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MEDICAL SCIENCES / DAHİLİ TIP BİLİMLERİ

# Evaluation of the Epidemiology, Risk Factors, Predictors and Fatality Associated with Extremely Drug-Resistant Infections in Burn Patients

## Yanık Hastalarında Antimikrobiyal Dirençli Enfeksiyonlarda Epidemiyoloji, Risk Faktörleri, Predikte Ettirici Faktörler ile Mortalite Oranlarının Değerlendirilmesi

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## Abstract

**Objectives:** Hospital-acquired infections are the leading causes of mortality in burn injuries following the initial resuscitation phase. Studies on healthcare associated antimicrobial-resistant infections in burn patients are limited. In this study, we aimed to evaluate the main risk factors and predictors of extremely drug-resistant infections in burn patients to highlight the need for optimal infection control approaches and antimicrobial stewardship.

**Materials and Methods:** This retrospective case-control study enrolled 92 adult patients with burn injuries admitted to the burn care department of our hospital from January 2015 to December 2018.

**Results:** Infection was observed in 47.8% of the burn patients (44/92), with 84 infection episodes noted among these patients. For the prediction of infection, only C-reactive protein/albumin ratio cut-off value was found to be a predictor after logistic regression analysis. Extremely drug-resistant infections accounted for 27% (23/84) of the episodes in 14 patients. The most common site of these infections was the lower respiratory tract. Extremely drug-resistant bacteria were isolated from nearly 80% of the respiratory samples. Broad spectrum and multiple antimicrobial usage were independent risk factors for the development of extremely drug-resistant infections and the presence of the resistant infection was the only independent risk factor for fatality (p=0.001; odds ratio 10.4; 95% confidence interval 1,923-56,359).

**Conclusion:** This study showed that extremely drug resistance was the major risk factor for fatality in burn patients. Infection control and antimicrobial stewardship programmes, which are crucial for limiting the development and spread of antimicrobial resistance, may decrease fatality in burn patients. We are able to cope with most of these factors with the infection control procedures.

**Key Words:** Antimicrobial Resistance, Burns, Fatality, Injury, Infection

## Öz

**Amaç:** Hastane kaynaklı enfeksiyonlar, ilk resüsitasyon evresini takiben yanık yaralanmalarında önde gelen ölüm nedenidir. Yanık hastalarında sağlık bakımıyla ilişkili antimikrobiyallere dirençli enfeksiyonlarla ilgili çalışmalar sınırlıdır. Bu çalışmada, optimal enfeksiyon kontrol yaklaşımları ve antimikrobiyal yönetim ihtiyacını vurgulamak amacıyla yanık hastalarında çok ilaca dirençli enfeksiyonların ana risk faktörlerini ve predikte ettiren faktörleri değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** Bu retrospektif olgu-kontrol çalışmasına Ocak 2015 ile Aralık 2018 tarihleri arasında hastanemizin yanık bakım bölümüne başvuran yanık yaralanmalı 92 erişkin hasta dahil edildi.

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**Bulgular:** Yanık hastalarının %47,8'inde (44/92) enfeksiyon geliştiği gözlendi ve bu 44 hastada 84 enfeksiyon epizodu kaydedildi. Lojistik regresyon analizi sonrası değerlendirilen parametreler içerisinde sadece C-reaktif protein/albümin oranının enfeksiyon varlığı için anlamlı olduğu bulundu. En sık Gram-pozitif mikroorganizmalar izole edilirken (42/84, %50), Gram-negatifler ikinci sıklıkta saptandı (39/84, %46). Çok ilaca dirençli enfeksiyonlar, 14 hastada atakların %27'sini (23/84) oluşturuyordu. Bu enfeksiyonların en sık görüldüğü yer alt solunum yoluydu. Dirençli bakteriler, solunum örneklerinin yaklaşık %80'inden izole edildi. Geniş spektrumlu ve çoklu antimikrobiyal kullanımı, çok ilaca dirençli enfeksiyonların gelişimi için bağımsız risk faktörleri olarak bulundu ve dirençli enfeksiyonun varlığı ölüm için tek bağımsız risk faktörü olarak saptandı (p=0,001; odds oranı 10,4; %95 güven aralığı 1.923-56.359).

**Sonuç:** Bu çalışma, çoklu ilaç direncinin yanık hastalarında ölüm için bağımsız risk faktörü olduğunu göstermektedir. Antimikrobiyal direncin gelişimini ve yayılımını sınırlamada en etkili yol olan enfeksiyon kontrolü önlemlerine sıkı uyum ve etkin antimikrobiyal yönetim programları, yanık hastalarında ölüm oranını azaltabilecek temel yaklaşımdır.

**Anahtar Kelimeler:** Antimikrobiyal Direnç, Yanık, Fatalite, Yaralanma, Enfeksiyon

## Introduction

Burn injuries are among the most serious forms of trauma and result in anatomic, physiologic, and immunologic stress. While innate and adaptive immunologic alterations that occur in association with burns can persist over long periods, the primary concern is often the wound itself. The type, size, and depth of burn injuries are important factors related to the healing process, presentation of complications, and survival (1). Immune system dysregulation and the loss of the natural cutaneous barrier predispose patients to infections. Furthermore, inhalation injury, the use of endotracheal intubation, central venous access, arterial lines and urinary catheters, and prolonged periods of hospitalisation contribute to an increased risk of infection in burn patients (2). The 2017 National Burn Repository Report of the American Burn Association found that seven of the 10 most frequently occurring complications in patients with burns have an infectious aetiology, with pneumonia, urinary tract infection (UTI), and cellulitis showing the highest prevalence rates in such settings (3).

Infections are the leading causes of mortality following the initial resuscitation phase. In addition to the features of the wound and the factors stated above, the length of stay at the burn centre is a major risk factor for antimicrobial-resistant pathogen infections. Previous antibiotic exposure and the use of invasive medical devices are additional risk factors. The treatment of infections caused by antimicrobial-resistant microorganisms is a challenge due to the limited number of treatment choices and rapid dissemination. Infection control approaches (hand hygiene, antimicrobial stewardship, optimisation of surgical interventions, the measured use of medical devices, and environmental control) are crucial for the prevention of multidrug-resistant infection spread. The involvement of an infectious disease specialist is essential for the day-to-day care of patients with such complexities (2). Studies on extremely drug-resistant (XDR) infections in burn care are limited. In this study, we aimed to evaluate the main risk factors and predictors of XDR infections to highlight the need for optimal infection control approaches and antimicrobial stewardship in burn patients.

## Materials and Methods

### Study Design

This retrospective case-control study enrolled patients with burn injuries, aged older than 18 years, with or without infections, who were admitted to the burn care department of our hospital from January 2015 to December 2018. There were 44 cases who developed infections after burn trauma and 48 controls who had burn trauma without infection. We analysed the patients' demographic data and laboratory findings as well as the risk factors and fatality rates and predictors across 84 infectious episodes. Data were collected retrospectively from the patients' medical records. If a patient died within 48 hours of admission, they were excluded from the study (Figure 1). Study approval was granted by the Başkent University Institutional Review Board (KA/18/273; 11.09.2018).

### Definitions

Burn size and depth were evaluated based on the 'rule of nines' and International Society of Burn Injuries guidelines. The rule of nines is based on the concept of dividing the adult body into anatomic regions for the calculation of the total burn surface area (TBSA) (4,5).

Infections (burn wound infection, pneumonia, blood stream infection, urinary system infection, etc.) were diagnosed based on the American Burn Association criteria using clinical and microbiological findings (6). We included only one of the duplicate cultures growing the same organism with the same susceptibility profile in the previous 14 days for the diagnosis of infection (7). Multiple antimicrobial treatment in the previous 30 days was defined as the reception of more than one antimicrobial treatment simultaneously or consecutively.

### Microbiological and Biochemical Analysis

Microbiological isolates were identified and antimicrobial susceptibility tests were performed using a Phoenix 100

automated analyser (Becton, Dickinson and Company; Franklin Lakes, NJ). The interpretation of antimicrobial resistance and susceptibility was performed using the European Committee on Antimicrobial Susceptibility Testing 2019 recommendations.

XDR infection was defined as one that was non-susceptible to at least one agent in all but two or fewer antibiotic categories (i.e. the bacterial isolates remain susceptible to only one or two categories) (8).

### Data Collection and Statistical Analysis

We collected data on the patients' demographics (sex and age); chronic diseases (diabetes mellitus, rheumatologic diseases, and malignancies that cause immunosuppression); burn degree, ratio, and cause; duration of hospital stay; number of infection episodes; isolates and resistance patterns; laboratory findings [total blood count, C-reactive protein (CRP) level, procalcitonin level, and albumin level]; antibiotic usage in the previous 30 days; and fatality. All data were recorded and analysed using SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY).

We used descriptive statistics for the analysis of demographic data, and chi-square tests were employed for multiple proportions. A p-value <0.05 was considered indicative of significance. The continuous numerical variables were not normally distributed and are presented as the median value; they were compared using the Mann-Whitney U test. Categorical data are presented as frequency (%) and were compared using a chi-square test. Comparisons of the episode development durations, by bacteria type, were performed using Kaplan-Meier analysis.

Univariate logistic regression analysis was conducted to evaluate the risk factors for the development of infection and XDR infection in burn patients. Multivariate logistic regression was employed for clinical and laboratory parameter estimation. Variables that were found to be statistically significant were included in the multivariable models using the kitchen sink approach. We analysed the ratios of the blood components if they could be used for the prediction of XDR infection or fatality using receiver operating characteristic (ROC) curve analysis. The risk factors and predictors of fatality were analysed using chi-square and logistic regression tests.

## Results

### Patients and Infection Episodes

This study enrolled 92 adult patients with burn injury and the demographics of the patients were shown in Table 1. The median duration of hospital stay was 12 days (range 1-110 days). Chronic diseases such as diabetes mellitus, rheumatologic

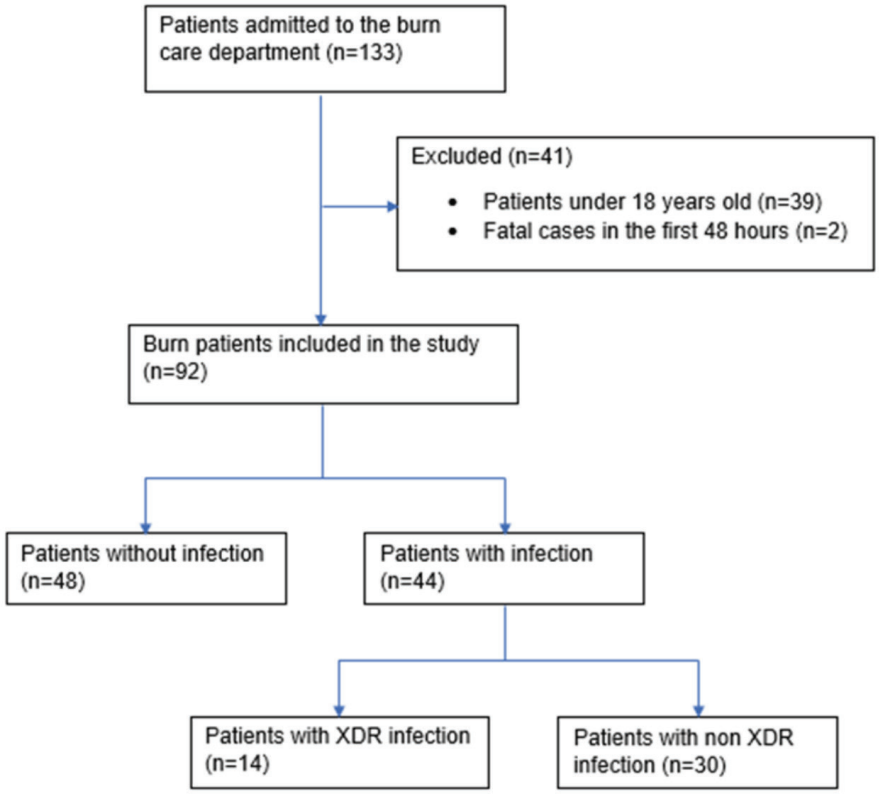


**Figure 1:** Patients included and excluded from the study

XDR: Extremely drug resistant

diseases, and malignancies that cause immunosuppression were present in 28.3% of the patients. The most commonly reported burn aetiology was hot liquid scalding, and two thirds of the hospitalised patients had second-degree burns (Table 1). During the follow-up of nine patients, mechanical ventilation was needed; six of these cases involved inhalation injury. The median duration of mechanical ventilation was 20 days (range 9-54 days).

Infection was observed in 47.8% of the burn patients (44/92), with 84 infection episodes noted among these patients. XDR infections accounted for 27% (23/84) of the episodes in 14 patients. Five patients had more than one XDR infection episode and no statistically significant relationship was observed between the presence of more than one XDR infection episode and the duration of hospital stay (p=0.374).

The most commonly observed site of XDR infection was the lower respiratory tract. Nearly 80% of the respiratory samples had XDR bacteria. Those who had inhalation injury had an XDR rate of 83.3% (5/6), whereas those who did not had a rate of 23.1% (18/78) and the difference was statistically significant (p=0.001). Details on the proportions of infection sites and XDR microorganisms are presented in Figure 2. Although the rates of XDR infections varied over the years, the difference was not statistically significant (p=0.693) (Figure 3).

The most common microorganisms isolated from burn infections were Gram-positives (42/84, 50%), while Gram-negatives were the second common (39/84, 46%). Extremely drug resistant bacteria were mostly Gram-negatives. All *Acinetobacter* isolates (17/17) and nearly half of Pseudomonas isolates (8/15) were resistant to carbapenems. Colistin resistance was seen in only one *Acinetobacter* isolate. The time taken for the development of Gram-negative infection episodes was significantly longer than Gram-positive infection episodes (27 days and 11 days, respectively). In addition, the difference between the median duration of development of XDR and non-XDR infection episodes was statistically significant (26 days and 14 days, respectively).

**Table 1: Demographic characteristics of the patients**

| Demographic characteristics | Value |
|---|---|
| **Sex, n (%)** | |
| Female | 35 (38%) |
| Male | 57 (62%) |
| **Median age, y** | 44.5 (21-89) |
| **Duration of stay (median)** | 12 (1-110) days |
| **Chronic disease** | 26 (28.3%) |
| **Burn cause** | |
| Flame burn | 28 (30.4%) |
| Hot liquid scald | 37 (40.2%) |
| Electrical burn | 17 (18.5%) |
| Others | 10 (10.9%) |
| **Burn degree** | |
| First-degree burn | 2 (2.2%) |
| Second-degree burn | 67 (72.8%) |
| Third-degree burn | 23 (25%) |
| **Total burn surface area (%), Median:** | 10 (1-76) |
| 1-10% | 49 (53.3%) |
| 11-25% | 28 (30.4%) |
| 26-50% | 10 (10.9%) |
| >50% | 5 (5.4%) |

## Risk Analysis

After univariate analysis we observed statistically significant differences in age, burn degree, TBSA, chronic disease occurrence and duration of stay between the patients with and without infection (p<0.05). However, the differences in sex and burn aetiology were not statistically significant. A collinearity test performed between the burn cause, burn degree, and TBSA showed the absence of collinearity problems. The results of the univariate analysis conducted in the burn patients with and without infections are shown in Table 2.

Multivariate logistic regression analysis revealed that age [p=0.035; 95% confidence interval (CI) 1,004-1,116] and duration of stay (p=0.0001; 95% CI 1,069-1,265) were independent risk factors for infection development.

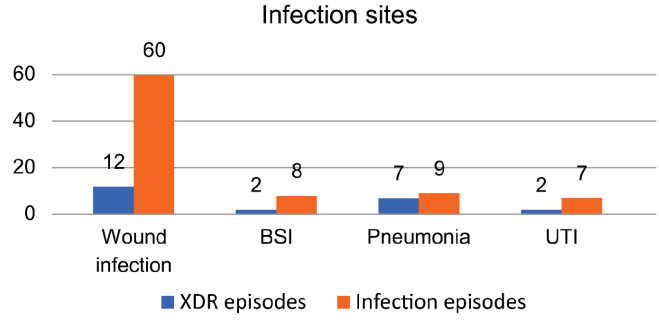


**Figure 2:** Distribution and comparison of the total rates of infection and XDR infection episodes

XDR: Extremely drug resistant, BSI: Bloodstream infection, UTI: Urinary tract infection

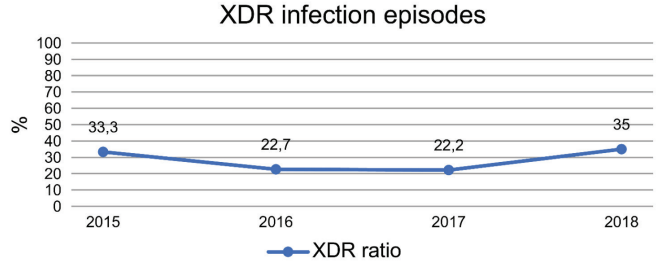


**Figure 3:** Rate of XDR infection episodes across different years

XDR: Extremely drug resistant, BSI: Bloodstream infection, UTI: Urinary tract infection

We also investigated the risk factors for the development of XDR infection for the infected group. The differences between the XDR and non-XDR infections, according to sex, duration of stay, hypoalbuminaemia, and antimicrobial treatment reception in the previous 30 days for all the broad-spectrum antibiotic groups (glycopeptides, carbapenems, beta-lactam/beta lactamase inhibitory combinations as piperacillin-tazobactam, ampicillin-sulbactam, amoxicillin-clavulanic acid) were statistically significant. All the patients with XDR infections had received antimicrobial treatment in the previous 30 days, and 95% of them were administered more than one antibiotic. The median duration of mechanical ventilation for pulmonary infections caused by XDR bacteria was 21 days (range 9-54 days), while this duration was 1.5 days (range 12-15 days) for non-XDR strains; however, the difference was not statistically significant. The results of the univariate analysis of the XDR and non-XDR infection episodes are presented in Table 3.

Piperacillin-tazobactam (p=0.020; 95% CI 1,449-73,227) and multiple antimicrobial usage (p=0.027; 95% CI 1,420-

**Table 2: Comparison of the risk factors between burn patients with and without infection**

| Risk factors for infection development | Infection (+) | Infection (-) | Univariate analysis OR (95% CI) | p-value |
|---|---|---|---|---|
| **Sex (Female/Male)** | 14/30 | 21/27 | 1.9 (0.925-3,998) | 0.080 |
| Median age, y | 55.5 (range 23-89) | 38.5 (range 21-88) | | 0.001 |
| Duration of stay (Median) | 25 (range 5-110) | 7 (range 1-39) | | 0.0001 |
| **Chronic disease (%)** Yes/No | 73.1/37.9 | 26.9/62.1 | 3.0 (1,246-7,210) | 0.014 |
| **Burn cause (%)** | | | | |
| **Flame burn** | **39.3** | **60.7** | **3.6 (1,635-8,030)** | **0.002** |
| **Hot liquid scald** | **62.2** | **37.8** | **0.2 (0.093-0.465)** | **0.0001** |
| Electrical burn | 41.2 | 58.8 | 2.0 (0.781-5,121) | 0.149 |
| Others | 70.0 | 30.0 | 0.2 (0.146-1,462) | 0.462 |
| **Burn degree (%)** | | | | |
| First-degree burn | 0 | 100 | - | - |
| Second-degree burn | 41.8 | 58.2 | 0.2 (0.102-0.547) | 0.002 |
| Third-degree burn | 69.6 | 30.4 | 5.2 (2,309-14,175) | 0.0001 |
| **Total burn surface area (Median)** | 15 (range 1-74) | 5 (range 1-76) | 1.1 (1,043-1,111) | 0.0001 |
| Hypoalbuminaemia (%) Yes/No | 88.0/35.3 | 12.0/64.7 | 17.5 (5,594-54,443) | 0.0001 |

OR: Odds ratio, CI: Confidence interval

**Table 3: Comparison of the risk factors between the XDR and non-XDR infection episodes**

| Risk factors for XDR infection episode | Univariate analysis XDR infection episode | Non-XDR infection episode | p-value |
|---|---|---|---|
| **Sex (Female/Male)** | 3/20 | 22/39 | 0.044 |
| Median age, y | 45 (min.: 23-max.: 87) | 56 (min.: 23-max.: 89) | 0.710 |
| Duration of stay (median) | 63 (min.: 15-max.: 110) | 42 (min.: 5-max.: 101) | 0.008 |
| **Chronic disease (%)** Yes/No | 25.8/28.3 | 74.2/71.7 | 0.805 |
| **Burn cause (%)** | | | |
| Flame burn | 32.6 | 67.4 | 0.033 |
| Hot liquid scald | 7.1 | 92.9 | 0.021 |
| Electrical burn | 33.3 | 66.7 | 0.231 |
| Others | 16.7 | 83.3 | 0.353 |
| **Burn degree (%)** | | | |
| Second-degree burn | 20.9 | 79.1 | 0.014 |
| Third-degree burn | 34.1 | 65.9 | 0.009 |
| **Total burn surface area (Median)** | 30 (range 1-74) | 25 (range 1-70) | 0.115 |
| Hypoalbuminaemia (%) (Yes/No) | 29.1/19.2 | 70.9/80.8 | 0.344 |
| Antimicrobial treatment in the previous 30 days (%) (Yes/No) | 38.3/0 | 61.7/100 | 0.001 |

XDR: Extremely drug resistant, min.: Minimum, max.: Maximum

355,929) were found to be independent risk factors for XDR infection after multivariate logistic regression analysis.

### Laboratory Findings

We compared the potential of CRP levels, the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and the CRP/albumin ratio as predictors of infection development in burn patients. We found statistically significant differences between the median CRP, NLR, PLR, and CRP/albumin ratio values of the patients with and without infection ($p<0.05$). The area under the curve (AUC) was 0.842 (95% CI 0.762-0.922; $p<0.001$) for CRP, 0.611 (95% CI 0.510-0.711; $p=0.040$) for the PLR, 0.667 (95% CI 0.565-0.769; $p=0.002$) for the NLR, and 0.889 (95% CI 0.826-0.952; $p<0.001$) for the CRP/albumin ratio. In addition, in the ROC curve analysis, the cut-off values for infection diagnosis were 61.0 for CRP (79.8% sensitivity and 75.7% specificity), 151.28 for the PLR (54.8% sensitivity and 72.7% specificity), 4.77 for the NLR (60.7% sensitivity and 72.7% specificity), and 19.3 for the CRP/albumin ratio (82.7% sensitivity and 82.9% specificity). In the univariate analysis, all results higher than the cut-off values were found to be statistically significant. However, in the logistic regression analysis, only the CRP/albumin ratio cut-off value was found to be a predictor ($p<0.05$). The ROC curve plot is shown in Figure 4.

The comparison of the value of CRP, procalcitonin, the PLR, the NLR, and the CRP/albumin ratio in the prediction of XDR in patients with infection in the ROC analysis did not yield statistically significant results ($p>0.05$).

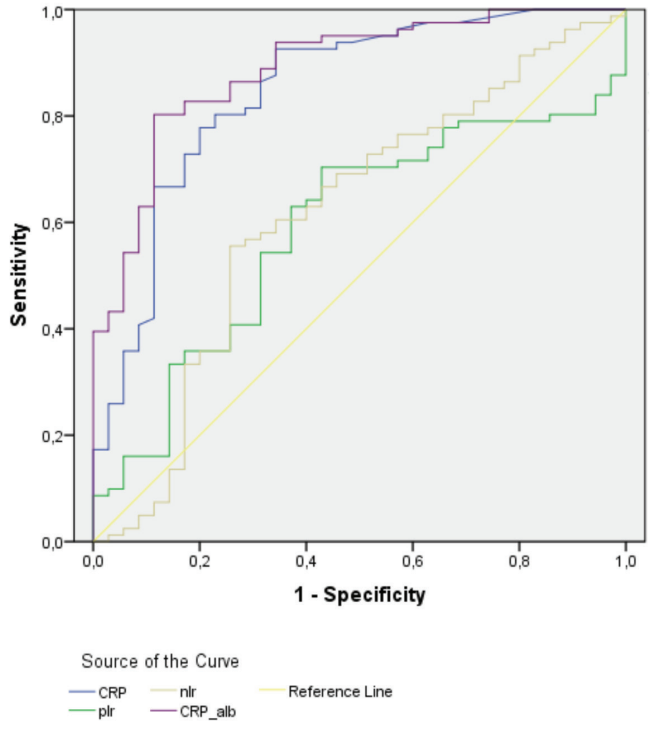


**Figure 4:** ROC curve plot of laboratory parameters

CRP: C-reactive protein, PLR: Platelet-lymphocyte ratio, NLR: Neutrophil-lymphocyte ratio

### Fatality

In our study, nine patients died, accounting for a fatality rate of 9.8% (9/92). Eight of these patients had one or more infection episodes. Accordingly, we analysed the fatality rates in the patients with infection and those with XDR infection separately. The fatality rate in those with infections was 9.5% (8/84), while the corresponding value in the patients with XDR infections was 26.1% (6/23). For the patients with infection; the median TBSA of fatal cases was 40,5% (min.: 1-max.: 74), while it was 25% (min.: 1-max.: 70) for non-fatal cases and the difference was statistically significant ($p=0.032$). For broad spectrum antibiotic groups, carbapenem group antibiotic usage in the last 30 days was statistically higher ($p<0.05$) in fatal cases. After multivariant logistic regression analysis, only XDR infection episode (95% CI 1,156-37,165; $p=0.039$) was found to be an independent risk factor for fatality.

## Discussion

In our study, nearly half of the burn patients had at least one infection episode (52%) and one third of these infections were antimicrobial resistant infections. Some previous studies, however, showed higher rates of nosocomial infection in such settings (1,9). Infections are the most important factor that influences the prognosis in burn patients after the acute phase has passed, as reported in previous studies. Despite all of the advancements in burn care, current studies suggest that infections are responsible for 42 to 65 percent of fatalities in patients with severe burn injury (1,9).

The most commonly reported infections in the present study were wound infections, followed by respiratory infections and UTIs. Wound infections and cellulitis are frequently observed in patients with scald and burn injuries involving contact with hot objects, consistent with our study (1) in which the most commonly noted cause of burn injury was scald injury. However, the aetiology differed by sex. While scald injury was observed in three-quarters of the women, flame burns were the most commonly reported cause followed by electrical burns in the men. However, in 1995, scalds accounted for only 5.3% of all adult thermal injuries (10). Two-thirds of the women with thermal injuries in our study were aged over 50 years, and 65% of them had scald burns caused by daily actions, while the men were frequently exposed to burn injuries resulting from an industrial or work-related accident, consistent with previous studies. Since legal action is taken in many of these cases, it is important to document the aetiology and extent of burn injuries (11,12).

Gram-positive isolates were the most commonly observed infection sources, followed by Gram-negative isolates in the present study. Additionally, Gram-positive infections occurred earlier while Gram-negative infection risk was correlated with the length of hospital stay, consistent with previous studies (1,2,9,13,14).

The Gram-negative isolates were associated with a stronger degree of antimicrobial resistance. Infections caused by XDR bacteria accounted for nearly one-quarter of the episodes and were also associated with longer durations of stay, compatible with the existing literature (2,14). Unlike in other studies, the rate of *A. baumannii* infection was higher than that of *P. aeruginosa* infection in our study.

The most commonly reported site of XDR microorganism infection was the lower respiratory tract. We isolated XDR bacteria from nearly 80% of the respiratory samples. Respiratory system infections were found to be related to mechanical ventilation (9/9) and inhalation injury (6/9) as in previous studies. Studies show that, inhalation injury impaires functions of alveolar macrophages, polymorphonuclear leukocytes and mucociliary clearance mechanism, causes atelectasis, complicates ventilator-associated pneumonia and increases rates of resistant infections (2,9,13). In our study, we also found significantly higher antimicrobial resistance rates in patients with inhalation injury (83,3% vs. 23.1%, p=0.001).

The treatment of antimicrobial-resistant infections is a major challenge due to limited treatment choices and rapid dissemination. In our study, we found yearly increases in the degree of resistance, consistent with previous reports (2,13).

A greater TBSA tends to be related to higher mortality and morbidity values (15); this affects the natural skin barrier of the immune system and increases the degree of susceptibility to infections (13). Among patients with severe burns and a TBSA exceeding 40%, 75% of all deaths are related to sepsis from burn wound infection or other infection-related complications (11). The TBSA was larger in the patients with infection and XDR infections in our study.

Prolonged hospitalisation leads to bacterial colonisation and increases the risk of infections, particularly antimicrobial-resistant infections (14). In this study, age, the presence of chronic diseases, burn cause, burn degree, TBSA, and hypoalbuminaemia were significantly associated with infection episode development; however, only the length of stay was found to be an independent risk factor.

Antimicrobial-resistant Gram-negative pathogens cause infections that are correlated with the length of hospital stay (1,2,13,14). Although resistant *Pseudomonas* spp. is the most important cause of burn infections, in our study, the most problematic pathogen was *A. baumannii*. XDR *Acinetobacter* was the most frequently observed cause of respiratory infection.

The length of hospital stay and history of the reception of antimicrobial treatment, particularly involving multiple antibacterial drugs, are major risk factors for drug-resistant infections in burn patients. The mis- or overuse of antibacterial agents facilitates resistance development (1,2,13,14). In the present study, the previous use of broad-spectrum antibiotics such as piperacillin-tazobactam and carbapenems in the last 30 days was found to be a risk factor for XDR infection. The rate of carbapenem resistance associated with *P. aeruginosa* and *A. baumannii* was 53.3% and 100%, respectively. These values are higher than those reported in previous studies (2,9).

Often, pathogen isolation is not sufficient for diagnosis. The distinction between colonisation and infection is a major challenge for clinicians. Swab cultures and tissue biopsy cultures cannot aid in decision-making owing to the presence of eschar and necrotic tissues (2). Respiratory samples are of low value unless collected using bronchoscopy, while the use of urinary samples can be confusing when they are obtained from urinary catheters (1,2). Among laboratory tests, the procalcitonin test is a promising method for the diagnosis of sepsis in burn patients. However, in our study, we were unable to evaluate the procalcitonin levels in all the patients and only compared these values for the prediction of XDR infection development; therefore, procalcitonin was not identified as a predictor (2,16-18). We evaluated the CRP, PLR, NLR, and CRP/albumin values using ROC curve analysis, and all the cut-off values were found to be statistically different between the infection and non-infection groups. However, in the logistic regression analysis, only the CRP/albumin ratio was found to be a predictor of infection. In recent studies, the CRP/albumin ratio has been investigated as an early predictor of infection, sepsis, and mortality in critically ill burn patients (19,20).

Sepsis is the main cause of mortality in this group of patients. Recent studies have shown that the fatality associated with Gram-negative bacteria infections, particularly owing to the limited number of antimicrobial options for resistant infections, is higher than that related to other types of infections (21). In this study, XDR infection development was found to be an independent risk factor for fatality, consistent with previous studies; while the median TBSA in the fatality group was statistically higher, in the multivariate analysis, it was not identified as an independent risk factor, unlike in previous reports (2,6,9,11,21).

## Conclusion

This study showed that XDR is the major risk factor for fatality. All burn centres should employ local data on antimicrobial

resistance for treatment-related decision-making. XDR infection prevention may decrease mortality rates. Our findings highlight the importance of shortening the lengths of hospital stay, infection control and antimicrobial stewardship programs in the management of burns and prevention of antimicrobial resistance. Prospective studies are needed to reveal the efficacy of infection control and antimicrobial stewardship programs in decreasing resistance and fatality in burn patients.

### Ethics

**Ethics Committee Approval:** Study approval was granted by the Başkent University Institutional Review Board (KA/18/273; 11.09.2018).

**Informed Consent:** Retrospective case-control study.

**Peer-reviewed:** Externally peer-reviewed.

### Authorship Contributions

Concept: Ç.E., M.H.D., E.G., C.A., A.H.A., M.H., Design: Ç.E., M.H.D., E.G., C.A., A.H.A., M.H., Data Collection or Processing: Ç.E., M.H.D., E.G., C.A., A.H.A., M.H., Analysis or Interpretation: Ç.E., M.H.D., E.G., C.A., A.H.A., M.H., Literature Search: Ç.E., M.H.D., E.G., C.A., A.H.A., M.H., Writing: Ç.E., M.H.D., E.G., C.A., A.H.A., M.H.

**Conflict of Interest:** The authors declare no conflicts of interest.

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