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Bloodstream Infections in Severe Burn Patients: Epidemiology, Microbiology, Laboratory Features, and Risk Factors Associated with Mortality

Ağır Yanık Hastalarında Kan Dolaşımı Enfeksiyonları: Epidemiyoloji, Mikrobiyoloji, Laboratuvar Özellikleri ve Mortalite için Risk Faktörleri

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Abstract

Introduction: Bloodstream infections (BSI) are a major cause of morbidity and mortality in burn patients. Early empiric antibiotic treatment directed against pathogens is critical. Studies on BSI are limited in burn patients. This study aimed to investigate the epidemiological, clinical, and laboratory features of cases with BSI detected in the burn unit and the factors affecting mortality.
Materials and Methods: Herein, we retrospectively studied sixty-eight inpatients diagnosed with BSI in the burn unit of our hospital during 2014-2018.
Results: Among the sixty-eight cases included in the study, 73.5% were male, and the median age was 38. We observed that 25% of the cases had two-degree burns and 75% had third-degree burns, and the median total burn surface area (TBSA) was 36%. Eighty-six bacteremia episodes were detected in sixty-eight cases. The most common isolated bacteria were (75.5%) Gram-negative bacilli (*Pseudomonas* spp. and *Acinetobacter* spp.). Carbapenem resistance was detected in 63% of Gram-negative bacteria. The overall mortality was 35.3% (24/68). In the deceased cases, the median time between bacteremia and mortality was 3.5 days. In addition, the mortality was statistically significantly higher in cases with a TBSA of >40% and thrombocytopenia ($p<0.05$). The mortality in non-fermenting Gram-negative bacteria and Enterobacteriaceae was 42.1% and 30.8%, respectively; it was higher mainly in non-fermenters and *Pseudomonas* spp. than in others (48%).
Conclusion: Burn patients are at high risk for infection. Unfortunately, if an infection develops, antibiotic treatment options are also limited due to the high resistance of microbial pathogens to carbapenem. High TBSA and thrombocytopenia appear to be significant prognostic factors for mortality. Therefore, infection control measures should be at a higher level, and the antibiotics to be started empirically should be broad spectrum.
Keywords: Bloodstream infections, burn patients, risk factor, mortality

Öz

Giriş: Kan dolaşımı enfeksiyonları (KDE), yanık hastalarında önemli bir morbidite ve mortalite nedenlerdendir. Bu nedenle olası etkenlere yönelik erken ampirik antibiyotik tedavisi çok önemlidir. Bu hasta grubunda KDE ile ilgili çalışmalar sınırlıdır. Bizde çalışmamızda yanık ünitesinde KDE saptanan ağır yanık olguların epidemiyolojik, klinik, laboratuvar özelliklerinin ve mortaliteye etki eden faktörlerin incelenmesi amaçlandı.
Gereç ve Yöntem: Çalışmamızda, hastanemiz yanık ünitesinde 2014-2018 yılları arasında yatarak tedavi gören ve bakteremi saptanan 68 olgu retrospektif olarak incelendi.

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Bulgular: Çalışmaya alınan 68 olgunun çoğu (%73,5) erkek olup yaş ortancası 38 olarak belirlendi. Olguların %25'inde ikinci derece, %75'inde üçüncü derece yanık olduğu ve yanık alanı ortancası %36 olarak belirlendi. Altmış sekiz olguda 86 bakteremi epizodu tespit edildi. Seksen altı etkenin çoğunun (%75,5) Gram-negatif olduğu (en sık *Pseudomonas* spp. ve *Acinetobacter* spp.) saptandı. Gram-negatif bakterinin %63'ünde karbapenem direnci belirlendi. Mortalite %35,3 (24/68) belirlendi. Eksitus olan olgularda bakteremi ile mortalite arası süre ortancası 3,5 gün saptandı. Toplam yanık yüzey alanı >%40 üzeri ve trombositopenisi olan olgularda mortalite istatistiksel olarak anlamlı olarak daha yüksek bulundu (p<0,05). Non-fermantatif bakterilerde ve *Enterobacteriaceae*'larda mortalite sırasıyla %42,1 ve %30,8 olup non-fermentatif bakterilerde mortalite daha yüksek saptandı. Ayrıca *Pseudomonas* spp. de mortalite *Pseudomonas* spp. dışı non-fermentatif bakterilere göre (%48) daha yüksek olduğu belirlendi.
Sonuç: Yanık hastaları enfeksiyon açısından yüksek risk altındadır. Enfeksiyon geliştiğinde de etkenlerin karbapenem direnci yüksek olması nedeniyle tedavi için antibiyotik tedavisi seçenekleri kısıtlı olmaktadır. Ayrıca olgularda yüksek toplam yanık yüzey alanı ve trombositopeni varlığı mortalitede önemli prognostik faktördür. Bu nedenle enfeksiyon kontrol önlemleri üst düzeyde olmalı ve ampirik başlanacak antibiyotiğin geniş spektrumlu olması önemlidir.
Anahtar kelimeler: Kan dolaşımı enfeksiyonu, yanık hastaları, risk faktör, mortalite

Introduction

Avascular necrotic tissue (eschar) provides a protein-rich environment suitable for proliferation and microbial colonization. It is detected in burn wounds due to the loss of the protective skin barrier[1-3]. The necrotic tissue disrupts the host immune cells' migration. It restricts the delivery of systemically administered antimicrobial agents and toxic substances released by eschar tissues, which reduces local host immune responses[2]. In these cases, several factors include impairment of the cellular and humoral immune systems, devitalization of tissues, translocation of intestinal microbial flora, loss of the protective skin barrier, multiple surgical procedures, and use of invasive devices, causing intense colonization and infection[4]. Patients with a total burn surface area (TBSA) greater than 20% are at an exceptionally high risk for infection and sepsis, which can occur even with a minor burn wound[5-8].

This study aimed to identify epidemiological, clinical, and laboratory features of burn cases that developed BSI and etiological agents causing BSI and investigate prognostic factors affecting mortality.

Materials and Methods

Study Design and Data Collection

This retrospective study examined sixty-eight cases of inpatients with severe burns diagnosed with bloodstream infections (BSI) between 2014-2018 in Ankara Numune Training and Research Hospital Burn Unit. The burn cases with bacteremia were divided into two groups, deceased and survivors; the relationship of relevant study variables with mortality was investigated by comparing the two groups. The patients' demographic data such as gender and age, type of burn (flame, electricity, hot water, and chemical), burn degree (two-degree and three-degree) [9] surface area, length of hospital stay, blood culture positivity (isolated agent and antimicrobial susceptibility), laboratory tests [hemogram and C-reactive protein (CRP)], post-treatment mortality, and the time between bacteremia to mortality was recorded. The documentation of all bacterial blood isolates from severe burn patients hospitalized in the burn unit was obtained from the medical records retrieved from a computerized hospital-wide database.

The normal CRP value ranged from 0-5 mg/L, and the normal leukocyte value ranged from 3.9-10.2 x 10^9/L.

Microbiological BSI Diagnostics

All blood cultures were processed in the hospital's microbiology laboratory. Blood culture samples, each consisting of an aerobic and anaerobic bottle, were incubated at 36.5 °C -37 °C for up to seven days in the semi-automated continuous-monitoring blood culture system BacT/ALERT 3D (BioMérieux, Marcy l'Etoile, France). Those with reproduction detected by the automation system were inoculated on 5% sheep blood agar and EMB agar plates; after 24 hours of incubation at 37 °C, the growth plates were examined. Vitek II (BioMerieux, Marcy l'Etoile, France) was used for microorganism identification and antibiotic susceptibility testing. Antibiotic susceptibility results were interpreted according to the Clinical Laboratory Standards Institute guidelines[10]. If a patient had more than one episode of BSI with the same pathogen, only the first BSI episode was used in the analysis.

Definitions

If the same microorganism was identified in the blood and burn wound cultures, the source of BSI was determined as a burn wound. Catheter-related BSI (CRBSI) is a clinical definition used by The Infectious Disease Society of America as follows: the detection of a recognized bacterial or fungal pathogen cultured from one or more blood cultures and the pathogen not related to an infection focus at another site; detection of a common commensal organism in two or more blood cultures from different sites, which is not related to an infection focus at another site in the setting of one of the following signs or symptoms: fever (38 °C), chills or hypotension; and in patients younger than one year of age: fever, hypothermia (<36 °C), apnea, or bradycardia. First, other sources of infection must be sought before diagnosing a CRBSI[11].

The Infectious Disease Society of America defines catheter-associated urinary tract infections (CAUTI) as the presence of signs/symptoms of a UTI with no other identified infection foci combined with the culture or growth of ≥1 bacterial species [$\geq 10^3$ colony-forming units per milliliter (CFU/mL)] in a single catheter urine sample or a freshly voided midstream urine sample in a patient whose catheter was removed in the previous 48 hours[12].

Ethics Committee Approval

Ethical approval was obtained from the Ankara Numune Training and Research Hospital Ethics Committee before initiating the study (date and number of approval: 06.09.2018 and 18-2175, respectively).

Statistical Analysis

The data were obtained by analyzing the Statistical Package for the Social Sciences (SPSS) software for Windows, version 24 (IBM SPSS Statistics for Windows, version 24. Armonk, NY: IBM Corp.). Quantitative variables were presented as the mean, standard deviation, and median values, while continuous data were presented as median, minimum (min), and maximum (max) values due to skewed distributions; categorical data were described as frequencies and percentages.

The relationships between categorical variables were evaluated using the chi-square or Fisher's Exact test. Mann-Whitney or Kruskal-Wallis tests were applied to compare the continuous variables. The effects of all variables on mortality were assessed by logistic regression analysis. Two-tailed p values of <0.05 were defined as statistically significant.

Results

Demographics, Laboratory Features, and Clinical Details

Out of the total cases, 73.5% (50/68) were male patients with a median age of 38 [interquartile range (IQR): 31, (min: 18, max: 91)], and the median length of hospital stay was twenty-eight days.

When the cause of burn was evaluated, flame burn (79.4%, 54/68) was detected as the most common, followed by electricity burn (8.8%, 6/68), hot water burn (7.4%, 5/68), and chemical burn (4.4%, 3/68). There were two-degree burns in 25% (17/68) and third-degree burns in 75% (51/68) of cases, and the median percentage of TBSA was determined to be 36% [IQR: 30, (min: 3, max: 97)].

The median white blood cell count of the patients studied was 11,000 [IQR: 8650, (min: 1100, max: 51000)], and the median CRP was 213 [IQR: 237.5 (min: 10, max: 399)].

Microbiological Characteristics of BSI

Eighty-six bacteremia episodes (two episodes in sixteen cases and three in two cases) were noted in sixty-eight cases. Most pathogens (75.6%, n=65) were Gram-negative (*Pseudomonas aeruginosa*, 24.4%, and *Acinetobacter baumannii*, 19.7%). After that, *Enterococcus* spp. (12.7%) and *Staphylococcus aureus* (6.9%) were the most common Gram-positive pathogens (Table 1).

The median time to first positive blood culture was 7.5 days. Bloodstream infection developed in the first week in 45.6% of cases, followed by BSI in the second week in 26.4%, the third week in 8.8%, and the fourth week in 19.1%.

Catheter-related BSI (CRBSI) (38.3%) was the most common source of bacteremia, followed by burn wounds (33.7%), CAUTI (17.4%), and unknown (10.4%). The distribution of BSI pathogens by sources is presented in Table 2.

Carbapenem resistance was detected in 63% (41/65) of Gram-negative bacteria. It was observed in 100% of *Acinetobacter* species and 60% of *Pseudomonas* species. Methicillin resistance was observed in 33% of *S. aureus*, and ampicillin resistance was observed in 9% of *Enterococcus* species.

Clinical Outcome

The mortality in this study was 35.3% (24/68); age and leukocyte values did not differ significantly between groups in terms of mortality (p>0.05). The median time between bacteremia and mortality in deceased cases was 3.5 days [IQR: 7, (min: 1, max: 30)] (Table 3).

Mortality was 53.1% (17/32) in cases with a TBSA >40% and 19.4% (7/36) in cases with a TBSA below 40%; these rates were found to be statistically significant (p=0.05) (Table 3).

When thrombocytopenia was evaluated according to mortality, a statistically significant difference existed between the groups (p=0.01). In deceased and survivor cases, the thrombocytopenia rate was 54.1% (13/24) and 22.7% (10/44), respectively. The other variables on mortality did not produce statistically significant differences (p>0.05).

When the effects of the isolated agents on mortality were examined, and Gram-negative and positive bacteria were compared, no statistically significant difference emerged between the groups (p>0.05). In 83.3% (20/24) of the deceased cases, the Gram-negative pathogen was isolated in the first episode. The mortality rate for non-fermenting Gram-negative pathogens and Enterobacteriaceae was 42.1% and 30.8%, respectively; it was also higher for non-fermenters. However, this result did not yield a statistically significant difference (p>0.05).

Non-fermenting bacteria other than *Pseudomonas* species had a higher mortality rate of 29.2%, with a much higher mortality rate of 48% for *Pseudomonas* species. However, no statistically significant difference was found (p>0.05) (Table 3).

Discussion

In 175 severe burn patients, infection was reported as the leading cause of death in 36% of the deceased patients[6]. Burns are a significant risk factor for developing BSIs, and the risk of BSI is increased sevenfold in burn patients[13-15]. A review examining 5,524 burn patients reported that BSI was the most common, followed by skin and soft tissue infections, urinary tract infections, and ventilator-associated pneumonia[16].

The development of sepsis and BSI are common infectious complications in severe burn patients[17]. A prominent case study of burn inpatients reported that mortality increased seven-fold (21.9% vs. 3.09%) in those patients that developed BSI[15]. In our study, a similar mortality rate of 35.3% was observed in burn cases with BSI. Similar studies have also revealed a 13-36% mortality in burn cases with BSI[18-22].

In our study, most of those affected by burns were men, and the median age was 38. However, it was concluded that age and gender did not affect mortality. A similar study reported that most cases were male, the mean age was 43, and age and gender were not associated with mortality[18].

We detected that significantly higher mortality was observed in cases where TBSA was 40% and above. Similarly, in a study of burn patients that developed sepsis, it was highlighted that mortality was higher in patients with high TBSA[23].

Our trial demonstrated that the median time to the first positive blood culture was 7.5 days. The first positive blood cultures were documented during the first week of hospitalization in 45.6% (31/68) of patients. The first blood culture positivity median has been mentioned as 5-7 days in parallel studies[15,18,24]. It has also been reported that BSI occurred in 68% (50/74) of cases in the first week[24]. Other previous studies have contributed

Table 1. Distribution of bloodstream infection pathogens

Pathogen	1. episode (%, n)	2. episode (%, n)	3. episode (%, n)	Total (%, n)
Gram-negative	75 (51)	75 (12)	100 (2)	75.5 (65)
Non-fermenting Gram-negative				
Acinetobacter baumannii	22 (15)	12.5 (2)		19.7 (17)
Acinetobacter spp.	4.4 (3)	18.7 (3)	50 (1)	8.1 (7)
Pseudomonas aeruginosa	27.9 (19)	12.5 (2)		24.4 (21)
Pseudomonas spp.	1.4 (1)	18.7 (3)		4.6 (4)
Enterobacteriaceae				
Enterobacter cloacae	5.8 (4)			4.6 (4)
Enterobacter spp.		6.2 (1)		1.1 (1)
Serratia marcescens	1.4 (1)			1.1 (1)
Klebsiella spp.	1.4 (1)	6.2 (1)	50 (1)	3.4 (3)
Klebsiella oxytoca	2.9 (2)			2.3 (2)
Klebsiella pneumoniae	7.3 (5)			5.8 (5)
Gram-positive	25 (17)	25 (4)		24.4 (21)
MRCNS	1.4 (1)			1.1 (1)
MSCNS	2.9 (2)			2.3 (2)
MRSA	2.9 (2)			2.3 (2)
MSSA	5.8 (4)			4.6 (4)
Enterococcus faecalis	5.8 (4)	18.7 (3)		8.1 (7)
Enterococcus faecium	1.4 (1)			1.1 (1)
Enterococcus spp.	2.9 (2)	6.2 (1)		3.4 (3)
Streptococcus mitis	1.4 (1)			1.1 (1)
Total	100 (68)	100 (16)	100 (2)	100 (86)

MRSA: Methicillin resistant *Staphylococcus aureus*, MSSA: Methicillin sensitive *Staphylococcus aureus*, MRCNS: Methicillin resistant coagulase-negative Staphylococcal spp., MSCNS: Methicillin sensitive coagulase-negative Staphylococcal spp.

to the literature by reporting the median time of bacteremia development between 16-17.6 days[20,22,25]. Based on these results, the first two weeks may be critical in developing bacteremia in burn cases.

Considering the bacteremia source in this study yielded the following implications: Catheter-related bacteremia (38.3%) was the most common source, followed by burn wounds (33.7%) and urinary tract-associated bacteremia (17.4%). In another analogous study, the most common source was demonstrated to be burn wounds and catheter-related bacteremia[21,22]. Therefore, placing a central catheter as far from burn wounds and bloody, donor, grafted areas would be helpful.

The most common etiologic agents isolated from the burn patients in this study were *Pseudomonas aeruginosa* (24.4%), *Acinetobacter baumannii* (19.7%), *Enterococcus* spp. (12.7%), and *S. aureus* (6.9%). In a study investigating 2,237 burn cases, similar to our study, *Pseudomonas aeruginosa* (30%), *Acinetobacter baumannii* (19%), *S. aureus* (14.4%), and *Enterococcus* spp. (12.3%) were found to be most frequently isolated in the blood cultures of 397 cases[22]. In another similar study, the most common pathogens were described as *Pseudomonas aeruginosa* (17.5%), *S. aureus* (16.5%), and *K. pneumoniae* (15.5%)[21]. One study reported the most frequently encountered agents as coagulase-negative *Staphylococci* (47%), *S. aureus* (41%), *Pseudomonas aeruginosa* (36%), and *Acinetobacter baumannii* (39%)[24]. Although the distribution of pathogens in BSI has been reported differently in burn patients in the literature, similar pathogens are causative to BSI in general. Each center should make an empiric antibiotic treatment plan considering possible microbial pathogens. However, in addition to determining the pathogens, knowledge of the resistance patterns of these agents also guide empiric antibiotic therapy. In our study, high carbapenem resistance was detected in 100% of *Acinetobacter* species, 60% of *Pseudomonas* species, and 33% of *S. aureus*. A similar trial showed high carbapenem resistance in *Pseudomonas aeruginosa* and *Acinetobacter baumannii* with rates of 95.9% and 95.3%, respectively[22]. Prolongation of hospital stay for burn patients may lead to clinicians viewing the treatment as problematic because it is a risk factor for developing highly resistant organisms. We detected that the median time between bacteremia and mortality in deceased cases was 3.5 days. Therefore, it is unlikely that antibiotic susceptibility will result in this period. It is essential to start early broad-spectrum antibiotic therapy, taking into account the local antibiotic resistance profile, without waiting for the result of antibiotic sensitivity.

Table 2. Distribution of bloodstream infection pathogens as reported by different sources

Sources of bacteremia					
Pathogens	**Unknown (n)**	**CAUTI (n)**	**CRBSI (n)**	**Burn wound (n)**	**Total**
Acinetobacter baumannii	1	2	7	7	17
Acinetobacter spp.	3	1	1	2	7
Pseudomonas aeruginosa	1	3	8	9	21
Pseudomonas spp.	1	1	0	2	4
Klebsiella oxytoca	0	0	2	0	2
Klebsiella pneumonia	0	3	1	1	5
Klebsiella spp.	1	0	1	1	3
Enterobacter cloacae	0	1	2	1	4
Enterobacter spp.	0	0	1	0	1
Serratia marcescens	0	0	0	1	1
Enterococcus faecalis	1	3	3	0	7
Enterococcus faecium	0	1	0	0	1
Enterococcus spp.	0	0	1	2	3
MRCNS	0	0	0	1	1
MRSA	0	0	2	0	2
MSCNS	0	0	1	1	2
MSSA	0	0	3	1	4
Streptococcus mitis	1	0	0	0	1
Total	9	15	33	29	86

MRSA: Methicillin resistant *Staphylococcus aureus*, MSSA: Methicillin sensitive *Staphylococcus aureus*, MRCNS: Methicillin resistant coagulase negative Staphylococcal spp., MSCNS: Methicillin sensitive coagulase negative Staphylococcal spp.

Table 3. Comparison of deceased and survivors in burn cases with bloodstream infections

	Survivors (n=44)	Deceased (n=24)	OR (95% CI)	p value
Age (median, min-max)	35 (18-92)	38 (21-91)	1.018 (0.993-1.045)	0.165
Sex (n, %)				
- Men	34 (68)	16 (32)	0.588 (0.195-1.773)	0.346
- Women	10 (55.6)	8 (44.4)		
Leukocyte count, mm^3 (median, min-max)	11300 (2800-42000)	11000 (1100-51000)	1.000 (1.000-1.000)	0.294
Leukocytosis	19 (65.5)	10 (34.5)	0.931 (0.334-2.593)	0.891
Anemia	40 (64.5)	22 (35.5)	1.1 (0.094-12.826)	0.939
Thrombocytopenia	10 (43.5)	13 (56.5)	4.16 (1.401-12.349)	0.010
CRP (mg/L) (median, min-max)	125 (10-399)	293.5 (213-300)	1.013 (1-1.026)	0.058
TBSA				
<40%	29 (80.6)	7 (19.4)	4.695 (1.597-13.806)	0.005
≥40%	15 (46.9)	17 (53.1)		
Lactate				
<2.5	13 (65)	7 (35)	4.179 (0.938-18.612)	0.061
≥2.5	4 (30.8)	9 (69.2)		
Source				
CAUTI	9 (20.5)	1 (4.2)	0.169 (0.02-1.426)	0.102
CRBSI	21 (47.7)	11 (45.8)	0.927 (0.342-2.512)	0.881
Burn wound	11 (25)	11 (45.8)	2.538 (0.885-7.281)	0.083
Unknown	3 (6.8)	1 (4.2)	0.594 (0.058-6.047)	0.660

*p<0.05 is considered as statistically significant.

CRP: C-reactive protein, CRBSI: Catheter-related bloodstream infection, CAUTI: Catheter-associated urinary tract infections, OR: Odds ratio, 95% CI: 95% confidence interval, TBSA: Total burn surface area, min-max: Minimum-maximum

In the current study, mortality was 42.1% and 30.8% in non-fermenting bacteria and *Enterobacteriaceae*, respectively; it was higher in the non-fermenters. Moreover, mortality was as high as 48% in *Pseudomonas* spp. A concordant literature study reported 21% and 35% mortality rates for Enterobacteriaceae and the non-fermenters, respectively, with a higher mortality rate of 41% for *Pseudomonas* spp. among the non-fermenters[20]. Several studies have also indicated that BSI-related mortality due to *Pseudomonas aeruginosa* is relatively higher in burn patients than in other Gram-negative organisms[18,26,27].

Thrombocytopenia is a common finding in sepsis patients in the intensive care unit (ICU). Cato et al.[28] reported that thrombocytopenia occurred in 47.6% of patients admitted to the ICU with severe sepsis or septic shock. Similar studies that specifically evaluated thrombocytopenia in patients with infection reported an incidence of 20-55%[29-31]. In our study, the incidence of thrombocytopenia was 33.8% in severe burns patients with BSI. Thrombocytopenia has been elucidated as a predictor of mortality and sepsis in burn cases[28]. Extensive clinical studies conducted in the ICU have shown that thrombocytopenia is predictive of multiorgan failure and mortality in sepsis[32-34]. Vandijck et al.[31] investigated the prognosis of thrombocytopenia in critically ill patients with nosocomial BSI. The ICU mortality was 55.8% for thrombocytopenia patients and 16.5% for non-thrombocytopenia patients with critically ill BSI. Thrombocytopenia occurred more frequently in nonsurvivors. In our study, mortality was 56.5% in thrombocytopenia patients. In deceased and survivor cases, the thrombocytopenia rate was 54.1% (13/24) and 22.7% (10/44), respectively. Our study revealed that thrombocytopenia plays a crucial role in mortality, supporting previous literature findings.

Study Limitations

The present study had several limitations. Antibiotic therapy was not evaluated, and our study is a retrospective single-center design. Furthermore, large-scale research on this topic is required.

Conclusion

Microbial pathogens in blood/wound cultures of patients in the burn units and their antimicrobial susceptibility patterns should be investigated routinely and evaluated for ultimate selection in empiric antibiotic therapy. Therefore, our study results can guide physicians to initiate appropriate empiric antibiotic therapy

when BSI, a leading cause of mortality, develops in burn patients. More importantly, our study found TBSA and thrombocytopenia to be significant prognostic factors for mortality. In addition, this study provides valid epidemiological data on the features of the pathogen composition of BSI in burn patients.

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Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ankara Numune Training and Research Hospital Ethics Committee before initiating the study (date and number of approval: 06.09.2018 and 18-2175, respectively).

Informed Consent: Retrospective study.

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Authorship Contributions

Surgical and Medical Practices: A.Ç.Y., Y.N.Y., İ.S., Concept: B.Ö., E.A., H.B., Design: B.Ö., E.A., H.B., Data Collection or Processing: B.Ö., A.B., S.K., Analysis or Interpretation: B.Ö., Literature Search: B.Ö., A.B., S.K., Writing: B.Ö.

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