Risk factors associated with bacteremia in burn children admitted to a specialized pediatric intensive care unit: A case-control study

Hugo Basílico, M.D.[a], Sebastián García, M.D.[a] and Lucas Pintos, M.D.[a]

ABSTRACT

Introduction. Infections due to bacteremia in burn patients are a common cause of complications and an extended length of stay. Knowing causative microorganisms and identifying associated risk factors allow to reduce infectious complications, morbidity, mortality, and health care expenditure. This study assesses the extent of the association between risk factors and bacteremia in burn patients and identifies the most common microorganisms found in blood cultures.

Population and methods. Case-control study conducted at the Burn Intensive Care Unit of Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan" between June 1st, 2014 and September 30th, 2019 in patients with bacteremia events and a positive blood culture (cases) and patients with a negative blood culture (controls).

Results. During the study period, 29 cases of bacteremia were identified. The median length of stay at the time of bacteremia was 23 days. The most commonly identified microorganism was *Pseudomonas* (7 cases). The only risk factor that showed a significant association was the presence of a central venous line for 7 days or more (OR: 3.18; 95 % confidence interval: 1.20-8.38). The overall mortality rate was 9.1%; 13.8% for cases and 3.4% for controls.

Conclusions. Central venous lines for more than 7 days are an independent risk factor for bacteremia in critically ill burn children. No statistically significant association was established with other studied risk factors. *Pseudomonas*, *Acinetobacter*, and coagulase-negative *Staphylococcus* were the most common microorganisms found in bacteremia.

Key words: *bacteremia, burn injuries, infections, morbidity, mortality.*

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a. Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan," Autonomous City of Buenos Aires, Argentina.

E-mail address:
Sebastián García, M.D.: seba_garcia2003@hotmail.com

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INTRODUCTION

Approximately 75 % of pediatric patients with burns are younger than 5 years; the main place where burns occur is their home. The most common etiology are hot liquids among children younger than 4 years and direct fire among older children.[1]

Infections are a cause of complications and a longer length of stay.[2] In addition, they are still a significant cause of morbidity and mortality and, although mortality has decreased as a consequence of advances in clinical and surgical management and complication prevention, mortality secondary to infection from a burn injury is still very high[3] and is the main cause of mortality among burn patients.[4]

Infections are common due to the damage in the skin barrier, the destruction of the local flora, and the alteration of immunity resulting in favorable conditions for bacterial colonization and the development of treatment-resistant microorganisms.[5] Patients become colonized by endogenous microorganisms from the skin, the gastrointestinal tract or the airways. Among hospitalized patients, colonization may occur in the hospital setting and involve multidrug-resistant microorganisms. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae* are the most frequent ones.[6-8] Bacteremia is usually the result of the invasion of microorganisms in the skin, although it may also develop at the time of a surgical debridement or due to central venous line colonization, urinary tract infection or bacterial translocation from the respiratory tract.[9] The American Burn Association (ABA) criteria for the diagnosis of sepsis

(3 or more of the following criteria: temperature > 39 °C or < 36.5 °C, progressive tachycardia, progressive tachypnea, thrombocytopenia, hyperglycemia, and feeding intolerance) have a limited correlation with the presence of bacteremia confirmed by blood culture, with a 78.2 % sensitivity and a 49.5 % specificity.[10,11]

The objective of this study was to assesses the extent of the association between risk factors and bacteremia in burn patients, and identify the most common microorganisms found in blood cultures and their respective antibiotic sensitivity.

POPULATION, MATERIALS, AND METHODS

Study conducted at the Burn Intensive Care Unit of Hospital de Pediatría S.A.M.I.C. "Prof. Dr. Juan P. Garrahan" in the Autonomous City of Buenos Aires between June 1st, 2014 and September 30th, 2019.

Design: Prevalent case-control study. Data were collected retrospectively from electronical medical records.

Inclusion criteria

- **Cases:** Patients aged 0-17 years and 11 months who, during hospitalization, developed bacteremia (positive blood culture) in the study period.
- **Controls:** Patients aged 0-17 years and 11 months admitted to the pediatric intensive care unit (PICU) in the same period with a negative blood culture that had been obtained for suspected bacteremia. Data were collected from the electronic medical records of all patients who developed bacteremia as reported by the Department of Epidemiology and Infectious Diseases and controls were randomly selected among the patients with a negative blood culture in a 1:2 case-control ratio.

Exclusion criteria

Bacteremia event confirmed in a different facility; ignorance of number of days since venous line placement or about admission to the operating room in the previous 24 hours in patients referred from another facility.

Description of outcome measures

- Dependent outcome measure (bacteremia): presence of isolated microorganism in blood culture in the 5 days after collecting the sample.
- Independent outcome measures (exposure): age in months, body surface area burned (percentage of damaged skin), length of stay (days since admission to our hospital), urinary catheter (presence or absence), time since placement and site of central venous line (7 days or less and more than 7 days, and anatomic site of insertion), mechanical ventilation (MV) (days of MV), immediate surgery (admission to the operation room 24 hours prior to bacteremia development).

Statistical analysis: Data were collected from the electronic medical records of patients who developed bacteremia as reported by the Department of Epidemiology and Infectious Diseases and controls' medical records were randomly selected. Qualitative outcome measures were compared using a χ^2 test, whereas quantitative ones with a normal distribution were compared using Student's t test and those with an asymmetrical distribution, with Wilcoxon's test. Odds ratios (ORs) were estimated to assess the extent of the association with risk factors. Data were processed with the InfoStat®, version 2020 (Universidad Nacional de Córdoba) and Epidat®, version 4.1 (Pan American Health Organization) software programs.

Bias control: All cases of bacteremia reported in the epidemiological surveillance sheets were identified and controls were randomly selected in compliance with the inclusion and exclusion criteria mentioned above for both groups.

Ethical aspects: This study was conducted in compliance with the laws and regulations in force in relation to ethical review guidelines and was approved by the hospital's Research Committee. Data were collected using encrypted identifiers and protecting patient identity. Given the observational and retrospective nature of the study, informed consents were not required.

RESULTS

During the study period, 230 burn patients were hospitalized, 61 % were males; the median age of the study population was 32 months, with a range between 2 months and 14 years. *Table 1* describes the characteristics of cases and controls. A total of 29 bacteremia events were diagnosed in 16 patients (6.96 %); 58 controls were selected.

Among patients younger than 12 months, 5 cases of bacteremia (17.8 %) and 6 controls (10.2 %) were identified, but no statistically significant association was established.

The percentage of total body surface area

(TBSA) burned ranged between 15 % and 87 %, with an average of 50 % and a standard deviation (SD) of 20.7, with no statistical differences in terms of number of bacteremia events at the cutoff of 30 % of TBSA burned.

The median length of stay at the time of bacteremia was 23 days, whereas the median use of mechanical ventilation (MV) was 21 days. None of these 2 outcome measures showed a statistically significant association.

The overall mortality rate among patients hospitalized in the study period was 9.1 %; 13.8 % for cases and 3.4 % for controls ($p = 0.003$).

A total of 27 bacteremia events were observed in patients who had a central venous line: 16 for > 7 days and 11 for ≤ 7 days after placement. The statistical analysis showed an association for a duration of central venous line higher than 7 days as a risk factor for bacteremia ($p = 0.017$; 95 % confidence interval [CI]: 3.18-8.38). The most common central venous line site was the femoral vein (74 %), followed by the jugular vein (18.5 %), and the subclavian vein (7.5 %); no association was established between the site of placement and a higher risk for infection (*Table 2*).

TABLE 1. *Case and control characteristics*

Characteristics	Cases (n = 29)	Controls (n = 58)	*p* value
Age (months)	32	113	0.01
Burn (%)	50	35	0.15
MV (days)	21	14	0.11
Length of stay (days)	23	16	0.12
Urinary catheter (%)	90	78	0.16
Mortality (%)	13.8	3.4	0.003
Admission to the operating room (%)	51	62	0.35

MV: mechanical ventilation.

Surgical management was proposed as a risk factor and patients who developed bacteremia in the 24 hours after admission were identified; no statistically significant association was established, as was the case with urinary catheter placement (*Table 3*).

The microorganisms most commonly isolated included *P. aeruginosa* (7 cases), *Acinetobacter* spp. (5 cases), and coagulase-negative *Staphylococcus* (4 cases). *Table 4* shows microbiological isolation by microorganism and site; *S. aureus* was identified only in 3 cases. In relation to resistance to the antibiotics used as initial empiric therapy for suspected sepsis or decompensation, meropenem resistance was considered in Gram-negative microorganisms and methicillin resistance, in Gram-positive ones; only 1 patient showed meropenem-resistant *P. aeruginosa* and there was a single case of methicillin-resistant *S. aureus* (MRSA).

DISCUSSION

A better knowledge of risk factors, etiology, and antibiotic sensitivity in bacteremia cases developed in critically ill burn patients allows to reduce morbidity and mortality. In the studied population, the burned body surface area ranged between 15 % and 87 %, with an average of 50 %, turning the population into critically ill and susceptible to multiple risk factors for infection.

Considering the severity of bacteremia in burn children and the fact that microbiological isolation varies from one facility to another, it is necessary to know the local epidemiology of each institution. In our hospital, the most commonly isolated microorganisms (*P. aeruginosa*, *Acinetobacter*, and *S. aureus*) account for approximately 50 % of cases, which is consistent with reports published by different specialized centers.[8,9,12-14] In a study conducted by Fochtmann-

TABLE 2. *Characteristics of central venous lines*

	Cases	Controls	*p* value	OR (95 % CI)
Duration				
> 7 days	16	1	0.017	3.18 (1.2-8.4)
≤ 7 days	11	35		
Site				
Femoral vein	20	38	0.36	2.10 (0.4-10.9)
Jugular vein	5	7	0.27	2.85 (0.4-19.6)
Subclavian vein	2	6	0.79	1.33 (0.14-2.4)

OR: odds ratio, CI: confidence interval.

Frana et al., bloodstream infections were caused by Gram-negative bacteria (46 %), Gram-positive bacteria (40 %), and fungi (14 %). The most commonly isolated microorganisms were *Enterococcus, Candida, Pseudomonas, Enterobacter, S. aureus*, coagulase-negative *Staphylococcus*, and *Klebsiella*.[12] In 2017, in a referral facility of Colombia, Ramirez-Blanco et al. reported the most commonly found microorganisms: *P. aeruginosa, A. baumannii, Escherichia coli, S. aureus*, and *Klebsiella pneumoniae*; [15] and the results observed were similar to those of our study. However, other studies identified Gram-positive bacteria as the most frequent cause of bacteremia in burn patients (66.4 %), followed by Gram-negative bacteria (22.1 %), and fungi (11.5 %), especially in the first week of admission.[7]

If a severe burn patient suffers a clinical decompensation, an infectious complication should be suspected and cultures should be performed to initiate or extend the antibiotic therapy.[16] An inadequate initial empiric therapy may increase mortality.[17,18] In a study conducted by Devrim et al., 8 out of 9 bacteremia cases evidenced carbapenem-resistant *P. aeruginosa*; 1 isolation of *K. pneumoniae* (12.5 %); 2 cases of positive extended-spectrum beta-lactamase (ESBL)-producing *E. coli* (22.2 %), and 27 out of 70 cases of methicillin resistence.[7] In our study, the rates of resistance to antibiotics used as initial empiric therapy (meropenem-vancomycin) for clinical decompensation were not high.

The systematic change of central venous lines is a controversial recommendation, although

Table 3. *Bivariate analysis of risk factors*

		Cases	Controls	Total	*p* value	OR (95 % CI)
Age	≤ 12 months	6	5	11	0.11	2.76 (0.77-9.98)
	> 12 months	23	53	76		
Admission to the operating room	Yes	15	36	51	0.36	0.65 (0.27-1.61)
	No	14	22	36		
Urinary catheter	Yes	26	45	71	0.17	2.5 (0.65-9.61)
	No	3	13	16		
Length of stay (days)	> 14 days	19	35	54	0.64	1.25 (0.49-3.16)
	≤ 14 days	10	23	33		
MV	> 14 days	14	21	35	0.27	1.64 (0.66-4.06)
	≤ 14 days	15	37	52		
CVL	> 7 days	16	16	32	0.017	3.18 (1.20-8.38)
	≤ 7 days	11	35	46		
Burn surface area	> 30 %	24	46	70	0.7	1.25 (0.39-3.97)
	≤ 30 %	5	12	17		

MV: mechanical ventilation, CVL: central venous line, OR: odds ratio, CI: confidence interval.

Table 4. *Microbiological isolation by microorganism and site*

Microorganism	Blood culture (n = 29)	Skin culture (n = 13)	Catheter tip (n = 12)	Urine culture (n = 5)
Pseudomonas	7	4	3	2
Acinetobacter	5	-	3	1
Coagulase negative *Staphylococcus*	4	4	2	-
S. aureus	3	3	-	-
Enterococcus	2	-	1	1
Klebsiella	2	-	-	-
Serratia	2	-	1	-
Stenotrophomonas	2	1	-	-
Providencia	1	-	1	-
Candida	1	1	1	1

placement for a prolonged time has been identified as a reversible risk factor.[10,12,19] In our hospital, the recommendation is to place a new central venous line every 7 days. Fochtmann-Frana et al. corroborated catheter tip colonization of the central venous line in 200 out of 472 patients (42 %) after a mean of 12 days. For this reason, we believe it is logical, timely, and wise to change the central venous line every week,[12] so as to reduce the risk evidenced in our study (OR: 3.18; 95 % CI: 1.20-8.38). No data have been published in recent years in relation to the cutoff point for the systematic preventive change of central venous lines.

In addition, 13.8 % of patients with bacteremia died, compared to 3.4 % in the control group. Although death is a multi-cause phenomenon,[20,21] patients with a greater burned body surface area, associated infections,[22] and a longer length of stay have a higher mortality rate.[14] Evidently, the high number of bacteremia cases in burn patients is a major problem for specialized centers due to its high morbidity and mortality, higher costs, and longer length of stay. Health care teams face major challenges in the future to reduce morbidity and mortality: knowing the local epidemiology, establishing an initial empiric antibiotic therapy protocol and bundles of measures for the placement and maintenance of central venous lines.[23-25]

It is worth noting that the main limitation of this study was the low prevalence of bacteremia events in the study period, which did not allow us to establish statistically significant associations. A prospective study design, with a larger sample size, where other factors and outcome measures affecting bacteremia can be assessed will allow to obtain statistically significant information and extrapolate data to the susceptible population.

CONCLUSION

In our study, the presence of a central venous line for more than 7 days showed a statistically significant association with bacteremia development; it was not possible to establish an association with other potential risk factors described in the bibliography. *Pseudomonas*, *Acinetobacter*, and coagulase-negative *Staphylococcus* were the most commonly identified microorganisms. ■

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