# SEPSIS AND SEPTIC SHOCK: EPIDEMIOLOGY, CLINICAL PARAMETERS, AND PROGNOSTIC FACTORS IN A BRAZILIAN INTENSIVE CARE UNIT

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**ABSTRACT:** Sepsis is an organ dysfunction caused by a dysregulated host response to infection and is associated with high morbidity and mortality. The identification of prognostic markers in this syndrome has been a strategy to increase treatment efficacy. The objectives of this study were: 1) to describe the epidemiological and microbiological profile of septic patients and 2) to investigate the association between laboratory/clinical parameters and mortality rate, identifying prognostic markers. Using a prospective observational protocol, epidemiological, clinical and laboratory data were collected from adult patients with sepsis or septic shock admitted to a Brazilian Intensive Care Unit. During the study period, 120 patients were diagnosed with sepsis and 71.67% (n = 86) were included in the protocol. The overall mortality was 69.76% and chronic diseases were identified in 79.07% of cases. The mortality rates for sepsis and septic shock were 51.06% and 92.31%, respectively. SOFA scores on the first, third, and seventh days of hospitalization gradually increased for patients who had clinical worsening. Hyperlactatemia and hyperglycemia were identified in 45.9% and 27% of patients, respectively, and were associated with mortality. INR values greater than 1.5 or thrombocytopenia were related to 92.9% and 88.6% mortality, respectively. In the study, gender, age, ICU stay, site of infection and microbiological agent were not associated with the risk of death. However, the presence of comorbidities, high SOFA scores, three or more organ dysfunctions, and sepsis severity correlated directly with mortality rate.
**KEYWORDS:** Sepsis; Septic Shock; Microbiology; Hyperlactatemia; Hyperglycemia; Thrombocytopenia.

# SEPSE E CHOQUE SÉPTICO: EPIDEMIOLOGIA, PARÂMETROS CLÍNICOS E FATORES PROGNÓSTICOS EM UMA UNIDADE DE TERAPIA INTENSIVA BRASILEIRA

**RESUMO:** A sepse é uma disfunção orgânica causada por uma resposta desregulada do hospedeiro à infecção e está associada a alta morbidade e mortalidade. A identificação de marcadores prognósticos nessa síndrome tem sido uma estratégia para aumentar a eficácia do tratamento. Os objetivos deste estudo foram: 1) descrever o perfil epidemiológico e microbiológico de pacientes sépticos e 2) investigar a associação entre parâmetros laboratoriais/clínicos e a taxa de mortalidade, identificando marcadores prognósticos. Por

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meio de um protocolo observacional prospectivo foram coletados dados epidemiológicos, clínicos e laboratoriais de pacientes adultos com sepse ou choque séptico internados em uma Unidade de Terapia Intensiva brasileira. No período do estudo, 120 pacientes foram diagnosticados com sepse e 71,67% (n = 86) foram incluídos no protocolo. A mortalidade geral foi de 69,76% e doenças crônicas foram identificadas em 79,07% dos casos. As taxas de mortalidade por sepse e choque séptico foram de 51,06% e 92,31%, respectivamente. Os escores SOFA no primeiro, terceiro e sétimo dias de internação aumentaram gradativamente para os pacientes que apresentaram piora clínica. Hiperlactatemia e hiperglicemia foram identificadas em 45,9% e 27% dos pacientes, respectivamente, tendo sido associadas à mortalidade. Valores de INR maiores que 1,5 ou trombocitopenia foram relacionados a 92,9% e 88,6% de mortalidade, respectivamente. No estudo, sexo, idade, permanência na UTI, local da infecção e agente microbiológico não se associaram ao risco de óbito. No entanto, a presença de comorbidades, altos escores SOFA, três ou mais disfunções orgânicas e a gravidade da sepse correlacionaram-se diretamente com a taxa de mortalidade.
**PALAVRAS-CHAVE:** Sepse; Choque Séptico; Microbiologia; Hiperlactatemia; Hiperglicemia; Trombocitopenia.

## SEPSIS Y SHOCK SÉPTICO: EPIDEMIOLOGÍA, PARÁMETROS CLÍNICOS Y FACTORES PRONÓSTICOS EN UNA UNIDAD DE CUIDADOS INTENSIVOS BRASILEÑA

**RESUMEN:** La sepsis es una disfunción orgánica causada por una respuesta desregulada del huésped a la infección y se asocia a una elevada morbilidad y mortalidad. La identificación de marcadores pronósticos en este síndrome ha sido una estrategia para aumentar la eficacia del tratamiento. Los objetivos de este estudio fueron: 1) describir el perfil epidemiológico y microbiológico de los pacientes sépticos y 2) investigar la asociación entre los parámetros de laboratorio/clínicos y la tasa de mortalidad, identificando marcadores pronósticos. Mediante un protocolo observacional prospectivo, se recogieron datos epidemiológicos, clínicos y de laboratorio de pacientes adultos con sepsis o shock séptico ingresados en una Unidad de Cuidados Intensivos brasileña. Durante el período de estudio, 120 pacientes fueron diagnosticados de sepsis y el 71,67% (n = 86) fueron incluidos en el protocolo. La mortalidad global fue del 69,76% y se identificaron enfermedades crónicas en el 79,07% de los casos. Las tasas de mortalidad por sepsis y shock séptico fueron del 51,06% y el 92,31%, respectivamente. Las puntuaciones SOFA en el primer, tercer y séptimo día de hospitalización aumentaron gradualmente en los pacientes que presentaron empeoramiento clínico. La hiperlactatemia y la hiperglucemia se identificaron en el 45,9% y el 27% de los pacientes, respectivamente, y se asociaron a mortalidad. Los valores de INR superiores a 1,5 o la trombocitopenia se relacionaron con un 92,9% y un 88,6% de mortalidad, respectivamente. En el estudio, el sexo, la edad, la estancia en la UCI, el lugar de la infección y el agente microbiológico no se asociaron con el riesgo de muerte. Sin embargo, la presencia de comorbilidades, las puntuaciones SOFA elevadas, tres o más disfunciones orgánicas y la gravedad de la sepsis se correlacionaron directamente con la tasa de mortalidad.
**PALABRAS CLAVE:** Sepsis; Shock Séptico; Microbiología; Hiperlactatemia; Hiperglucemia; Trombocitopenia.

## 1. INTRODUCTION

Sepsis is the leading cause of death among critically ill patients and has been associated with many sequelae in survivors (PRESCOTT; ANGUS, 2018). The Institute for Health Metrics and Evaluation (IHME) estimated an incidence of 48.9 million sepsis cases in 2017 and reported 11 million sepsis-related deaths worldwide, representing 19.7% of all global deaths in the same period (RUDD et al., 2020).

This syndrome represents a great challenge for health systems worldwide because of its high treatment costs and long hospitalization periods. The cost of sepsis-related care in the United States is more than $20.3 billion annually (LIANG; MOORE; SONI, 2006). In a cohort study that included about 2.5 million cases of sepsis, the costs varied from $16,324 to $38,298, in sepsis or septic shock with a mortality of 12.4%, and 34.2%, respectively (PAOLI et al., 2018). A study conducted in 21 public and private Brazilian Intensive Care Units (ICU) estimated that the average cost associated with sepsis treatment was $9,632 per patient. The mean daily cost per intensive care patient was significantly higher in non-survivors than survivors (SOGAYAR et al., 2008).

A multicenter study conducted in 198 ICUs from 24 European countries showed that the incidence of sepsis was 37.0 %, with an overall mortality of 24.1%. In patients with severe sepsis and septic shock, mortality was 32.2% and 54.1%, respectively (VINCENT et al., 2006). The *Brazilian Sepsis Epidemiological Study* (BASES), conducted from 2001 to 2002 in ICUs located in the south and southeast regions of the country, showed that the incidence of sepsis, severe sepsis, and septic shock was 46.9%, 27.3%, and 23.0%, respectively. In these patients, the mortality rate was 33.9%, 46.9%, and 52.25%, respectively (SILVA et al., 2004).

According to the Third International Consensus (Sepsis-3), sepsis is an “organ dysfunction caused by a dysregulated host response to infection”. It can also be described as a heterogeneous syndrome with extensive physiological and biochemical abnormalities, caused mainly by an immunological imbalance of inflammation and anti-inflammation response (SINGER et al., 2016).

Despite decades of studies, the treatment approaches to sepsis are based mainly on timely fluid resuscitation and early administration of broad-spectrum antibiotics. Accurate diagnoses and early clinical interventions remain important for a favorable outcome, improving patient survival (JARCZAK; KLUGE; NIERHAUS, 2021).

The physiological changes resulting from sepsis, directly or indirectly, influence several clinical and laboratory parameters that have been studied to identify prognostic markers and guide the treatment of patients. The failure of three or more organs, oliguria, and elevated blood lactate detected at the time of Intensive Care Unit (ICU) admission have been associated with a higher risk of death (FAN et al., 2016, REBOUÇAS et al., 2023).

In 2021, there was an update of the clinical approach guide for septic patients (Surviving Sepsis Campaign) as an effort to unify the evaluation criteria and treatment protocols. However, due to the heterogeneity of the syndrome and its individual variability, there is still not an absolutely efficient score for its diagnosis and prognosis (EVANS et al., 2021).

Early diagnosis and rapid intervention with supportive therapies and antibiotics correlate directly with better clinical outcomes (SINGER et al., 2016). The syndrome may be self-limited or progress to septic shock, where circulatory abnormalities such as intravascular volume depletion, peripheral vasodilation, coagulation system activation, myocardial depression, and increased metabolic rate lead to an imbalance between oxygen need and demand, resulting in global hypoxia or shock. Tissue hypoxia reflects the severity of the disease and is predictive of the development of multiple organ dysfunction (DUGAR; CHOUDHARY; DUGGAL, 2020).

Data on the incidence and progression of sepsis in ICUs in Latin America, including Brazil, are rare (VINCENT, 2009; QUINTANO NEIRA; HAMACHER; JAPIASSÚ, 2018). Thus, the true impact of this syndrome on developing countries is not yet fully understood (RUDD et al., 2020). It is important that, in Brazil, a country with wide regional heterogeneity, studies are carried out to trace the real profile of septic patients to define priorities and improve patient care.

The present study aims to evaluate the association of the epidemiological, microbiological, clinical, and laboratory parameters with the outcomes of adult septic patients admitted to the ICU of a Brazilian public hospital, identifying prognostic markers.

## 2. MATERIAL AND METHODS

The study was carried out in the Otávio de Freitas Hospital ICU in the State of Pernambuco, Brazil. The Hospital belongs to Brazilian Public Health System and consists

of 485 beds, including 20 ICU beds for adults. The study model was a prospective, observational cohort with non-random sampling, carried out in a period of 17 months.

Inclusion criteria were patients admitted to the ICU, aged 18 years or older, who presented clinical and/or laboratory manifestations of sepsis at the time of admission or during hospitalization. The criteria for diagnosis of sepsis and its stages (sepsis or septic shock) followed the definitions established by the Third International Consensus - Sepsis-3 (SINGER et al., 2016). Exclusion criteria were patients with a length of stay in the ICU of less than seven days.

Data collection was performed through a questionnaire, ensuring the uniformity of the information. SOFA (Sequential Related Organ Failure Assessment) scores were used to monitor organic dysfunctions and were calculated on the first, third, and seventh days of ICU stay (VINCENT et al., 1996).

The patients were evaluated for seven days through laboratory and blood gas analysis and followed up to define the clinical outcome (death or discharge from the ICU). Sepsis was classified as community in patients with less than 72 hours of hospitalization or nosocomial when its onset occurred after 72 hours of hospitalization, according to the methodology of Koury et al. (2006). The following aspects were analyzed: demographic patients characteristics, microbiological profile (source of infection and etiological isolation), presence of comorbidities, time of hospitalization, medical procedures performed for clinical support, laboratory parameters (complete blood count, biochemical analysis), arterial blood gas profile (lactate, bicarbonate, and pH dosage) and mortality rate.

### 2.1 Statistical Analysis

Statistical analyses were performed using GraphPad Prism 8 Software. All tests were applied with 95% confidence. The results are presented in table form with their respective absolute and relative frequencies. Quantitative variables were expressed as mean and standard deviation. The Chi-Square Test and Fisher's Exact Test were used to verify the association between categorical variables. The student’s t-test (normal distribution) and Mann-Whitney (non-normal distribution) were used to compare the two groups.

## 2.2 Ethical Considerations

The research was approved by the local Ethics Committee (Protocol No. 0027.0.344.172-10), and all patients or their legal representatives signed a Free and Informed Consent Form before their inclusion in the study.

## 3. RESULTS

During the study, 120 ICU patients were diagnosed with sepsis; 71.67% (n=86) met the inclusion criteria established in the protocol. The exclusion of 28.33% of patients was due to the following factors: 24 patients were hospitalized for a period of fewer than seven days and 10 patients were under 18 years of age.

### 3.1 Demographic, Epidemiological, and Clinical Characteristics of Patients

Approximately 53% (n=46) of the patients in the study were male, and the mean age observed was 57.49±19.77 years.

The length of stay in the ICU ranged from 7 to 90 days, with a general average of 21.79 days. Patients were admitted to the ICU because of clinical complications in 89.53% of the cases, followed by post-surgical (8.12%) or polytraumatic (2.32%) events. Sepsis was classified as community or nosocomial in 51.2% and 48.8% of cases, respectively. Regarding ICU procedures, 81.40% of patients underwent artificial ventilation, 43.02% required tracheostomy, and 20.93% received parenteral nutrition.

The patients' epidemiological, demographic, and clinical characteristics are compiled in Table 1.

Table 1. Epidemiological, demographic, and clinical characteristics of patients diagnosed with sepsis in the ICU.

| Variables | n (%) |
|---|---|
| Male | 46 (53.49) |
| Female | 40 (46.51) |
| Age (mean ± SD) | 57.49 ± 19.77 |
| **Presence of comorbidities** | **68 (79.07)** |
| Systemic Arterial Hypertension | 19 (27.94) |
| Diabetes Mellitus (DM) | 14 (20.59) |
| Chronic Liver Disease | 13 (19.12) |
| Chronic kidney disease | 10 (14.71) |
| Cancer | 8 (11.76) |
| Tuberculosis (TB) | 7 (10.29) |
| Acquired Immunodeficiency Syndrome (AIDS) | 5 (7.35) |
| Chronic Obstructive Pulmonary Disease (COPD) | 4 (5.88) |
| SN (Neurological Sequelae) | 3 (4.41) |
| **Sepsis Classification** | |
| Sepsis | 47 (54.65) |

| | |
|---|---|
| Septic Shock | 39 (45.35) |
| Community sepsis | 44 (51.16) |
| Nosocomial sepsis | 42 (48.84) |
| **Site of infection** | |
| Respiratory system | 42 (48.84) |
| Urinary System | 20 (23.26) |
| Gastrointestinal tract | 19 (22.09) |
| Hematological system | 3 (3.49) |
| Others | 2 (2.32) |
| **Isolated etiological agent** | **55 (63.95)** |
| Gram-positive bacteria | 21 (38.18) |
| Gram-negative bacteria | 20 (36.36) |
| Fungi | 10 (18.18) |
| Polymicrobial | 4 (7.27) |
| **Reasons for ICU admission** | |
| Hospitalization for clinical reasons | 77 (89.53) |
| Post-surgical events | 7 (8.12) |
| Polytraumatic events | 2 (2.32) |
| **ICU procedures** | |
| Artificial ventilation | 70 (81.40) |
| Tracheostomy | 37 (43.02) |
| Parenteral nutrition | 18 (20.93) |
| **Outcome** | |
| Length of stay in the ICU (mean ± SD) | 21.79 ± 20.08 |
| Overall mortality rate | 60 (69.76) |

Source: prepared by the authors

In the study, 54.65% (n=47) of the patients were diagnosed with sepsis and 45.35% (n=39) with septic shock. The overall mortality rate was 69.76% (n=60). In sepsis and septic shock patients, the mortality rate was 51,06% (24/47) and 92.31% (36/39), respectively. There was a significant association between the severity of sepsis and the observed mortality rate ($p<0.001$).

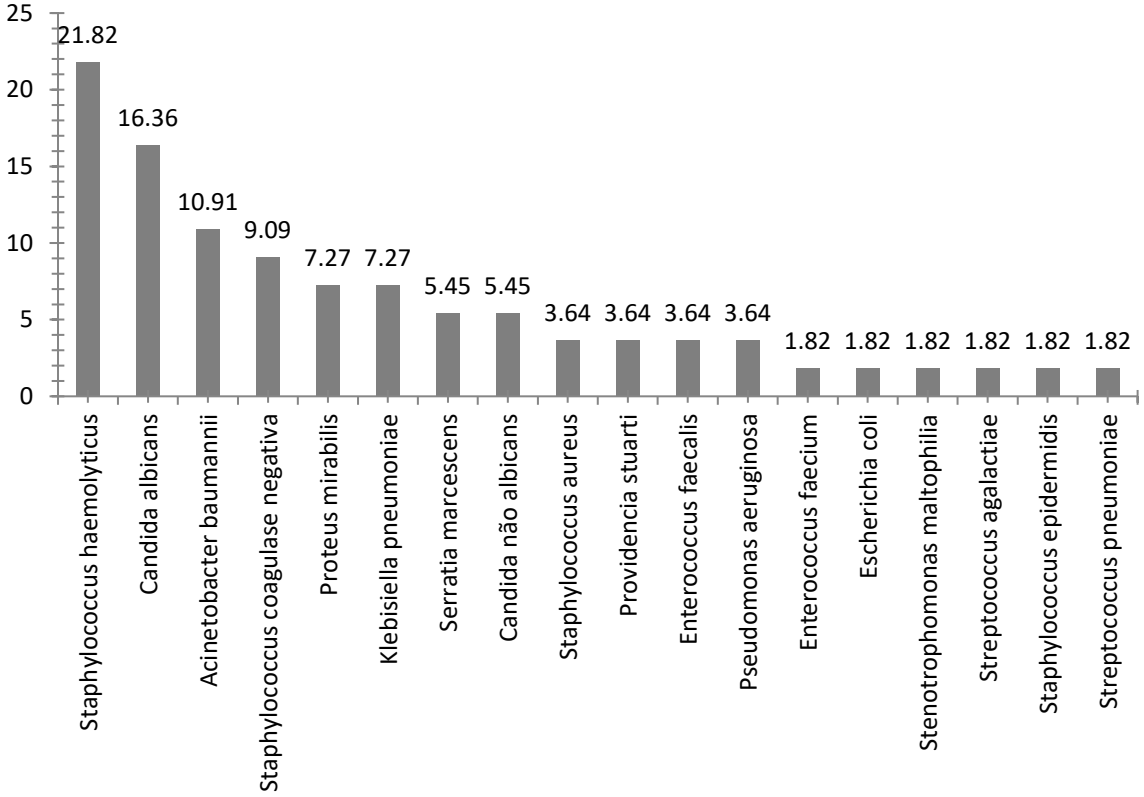
Comorbidities were present in 79.07% (n=68) of the cases. There was a high frequency of systemic arterial hypertension (27.94%), Diabetes Mellitus (20.59 %), and chronic liver disease (19.12 %). Chronic comorbidities were significantly associated with mortality ($p < 0.001$). Dissimilarly, there was no significant association between death outcome and age ($p = 0.280$), sex ($p = 1.00$), use of parenteral nutrition ($p =0.550$), use of artificial ventilation ($p = 0.550$) and tracheostomy procedure ($p = 0.272$).

### 3.2 Infection Sites and Pathogens

The analysis of the primary source of infection indicated that the main focus was pulmonary (48.84%), followed by the urinary system (23.26%), gastrointestinal tract (22.09%), and hematological system (3.49%) and others (2.32%). In 63.95% (n = 55) of the patients, the etiological agent was isolated, 38.18% were gram-positive bacteria,

36.36% gram-negative bacteria, 18.18% fungi and 7.27% polymicrobial bacteria. Figure 1 describes the isolated etiological agents and their relative percentages.

Figure 1. Percentage of etiological agents isolated after diagnosis of sepsis.




The etiological agents were isolated from blood, urine, and tracheal secretion cultures. In four patients were isolated more than one microorganism.
Source: prepared by the authors

The etiological agent in septic patients showed no relationship with a clinical outcome (p =0.921). Similarly, the site of infection was not associated with mortality (p = 0.297). However, the indirect action of these agents is not ruled out.

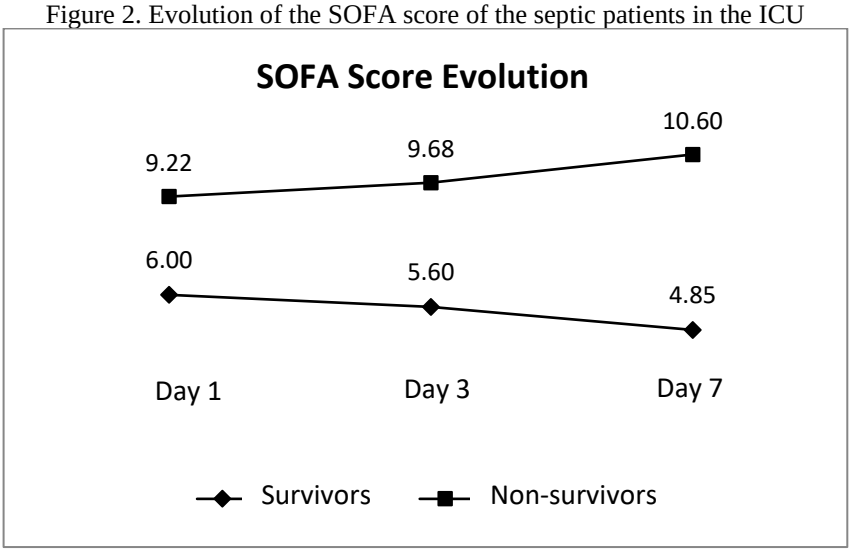
### 3.3 SOFA Score

To monitor clinical deterioration or organic dysfunction, SOFA scores were recorded on the first, third, and seventh days of ICU stay. On all days analyzed, SOFA values were correlated to the mortality of septic patients. Regarding organic dysfunction, 72.3% of patients had a failure in three or more organs during hospitalization.

Mortality rates ranged from 20% for patients with less than three organ failures to 93.20% for those with three or more organ failures (p<0.001).

There was a gradual increase in SOFA scores for patients whose clinical condition worsened, which culminated in death, as shown in Figure 2.

Figure 2. Evolution of the SOFA score of the septic patients in the ICU




Mean of SOFA score values of the septic patients, survivors and non-survivor, analyzed on the first, third and seventh day of ICU stay.
Source: prepared by the authors

### 3.4 Biochemical Parameters

Some laboratory parameters were analyzed in the first 24 hours of hospitalization to evaluate metabolic dysfunctions, as described in Table 2.

Table 2. Association between laboratory parameters and the clinical outcome of septic patients admitted to the ICU.

| **Laboratory Parameters** | **Survivors** (Mean ± SD) | **Non-survivors** (Mean ± SD) | **p-value*** |
|---|---|---|---|
| Leukocytes ($mm^3$) | 19311.76 ± 11702.34 | 18431.33 ± 11813.26 | 0,794 |
| Hematocrit (%) | 29.60 ± 7.86 | 26.41 ± 8.68 | 0.310 |
| Creatine (mg/dL) | 1.40 ± 1.10 | 2.29 ± 1.98 | 0.113 |
| Albumin (g/dL) | 2.42 ± 0.65 | 1.92 ± 0.46 | 0.004** |
| Urea (mg/dL) | 91.36 ± 103.30 | 85.58 ± 63.11 | 0.816 |
| Blood pH | 7.36 ± 0.11 | 7.35 ± 0.10 | 0.683 |
| Bicarbonate (mEq/L) | 18.84 ± 5.06 | 18.12 ± 5.34 | 0.649 |

(*) student's t-test, (**) $p<0.05$
Source: prepared by the authors

The mean values of leukocytes, hematocrit, creatinine, and urea, despite having shown differences between the groups of survivors and non-survivors, were not statistically significant. The same was observed about the acid-base balance parameters. However, the albumin concentration was significatively lower in non-survivors patients.

Other biochemical parameters, such as lactate level, blood glucose, and parameters of the coagulation system, were shown, in the stratified analysis, to be extremely relevant for the clinical evolution of the septic patient (Table 3).

Table 3. Stratification analysis of biochemical parameters and mortality rate of the ICU septic patients

| Laboratory parameters | Non-survivors | | Survivors | | p-valor |
|---|---|---|---|---|---|
| | N | % | N | % | |
| **INR** | | | | | |
| ≥ 1.5 | 39 | 92.9 | 3 | 7.1 | <0.001 * |
| < 1.5 | 7 | 20.0 | 28 | 80.0 | |
| **Lactate** | | | | | |
| ≥ 4 mmol/L | 29 | 85.3 | 5 | 14.7 | <0.001 * |
| < 4 mmol/L | 16 | 40.0 | 24 | 60.0 | |
| **Platelet** | | | | | |
| > 100.000/mm$^3$ | 17 | 40.5 | 25 | 59.5 | <0.001 * |
| < 100.000/mm$^3$ | 31 | 88.6 | 4 | 11.4 | |
| **Glucose** | | | | | <0.001 * |
| < 200 mg/dL | 32 | 62.7 | 19 | 37.3 | |
| ≥ 200 mg/dL | 15 | 78.9 | 4 | 21.1 | |

INR (International Normalized Ratio). *Chi-square test: p < 0.001.
Reference value: Serum lactate: ≤ 2 mmol/L; INR: 0.8 to 1.0; Platelet: 150000 to 400000/mm$^3$; glucose under ICU insulin therapy: 140 to 180 mg/dL.
Source: prepared by the authors

Serum lactate levels were shown to have a significant association with the patient mortality rate (p<0.001). About 45% of patients (n=34) had hyperlactatemia (serum lactate level ≥4.0 mmol/L), corresponding to a mortality rate of 85.3% versus 40% observed in patients with lactate levels below 4.0 mmol/L. Similarly, hyperglycemia events (glucose > 200 mg/dL) were identified in 27% of patients, of which 78.9% died (p<0.001).

Platelet count and INR (International Normalized Ratio) values were evaluated to assess the sepsis impact on the coagulation system. These variables of hemostasis proved to be good indicators of patient survival. A platelet count below 100.000/mm$^3$, and an INR value equal to or greater than 1.5 were associated with a higher risk of death, corresponding to 88.6% and 92.9%, respectively.

## 4. DISCUSSION

Sepsis is a heterogeneous syndrome and its epidemiology differs considerably between the countries being influenced by several aspects, such as the pattern of infectious diseases, population comorbidities, and resources for diagnosis and treatment (FLEISCHMANN-STRUZEK et al., 2020). Therefore, the data obtained in European and South American countries could not represent the reality of other regions.

In this single-center study carried out in the ICU of a Brazilian hospital, we evaluate the sepsis characteristics and management of 86 adult patients. Approximately 45% of the septic patients admitted to the ICU were elderly (over 60 years), with a slight predominance of males, as described in previous studies (PAOLI et al., 2018; VINCENT et al., 2009; QUINTANO NEIRA; HAMACHER; JAPIASSÚ, 2018). It is believed that this percentage of the elderly was not higher because the study was conducted in a hospital belonging to the public health system that serves a disadvantaged population with less access to health services and, consequently, a lower life expectancy. In addition, this population is more susceptible to chronic diseases, malnutrition, and infectious diseases.

The association between patient age and the mortality rate from sepsis is no consensus in the literature (QUINTANO NEIRA; HAMACHER; JAPIASSÚ, 2018; JUNCAL et al., 2011; ZAHAR et al., 2011). However, according to the statistical analysis of this study, age was not directly associated with the mortality rate.

The mean length of stay in the ICU was 21.79 ± 20.08 days, considered high when compared to the study conducted by Sales et al. (2006), which had a mean of 15.5 ± 11 days (SALES JÚNIOR et al., 2006). Nonetheless, in our analysis, the length of stay in the ICU was not related to clinical evolution, following the trend of other studies (JUNCAL et al., 2011).

The presence of comorbidities was associated with a higher risk of mortality ($p<0.001$), probably due to the negative effect on the physiological changes derived from intensive care, aggravating the general condition of the septic patient. According to Vicent, et al. (2009) and Koury, et al. (2006), comorbidities are associated with the outcome of death, suggesting an increased susceptibility of patients with chronic diseases to develop severe complications (VINCENT, 2009; KOURY; LACERDA; BARROS NETO, 2006).

A data that should be viewed with great concern is the high mortality rate observed in this study. The overall mortality rate was 69.76%, ranging from 51.06% to 92.31% according to the diagnosis of sepsis and septic shock, respectively. A Brazilian study that evaluated sepsis mortality in ICU patients in the period between 2006 to 2015, registered a global rate of 64.5% (QUINTANO NEIRA; HAMACHER; JAPIASSÚ, 2018). However, other countries presented better outcomes, such as 57.5% in China (CAO et al., 2021) and 30.4% in Mexico (CARRILLO-ESPER; CARRILLO-CÓRDOVA; CARRILLO-CÓRDOVA, 2009). A global epidemiological study of sepsis revealed that

the highest mortality occurred in countries with the lowest socio-demographic index, that is, in less developed areas (RUDD et al., 2020). The reasons for this include insufficient health care professionals, and a lack of adequate training and education on sepsis diagnosis and management (TUFAN, 2015; SCHULTZ et al., 2017).

The comparison between ICUs is complex due to the various parameters that profoundly interfere with the relationship between them, especially the profile of patients. In this study, patients presented a high degree of sepsis severity and multiple organ dysfunctions, which directly interfered with the mortality rate. It is interesting to highlight that Koury et al. (2006), in a study methodologically similar to ours, conducted in a private hospital ICU in Pernambuco, obtained different findings related to the predominance of comorbidities, microbiota, hospitalization time and risk of death, reaffirming the complexity of the topic (KOURY; LACERDA; BARROS, 2006). A Brazilian multicenter study also elucidated the differences in the lethality rate in public and private hospitals (55.5% versus 37.0%) (QUINTANO NEIRA; HAMACHER; JAPIASSÚ, 2018).

An important contribution of the BASES study, which compared the clinical profile on septic patients admitted to public and private hospitals, was the data of lower mortality rate observed in patients admitted to private hospitals, which suggests that access to the highest standards of care is directly related to prognosis (SILVA et al., 2004). Our data reiterate that the classification of sepsis severity is directly related to mortality. This association was readily acceptable since the severity of sepsis is directly related to the degree of organic dysfunction and the deterioration of the general state of health of the patient (ZÁHOREC et al., 2005; ENGEL et al., 2007).

Sepsis due to lung infections, unknown causes, and multiple sources had the highest rates of multi-organ failure, whereas patients with sepsis due to genitourinary and skin/soft tissue had the lowest rates. Multisource sepsis causes a significantly higher ICU length of stay and hospital cost (JEGANATHAN et al., 2017). The prevalence of the respiratory system as the primary focus of infection in this study (48.84%) was corroborated by other authors (VINCENT et al., 2009). We believe that the main factors contributing to this result were: the large percentage of elderly patients (45.34%), who are more likely to develop lung diseases and a long period of ICU stay under artificial ventilation.

A microbiological diagnosis is an important tool for the treatment of patients with sepsis. However, in only 55 patients (63.95%) it was possible to isolate the etiological agent. Among the identified agents, about 38% were gram-positive bacteria. The main microorganisms isolated were *Staphylococcus haemolyticus*, *Candida albicans*, *Acinetobacter baumannii*, and *Staphylococcus* coagulase negative.

Most sepsis studies in Latin America show a predominance of infections caused by gram-negative bacteria (VINCENT et al., 2009; RODRÍGUEZ et al., 2011), but others conducted in Brazil revealed the prevalence of gram-positive bacteria (KOURY; LACERDA; BARROS NETO, 2006; ZANON et al., 2008), as confirmed by our results. Studies in the USA and Europe report a predominance of gram-positive bacteria, especially enterococci and staphylococci (VINCENT et al., 2009; ZAHAR et al., 2011). Interestingly, the incidence of fungi in microbiological isolates of patients increased considerably in most studies conducted in ICU (RODRÍGUEZ et al., 2011).

This study did not observe a direct relationship between etiological agent, site of infection, and mortality rate, and this correlation remains controversial in the literature (VINCENT et al., 2006; ZAHAR et al., 2011).

In a systematic review, Li et al. (2021) showed that culture positivity or negativity was not associated with the mortality of sepsis or septic shock patients (LI et al., 2021). We emphasize that the main consequence of the lack of identification of pathogens is the disproportionate use of broad-spectrum antibiotics and the inability to de-escalation of antimicrobials, which increases bacterial resistance and care costs (NIEDERMAN et al., 2021).

The high SOFA scores correlate with worse clinical outcomes and the risk of death, as reported in studies conducted in North America, Europe, and Brazil (VINCENT et al., 2006; KOURY; LACERDA; BARROS NETO, 2006; JUNCAL et al., 2011; CAO et al., 2021). Among the patients analyzed, 72.3% presented dysfunction in more than three organs corresponding to a mortality rate of about 93%.

Despite several studies to establish diagnostic, predictive, and prognostic biomarkers in septic patients, laboratory parameters such as blood glucose, lactate level, and blood cell composition continue to be widely used in clinical practice as indicators for treatment and outcome.

Sepsis is associated with a hypermetabolic state, in which the activation of the inflammatory response contributes to a sympathetic mimetic response with increased

levels of catecholamines, inducing an increase in insulin resistance which contributes to a state of hyperglycemia (LEVERVE, 2003). A single episode of hyperglycemia (glycemia > 200 mg/dL) in the first periods of hospitalization has been directly associated with a higher risk of death in non-diabetic septic patients. However, this correlation does not seem significant among diabetic patients (SCHUETZ et al., 2011).

In our study, the hyperglycemia events appear to be predictive of a worse clinical prognosis, and it was detected in 31.9% of non-surviving patients. The percentage of patients with hyperglycemia in the study (27%) was higher than the 9% margin described by Green et al. (2012), which can be explained by the high rate of patients with septic shock in our cohort (45.35%).

Hyperlactatemia has demonstrated a direct association with the mortality rate in septic patients[13]. Several factors may be related to the high serum lactate levels observed in septic patients, such as increased anaerobic metabolism due to tissue hypoperfusion, inhibition of pyruvate-dehydrogenase enzyme activity, and increased lactate synthesis induced by increased catecholamines, and reduced clearance due to liver dysfunction. The proportion of patients with hyperlactatemia in our study (45.96%) was higher than that reported by other studies, which tend to range from 6 to 13% (GREEN et al., 2012; ARNOLD et al., 2009). Hyperlactatemia proved to be an independent parameter for evaluating the prognosis of patients with a clear association with the mortality rate ($p<0.001$).

Tissue hypoxia and other inflammatory processes associated with sepsis can directly or indirectly activate the coagulation cascade, generating the formation of thrombi in the microcirculation, further aggravating tissue perfusion, resulting in acute organ dysfunction (UENO et al., 2002). During the septic condition, the activation of the inflammatory response and the coagulation system occur concomitantly, leading to an imbalance of hemostasis. Currently, several studies have shown that platelets can be activated both by immune system components and directly acting in cell recruitment and defense against infectious agents. Thus, parameters related to the coagulation system are increasingly relevant as indications of severity and conduct in the treatment of septic patients (JACOBI, 2022).

INR values higher than 1.5 and platelet count below 100.000/mm$^3$ were the parameters that presented the highest correlation with the mortality rate in our analyses, corresponding to 92.9% and 88.6% ($p<0.001$), respectively. However, some authors

characterize these variables as moderate predictive markers (DAUDEL et al., 2009; ADAMZIK et al., 2012).

In the present work, we evaluated the association of epidemiological, microbiological, clinical and laboratory parameters with the outcomes of septic patients in the ICU. Taken together, our data revealed that the presence of comorbidities, high SOFA scores, more than three organ dysfunctions, and sepsis severity are associated with a high mortality rate. These results may contribute to support clinical decisions by establishing priorities for rapid intervention with supportive therapies, promoting better care for septic patients.

This study presented some limitations that should be considered. The correlation between lactate levels and patients' risk of death was performed from direct dosages, and clearance capacity was not evaluated. It has been shown that clearance values may have a higher sensitivity as prognostic markers in septic patients (MONTIEL-JARQUÍN et al., 2012). The study population showed a tendency to high severity sepsis, which may have interfered with the correlations found. In addition, the data comes from a single center. A future multicenter study could corroborate the relationships described, consolidating the influence of the parameters studied in the population of northeastern Brazil.

## 5. CONCLUSION

Our results demonstrated a high mortality rate, suggesting that economic and social conditions may be related to the clinical outcomes observed in patients. However, to verify the existence of this association, multicentric research is necessary to address a significant number of public and private hospitals in the Northeast Region. In addition, our study observed that gender, age, ICU stay, site of infection, and type of agent causing the infection are not associated with the risk of death. However, the presence of comorbidities, high SOFA scores, three or more organ dysfunctions, and the severity of sepsis directly correlated with an overall increase in mortality.

Thus, the establishment of strategies to stabilize the disorders generated by the presence of comorbidities can positively influence the prognosis. In this context, the time is of reflection for all professionals, directly and indirectly, involved in the care of these patients to adapt the Surviving Sepsis Campaign approach to the hospital reality, using all available resources in the best possible way.

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