

# Bloodstream infections by multidrug-resistant bacteria in patients in an intensive care unit for the treatment of burns: a 4-year-experience

*Infecções de corrente sanguínea por bactérias multirresistentes em UTI de tratamento de queimados: experiência de 4 anos*

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## ABSTRACT

**Background:** Knowledge of the profile of antibiotic resistance in bacteria in a hospital is essential for guiding appropriate patient treatment. This is especially important for the severely ill patients, because treatment must be initiated before the results of cultures can be obtained. In this study, we aimed to analyze the profile of multidrug-resistant bacteria (MR) found in blood cultures from patients admitted to the intensive care unit (ICU) of the Burns Unit of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. **Methods:** We evaluated 178 patients (131 men) admitted to the ICU for the treatment of burns from 2009 to 2011, with a mean age of 29.2 years. **Results:** Eighty (44.9%) patients indicated positive results in peripheral blood cultures, and there were 66 (82.5%) cases with MR bacteria. *Staphylococcus* sp. was isolated in 48 cases, of which 33 cases showed resistance to oxacillin. *Acinetobacter baumannii* was isolated in 11 cases, and 8 of these cases were resistant to imipenem. *Pseudomonas* sp. was isolated in 19 cases, and 16 of these cases were resistant to imipenem. *Enterobacter* sp. was isolated in 10 cases, and 2 of these cases were resistant to ciprofloxacin and amikacin. The presence of MR bacteria was not associated with a higher incidence of deaths but was associated with longer hospital stay (52.6 vs. 36.3 days for those with and without MR bacteria, respectively,  $P = 0.0306$ ). There was no significant association between burned body surface and the presence of MR bacteria. **Conclusions:** The presence of MR bacteria is an important problem, because of the prevalence and associated morbidity and mortality.

**Keywords:** Burn units. Intensive care. Drug resistance, bacterial.

## RESUMO

**Introdução:** O conhecimento do perfil de resistência aos antibióticos das bactérias de um nosocômio é essencial para orientar tratamento adequado dos pacientes. Isso é especialmente importante para os pacientes mais graves, já que o tratamento deve ser instituído antes do resultado das culturas. O objetivo deste estudo foi analisar o perfil das bactérias multirresistentes encontradas nas hemoculturas de pacientes admitidos na Unidade de Tratamento Intensivo (UTI) da Unidade de Queimados do Hospital das Clínicas da Faculdade

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de Medicina da Universidade de São Paulo. **Método:** Foram analisados 178 pacientes internados na UTI para tratamento de queimados, no período de 2009 a 2011, sendo 131 do sexo masculino, com média de idade de 29,2 anos. **Resultados:** Entre os pacientes analisados, 80 (44,9%) apresentaram hemocultura periférica positiva, sendo 66 (82,5%) casos com bactérias multirresistentes. Em 48 pacientes, foram isoladas *Staphylococcus sp.*, que se apresentaram resistentes à oxacilina em 33 deles. Em 11 pacientes, foram isoladas *Acinetobacter baumannii*, que se apresentaram resistentes a imipenem em 8 casos. Em 19 pacientes, foram isoladas *Pseudomonas sp.*, resistentes a imipenem em 16 casos. Em 10 pacientes foram isoladas *Enterobacter sp.*, resistentes a amicacina e ciprofloxacina em 2 casos. A presença de bactérias multirresistentes não foi associada a maior ocorrência de óbitos, porém foi verificado maior tempo de internação (52,6 dias vs. 36,3 dias para os grupos com e sem bactérias multirresistentes, respectivamente;  $P = 0,0306$ ). Não foi encontrada interação significativa entre superfície corpórea queimada e presença de bactérias MR. **Conclusões:** A presença de bactérias multirresistentes é um problema grave, tanto pela prevalência como pela morbidade e mortalidade associadas.

**Descritores:** Unidades de queimados. Terapia intensiva. Farmacorresistência bacteriana.

## INTRODUCTION

Severely burned patients are more susceptible to infections because of immunosuppression and loss of cutaneous coverage<sup>1</sup>. Furthermore, prolonged hospitalizations associated with invasive measures such as mechanical ventilation, and vascular and bladder catheterization, further expose these patients to nosocomial infections<sup>2</sup>.

Recent changes in patient care in the intensive care unit (ICU), such as reduced time of catheter presence, greater care with patient manipulation, attempted earlier weaning from mechanical ventilation, better patient nutrition, prophylaxis for deep venous thrombosis and stress ulcers, and tighter controls for blood glucose, have resulted in increased survival of these patients. However, this has been accompanied by increases in nosocomial infection rates<sup>3</sup>.

Knowledge of the profile of antibiotic resistance in bacteria is essential for guiding appropriate treatment of patients. This is especially important for seriously ill patients, because treatment must be initiated before the results of cultures can be obtained.

In 2003, a study performed in our ICU showed that bloodstream infections are the most common; 24%, 18%, 14%, 12%, and 8% of these infections were caused by *Staphylococcus sp.*, *Pseudomonas aeruginosa*, *Acinetobacter spp.*, coagulase-negative staphylococci, and *Candida spp.*, respectively<sup>1</sup>.

However, the presence of multidrug-resistant bacteria is more common in burn units<sup>4</sup>. This is because cross-infection is common and patients are often treated with topical and systemic antimicrobial therapies at some point during their long hospitalization period. *Acinetobacter baumannii*<sup>2,5</sup>, *P. aeruginosa*<sup>6</sup>, and *Staphylococcus aureus*<sup>7</sup> are the most

common multidrug-resistant bacteria. However, others such as *Serratia marcescens*<sup>8</sup> are also found.

In this study, we aimed to analyze the profile of multidrug-resistant bacteria found in blood cultures from patients admitted to the ICU of the burn unit of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP, São Paulo, SP, Brazil).

## METHODS

This was a retrospective study that analyzed all patients admitted to the ICU for the treatment of burns from 2009 through 2011.

Data including identification; age; cause of burn; percentage of body area burned; presence of inhalation injury; and dates of admission, discharge, or death were obtained from the burns unit. Data related to bacteria isolated in blood cultures were obtained from the electronic database. The profiles of antibiotic resistance from species identified to be multidrug resistant were analyzed.

According to the National Health Surveillance Agency (ANVISA), multidrug-resistant microorganisms are defined as follows:

- Gram-negative
  - *Escherichia coli*, *Enterobacter*, *Proteus*, and *Klebsiella* resistant to any 2 of the following antibiotics: amikacin, ceftriaxone, cefepime, and ciprofloxacin.
  - Large-spectrum beta lactamase-producing *Escherichia coli* and *Klebsiella* (ESBL).
  - *Pseudomonas* and *A.* resistant to imipenem or sensitive only to imipenem and polymyxin

- Gram-positive
  - *Staphylococcus*: resistant to oxacillin.
  - *Enterococcus*: resistant to vancomycin or teicoplanin<sup>9</sup>.

During the study period, 178 patients were hospitalized in the ICU of the burn unit of the HCFMUSP, including 131 (73.6%) men. The mean age of the patients was 29.2 years, ranging from 3 months to 95 years.

## RESULTS

The most common cause of burns was fire (54 cases; 30.3%), followed by alcohol combustion (36 patients, 20.2%), blasts (29 cases; 16.3%), and other causes (59 cases; 33.2%). The mean percentage of body surface area burned was 30.6% (range: 0.2–96.5%).

Inhalation injury confirmed by bronchoscopy was present in 45 (25.3%) of the patients admitted and was usually caused by fire (17 cases, 37.8%) or explosion (12 cases, 26.7%).

Eighty (44.9%) patients had positive results on peripheral blood cultures, and 66 patients had multidrug-resistant bacteria (82.5% of cases with positive results on blood culture and 37% of all patients).

*Staphylococcus* sp. was isolated from 48 patients; 33 (68.8%) of these cases indicated resistance to oxacillin. *Acinetobacter baumannii* was isolated from 11 patients; 8 (72.7%) of these cases indicated resistance to imipenem. *Pseudomonas* sp. was isolated from 19 patients; 16 (84.2%) of these cases indicated resistance to imipenem. *Enterobacter* sp. was isolated from 10 patients; 2 (20%) of these cases indicated resistance to ciprofloxacin and amikacin.

The presence of multidrug-resistant bacteria was not associated with increased mortality (25 deaths in the group with multidrug-resistant bacteria vs. 32 deaths in the group without multidrug-resistant bacteria,  $P = 0.2445$ ) but was associated with longer hospitalization in those who were discharged (mean of 52.6 days for those with multidrug-resistant bacteria vs. 36.3 days for those without multidrug-resistant bacteria,  $P = 0.0306$ ).

Logistic regression analysis of the variables of percentage of body surface burned and the presence of multidrug-resistant bacteria in blood cultures revealed no significant association (confidence interval 95% of the odds ratio = 0.9901 to 1.0161).

## DISCUSSION

Infection followed by sepsis is the major cause of death in burn units. This is due to immunosuppression resulting from burns, the low level of T lymphocytes in the bloodstream,

and increase in suppressive cellular activity<sup>10,11</sup>. Furthermore, the need for monitoring critical patients with vascular and urinary catheters and nasogastric enteral probes, and those who have undergone tracheal intubation, coupled with a lack of skin coverage, are important risk factors for infection<sup>7</sup>.

Burn patients are also more susceptible to serious staphylococcal infection; the increasing rates of multidrug-resistant *Staphylococcus aureus* in ICU burn units have resulted in a remarkable increase in morbidity and mortality in these centers<sup>7</sup>.

The emergence of multidrug-resistant bacteria in burn units is not a new concern. Since the 1970s, bacteria have already become resistant to multiple antibiotics<sup>12</sup>. The presence of such microorganisms can worsen the clinical course of patients<sup>13</sup>.

Critically ill patients usually undergo lengthy hospitalizations, which is associated with a higher incidence of infections by multidrug-resistant bacteria. However, this study did not demonstrate increased mortality associated with infections by multidrug-resistant bacteria, but such infections were associated with a longer hospital stay. The importance of preventing infections by multidrug-resistant bacteria is critical, since many studies indicate that this results in a significant reduction in the costs of hospitalization and antibiotic treatment<sup>14</sup>.

In this study, 25.3% of patients had some type of inhalation injury; the most common causes of burns were fire (37.8%) and blasts (26.7%). The factor of inhalation injury is less important than the need for intubation for acquiring nosocomial infections, because prolonged mechanical ventilation is strongly associated with pneumonia, wound infections, and bacteremia<sup>15</sup>.

Besides endotracheal intubation, a burned body surface exceeding 50% is strongly associated with the acquisition of nosocomial infections<sup>2</sup>. In this study, the mean percentage of body surface area burned was 30.6%, which was not associated with the presence of multidrug-resistant bacteria.

*Staphylococcus aureus*, *A. baumannii*, and *P. aeruginosa* are the most common multidrug-resistant bacteria in the ICU of the burn unit of the HCFMUSP.

In this study, 18.5% of patients showed positive results in blood cultures for multidrug-resistant *Staphylococcus aureus*. Patients colonized with methicillin-resistant *Staphylococcus aureus* (or methicillin-resistant *Staphylococcus aureus*; MRSA) represent reservoirs for the spread of these bacteria to other hospital departments. However, a greater extent of burns favors colonization by MRSA<sup>7</sup>. Experiences from other burn units attempting to contain MRSA outbreaks show that burn patients are more vulnerable to these bacteria and that it is harder to contain outbreaks in burn units than other ICUs<sup>7</sup>.

Among the patients studied, 9% indicated the presence of multidrug-resistant *P. aeruginosa* in their blood culture. Morbidity and mortality associated with *Pseudomonas* infections in burn patients are higher in some studies than in the present study<sup>16</sup>. However, this study found no increase in mortality due to multidrug-resistant bacteria, although such infections were associated with morbidity and prolonged hospitalization. Environmental reservoirs represent a major factor in the spread of *Pseudomonas*. In such cases, the prevention of barrier contact, patient isolation, and restricting visits are very effective<sup>16</sup>. It is assumed that restricting antibiotics from being prescribed prior to confirmation by blood culture is also a way to contain the spread of *P. aeruginosa*.

*Acinetobacter baumannii* was present in 6.2% of patients in this study and was multidrug resistant in 72.7% of cases. The high prevalence of *Staphylococcus aureus* and *P. aeruginosa* identified in this study is similar to other studies<sup>1</sup>. However, the high incidence of *A. baumannii* in our center contrasts with the literature but is consistent with a study conducted in a hospital in Singapore. The authors of that study suggest the hot and humid climate is responsible for the increased colonization and nosocomial infection<sup>2</sup>. Other studies report on endemic *A. baumannii* in Hong Kong<sup>17</sup> as well as increases in *A. baumannii* infections in hospitals in France<sup>18</sup> and England<sup>19</sup> in the summer months.

Some initial steps must be taken to contain the spread of these bacteria, such as training health professionals to improve the practice of appropriate aseptic techniques for handling these patients, identifying environmental reservoirs (e.g., stethoscopes, cuffs, injection pumps, etc.), screening for the colonization of patients, preventing cross-infection, and reinforcing the importance of barrier contact (i.e., aprons, gloves, masks, and caps). However, these measures alone are insufficient. Although limited, restricting the use of antibiotics has been shown to be effective<sup>20</sup>.

At the time of the identification of multidrug-resistant bacteria in the blood culture of a critically ill patient, initial regimens of antibiotics (mixed or not) with increasingly larger spectra<sup>11</sup> and even some unusual antibiotics are administered<sup>21</sup>. This can lead to a vicious cycle by selecting increasingly multidrug-resistant strains.

## CONCLUSIONS

The presence of multidrug-resistant bacteria is a major problem because of its prevalence and associated morbidity and mortality.

This study shows the resistance profiles of bacteria found in the blood cultures of patients in an ICU burn unit, which can guide better treatment and the rational use of antibiotics.

## REFERENCES

1. Santucci SG, Gobara S, Santos CR, Fontana C, Levin AS. Infections in a burn intensive care unit: experience of seven years. *J Hosp Infect.* 2003;53(1):6-13.
2. Chim H, Tan BH, Song C. Five-year review of infections in a burn intensive care unit: high incidence of *Acinetobacter baumannii* in a tropical climate. *Burns.* 2007;33(8):1008-14.
3. Wahl WL, Arbabi S, Zaleski C, Wang SC, Hemmila MR. Intensive care unit core measures improve infectious complications in burn patients. *J Burn Care Res.* 2010;31(1):190-5.
4. Thabet L, Messadi A, Mbarek M, Turki A, Meddeb B, Ben Redjeb S. Surveillance of multidrug resistant bacteria in a Tunisian hospital. *Tunis Med.* 2008;86(11):992-5.
5. Simor AE, Lee M, Vearncombe M, Jones-Paul L, Barry C, Gomez M, et al. An outbreak due to multiresistant *Acinetobacter baumannii* in a burn unit: risk factors for acquisition and management. *Infect Control Hosp Epidemiol.* 2002;23(5):261-7.
6. Lamia T, Bousselmi K, Saida BR, Allah MA. Epidemiological profile and antibiotic susceptibility of *Pseudomonas aeruginosa* isolates within the burned patient hospitalized in the intensive care burn unit. *Tunis Med.* 2007;85(2):124-7.
7. Safdar N, Marx J, Meyer NA, Maki DG. Effectiveness of preemptive barrier precautions in controlling nosocomial colonization and infection by methicillin-resistant *Staphylococcus aureus* in a burn unit. *Am J Infect Control.* 2006;34(8):476-83.
8. Edgar P, Mlcak R, Desai M, Linares HA, Phillips LG, Heggers JP. Containment of a multiresistant *Serratia marcescens* outbreak. *Burns.* 1997;23(1):15-8.
9. Agência Nacional de Vigilância Sanitária. Investigação e controle de bactérias multirresistentes. Brasília: ANVISA; 2007. 21p.
10. Zedler S, Bone RC, Baue AE, von Donnersmarck GH, Faist E. T-cell reactivity and its predictive role in immunosuppression after burns. *Crit Care Med.* 1999;27(1):66-72.
11. Nseir S, Di Pompeo C, Diarra M, Brisson H, Tissier S, Boulo M, et al. Relationship between immunosuppression and intensive care unit-acquired multidrug-resistant bacteria: a case-control study. *Crit Care Med.* 2007;35(5):1318-23.
12. Ayliffe GA, Green W, Livingston R, Lowbury EJ. Antibiotic-resistant *Staphylococcus aureus* in dermatology and burn wards. *J Clin Pathol.* 1977;30(1):40-4.
13. Williams FN, Herndon DN, Hawkins HK, Lee JO, Cox RA, Kulp GA, et al. The leading causes of death after burn injury in a single pediatric burn center. *Crit Care.* 2009;13(6):R183.
14. Vandijck DM, Depaemelaere M, Labeau SO, Depuydt PO, Annemans L, Buyle FM, et al. Daily cost of antimicrobial therapy in patients with intensive care unit-acquired, laboratory-confirmed bloodstream infection. *Int J Antimicrob Agents.* 2008;31(2):161-5.
15. Wurtz R, Karajovic M, Dacumos E, Jovanovic B, Hanumadass M. Nosocomial infections in a burn intensive care unit. *Burns.* 1995;21(3):181-4.
16. Kerr KG, Snelling AM. *Pseudomonas aeruginosa*: a formidable and ever-present adversary. *J Hosp Infect.* 2009;73(4):338-44.
17. Siau H, Yuen KY, Wong SS, Ho PL, Luk WK. The epidemiology of acinetobacter infections in Hong Kong. *J Med Microbiol.* 1996;44(5):340-7.
18. Fournier PE, Richet H. The epidemiology and control of *Acinetobacter baumannii* in health care facilities. *Clin Infect Dis.* 2006;42(5):692-9.
19. McDonald LC, Banerjee SN, Jarvis WR. Seasonal variation of acinetobacter infections: 1987-1996. *Nosocomial Infections Surveillance System.* *Clin Infect Dis.* 1999;29(5):1133-7.
20. Leverstein-van Hall MA, Fluit AC, Blok HE, Box AT, Peters ED, Weer-

sink AJ, et al. Control of nosocomial multiresistant Enterobacteriaceae using a temporary restrictive antibiotic agent policy. *Eur J Clin Microbiol Infect Dis.* 2001;20(11):785-91.

21. Gang RK, Sanyal SC, Mokaddas E, Lari AR. Rifampicin as an adjunct to vancomycin therapy in MRSA septicaemia in burns. *Burns.* 1999; 25(7):640-4.

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