Clinical and microbiological characteristics of bloodstream infections in a tertiary hospital in Maceió, Alagoas, Brazil

ABSTRACT

We observed the clinical and microbiological characteristics of several stages of bloodstream infections (BSI), as well as the mortality attributed to it in a tertiary hospital in the northeast of Brazil (in the city of Maceió, Alagoas). A prospective cohort of 143 patients who had at least one positive blood culture was enrolled in the study. Their clinical evolution was followed up for 30 days from October 2005 to December 2006. The relation among the qualitative variables was verified through Chi-square test. The significance level was 5%. The statistical package adopted was SPSS 15.0 for Windows. Up to the thirtieth day, 30.1% of the patients presented bacteremia and 69.9% developed sepsis. Among these, 20.3% developed severe sepsis and 10.5% septic shock. The mortality attributed to it was 37.8%. In bacteremia, sepsis, severe sepsis, and septic shock conditions, mortality rates were 9.3%, 50%, 65.5%, and 84.6%, respectively. Respiratory (32.2%) and urinary (14%) sources and the ones related to central venous catheter (14%) were prevalent. In the wards 55.12% of the cases developed sepsis, whereas in the intensive care units, the rate was 87.69% ($p < 0.05$). Chronic renal failure, diabetes melitus, and neuropathy were present in 21.7%, 26.6%, and 29.4% of the cases, respectively. Coagulase-negative *Staphylococcus* (25.9%), *Staphylococcus aureus* (21%), and *Klebsiella pneumoniae* (14%) were the most present microorganism in the sample. The high morbidity and mortality rates in this study are attributed to the lack of knowledge on BSI characteristics and on instituted protocols for detection and treatment in early stages.

Keywords: bloodstream infections, blood cultures, bacteremia, spesis.

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INTRODUCTION

The aging process of the population combined with technological advances and survival quality of immunosuppressed and severely ill patients has led to a significant increase in the incidence of mortality due to bloodstream infections (BSI) in recent years, posing major problems to public health all over the world, both economically and socially.[1-4]

However, the actual impact of such disease has not been widely established in distinct communities. It is mandatory that specialists in the area collect epidemiological data in order to provide authorities and health professionals contextualized and more based information regarding the extent of problem locally. The concern among health professionals about using empirical therapeutics of large spectrum, due to lack of knowledge about evolution, the clinical and microbiological characteristics of such infections in our hospitals worsened microbial resistance of adverse events and increased costs related to it, most of the time without decreasing morbidity and mortality of patients harmed by disease.

Besides the classic clinical condition, sepsis may present as severe sepsis and septic shock. Some knowledge about the definition criteria of the different stages of sepsis among physicians is primordial, once it can promote an early diagnosis, immediate treatment, and contributes positively in the prognosis of BSI patients.[5,6] Septic shock and multiorgan dysfunction are the most common causes of death in patients with sepsis. The mortality rates associated with severe sepsis and septic shock described in literature are 25% to 30% and 40% to 70%, respectively.[7,8]

Localizing the source of infection is primordial, considering that the mortality rate may vary between 15.4% and 41.2%, depending on its origin,[9] and that empirical antibiotics

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therapy will differ according to the site of infection.[10] The elderly, immunocompromised, diabetic, individuals with dialytic chronic renal failure, alcoholics, and patients admitted in the intensive care unit (ICU) are the main groups at risk of developing such infections.[11]

In this study, we evaluated the clinical and microbiological characteristics of BSI in patients admitted in a tertiary hospital in the northeast of Brazil that attends about 49,000 patients per year in its emergency unit. It has 330 beds, of which 47 is for adult and pediatric intensive care units (ICU). The incidence of BSI in 2006 was 41.34 cases in 1,000 discharges. Published data reported lower rates in American hospitals, although they have registered an increase from 5% to 14% in the last past two decades,12 raising incidence density from 2-4 episodes to 15-20 per 1,000 discharges.

The high incidence of BSI and the lack of knowledge of its clinical and microbiological characteristics according to its distinct evolutive stages motivated us to carry out this research. The aim of this study is to establish the epidemiological profile of such infections in order to guide towards measures to reduce the incidence and mortality due to BSI in our setting.

MATERIAL AND METHODS

We carried out a study of prospective panel in which we assessed 143 patients with positive blood cultures, in a tertiary hospital in Maceió, Alagoas, northeast of Brazil, from October 2005 to December 2006. Patients of all ages and both genders who were admitted to medical wards and ICU were enrolled in the study. They presented at least one positive blood culture and remained in the hospital for at least 24 hours. Sixty five cases of positive blood culture of patients who were either transferred or died within the first 24 hours of evolution, or yet had not signed the informed consent were excluded. The identification data, characteristics, and disease evolution were recorded systematically up to the thirtieth day of evolution in a protocol developed for this very purpose and then submitted to statistical studies. The definitions for sepsis and its variations were in accordance with the American College of Physicians and the Society of Critical Care Medicine, 1991.[13] The adult ICU patients were grouped in 5 categories: A, B, C, D, E, whose estimated risks are 4.9%, 11.5%, 25.1%, 29.9%, and 42.4%, respectively, according to the prediction system for infection risk "Average Score of Illness System" (ASIS), modified by Pinheiro.[14]

Descriptive analysis of all variables in the study was performed. Qualitative variables were presented in terms of their absolute and relative values. Quantitative variables were presented according to their central tendency and dispersion. In order to verify the relationship among the qualitative variables, Chi-square test was applied. The level of significance was 5%. The statistical package was SPSS15.0 for Windows. This study was approved by the UNCISAL Research Ethics Committee under the protocol number 430.

RESULTS

Table 1 shows demographic characteristics of the sample, such as gender, age, and origin, number of samples analyzed, kind of clinical condition, and place of admission.

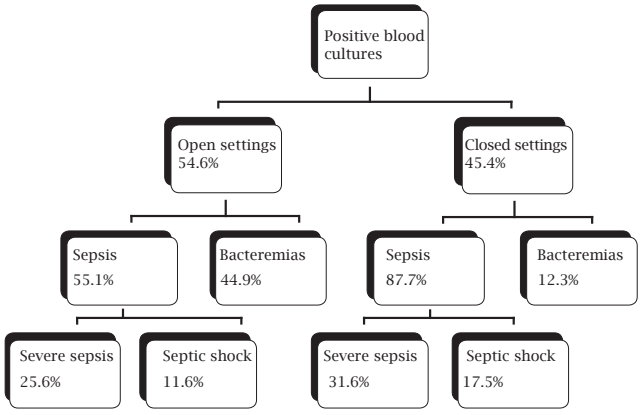
The episodes of bacteremia or candidemias in the study meant 68% in all positive culture recorded in the headquarters hospital in the research during the period studied. Among the specialties that contributed to the casuistic, the most prevalent were neurology, cardiology, medical clinic and oncology, corresponding to 67.9% of the overall analyzed.

It was observed that 55.12% of the patients with positive blood culture developed sepsis in the open settings (individual rooms and wards), whereas in the closed setting (ICU), this rate increased significantly to 87.69% ($p < 0.05$). Among these 14.10% developed severe sepsis in the open settings, whereas in the ICU, 27.69% evolved to such complication ($p < 0.05$). Septic shock was present in 6.41% of the patients admitted in the open units and in 15.34% in closed units ($p < 0.05$) (Figure 1).

Table 1. Demographic characteristics of the sample studied (n = 143 patients related to 68% of overall positive samples). Santa Casa de Misericórdia de Maceió from October 2005 to December 2006

Variable	n	%
Gender	Male	60.1
	Female	39.9
Clinic	Medical	76.9
	Surgical	23.1
Age	= 60 yrs	57.3
	> 60 yrs	42.7
Origin	Home	68.5
	The very hospital	11.2
	Other hospitals	19.6
Number of blood cultures analyzed	One	38.5
	Two	16.1
	Three	45.5
Admission setting	Ward	19.6
	Apartment	35.0
	Coronary ICU	0.7
	Neonatal ICU	7.7
	Pediatric ICU	9.8
	General ICU	11.9
	Neuro ICU	11.9
	Cardiac ICU	3.7

Figure1: Clinical evolution of patients with positive blood culture in open ans closed admission settings during the period studied. Santa Casa de Misericórdia de Maceió from October 2005 to December 2006.



It was observed that, among patients from adult ICU, the susceptibility to infection development was higher than 29.9% (categories D and E) in 36.0% of the cases.

Among the comorbidities, it was verified that diabetes *mellitus* was incident in 26.6% of the cases, chronic renal failure in 21.7%, neuropathy in 29.4%, chronic obstructive pulmonary disease (COPD) in 11.2%, neoplasia in 17.9%, and neutropenia in 8.4%.

The main etiological agents isolated in blood culture of patients in this study were Coagulase-negative *Staphylococcus* (CNS) 25.9%, *Staphylococcus aureus* (21%), *Klebsiella pneumoniae* (14%), *Escherichia coli* (9.1%), and *Candida* spp. (8.4%).

The main pathogen isolated from blood cultures of patients who died was *S.* aureus, present in 24.1% of the cases. In addition, only 17.5% of BSI patients due to *S. aureus* were discharged by the thirtieth day of follow-up. On the other hand, Coagulase-negative Staphylococcus (CNS) showed important correlation, considering evolution to discharge (38.6%) in this research.

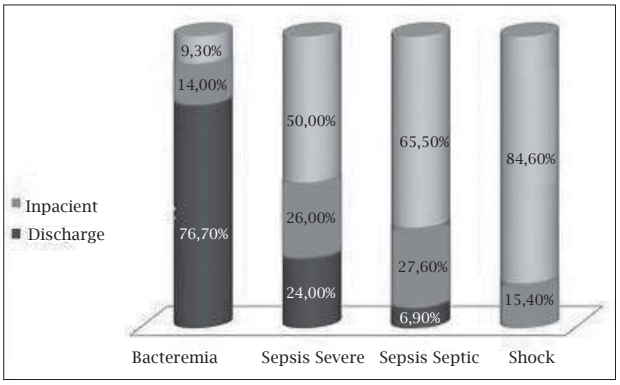
Sources that contributed most to mortality in this study were respiratory tract (37%), urinary (16.7%), and intra-abdominal (11.1%). It was observed that the respiratory source was a predictor to evolution from bacteremia to sepsis, considering that its presence (36.0%) was significant when compared to other sources responsible for infection ($p < 0.05$).

It was observed that 60.8% of the patients in the sample used antibacterial drugs and 4.9% received antifungal drugs before the occurrence of bacteremia and candidemia. All patients who developed multiresistant microorganisms in blood cultures had undergone at least one antimicrobial treatment a couple of weeks before the occurrence of bacteremia (92.6% with therapeutic purpose and 7.4% as prophylactic).

In this casuistic, 30.1% of the patients presented only bacteremia and 69.9% developed sepsis. Among these, 20.3% developed severe sepsis and 10.5% septic shock by the thirtieth day of follow up after BSI detection. On the thirtieth day, 39.9% of the patients had been discharged, 37.8% died, and 22.4% remained in the hospital.

Figure 2 shows the evolution of patients from admission to discharge, death, and the ones who remained in the hospital by the thirtieth day, after the collection of blood culture. At that time, they had only presented bacteremia or had developed distinct progressive stages of sepsis during the period studied. Up to the thirtieth day, none of the patients who presented septic shock were discharged; however, 84.6% of the patients in this group died, and 15.4% remained in the hospital for this period.

Figure 2: Evolution of patients up to 30th day of follow up, when they had presented only bacteremia, and when they evolved to sepsis, severe sepsis and septic shock. Santa Casa de Misericórdia de Maceió from October 2005 to December 2006 (n = 143).



DISCUSSION

Understanding basic concepts on the several ways the pathology may occur is crucial in order to manage it. Different from other diseases, sepsis may represent clinical conditions in its evolutive aspect distinct from those of physiopathological condition.[15] Aiming to standardize concepts, the American College of Physicians and the Society of Critical Care Medicine elaborated a consensus for sepsis definitions and its clinical variation in 1991.[13]

The first American epidemiological study that used the 1991 Consensus definition about sepsis clinical variation is the study by Rangel-Frausto's *et al.*[16] This study showed the incidence of BSI (68%), of which 17% developed sepsis, 13% severe sepsis, and only 3% developed septic shock. More recently, Albert *et al.*[17] observed that 8.2% of the cases studied developed septic shock. In our study, sepsis was present in

70% of BSI episodes. Severe sepsis corresponded to 20.3% of the population under study, and 10.5% of the cases developed septic shock.

The sample demographic characteristics showed that male was predominant in 60.1%, among the 143 patients who took part of the study. A similar finding published by Martin *et al.*[18] confirmed this predisposition when both genders were compared. In relation to mortality, it was verified that patients who developed severe sepsis and septic shock and were older than 60 had a mortality rate of 86.7% ($p < 0.05$; relative risk of 8.7), against 50% when all ages were included ($p < 0.05$; relative risk of 5.4%). Lemos *et al.*[19] found that the elderly were the principal risk group for BSI development and for the increase of morbidity ad mortality.

Brun-Buisson *et al.*[20] in their study on the relationship between bacteremia and severe sepsis in French hospitals identified patient's age, intra-abdominal and pulmonary septic sources among other independent risks. In our study, we also highlighted that, when the respiratory source was present, the development of sepsis was significant in 78.3% of the cases ($p < 0.05$). Moreover, the absence of respiratory source as BSI origin was so significant that patients did not develop the most severe degrees of such pathology ($p = 0.020$).

According to Medeiros *et al.*,[21] the presence and severity of base pathologies, such as chronic obstructive pulmonary disease, diabetes *mellitus*, chronic renal failure, congestive cardiac failure, and the consequent need for invasive procedures favored colonization of microorganisms, predisposing patients to the development of infections. In our study, patients who had cardiovascular pathologies presented significant correlation between comorbidity and respiratory source, presenting 65.2% of the cases in this condition ($p < 0.05$).

Chronic renal failure showed a prevalence of 21.7% in this study, having 61.3% of these patients under dialysis by the time they had bacteremia/candidemia. Among the patients who presented positive blood culture, 14% had dialytic chronic renal failure. Diabetes *mellitus* was incident in 26.6% of the cases and 11.2% of the patients had chronic obstructive pulmonary disease.

S. aureus were isolated in 21% of the samples analyzed in patients with sepsis, corresponding to 70% of positive cultures for this pathogen in diagnosed BSI, of which 50% were methicillin-resistant (MRSA). This frequency presented statistical significance ($p < 0.05$) in relation to the other pathogens identified in this group. NNIS data, published by CDC,[22] reported that 59.5% of the isolated *S.aureus* in American hospitals was methicillin-resistant. Recent studies suggest that the epidemiology of MRSA may get worse, once the isolation of these strains is no more limited to hospital environment, having spread out to the community.[23,24]

Concerning patients' clinical evolution in different settings of the hospital, it was observed that, in the open ones, 14.10% of the patients developed severe sepsis. However, when ICU were analyzed separately, it was verified that 27.69% of the patients developed severe sepsis ($p < 0.05$), showing two times more the incidence in open settings. It reflects the susceptibility of patients admitted in such units in accordance with infection risk prediction ASIS (Average of Severity of Illness Score), modified by Pinheiro.14 In this study, it was detected that the probability of adult ICU patients to develop infection is higher than 29.9% (categories D and E) in 36.0% of the cases. Among the studies revised by Silvia *et al.*,[25] the occurrence rate of severe sepsis was 0.26% when ward patients were included, 27% when only ICU patients were investigated.

The overall mortality rate in hospital during research was 3.7%, whereas the mortality due to BSI by the thirtieth day of follow up was 37.8%. Data based on literature[25,26] showed overall mortality around 30%, similar to the findings in our study. However, it was observed that among patients who presented sepsis, 50% died by the thirtieth day after diagnosis. Data published in Spain in 1993[26] presented a mortality rate of 65.7%, straightly linked to sepsis. Mortality rate due to sepsis in BASES study was 33.9%,[27] whereas Brun-Buisson *et al.*[20,28] observed death probability of 25% by the 28th day. It was observed that on the thirtieth day after diagnosis for severe sepsis, 65.5% of the patients died, presenting a higher rate than in literature analyzed. Rangel-Frausto *et al.*[16] observed a mortality rate of 20% in their study. Sands *et al.*[29] found a rate of 34% by the 28th day of evolution, and BASES study showed a mortality rate of 46.9% for severe sepsis.[27] In cases of septic shock, 84.6% of the patients in our study had died by the 30th day of follow up. The mortality rate was 52.2% in BASES study[27] and varied between 47.2% and 63.8% in the study by Alberti *et al.*[17]

The high rates of evolution to more severe stages of severe sepsis and mortality attributed to these conditions in this study can be a consequence of the lack of knowledge on BSI characteristics in our area and the absence of instituted protocols in hospitals. Several studies report that the lack of knowledge of such aspects contributes to the increase of morbidity and mortality of patients affected by this infection.[6,9,10]

In 2004, Dellinger[30] proposed a Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock in order to establish a model based on better scientific evidences available to manage patients with sepsis and septic shock. According to him, not changing medical behavior practice at bedside, despite the alarming levels of BSI incidence and mortality, means an unforgivable failure. In 2008, it was published in Critical Care[31] an update on these guidelines proposing key recommendations, listed by categories of evidence to help in management of severe sepsis and septic shock.

We understand that the early diagnosis of the different stages of BSI and the institution of adequate and immediate treatment are essential in order to avoid the evolution to more severe, and many times, irreversible stages of the disease.

CONCLUSION

According to the study, the most relevant characteristics that may lead to increase of morbidity and mortality rates due to BSI were the presence of respiratory source of infection, isolation of *S. aureus* in blood cultures, age of patients older than 60 years, and severity of patients in ICU. Being aware of such results may contribute to the adoption of preventive measures and effective therapeutics capable to improve the survival of BSI patients.

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