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Original Article

# Mortality risk associated with blood sugar levels in patients with septicemia in Intensive Care

## Risco de mortalidade associado aos níveis glicêmicos em pacientes com septicemia na Terapia Intensiva

Adriana Cristina Moreira[1], Luciano Garcia Lourenção[1], Natália Sperli Geraldes Marin Santos Sassaki[2], Claudia Eli Gazetta[1], Silvia Helena Figueiredo Vendramini[1], Maria de Lourdes Sperli Geraldes Santos[1]

**Objective:** to estimate the mortality risk associated with blood sugar levels in patients with septicemia in an Intensive Care Unit. **Methods:** this is a retrospective cohort study, performed with 263 patients with septicemia admitted to an intensive care unit, using the hospital management system data. **Results:** there was a higher frequency of patients aged from 14 to 59 years old (52.1%), male (55.9%), white (85.9%) of clinical specialties (65.8%); the hospitalization period ranged from 2 to 132 days; 91.6% of patients (n=241) were hyperglycemic at the time of hospitalization. There were 37 (14.1%) deaths, more frequent in patients with hyperglycemia during hospitalization (1.49 deaths/1,000 patients). **Conclusion:** hyperglycemia was a risk factor for mortality in patients admitted to the Intensive Care Unit.
**Descriptors:** Hyperglycemia; Sepsis; Mortality; Intensive Care Units.

**Objetivo**: estimar o risco de mortalidade associado aos níveis glicêmicos em pacientes com septicemia em uma Unidade de Terapia Intensiva. **Métodos**: estudo de coorte retrospectivo com 263 pacientes com septicemia internados em uma unidade de terapia intensiva, utilizando dados do sistema de gestão hospitalar. **Resultados:** houve maior frequência de pacientes na faixa etária de 14 a 59 anos (52,1%), sexo masculino (55,9%), raça branca (85,9%), de especialidades clínicas (65,8%); o período de internação variou de 2 a 132 dias; 91,6% dos pacientes (n=241) estavam hiperglicêmicos no momento da hospitalização. Ocorreram 37 (14,1%) óbitos, sendo mais frequentes nos pacientes que apresentaram hiperglicemia na hospitalização (1,49 óbitos/1000 pacientes). **Conclusão:** a hiperglicemia mostrou-se fator de risco para mortalidade em pacientes internados na Unidade de Terapia Intensiva.
**Descritores:** Hiperglicemia; Sepse; Mortalidade; Unidade de Terapia Intensiva.

[1]Faculdade de Medicina de São José do Rio Preto. São José do Rio Preto, SP, Brazil.
[2]União das Faculdades dos Grandes Lagos. São José do Rio Preto, SP, Brazil.

Corresponding author: Maria de Lourdes Sperli Geraldes Santos
Av. Brigadeiro Faria Lima, 5416. Vila São Pedro. CEP: 15090-000. São José do Rio Preto, SP, Brazil. E-mail: mlsperli@gmail.com


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## Introduction

Sepsis is a complex syndrome caused by the systemic inflammatory response of infectious origin, characterized by multiple manifestations, which can determine dysfunction or failure of one or more organs, or even death[1].

Over the past 20 years, although the overall mortality rate among patients has been reduced, there was an increase in incidence and deaths related to sepsis[1], considered the second cause of death in non-cardiac intensive care units worldwide[2].

Factors such as infectious focus, pneumonia as a cause of septic shock, more than three organ failures, oliguria and elevated lactate, detected at the admission to the Intensive Care Unit, showed relationship with the sepsis prognosis, that is a challenge for system health throughout the world, especially in the socioeconomic aspect[3].

In Brazil, sepsis mortality rates are higher than countries such as Argentina and India, placing it as an important public health problem[3-5].

Several factors contribute to the emergence of this panorama, and the most important are: increase of the elderly population; longer survival compared to many debilitating diseases; more frequent use of invasive techniques such as bladder and intravascular catheters, endotracheal tubes, among others; more immunosuppressed patients and hospital infections[2-4].

Hyperglycemia in critically ill patients, even in the absence of Diabetes *Mellitus*, is also a common problem and is associated with increased morbidity and mortality[6]. Once proven the benefit of performing intensive glycemic control in critically ill patients, studies were conducted to replicate these findings in critically ill patients with hyperglycemia in different situations[7-8].

Hyperglycemia, could have an etiological role in the prognosis of critical patients, or be just a marker of the severity of the patient. The mechanisms for the development of hyperglycemia in these patients include the release of hormones against stress (corticoid and catecholamine), inflammation mediators, vasopressors and glucose in parenteral solutions[7]. As a consequence of this stress response occurs the inhibition of insulin release and its action, enhancing glycogenolysis and inhibiting tissue uptake of glucose insulin-dependent[7].

It is believed that hyperglycemia causes an imbalance of the immune system and the inflammatory response that becomes unspecific, resulting in oxidative stress, mitochondrial dysfunction, cell death, and tissue injury with resultant organ failure[9].

Seriously ill patients frequently present persistent hyperglycemia. It is probable that hyperglycemia perpetuates the inflammatory response and interferes with coagulation mechanisms, resulting in organ failure[8]. In surgical patients with hyperglycemia, changes occur in mitochondrial structure and function of its oxidative complex[10].

Based on the previous, this article aimed to estimate the mortality risk associated with blood sugar levels in patients with septicemia in an Intensive Care Unit.

## Methods

This is a retrospective cohort study performed with 263 patients with septicemia admitted to an Intensive Care Unit of a referral hospital in a city in *São Paulo* Northwest. The study period was defined by researchers from January 2010 to December 2014.

The study included clinical and surgical patients diagnosed with septicemia (ICD A41 - another septicemia; ICD A41.9 - unspecified septicemia), admitted to the Intensive Care Unit for more than 24 hours.

Data were collected from the electronic patient record. After identifying the registration of medical septicemia diagnosis proceeded to the collection of study variables for the period between the hospitalization and the clinical outcome, i.e., discharge to the room or death. A form was elaborated to collect

the data containing socio-demographic variables (age group, gender, color) and clinical (hospitalization unit - clinical or surgical, diabetes mellitus, glucose values in the first 24 hours of admission, hospitalization stay in Intensive Care Unit - in days, hospitalization outcomes – discharge to the room, death).

After collection, the data were entered into a Microsoft Excel® spreadsheet and imported into the *Statistical Package for Social Sciences* Program, version 17.0. Descriptive analyses were performed with single frequency for nominal or categorical variables and central trend analysis (average and median) and dispersion (standard deviation) for continuous variables. The Fisher exact test was used to verify possible associations between the socio-demographic and clinical variables and the outcome variables (discharge to the room or death). The calculation of the Relative Risk was used to verify the mortality risk associated with blood sugar levels.

The study complied with the formal requirements contained in the national and international standards, regulatory of research involving human beings.

## Results

Two hundred and sixty-three patients were evaluated, 147 (55.9%) were male, 226 (85.9%) whites and 216 (82.1%) non-Diabetes *Mellitus* patients.

The age group ranged from 14 to 98 years old, average age of 55.85 years old (SD: ± 19.28), and 137 (52.1%) were between 14 and 59 years old, and 126 (47.9%) were 60 years or older.

Regarding inpatient unit, it was observed that 173 (65.8%) patients were clinical. The total hospitalization time ranged between 2 and 132 days with a mean of 28.5 days (SD: ± 1.3).

There were 37 (14.1%) deaths, 24 (64.9%) clinical and 13 (35.1%) surgical. The results showed that 241 (91.6%) patients had hyperglycemia, and there was a higher occurrence of deaths among these patients (36 to 97.3%).

**Table 1** - Characteristics of patients with septicemia admitted to the Intensive Care Unit, according to socio-demographic and clinical variables

| Variables | Population n(%) | Discharge to the room n(%) | Death n(%) | p |
|---|---|---|---|---|
| Age group (years) | n=263 (100.0) | n=226(100.0) | n=37 (100.0) | 0.032 |
| 14-59 | 137(52.1) | 124(54.9) | 13(35.1) | |
| ≥60 | 126(47.9) | 102(45.1) | 24(64.9) | |
| Gender | | | | 0.374 |
| Male | 147(55.9) | 129(57.1) | 18(48.6) | |
| Female | 116(44.1) | 97(42.9) | 19(51.4) | |
| Color* | | | | 0.413 |
| White | 226(85.9) | 198(87.6) | 28(75.7) | |
| Nonwhite | 37(13.0) | 28(12.3) | 6(16.2) | |
| Inpatient Unit | | | | 1.000 |
| Clinic | 173(65.8) | 149(65.9) | 24(64.9) | |
| Surgical | 90(34.2) | 77(34.1) | 13(35.1) | |
| Diabetes *Mellitus* | | | | 0.819 |
| Yes | 47(17.9) | 40(17.7) | 7(18.9) | |
| No | 216(82.1) | 186(82.3) | 30(81.1) | |
| Hyperglycemia | | | | 0.331 |
| Yes | 241(91.6) | 205(90.7) | 36(97.3) | |
| No | 22(8.4) | 21(9.3) | 1(2.7) | |
| Hospitalization stays (in days) | | | | 1.000 |
| Minimum | 2 | 5 | 2 | |
| Maximum | 132 | 132 | 69 | |
| Average ± Standard deviation | 28.5 ± 1.3 | 29.21 ± 1.43 | 24.3 ± 2.95 | |
| Median | 22 | 22.5 | 20 | |

*Color: three patients had no record of color and are not presented in the table

The results showed higher mortality among patients with hyperglycemia on admission at the Intensive Care Unit (1.49 deaths/1,000 patients). As noted in Table 2, the presence of hyperglycemia at the admission to the Intensive Care Unit tripled the risk of mortality of these patients (RR=3.31).

**Table 2** - Distribution of the number of deaths of patients with septicemia admitted to the Intensive Care Unit, according to the presence of hyperglycemia

| Variable | Deaths in the Intensive Care Unit | | | Incidence Coefficient/1000 patients | Relative risk |
|---|---|---|---|---|---|
| | Yes n(%) | No n(%) | Total n(%) | | |
| Hyperglycemia | | | | | |
| Yes | 36(97.3) | 205(90.7) | 241(91.6) | 1.49 | 3.31 [$IC_{95\%}$=0.47-22.84] |
| No | 1(2.7) | 21(9.3) | 22(8.4) | 0.45 | |
| Total | 37(14.1) | 226(85.9) | 263(100.0) | 1.40 | |

## Discussion

This study presents as a limitation, the sample of septic patients obtained from a single hospital, not allowing generalizing the results to other services. However, estimating the risk of mortality associated with blood sugar levels, contributes to the health professionals involved in the care of these patients to orientate the assistance actions for the control of blood sugar levels, preventing clinical complications and reducing mortality.

The average age of patients in this study was similar to that found in studies with a similar population in *Campinas/São Paulo* and *Teresina/Piauí*, whose average age was 53.8 and 51.5 years old, respectively[3,11]. The results corroborate with the literature that indicates that sepsis is more common in the elderly, because of increased susceptibility[4-7].

The results showed a prevalence of male patients, corroborating other authors who also found a prevalence of male patients with sepsis, admitted to Intensive Care Units in *Salvador* (55.2%)[5], *Campinas* (59.6%)[11] and in the south of *Minas Gerais* (56.2%)[12]. Previous studies showed that the highest incidence of sepsis and worse outcomes in male might be caused by hormonal differences between the both genders and higher levels of inflammatory mediators in women[5,13-14].

Regarding the stay in the Intensive Care Unit, the results of this study were higher than those observed in studies in *Salvador* and *Campinas*, in which the average length of stay was 9.3 and 8.2 days, respectively[5-11]. This difference may be due to the severity of the patients in this study since the hospital is a regional referral that serves high-complexity patients.

The higher prevalence of clinical admissions observed among patients in this study, was also identified in a study conducted in *Salvador* (89.7%)[5]. It is noteworthy, however, that sepsis is a frequent event in admissions due to surgical complications and in obstetric patients, is one of the five major causes of maternal mortality[15-16].

The presence of comorbidities may reflect the greater susceptibility of the population with chronic diseases in developing sepsis. Among the most frequent comorbidities, are: heart failure, Diabetes *Mellitus*, Malignant neoplasia, chronic renal failure, chronic liver disease, high blood pressure and squeals of neurological diseases[6-10,16-17], but this study showed more not diabetics patients.

It is described in the Brazilian consensus that the most common cause of death in septic patients is multiple organ dysfunctions. Every new dysfunction of an organic system adds approximately 15 to 20.0% to the initial risk of death[6.15]. The most commonly affected organs are the lungs, kidneys, heart and liver.

Therefore, despite the great advances in advanced life support contributing to increased survival, a better understanding of the complex pathophysiological mechanisms involving sepsis, especially by nurses, allows establishing a better quality care, corroborating the reduction in mortality.

The results of this study showed that the presence of hyperglycemia in the first 24 hours of hospitalization is a risk factor for mortality. Similar results were found in a study of patients in a hospital in southern *Minas Gerais*, which concluded that hyperglycemia is among the risk factors associated with increased mortality in patients with sepsis[12].

Thus, even though the clinical evidence has

contributed significantly to the advance of the sepsis treatment, the nurse has a key role in the patient's identification with sepsis and optimization of treatment[18], which requires the work of skilled professionals with in-depth knowledge about this theme.

However, a study about the knowledge of nurses in an Intensive Care Unit about sepsis stages, performed in *Rondônia*, showed that professionals have knowledge about the sepsis concept, but present knowledge deficit about Systemic Inflammatory Response Syndrome, Sepsis, Severe Sepsis, Septic Shock, and about treatment methods[19]. Another research about the application of sepsis algorithm by nurses in the Intensive Care Unit identified difficulties of professionals with some questions about the theme and showed that it is important for nurses to know about the subject, to work in a fast and precise manner, as standardizes the science literature[18].

These studies reinforce the need for further development of nursing professionals about sepsis actuation mechanism, which is one of the main causes of death in the Intensive Care Unit[2-3]. Therefore, permanent education is essential to improve the knowledge of professionals, increasing the quality of care and reducing sepsis mortality.

It is believed, finally, that new research with patient samples from different services could contribute to the elucidation of the profile and confirmation of hyperglycemia risk for mortality of these patients.

## Conclusion

Most patients in this study were male, not elderly, white, coming from clinical and while not diabetic, showed hyperglycemia in the first 24 hours of admission to the Intensive Care Unit. In response to the purpose of the study, it was found that hyperglycemia is a risk factor for mortality among patients with sepsis admitted to the Intensive Care Unit.

## Collaborations

Moreira AC and Santos MLSG contributed to the project design, collection, organization, analysis and interpretation of data, article writing and final approval of the version to be published. Lourenção LG contributed to the analysis and interpretation of data and relevant critical review. Sassaki NSGMS, Gazetta EC and Vendramini SHF contributed in drafting the article and relevant critical review of the article.

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