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Infections in burned children: epidemiological and risk factor analysis

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ABSTRACT

Introduction. Burns are the third cause of accidental deaths among children. Approximately 50-60% of these deaths are the result of an infection.

Objective. To determine infection related risk factors in burned children.

Population and Methods. All patients admitted to the Burn Unit of Hospital "Prof. Dr. Juan P. Garrahan" between June 2007 and December 2009 were included. The epidemiology of hospital-acquired infections and the associated outcome measures were determined. Groups of infected and non-infected children were compared using Student's t test or the Mann-Whitney Rank Sum test, as applicable.

Dichotomous outcome measures were analyzed with the X2 test using Yates' correction. In order to assess the predictive value of independent outcome measures, the multiple logistic regression model was applied.

Results. In this cohort of 110 children, 128 hospital-acquired infections were recorded in 84 patients. There were 17 deaths (15%); 14 out of these 17 (82%) were related to infection. Infection-related factors included the percentage of burned body surface area; the highest Garces' index; burn depth; antibiotic prophylaxis; the use of topical antibiotics; the presence of a central venous line, an arterial line, a urinary catheter, mechanical ventilation support, escharotomy, and the need of a graft. The multivariate analysis showed a higher risk of infection with the use of central venous lines (RR: 5.15; 95% CI: 1.44-18.46), antibiotic prophylaxis (RR: 5.22; 95% CI: 1.26-21.63), and graft requirement (RR: 3.65; 95% CI: 1.08-12.37).

Conclusions. The presence of lines or catheters, antibiotic prophylaxis, and graft requirement were independent risk factors for infection in burned children.

Key words: *burned, infections, children.*

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INTRODUCTION

According to the Argentine Burn Association, the annual incidence of burns in Argentina is 5/1000, and accounts for the third cause of they account death among children.[1]

Infection leads to death in 50-60% of burned patients.[1-3] The identification of risk factors for infection, understudied in children, would enable the implementation of measures aimed at reducing their incidence.[1]

Our main objective was to assess risk factors of hospital-acquired infections in burned children and to determine the epidemiology of these infections in this population.

POPULATION AND METHODS

Prospective cohort of all burned pediatric patients admitted to the Hospital "Prof. Dr. Juan P. Garrahan" between June 2007 and December 2009.

Children aged from 1 month to 18 years old admitted to the burn unit due to any degree burns with one week evolution were included.

Patients with infection at the time of admission were excluded.

Independent outcome measures were: age in months; sex; type of burn: superficial or A, intermediate or AB, and deep or B; cause of burn (fire, hot liquids, electrical, others); burned surface area expressed as a percentage of the body surface area; history of event related hospitalization, including days, type and duration of prophylactic antibiotic therapy used at the time of admission to this hospital, and type of treatment (surgical, topical or systemic antimicrobial therapy); use and length of balneotherapy; use of mechanical ventilation support; central or peripheral lines; parenteral nutrition, and length of treatment with each of these procedures.

The primary dependent outcome measure was the presence of a hospital-acquired infection. A hospital-acquired infection was defined as an infection developed in the 48 hour period following the admission to a hospital and not

present at the time of admission.

The secondary outcome measures were:

a. Type of microorganism.
b. Length of treatment in days.
c. Progress. In case of death, progress was considered related to the infection if death occurred in the presence of positive cultures or clinical signs of infection.
d. Length of hospital stay.

Definitions

Garces' index: [1-3] this a severity and mortality prediction index calculated as follows: 40 minus patient's age, plus burn percentage, multiplied times 1 (if type A burn), times 2 (if type AB burn), or times 3 (if type B burn).

From 0 to 60 points: grade 1 (mild risk).
From 61 to 90 points: grade 2 (moderate risk).
From 91 to 120 points: grade 3 (severe risk).
Over 121 points: grade 4 (critical risk).

Inhalation syndrome: suspected: if the patient exposed to smoke or heat had a nasal or mouth burn, carbonaceous sputum, dysphonia, cough, rales, nasopharyngeal erythema or edema, or carbon monoxide poisoning; certain: if the patient's fibrobronchoscopy shows a lesion in the respiratory tract mucous membrane.

Type of infections: according to the American Burn Association (ABA),4 the following types of infections have been defined: a) burn wound infection: if there were local signs of infection or a positive microbiological culture in viable tissue samples; b) sepsis associated with a burn wound: if there was evidence of a wound infection and concurrent organ failure; c) line or catheter-associated infection: presence of positive blood culture in patients with a central line with no other apparent cause of infection.

Statistical Analysis

The SPSS software for Windows, version 11.5, was used. Logistic regression was performed applying the forward stepwise method. In order to assess differences between groups in terms of continuous outcome measures, Student's t test or the Mann-Whitney Rank Sum test was used, as applicable, with the outcome distribution.

The X2 test was used for dichotomous outcome measures (with Yates' correction). For the assessment of the predictive value of independent outcome measures, a multiple logistic regression model integrating outcomes that showed an association with a <20% confidence interval to the specified endpoint was used. The power of the association between outcome measures was expressed as relative risk (RR).

RESULTS

A hundred and ten patients participated, and their clinical and epidemiological characteristics are summarized in Table 1. In relation to invasive procedures, 90 patients (82%) had a venous line, with a mean dwell time of 16.5 days (r: 1-90); 83 patients (75.5%) had an arterial line (mean: 16 days; r: 1-87 days), and 86 patients (78%) had a urinary catheter (mean: 16 days; r: 1-80). Only 1 patient (1%) required parenteral feeding during 7 days. A total of 75 patients (68%) required mechanical ventilation, with a mean use of 14 days (r: 1-180). Balneotherapy was used in 93 patients (85%) during 7 days (mean: 7 days; r: 1-44). Topical antibiotics were prescribed in 95 patients (86%), while 92 (84%) received systemic antibiotics, either as prophylaxis or treatment. Colistin was used in 68 children (62%).

In total, 128 hospital-acquired infections were recorded in 84 patients; the most common clinical presentation was burn-related sepsis. Bacterial infections accounted for the most frequent type of infections, the multidrug-resistant Gram-negative bacteria, *Pseudomonas aeruginosa* and *Acinetobacter spp.*, were the most commonly isolated bacteria. The (mean) time until development was 10 days (r: 2-84). The most common fungal infections were caused by *Candida albicans* and *no albicans*, and in this case, the (mean) time until development was 10.5 days (r: 2-60). *S. aureus* was the most common Gram-positive bacteria (mean time until isolation: 6.5 days; r: 2-56) (see *Table 2*).

A baseline escharotomy was performed in 90 patients (82%; mean: 5 days; r: 1-19). A total escharotomy was completed at 5 days (r: 1-45). Eighty-two patients (74.5%) required a graft, with a mean of 17 days (r: 1-81).The median hospital length of stay was 37 days (r: 1-139).

A total of 93 patients (85%) were discharged, and 17 patients (15%) died. The cause of death was related to the infection in 14 of these cases (82%).

A bivariate analysis of infected and non-infected patients showed no significant differences between both groups in terms of age ($p = 0.079$), distribution by sex ($p = 0.131$), burn etiology (mechanism) ($p = 0.216$), location of the burn injury ($p = 0.07$), or the presence of an inhalation syndrome ($p = 0.139$).

The percentage of burned body surface area, a higher Garces' index, and the type of burn

(depth) showed a significant association with the development of an infection; type B burns had the highest risk of infection.

Antibiotic prophylaxis was observed to be related to the development of an infection, as well as the use of topical antibiotics, the presence of a central venous line, an arterial line, a urinary catheter, mechanical ventilation, an escharotomy, and graft requirement. Significant differences were found in the number of days until a complete graft placement between the patients with and without infection (p= 0.026).

The non-infected group completed the graft placement on day 10, in average, versus 22.5 days in the infected group. The mean difference was 12 days (95% CI: 5-20). Balneotherapy was associated with a higher risk of infection (see *Table 3*).

Multivariate Analysis

By integrating all significant outcome measures used in the bivariate analysis, it was possible to establish that the use of central venous lines, antibiotic prophylaxis, and graft requirement were independent risk factors for infection (*see Table 4*).

DISCUSSION

Infections in burned patients are a determining factor of morbidity and mortality; therefore, it is important to know which factors are associated with the development of infections in children, a population in whom studies are scarce.

Patients' age has been suggested as a risk factor of infection in children, but as commented by Rodgers, et al.,[2] in our study, patients' age did not play this role. Although men had a higher risk of infection in a series of adult patients, this was not observed in our study.[5]

The risk of infection is higher when the burned body surface area is over 30% due to the associated immune complications,[2-6] but it was not an independently associated factor in this series.

Patients with a higher Garces' index were more prone to infection. Garces' index considers, among other parameters, age, surface and depth of burn; therefore, by including these outcome

TABLE 1. *Characteristics of patients (n: 110)*

Outcome measure	*n* (patients)	Percentage	Median
Age			31.5 months old (r: 1-24 months old)
Male	71	66	
Underlying disease	6	5	
Burn mechanism	Fire: 43	39	
	Liquid: 31	28	
	Others: 36	33	
Burned surface area			27% (r: 1-95%)
Garces' index			
1	14	13	
2	39	35	
3	24	22	
4	33	30	
Type of burn			
A	39	36	
AB	19	17	
B	52	47	
Inhalation syndrome	52	47	
Antibiotic prophylaxis	92	85	
Invasive procedures:			
Venous line	90	82	
Arterial line	83	75	
Urinary catheter	86	78	
MV	75	68	
Balneotherapy	93	85	

measures, depth would not be a risk factor by itself.

Burns in the lower limbs or the perianal area have been considered to be more prone to infection, but as in Rodgers, et al.[2] paper, in our study the location of the burn was not related to infection.

The presence of inhalation syndrome has been related to infections, especially respiratory infections. However, this is more common in adults with a higher rate of burns by fire than in children, who usually suffer hot liquid burns. This is confirmed by our study given that patients with this type of burns did not have a higher risk.[6-10]

Line or catheter-related infectious complications are very common. The incidence of line or catheter related infections in critical patients is variable, with an incidence rate of 2-30 episodes due to bacteremia for every 1000 days of catheter use. In this study, the presence of a line or catheter was an independent risk factor for infection and, since this could be a modifiable risk factor, prevention measures should be maximized at the time of line or catheter insertion and while the vascular access is maintained. It has been attempted to prevent infections with the use of antibiotic-impregnated lines or catheters, more frequent line or catheter replacements, a strict control of the insertion procedure, among other measures; results have been variable.[11-14]

Ramos, et al.[15] conducted a study to evaluate the relationship between the line or catheter-insertion distance to the burned area and infection in adults. Colonization was registered more frequently in the catheter close to the burned area; so Ramos, et al. concluded that the line or catheter should not be inserted near the burned area or replacements should be more frequent.

In pediatric patients, this is complicated by the lack of venous accesses and burn extension on the child's total body surface area. A periodic replacement of IV lines has also been proposed as prevention of related bacteremias. However, the systematic rotation of lines or catheters is controversial.[16] Kowalewska-Grochowska, et al.[17] compared line or catheter removal on Day 7 versus line or catheter replacement using a guidewire on Day 3 and removal on Day 7, but no significant differences were observed.

Mechanical ventilation has been related to ventilator-associated pneumonia in critical patients; in our study, it was not an independent risk factor for infection.[2,11]

Urinary catheter is associated with the risk of urinary tract infection. Among our patients, it was not an independent risk factor for infection.

Balneotherapy can be a potential source for microorganism transmission, which could be avoided if recommendations for prevention were adequately followed.[18] In this study, balneotherapy was not an independent risk factor for infection.

The escharotomy of necrotic tissue has been indicated as a protection factor against infection. Lloyd, et al.[19] reported that the incidence of sepsis decreased from 6% to 1% with an early incision, and confirmed a significant reduction of mortality with an early escharotomy when compared to conventional surgical management. In these patients, escharotomy was not an independent risk factor, probably due to the higher number of necessary procedures and the possibility of bacteremia secondary to the escharotomy, or because the non-infected group had this procedure performed earlier.

One of the challenges in burn units at the time of preventing infections is the adequate use of antibiotics, whether topical or systemic.[20,21] The study conducted by Ergün, et al.[22] was not able to demonstrate that systemic antibiotic prophylaxis could prevent infections. On the contrary, it was related to higher rates of infection, which is consistent with the observations of this series. Rodgers, et al.[23] concluded that, in children, the use of perioperative antibiotics is not beneficial.

A graft is considered as the best definitive treatment and has proven to be useful for infection prevention.[27-29] Graft requirement was an independent predictive factor for infection in our patients.

However, since this is correlated with burn depth and a greater burned body surface area, it could be concluded that these factors would be related to the fact that the graft was not a protection factor against infection or that, in average, the graft was placed later in the infected group.

Reported mortality varies between 3.5% and 7%, and infections are the main cause of death in burn units.[30] The high mortality rate (15%) in these patients could be attributed to the fact that our facility is a referral center for critical patients and, among them, infection was the leading cause of death.

Although the sample size is not large enough for some of the studied outcome measures to make definitive conclusions, we believe that since this is, as far as we know, the first study

about risk factors for infection in pediatric burned patients conducted in Argentina, these findings are greatly significant and serve as the foundation to continue gathering patients to involve a larger population. Nonetheless, this is a referral tertiary care center and data obtained could correspond to a group of patients with a more severe status and could not be extrapolated to the entire population of burned children.

CONCLUSIONS

In this study, the presence of venous lines, antibiotic prophylaxis, and graft requirement were independent risk factors for infection in burned children.■

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ELECTRONIC ANEX

TABLE 2. *Sources of infection and etiologic agents (n: 128 sources in 84 patients)*

Source	n (%)	Microorganismganism	*n*
Sepsis associated to burn wound	48 (37)	**Gram-negative bacilli**	
		MDR *Pseudomonas aeruginosa*	21
		MDR *Acinetobacter* sp.	20
		Stenotrophomonas maltophilia	4
		Enterobacter aglomerans	3
		Escherichia coli	3
		Serratia	2
		Klebsiella pneumoniae	2
		Burkhordelia	1
		Non-fermenting Gram-negative bacillus	1
		Gram-positive	
		MR *Stahylococcus aureus*	8
		MS *Stahylococcus aureus*	5
		Enterococcus faecium	6
		Bacillus spp.	1
		Nocardia	1
		Fungi	
		Candida albicans	5
		Non-typified filamentous	4
		Non-typified no albicans	3
		Candida guillermondie	2
		Trichosporum asahi	2
		Candida tropicalis	1
		Candida lusitanae	1
		Candida glabrata	1
		Mucor	1
Burn wound infection	29 (23)	**Gram-negative bacilli**	
		MDR *Pseudomonas aeruginosa*	9
		MDR *Acinetobacter* sp.	5
		Klebsiella sp.	2
		Enterobacter aglomerans	1
		Alcaligenes xiloxosidans	1
		Gram-positive	
		MR Stahylococcus aureus	4
		MS Stahylococcus aureus	2
		Bacillus sp.	3
		Corynebacterium sp.	2
		Enterococcus sp.	1
		S. pyogenes	1
		Fungi	
		Fusarium	5
		Aspergillus fumigates	5
		Alternaria sp.	3
		Candida albicans	1
		Candida tropicalis	3
		Aureobasidium pullulans	1
		Dreschelera	1
		Non-typified filamentous	1
		Penicilium	1
		Mucor	1
		Rodhotorula	1

Line or catheter-associated infection	11 (8,5)	**Gram-negative bacilli**	
		MDR *Pseudomonas aeruginosa*	3
		MDR *Acinetobacter* sp.	1
		Klebsiella pneumoniae	1
		Serratia marcescens	1
		Alcaligenes xylosoxidans	1
		Gram-positive	
		MS *S. aureus*	1
		Enterococcus faecium	1
		Bacillus sp.	1
		Fungi	1
		Candida albicans	3
		Candida parapsilopsis	3
		Candida no albicans	1
Urinary tract infection associated with urinary catheter	15 (12)	**Gram-negative bacilli**	
		MDR *Pseudomonas aeruginosa*	7
		Enterobacter aglomerans	2
		Klebsiella pneumoniae	1
		MDR *Acinetobacter* spp.	1
		Fungi	
		Candida albicans	3
		Candida tropicalis	1
MV-associated pneumonia	8 (6)	**Gram-negative bacilli**	
		MDR *Pseudomonas aeruginosa*	6
		MDR *Acinetobacter* sp.	2
		Klebsiella pneumoniae	1
		Alcaligenes xylosoxidans	1
		Positive cocci	
		MDR *S. aureus*	1
		Fungi	
		Candida albicans	2
Osteomyelitis	5 (4)	MDR *S. aureus*	2
		Enterococcus faecalis	2
		MDR *Pseudomonas aeruginosa*	1
Pneumonia	4 (3)	*Streptococcus pneumoniae*	1
		Negative cultures	3
Corneal abscesses	3 (2)	MDR *Pseudomonas aeruginosa*	3
Chondritis	2 (1.5)	MDR *Pseudomonas aeruginosa*	2
Toxic shock	1 (1)	*Streptococcus pyogenes*	1
Probable endocarditis	1 (1)	MDR *Acinetobacter* spp.	1
Burn zoster rash	1 (1)	Varicella-zoster virus	1

MR: multi-drug resistant; MR: methicillin-resistant; MS: methicillin-sensitive.

TABLE 3. *Bivariate analysis (n: 110 patients)*

Outcome measure	**Infected n (%)**	**Non-infected n (%)**	**Total n (%)**	**RR (95% CI)**	***p***
Type B burn	47 (43)	5 (4)	52 (47)	1.42 (1.14-0.75)	<0.001
Percentage of burned body surface area	Md 34%	Md 19%		Difference CI (5-25%)	<0.0001
Systemic antibiotic prophylaxis	79 (72)	13 (12)	92 (84)	3.09 (1.46-6.54)	<0.0001
Topical antibiotics	78 (71)	17 (15)	95 (86)	2.05 (1.10-3.84)	<0.01
Venous line	77 (70)	13 (12)	90 (82)	2.44 (1.34-4.47)	<0.0001
Arterial line	72 (65)	11 (10)	83 (75)	1.95 (1.27-3)	<0.0001
Urinary catheter	73 (66)	13 (12)	86 (78)	1.85 (1.19-0.89)	<0.0001
Mechanical ventilation	64 (58)	11 (10)	75 (68)	1.49 (1.10-0.02)	<0.01
Escharotomy	77 (70)	13 (12)	90 (82)	2.44 (1.34-0.47)	0.0001
Graft requirement	71 (64.5)	11 (10)	82 (74.5)	2.05 (1.33-0.17)	0.0001
Balneotherapy	78 (71)	15 (14)	93 (85)	5.92 (2.43-4.46)	0.0001

TABLE 4. *Multivariate analysis of infection risk*

Outcome measure	**RR**	**95% CI**	***p***
Central venous line	5.15	1.44-18.46	0.012
Antibiotic prophylaxis	5.22	1.26-21.63	0.023
Graft requirement	3.65	1.08-12.37	0.038