin value of all subjects (control group and patient group) was 6.8 ng/mL. Among patients with procalcitonin values of <6.8 ng/mL, the mortality rate was 39.7%, while this rate was 66.7% in patients with procalcitonin values of >6.8 ng/mL (Table 2).

Mean APACHE II score was 21.33 ± 6.17 in the BSI group and 13.39 ± 16.67 in the control group. This difference was statistically significant ($P = 0.001$). Mean APACHE II score of all subjects (control group and patient group) was 17. The mortality rate of patients with APACHE II score of <17 was 29.2%, while this rate was 71.2% in patients with APACHE II score of >17 (Table 2).

3.2. Distribution of pathogenic microorganisms

Gram-positive bacteremia was determined in 27 (42.1%) of BSI patients. Of these isolates, 21 (32.8%) were staphylococci and 6 (9.3%) were *Enterococcus* spp. Among staphylococci, 85% were coagulase-negative. The identification of staphylococci types revealed *S. haemolyticus* in 6 (9.3%) patients, *S. hominis* in 7 (7%), *S. epidermidis* in 5 (7.8%), and *S. aureus* in 3 (4.6%). Distribution of gram-negative bacteria was as follows: 12 (18.75%) cases of *Acinetobacter* spp., 2 (3.1%) *Pseudomonas* spp., 3 (4.6%) *Klebsiella* spp. and 5 (7.8%) *E. coli*. Fifteen (23.4%) samples of *Candida* spp. were isolated and the types were determined as *Candida albicans* in 6 patients (40%) and nonalbicans *Candida* in 9 (60%) patients (Table 3).

3.3. Comparison of patients with candidemia

In candidemia patients as compared with the control group, age, duration of stay in the CICU, duration of stay in the hospital prior to the CICU, presence of CRF and DM, rate of intubation, rate of arterial catheter use, rate of tracheostomy, duration of CVC, mean duration of urinary catheter use, rate of enteral nutrition, rate of mortality, and mean APACHE II score were found to be statistically significant in terms of development of candidemia (Table 4). The number of antibiotic agents used in patients with candidemia was significantly higher than in the control group.

3.4. Logistic regression analysis in development of candidemia

Risk factors of CRF, DM, and coexistence of CRF and DM, determined significant at $P < 0.05$ by bivariate statistical analysis method, were evaluated in a binary logistic regression model. As per this assessment, the presence of CRF increased the risk of candidemia by 4.9-fold, the presence of DM caused an increase of 3.6-fold, and coexistence of CRF and DM elevated the risk by 9.3-fold (Table 5).

Table 1. Comparison of patient and control groups.

		Patient group	Control group	P
Sex	M/F (75/68)	37/27	38/41	0.248
Age		58.19 ± 19.40	53.27 ± 19.79	0.138
Duration of stay in CICU		21.95 ± 16.37	8.71 ± 6.21	0.001
Duration of stay in hosp. prior to CICU		11.42 ± 7.15	6.5 ± 5.57	0.001
APACHE II score		21.33 ± 6.17	13.39 ± 6.67	0.001
Underlying diseases				
	CRF	23 (35.9)	12 (15.2)	0.004
	DM	26 (40.6)	15 (19.0)	0.004
	COPD	7 (10.9)	9 (11.4)	0.932
	Liver cirrhosis	4 (6.3)	12 (15.2)	0.092
	Malignity	10 (15.6)	14 (17.7)	0.739
Rate of invasive procedures				
	CVC	57 (89.6)	70 (88.6)	0.932
	Intubation	57 (89.1)	32 (40.6)	0.000
	AC	49 (76.6)	46 (58.2)	0.021
	NG	44 (68.5)	47 (59.5)	0.253
	Tracheostomy	21 (32.8)	3 (3.8)	0.000
Duration of invasive procedures				
	CVC days	11.34 ± 4.21	7.54 ± 4.61	0.000
	Intubation days	9.30 ± 6.11	6.34 ± 4.09	0.021
	AC days	7.78 ± 4.03	6.48 ± 3.10	0.084
	NG days	8.77 ± 4.48	6.35 ± 3.39	0.004
	UC days	9.86 ± 3.79	7.06 ± 3.83	0.001
Implemented treatments				
	Sedation	37 (57.8)	32 (40.05)	0.039
	Steroid treatment	28 (43.8)	30 (37.98)	0.484
	Enteral nutrition	34 (64.2)	24 (30.40)	0.016
Mortality rates		47 (73.4)	28 (35.4)	0.000
Procalcitonin		8.13 ± 17.48	5.69 ± 16.62	0.264
History of surgery		14 (21.9)	16 (20.3)	0.813

AC: Arterial catheterization, UC: urinary catheterization, NG: nasogastric catheter, CVC: central venous catheter, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, CRF: chronic renal failure.

4. Discussion

Nosocomial infections are one of the leading causes of mortality and morbidity, particularly in critically ill patients. The nosocomial infection rate is estimated as 2%, and this rate can increase to up to 54% in patients staying in ICUs (6). Nosocomial BSIs extend the time of stay and increase the mortality risk and the cost of treatment.

In the current study, BSIs developed in 64/407 (15.7%) of the patients, while the incidence rate was determined as 18.2 per patient days (18.2/1000). In a multicenter study conducted in Turkey at 12 hospitals (including 11 university hospitals) among members of the International Nosocomial Infection Control Consortium from 10 cities, the mean rate of device-associated hospital acquired infections for a 3-year period was determined as 33.9 per 1000 patient days. Rate of bloodstream infections associated with CVCs was 19.6 (5.3/1000 to 41.5/1000) per 1000 catheter days. These rates are similar to our results (7).

Another risk factor that was determined for development of BSIs is arterial catheterization. Duration of catheterization, frequent manipulation of catheter,

Table 2. Correlation of APACHE II scores and procalcitonin values with mortality.

	Result	≤17	>17	P
APACHE II	Exitus	23 (29.2%)	47 (71.2%)	0.000
	Recovered	56 (70.8%)	19 (28.8%)	
		≤6.8 ng/mL	>6.8 ng/mL	
Procalcitonin	Exitus	48 (39.7%)	18 (66.7%)	0.011
	Recovered	70 (60.3%)	9 (33.3%)	

Table 3. Distribution of agent pathogen microorganisms in patients with BSIs.

Agent microorganism		n = 64	%
Gram-positive	*S. hominis*	7	10.9
	S. haemolyticus	6	9.3
	S. epidermidis	5	7.8
	S. aureus	3	4.6
	Enterococcus spp.	6	9.3
Gram-negative	*Acinetobacter* spp.	12	18.7
	E. coli	5	7.8
	Pseudomonas spp.	2	3.1
	Klebsiella spp.	3	4.6
Candida	*C. albicans*	6	9.3
	Nonalbicans	9	14

location of catheter, type of catheter, underlying diseases, suppression of immune system, and types of fluids administered through the catheter are significant risk factors in development of BSIs (8). The correlation between development of BSIs and use of arterial catheters in our study was found to be statistically significant. Use of arterial catheters is not a routine procedure during monitoring in ICUs; the procedure is performed in cases of increased requirements for vasopressors. Since arterial catheters are generally applied under emergency conditions, the required aseptic conditions may not have been provided.

Intubation was assessed as a risk factor for development of BSIs in our study. The following mechanisms are responsible for this. Endotracheal intubation disturbs defense mechanisms of the host and cough and mucociliary activity; also, during mechanical ventilation in particular, this condition is more prominent in the development of ventilation-associated pneumonia (9). Prolonged duration of intubation and respiratory failure increases the rate of acquired infections in ICUs and, as a result, secondary bacteremia can develop (9–12). In our hospital, tracheostomy is performed after the 10th day and causes prolongation of hospital stay; the presence of tracheostomy may also be a risk factor for primary bacteremia (13). Therefore, the relation between tracheostomy and BSI is thought to be a result of both of these factors.

It is known that the risk of infection associated with bacterial translocation secondary to intestinal mucosal atrophy is increased with parenteral nutrition. It is recommended to switch patients to enteral nutrition as early as possible. However, enteral nutrition was determined as a risk factor for development of BSIs in this study. Similarly, enteral nutrition in the ICU was designated as a risk factor for development of BSIs in various studies (14,15). Usually for enteral nutrition, nasogastric tubes are used in the ICU. It is thought that colonization of the tube results in bacteremia (15). In our study, not the use of nasogastric tube but rather the duration of nasogastric tube was found to be significant as a risk factor for BSIs.

Sedation was also specified as a risk factor for BSIs. A 3.34-fold increase was reported in nosocomial infections among sedated patients (16). In a similar study, sedative medication was determined to increase the risk of nosocomial infections in the ICU (17). In patients with suppressed swallow reflex due to sedation, development of aspiration and associated pneumonia may increase the risk of secondary BSIs.

Table 4. Comparison of patients with candidemia and control group.

		Candidemia	Control group	P
Sex	M/F (48/46)	10/5	38/41	0.138
Age		56.53 ± 22.66	53.27 ± 19.79	0.000
Duration of stay in CICU		21.20 ± 4.67	8.71 ± 6.21	0.005
Duration of hosp. prior to CICU		17.27 ± 7.73	6.40 ± 5.54	0.001
APACHE II score		22.73 ± 6.15	13.39 ± 6.67	0.001
Underlying diseases				
	CRF	8 (53.3)	12 (15.2)	0.015
	DM	8 (53.3)	15 (19.0)	0.004
	COPD	1(11.4)	9 (11.4)	0.586
	Liver cirrhosis	0 (0)	12 (15.2)	0.106
	Malignity	2 (13.3)	14 (17.0)	0.678
Rate of invasive procedures				
	CVC	14 (93.3)	70 (88.6)	0.586
	Intubation	14 (93.3)	32 (38.3)	0.000
	AC	13 (86.7)	46 (58.2)	0.006
	NG	8 (53.3)	47 (59.5)	0.657
	Tracheostomy	5 (33.3)	3 (3.8)	0.000
Duration of invasive procedures				
	CVC days	11.64 ± 4.37	7.54 ± 4.21	0.001
	Intubation days	9.71 ± 6.46	6.34 ± 4.09	0.091
	AC days	7.78 ± 4.80	6.43 ± 3.09	0.060
	NG days	10.13 ± 4.25	6.21 ± 3.38	0.005
	UC days	9.93 ± 3.84	7.06 ± 3.83	0.009
Implemented treatments				
	Sedation	5 (33.3)	32 (40.05)	0.062
	Enteral nutrition	9 (60)	24 (30.40)	0.028
Mortality rates		15 (100)	28 (35.4)	0.000
Procalcitonin		9.04 ± 9.34	5.69 ± 16.62	0.454

AC: Arterial catheterization, UC: urinary catheterization, NG: nasogastric catheter, CVC: central venous catheter, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus, CRF: chronic renal failure.

It was determined that prolonged stay in the ICU increases the risk of infection (16–19). In the current study, prolonged duration of stay in the ICU was found as a risk factor for development of BSIs. Mean duration of stay was determined as 21.95 ± 7.15 days in the BSI group and 8.71 ± 6.21 days in the control group. Evaluation of mean duration of hospitalization prior to admission to the ICU revealed prolonged duration of hospitalization as a risk factor for BSIs. During long hospitalizations, patients are more frequently exposed to nosocomial pathogens and development of nosocomial infections is thought to be associated with increased colonization. ICU stays of 3–4 days increase the risk of infection by 3-fold as compared to stays of 1–2 days (20). This period was determined as 11 ± 6.72 days in our study. The BSI development period from admission to the ICU was reported as 12 days and 11.5 ± 5.7 days in 2 different studies (21,22).

A significant correlation exists between APACHE II score and mortality (16,19). Invasive procedures are more frequently performed in patients with high APACHE II scores during their stay in ICUs; increased numbers of invasive procedures and longer stays in the hospital in

Table 5. Risk factors for candidemia in logistic regression analysis.

	P	OR	Lower limit	Upper limit
DM	0.009	3.601	1.049	12.360
CRF	0.012	4.937	1.429	17.051
CRF and DM	0.003	9.375	2.153	40.817

patients with high APACHE II scores may lead to higher rates of BSIs in this patient group. In the current trial, high APACHE II score was determined as a risk factor for development of BSIs. Similarly, the rate of mortality was significantly higher in patients with high APACHE II scores.

For the time being, nosocomial BSIs are infectious diseases with the highest mortality rate, despite significant improvements in medical technology and antimicrobial treatment. Trials conducted on this topic indicate crude mortality rates associated with BSIs of 12%–80%, with a mean rate of 35%. The rate of mortality related to infection was reported as 27% (23,24). In the current study, development of BSI was determined to increase the mortality rate. A significant correlation was found between BSI and mortality (17,25). Development of such a disease in ICU patients with poor general medical condition, high APACHE scores, and comorbidities, caused by resistant microorganisms, will definitely lead to a poorer outcome.

In a metaanalysis covering 12 studies comparing procalcitonin and C-reactive protein levels, procalcitonin was reported to be more beneficial than C-reactive protein in terms of differentiation of bacterial infections from other noninfectious systemic inflammatory responses (26). In the current study, procalcitonin levels of patients with BSIs did not reveal a significant difference compared to controls; however, a direct correlation was determined between high procalcitonin values and mortality.

Distributions of the microorganisms isolated as agent pathogens in a similar study were *P. aeruginosa* at 20.8%, *Staphylococcus aureus* at 18.2%, *Acinetobacter* spp. at 18.2%, and *Klebsiella* spp. at 16.1% (15). The distributions in our study were as follows: staphylococci at 32.8%, *Enterococcus* spp. at 9.3%, *Acinetobacter* spp. at 18.7%, *P. aeruginosa* at 4.6%, *Klebsiella* spp. at 4.6%, *E. coli* at 7.8%, and *Candida* spp. at 23.4%. In our study, gram-positive agents were more frequent, and another remarkable result is the high candidemia rates. In recent years, a significant increase has been seen in systemic mycoses cases in ICUs, with trials conducted in Europe and the United States indicating that fungi infections, and mainly *Candida* infections, have the highest mortality rates (27). In the current study, 6 of the *Candida* samples specified as agent pathogens of BSIs (40%) were determined as *Candida albicans* and 9 (60%) were specified as nonalbicans *Candida*. Nonalbicans *Candida* included *C. parapsilosis* (n = 3), *C. glabrata* (n = 2), *C. tropicalis* (n = 2), *C. krusei* (n = 1), and *C. lusitaniae* (n = 1). In a study performed in the United States investigating the national epidemiology of mycoses, *Candida* species similarly ranked fourth among the most common causes of hospital-acquired BSIs in 7 surgical ICUs and 6 newborn ICUs, and species-based distribution of *Candida* was determined as *C. albicans* at 48%, *C. glabrata* at 24%, *C. tropicalis* at 19%, *C. parapsilosis* at 7%, and other species at 2% (28). In a similar study, 49% of 74 strains isolated from blood cultures were designated as *C. albicans*, 23% as *C. parapsilosis*, 14% as *C. tropicalis*, 12% as *C. glabrata*, 1% as *C. guilliermondii*, and 1% as *C. krusei* (29). In our study, *Candida* ranked third among agent pathogens. No azole resistance was found among *Candida* species in the current study. Only in *C. krusei* was decreased sensitivity determined against fluconazole. Resistance against azoles in *C. glabrata* and *C. krusei* is found to increase due to the increase of candidemia rates and the use of azoles (30).

Assessment of underlying diseases in patients with candidemia indicated the presences of CRF and DM as risk factors (31,32). In different studies, invasive procedures, duration of invasive procedures, duration of stay in hospital, immunosuppressive treatment, and long-term use of antibiotics were regarded as risk factors for candidemia (33–35). In the current study, use of arterial catheters, enteral nutrition, intubation, tracheostomy, duration of CVC use, duration of urinary catheter use, high APACHE II score, duration of stay in CICU, duration of hospitalization prior to admission to CICU, and underlying DM and CRF were designated as risk factors for development of candidemia. The duration as well as presence of invasive procedures were also determined as risk factors. Among implemented treatments, enteral nutrition was determined as a risk factor for development of candidemia.

BSIs detected in ICUs have high mortality and morbidity rates. Today BSIs remain associated with microorganisms that are resistant to antibiotics and can easily be spread by hospital personnel (36). Being informed about the risk factors associated with BSIs in this patient group will create consciousness among health care providers and physicians in terms of approaches to the patients and conventional behavior models. The goal of determining the risk factors of BSIs is to decrease infection rates and thus decrease the mortality associated with BSIs.

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