Clinical impact of sepsis at admission to the ICU of a private hospital in Salvador, Brazil*

Impacto clínico do diagnóstico de sepse à admissão em UTI de um hospital privado em Salvador, Bahia

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Abstract

Objective: To describe the clinical characteristics, laboratory data, and clinical outcomes of patients with and without sepsis admitted to the ICU of a private hospital in the city of Salvador, Brazil, and to identify clinical variables related to a worse prognosis in those with sepsis. **Methods:** This was a longitudinal study including all patients admitted to the general ICU of the *Hospital Português*, in the city of Salvador, Brazil, between June of 2008 and March of 2009. At ICU admission, two groups of patients were identified: with sepsis and without sepsis. Epidemiological, clinical and laboratory data were collected, and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated. **Results:** Of the 144 patients in the study, 29 (20.1%) had sepsis. Among the patients with sepsis, males accounted for 55.2%, the mean age was 73.1 ± 14.6 years, and the mean APACHE II score was 23.8 ± 9.1, compared with 36.3%, 68.7 ± 17.7 years, and 18.4 ± 9.5, respectively, among those without sepsis. There were significant associations between a diagnosis of sepsis and the following variables: APACHE II score; in-hospital mortality; ICU mortality; HR; mean arterial pressure; hematocrit level; white blood cell count; and antibiotic use. The use of life support measures and lower hematocrit levels were associated with a worse prognosis in the patients with sepsis. **Conclusions:** The patients diagnosed with sepsis presented worse clinical outcomes, probably due to their greater severity. Hematocrit level was the only variable that was a predictor of mortality risk in the patients with sepsis.

Keywords: Sepsis/epidemiology; Sepsis/mortality; Intensive care units.

Resumo

Objetivo: Descrever as características clínicas, os dados laboratoriais e o desfecho clínico de pacientes sépticos e não sépticos admitidos em UTI de um hospital privado na cidade de Salvador, Bahia, e identificar variáveis clínicas relacionadas ao pior prognóstico dos pacientes sépticos. **Métodos:** Foi realizado um estudo longitudinal que incluiu todos os pacientes admitidos na UTI geral do Hospital Português, Salvador (BA), entre junho de 2008 e março de 2009. Na admissão na UTI, dois grupos de pacientes foram identificados: sépticos e não sépticos. Foram coletados dados epidemiológicos, clínicos e laboratoriais, e o escore *Acute Physiology and Chronic Health Evaluation II* (APACHE II) foi calculado. **Resultados:** Dos 144 pacientes do estudo, 29 (20,1%) eram sépticos. Entre os pacientes sépticos, 55,2% eram do sexo masculino, a média de idade foi de 73,1 ± 14,6 anos, e a média do escore do APACHE II foi de 23,8 ± 9,1. No grupo não séptico, 36,3% eram do sexo masculino, a média de idade foi de 68,7 ± 17,7 anos, e a média do escore do APACHE II foi de 18,4 ± 9,5. Houve associações estatisticamente significantes entre o diagnóstico de sepse e as seguintes variáveis: escore do APACHE II, mortalidade na UTI, mortalidade hospitalar, FC, pressão arterial média, valor de hematócrito, contagem de leucócitos e uso de antibioticoterapia. O uso de medidas de suporte e valores reduzidos de hematócrito se relacionaram com um pior prognóstico entre os pacientes sépticos. **Conclusões:** Os pacientes diagnosticados com sepse apresentaram piores desfechos clínicos, provavelmente por causa de sua maior gravidade. O nível de hematócrito foi a única variável capaz de predizer o risco de morte entre pacientes sépticos.

Descritores: Sepse/epidemiologia; Sepse/mortalidade; Unidades de terapia intensiva.

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Introduction

The establishment of ICUs, which bring state-of-the-art equipment and specialized multidisciplinary teams together in one place, has improved the treatment and care of critically ill patients over the years.[1] In Brazil, the first ICUs were inaugurated in the 1970s. Since then, there have been studies evaluating the clinical, epidemiological, and biochemical data of ICU patients in Brazil in order to determine disease severity and improve the management of intensive care in the country.[2]

Among all diseases that affect critically ill patients, sepsis is a cause of great concern. a study conducted in the United States having shown it to be the leading cause of death in the ICU and one of the leading causes of death overall.[3] Sepsis is defined as a clinical syndrome consisting of a systemic inflammatory response associated with a focus of infection.[4] When not treated appropriately, sepsis can rapidly progress to septic shock, potentially resulting in organ failure and death. In the United States, the reported incidence of sepsis increased from 82.7 to 240.4 cases per 100,000 population from 1979 through 2000.[3] The incidence of sepsis in ICU patients ranges from 9% to 31%.[5-9] Mortality from sepsis varies according to the severity of the clinical profile. Although mortality from sepsis in the United States was shown to have decreased from 27.8% to 17.9% over a 22-year period (1979-2001),[3] the proportion of individuals affected remains quite high. Studies in the literature, including some conducted in Brazil, have revealed that the mean ICU mortality for patients with sepsis ranges from 10% to 64%.[5-13] In contrast, other studies evaluating ICU patients, with and without sepsis, have found mortality rates ranging from 25% to 38%.[1,2,13]

The first large study of sepsis conducted in Brazil was the Brazilian Sepsis Epidemiological Study (BASES), which evaluated the profile of ICU patients in the southern and southeastern regions of the country in order to determine the incidence of sepsis in these patients.[5] In that study, the incidence of sepsis in ICU patients was found to be 30.5%, and the difference in survival rate between patients with and without sepsis 28 days after admission was established to be 66% and 88%, respectively.[5] Many studies conducted in Brazil have evaluated exclusively ICU patients with sepsis,[8,10-12] whereas others have characterized the clinical and epidemiological profile of all ICU patients.[1,2,13] However, few researchers have performed a clinical and epidemiological comparison of ICU patients with and without sepsis, a process that could identify clinical variables related to prognosis in these patients. Data in the literature indicate that patients with sepsis have worse clinical outcomes, such as death and prolonged hospital stay, as well as deterioration of vital signs and less favorable laboratory test results.[8,10,11] It is necessary to verify these aspects in this specific population in order to establish appropriate protocols and plan future interventions.

The objective of the present study was to describe the clinical characteristics, laboratory data, and clinical outcomes of patients with and without sepsis admitted to the ICU of a private hospital in the state of Bahia, Brazil, and to identify clinical variables of prognosis value in those with sepsis.

Methods

This was a longitudinal study of adult patients admitted to an ICU and monitored throughout their hospital stay. The study was carried out in the general ICU of the *Hospital Português*—a private charity hospital with 300 beds in the infirmary and 24 beds in the ICU—located in the city of Salvador, Brazil. On average, the *Hospital Português* admits 1,000 patients/month, with no predominance of any particular ward.

We included all patients admitted to the general ICU between June of 2008 and March of 2009. The exclusion criteria were staying in the ICU for less than 24 h and being under 18 years of age. The study was approved by the Research Ethics Committee of the *Hospital Português*. All participating patients or, in case of incapacitation, their legal guardians or designated family members, gave written informed consent.

The medical charts of 144 patients were reviewed, and the data obtained were recorded on a confidential data collection form. The following data were collected: age; gender; dates of admission, ICU discharge, and hospital discharge; reason for admission; focus of infection; clinical outcome in the ICU and in the infirmary; and use of life support measures

(enteral feeding, prophylaxis for venous thromboembolism, prophylaxis for acute gastric mucosal injury, mechanical ventilation, antibiotic therapy, corticosteroid therapy, or noradrenaline administration) within the first 24 h after ICU admission. In addition, the worst values obtained in the first 24 h after admission were recorded for the following variables: hematocrit level; white blood cell count; platelet count; glycemia; activated partial thromboplastin time; prothrombin activation time with international normalized ratio; creatinine level; sodium level; potassium level; blood pH; PaO_2; $PaCO_2$; bicarbonate level; SaO_2; base excess; lactate level; HR; RR; temperature; and mean arterial pressure.

At ICU admission, the patients were screened for sepsis, which was defined, on the basis of the recommendations of the 1991 International Sepsis Definitions Conference,[4] as an infectious process associated with two or more of the following criteria: temperature > 38°C or < 36°C; HR > 90 bpm; RR > 20 breaths/min or $PaCO_2$ < 32 mmHg; and white blood cell count > 12,000 cells/mm^3 or < 4,000 cells/mm^3. After classification, two groups were identified: patients with sepsis and patients without sepsis.

We used the worst clinical and biochemical values obtained in the first 24 h after ICU admission in order to calculate the Acute Physiology and Chronic Health Evaluation II (APACHE II) score for all of the ICU patients evaluated.

The statistical analysis was performed with the Statistical Package for Social Sciences, version 14.0 (SPSS Inc., Chicago, IL, USA). For continuous variables, data distribution was evaluated by the Kolmogorov-Smirnov test. The Student's t-test was used for analyzing the differences of the continuous variables if their distribution was found to be parametric. For non-parametric data, the Mann-Whitney test was used. The chi-square test was used for analyzing proportions. Continuous variables are expressed as mean ± SD, whereas categorical variables are expressed as absolute values and percentages. Values of $p < 0.05$ were considered statistically significant.

Results

We evaluated 144 ICU patients, of whom 29 (20.1%) had sepsis and 115 (79.9%) did not. Among the patients with sepsis, the mean age was 73.1 ± 14.6 years and males accounted for 55.2%. Among those without sepsis, the mean age was 68.7 ± 17.7 years and males accounted for only 36.3%. The mean APACHE II score was 23.8 ± 9.1 and 18.4 ± 9.5 among the patients with and without sepsis, respectively. In terms of the variables listed above, a diagnosis of sepsis showed a statistically significant association with mean APACHE II score ($p = 0.012$) and with the reason for admission ($p = 0.049$; Table 1).

In both groups, most of the patients (89.7% and 72.1% of those with and without sepsis, respectively) were non-surgical patients. The reasons for ICU admission of all patients and the foci of infection in the patients with sepsis are shown in Tables 2 and 3, respectively.

The mean length of ICU stay was greater for the patients with sepsis than for those without

Table 1 - Demographic and clinical variables of the patients with and without sepsis.[a]

Variable	With sepsis	Without sepsis	p
Male/female, %/%	55.2/48.8	36.3/63.7	0.064
Age, years	73.1 ± 14.6	68.7 ± 17.7	0.176
Admission for non-surgical reasons, %	89.7	72.1	0.049
APACHE II	23.8 ± 9.1	18.4 ± 9.5	0.012
Length of stay, days			
ICU	9.3 ± 10.1	6.9 ± 9.6	0.276
Overall	31.9 ± 30.0	20.8 ± 22.7	0.088
Mortality, %			
ICU	38.5	15.2	0.003
In-hospital	60.0	20.6	0.000

APACHE II: Acute Physiology and Chronic Health Evaluation II. [a]Values expressed as mean ± SD, except where otherwise indicated.

(9.3 ± 10.1 days vs. 6.7 ± 9.6 days), as was the mean length of hospital stay (31.9 ± 30.0 days vs. 20.8 ± 22.7 days). However, there were no significant associations between these variables (Table 1).

For the patients with sepsis, ICU mortality was 38.5%, compared with 15.2% for those without. In contrast, in-hospital mortality was 60.0% and 20.6% for the patients with and without sepsis, respectively. A diagnosis of sepsis was found to be associated with ICU mortality (p = 0.003) and with in-hospital mortality (p < 0.001; Table 1).

The mean temperatures were very similar in the two groups (36.5 ± 1.3°C and 36.3 ± 0.9°C in the patients with and without sepsis, respectively). The mean arterial pressure was lower in the patients with sepsis than in those without sepsis (87.6 ± 26.4 mmHg vs. 102.2 ± 29.0 mmHg). In addition, 34.5% of the patients with sepsis were hypotensive at admission, compared with 9.6% of those without sepsis. The mean HR was higher in the patients with sepsis (110.5 ± 26.7 bpm vs. 93.9 ± 27.3 bpm). However, the mean RR was above normal in both groups (25.9 ± 5.8 breaths/min and 23.8 ± 6.3 breaths/min in the patients with and without sepsis, respectively). A diagnosis of sepsis at ICU admission showed a statistically significant association with mean arterial pressure (p = 0.013) and with HR (p = 0.005; Table 4).

White blood cell counts > 10,000/mm^3 were more common in the patients with sepsis than in those without sepsis, and hematocrit levels were lower in the former than in the latter. There were no significant differences in platelet counts, international normalized ratio, base excess, or lactate levels between the groups, nor were there any statistically significant differences in pulmonary gas exchange parameters ($PaCO_2$, PaO_2, SaO_2, or bicarbonate levels; Table 4).

The use of life support measures was more common among the patients with sepsis than among those without sepsis—vasoactive drug administration (35.5% vs. 15.0%; p = 0.05), antibiotic therapy (100.0% vs. 74.8%; p < 0.001), corticosteroid therapy (72.4% vs. 58.0%; p = 0.081), and mechanical ventilation (41.4% vs. 25.0%; p = 0.081).

In the patients with sepsis, certain variables were found to be related to the clinical outcome of mortality in the ICU or in the infirmary. The mean hematocrit level in those who died was 23.45 ± 8.62%, compared with 29.84 ± 5.70% in those who survived (p = 0.028). The use of mechanical ventilation in the first 24 h after ICU admission also showed a statistically significant association with the outcomes of the patients with sepsis, because among those submitted to this intervention, 63.6% died in the ICU (p = 0.045) and 90.1% died in the hospital (p = 0.013). Mortality was also higher in the patients who used corticosteroids (55.6% vs. 7.4%; p = 0.029) and in those who used vasoactive drugs (88.9% vs. 50.0%; p = 0.049).

Table 2 - Reasons for ICU admission of the patients with and without sepsis.[a]

Reason	With sepsis	Without sepsis
Pulmonary	27.6	22.1
Cardiovascular	0.0	5.3
Neurological	0.0	28.3
Gastroenterological	0.0	4.4
Urological	10.3	4.4
Sepsis	48.3	0.0
Post-operative recovery	10.3	27.9
Other	3.5	7.6
Total	100	100

[a]Values expressed as %.

Discussion

In the present study, the proportion of patients diagnosed with sepsis at admission to the ICU was high. The rate found was similar to those reported in two multicenter studies of sepsis in the ICU conducted in Brazil: the BASES showed an incidence of 20.3% and the study called *Sepse Brasil* showed an incidence of 16.7%.[5,8] However, sepsis is a dynamic process, and many patients who do not meet the criteria for sepsis at ICU admission might do so within a few days after admission. The BASES, for example, revealed that 9.6% of all patients

Table 3 - Foci of infection in the patients with sepsis (n = 29).

Focus	%
Respiratory	48.3
Urinary	27.6
Blood	3.4
Catheter	6.9
Abdominal	6.9
Other	6.9

Table 4 - Arterial blood gas analysis results, blood workup, and vital signs of the patients with and without sepsis.[a]

Variable	With sepsis	Without sepsis	p
Arterial pH	7.38 ± 0.074	7.39 ± 0.09	0.577
$PaCO_2$, mmHg	36.02 ± 9.05	40.24 ± 15.43	0.061
PaO_2, mmHg	104.12 ± 41.41	120.57 ± 62.21	0.094
Bicarbonate, mEq/L	21.64 ± 5.68	23.25 ± 5.23	0.174
SaO_2,%	93.21 ± 14.60	96.62 ± 8.50	0.236
Temperature, °C	36.5 ± 1.3	36.3 ± 0.1	0.443
Mean arterial pressure, mmHg	87.6 ± 26.4	102.2 ± 29.0	0.013
HR, bpm	110.5 ± 26.7	93.1 ± 27.3	0.005
RR, breaths/min	25.9 ± 5.8	23.8 ± 6.3	0.093
Hematocrit level, %	27.4 ± 7.4	36.4 ± 7.2	< 0.001
White blood cell count, cells/mm^3	18.569 ± 9.254	11.873 ± 5.877	0.001
Platelet count, /mm^3	234.717 ± 132.948	233.867 ± 123.043	0.975
International normalized ratio	1.53 ± 0.95	1.42 ± 0.84	0.566
Base excess, mmol/L	−3.24 ± 5.56	−1.56 ± 5.09	0.050
Lactate level, mg/dL	1.88 ± 1.09	1.90 ± 1.58	0.909

[a]Results expressed as mean ± SD.

included were diagnosed with sepsis only after ICU admission.[5]

The high mean age (> 60 years) of the ICU patients in the present study, regardless of the diagnosis of sepsis, is also a constant finding in studies conducted in Brazil and in developed countries, such as the United States, the United Kingdom, France, and Spain, because life expectancy has increased and elderly individuals are at a higher risk of having severe diseases that can result in ICU admission.[2,3,5-10,12-14] A study conducted in the United States demonstrated that the mean age of patients with sepsis increased from 57.4 years to 60.8 years over a 22-year period.[3] In addition, that same study supports data in the literature in that the mean age of ICU patients with sepsis was higher than was that of those without sepsis, which might reflect a greater vulnerability of the immune system of older individuals to infectious processes.

In the present study, male gender was associated with ICU admission for sepsis, although the study design did not allow a causal inference. The literature corroborates this finding,[8,10,13,15] and some authors argue that gender-related hormonal differences and higher levels of anti-inflammatory mediators in women are the likely causes of the higher incidence of sepsis and worse outcomes in men.[15,16]

The APACHE II score was higher in the ICU patients with sepsis than in those without, there being a significant difference between the means of the two groups of patients, as was also observed in the BASES.[5] This is attributable to the fact that comorbidities and acute disorders that affect vital signs and the results of many laboratory tests, which form the APACHE II criteria, are more common among patients with sepsis.[5,8] In addition, the mean APACHE II scores found in the present study (18.4 ± 9.5 and 23.8 ± 9.1 for patients without and with sepsis, respectively) were similar to those reported in the literature. In studies conducted in Brazil, the reported mean APACHE II scores for all ICU patients range from 15.0 to 18.4.[2,5,13] In contrast, in most studies evaluating patients with sepsis as a separate group, the mean APACHE II score ranges from 18 to 20, there being some exceptions, such as a study conducted in Spain, in which the mean was 25.5 ± 7.1.[5,8-10,12] The slightly higher APACHE II scores found in the present study might be explained by the profile of the ICU studied, in which older patients with chronic diseases predominate and there are a fewer postoperative admissions. Although the association of the APACHE II score with severity of illness and mortality in ICU patients has already been proven, the present study also underscores the association of this score with a diagnosis of sepsis, because this is an illness of significant severity.

Among the patients with sepsis, ICU mortality and in-hospital mortality were higher

than among the patients without sepsis, which reveals the impact of this clinical syndrome and underscores the importance of early treatment to minimize its effects on the clinical outcomes. In addition, among the patients with sepsis, in-hospital mortality (60.0%) was much higher than was ICU mortality (38.5%). This fact can promote a more careful approach of these patients, including at ICU discharge. One study showed that patients with a history of sepsis can be threatened by its complications even 5 years later, given that an acute episode of sepsis can lead to irreversible organic changes that can result in late effects, such as the worsening of chronic diseases.[17]

In the present study, ICU mortality among the patients without sepsis was 15.2%, slightly higher than the 12% reported in the BASES.[5] In contrast, ICU mortality among the patients with sepsis was 38.5%, similar to that reported in other studies.[5,8,10,12,13] Within the group of patients with sepsis, we did not identify those with severe sepsis and those with septic shock. Therefore, it was not possible to perform a more accurate comparison of our mortality findings with those reported in the literature, because many studies make this distinction and report a much higher mortality rate among the patients who meet the criteria for severe sepsis or septic shock.

Length of ICU stay and length of hospital stay were much higher in the group of patients with sepsis than in the group of those without sepsis, because, in general, patients with a history of sepsis require long-term follow-up and are more likely to have complications. The mean length of ICU stay found in the present study among the patients with sepsis was shorter than those found in studies conducted in the Brazilian states of Pernambuco and Acre, as well as than that found in the multicenter study called *Sepse Brasil*,[2,8,10] although it was longer than that found in a study conducted in the Brazilian state of Rio Grande do Sul.[12] It is important to point out the prolonged hospital stay found in the present study among the patients with sepsis (31.9 ± 30.0 days), because this might indicate that the patients had complications after leaving the ICU or even had to be readmitted to the ICU.

It should be noted that temperature alone should not be considered a major criterion in the diagnosis of sepsis, because the temperatures recorded in the ICU patients with sepsis were not significantly different from those recorded in those without sepsis.

Although the use of life support measures, such as antibiotic therapy, corticosteroid therapy, vasoactive drug administration, and mechanical ventilation, has been associated with mortality in ICU patients, the present study underscores the fact that patients with sepsis more often require the use of such measures, there being a significant association between their use and a diagnosis of sepsis.[2,8] In addition, the present study presented a population of patients with severe sepsis, as determined on the basis of the relationship between the use of the abovementioned measures and mortality.

The high prevalence of the lungs as a source of infection for sepsis, as demonstrated in the present study and corroborated by other authors, is consistent with the proportion of patients admitted with lung diseases, especially respiratory infections. It should be noted that this finding is favored by the composition of the sample, which consisted primarily of elderly individuals, who are generally at a greater risk of developing respiratory infections, as well as by the increasing number of patients submitted to mechanical ventilation in the ICU.[5,8,10]

Hematocrit level was the only biochemical marker that was found to be related to a worse prognosis in the patients with sepsis. Although there have been few studies on the subject, the high levels of inflammatory mediators produced during the acute response to sepsis are believed to result in decreased erythrocyte half-life, due to a deformity in the membranes of these cells, caused by the circulating reactive oxygen species. Despite the need for the bone marrow to compensate, the production of new red blood cells is ultimately insufficient, because erythropoietin production and bone marrow response to erythropoietin stimulation are also affected by the inflammatory process. Therefore, the reduction in erythrocyte mass together with the hemodilution caused by fluid expansion can result in decreased hematocrit levels and indicate a more exacerbated inflammatory process in these patients.[18-20] However, it is essential that further studies be conducted in order to confirm these hypotheses.

The present study has some limitations. Although the patients were divided into those

with sepsis and those without, the small size of our sample limited the statistical power of the study, preventing us from assessing the presence of septic shock and severe sepsis in isolation. Another limitation was that the patients were screened for sepsis only at ICU admission, because the course of sepsis is dynamic and patients initially classified as not having sepsis might develop sepsis within a few days after admission. It would have been interesting to correlate mortality with the underlying diagnosis and with the focus of infection in the patients with sepsis. However, the small sample size precluded such an analysis.

In the present study, mortality was high among the ICU patients with sepsis and the presence of sepsis was associated with a prolonged hospital stay. In addition, we found that sepsis affects vital signs and laboratory test results. However, hematocrit level was the only variable that was found to be an isolated predictor of mortality in the patients with sepsis. It should be noted that the frequency of the use of life support measures was high among the patients with sepsis, demonstrating the severity of the disease and the relationship between the use of such measures and a worse prognosis in these patients, who are, intrinsically, more critically ill. Studies involving multiple ICUs in the state of Bahia should be conducted in order to draw conclusions about any regional differences related to sepsis in the ICU.

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