

Risk factors associated with increased mortality in septic patients admitted to the intensive care unit

Fatores de risco associados ao aumento da mortalidade em pacientes sépticos admitidos na unidade de terapia intensiva

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ABSTRACT

Sepsis is a potentially fatal clinical syndrome characterized by an abnormal response to infection associated with organic dysfunction. It is a relevant cause of admission to intensive care units (ICUs) and related to increased morbidity and mortality rates. This study aimed to evaluate the epidemiological profile of adult ICU patients of Lauro Wanderley University Hospital (HULW) in the municipality of João Pessoa (PB) to determine the risk factors associated with increased mortality in patients with sepsis. This retrospective and observational methodological study evaluated the epidemiological profile and characteristics of patients with sepsis, aiming to analyze the risk factors related to increased mortality. The mortality risk analysis was performed in two parts. The first was made from Pearson's chi-square test to determine the association between categorical

variables. Thus, only those variables with p values < 0.05 were included in the final logistic regression model to neutralize the effects of the confounding variables, for which values of $p < 0.05$ were considered significant. This study's findings suggest that septic shock and IMV and CVC use are the factors that deserve greater attention in patients with sepsis. However, among them, IMV is the main risk factor for death in ICU patients with sepsis. Variables such as sex, age, and comorbidities did not inflate the death rate for the patients studied.

Keywords: Sepsis, Intensive Care Unit, Epidemiology, Risk Factor.

RESUMO

A sepse é uma síndrome clínica potencialmente fatal caracterizada por uma resposta anormal a infecções associadas a disfunções orgânicas. É uma causa relevante de admissão em unidades de terapia intensiva (UTIs) e está relacionada ao aumento das taxas de morbidade e mortalidade. Este estudo teve como objetivo avaliar o perfil epidemiológico de pacientes adultos em UTI do Hospital Universitário Lauro Wanderley (HULW) no município de João Pessoa (PB) para determinar os fatores de risco associados ao aumento da mortalidade em pacientes com sepse. Este estudo metodológico retrospectivo e observacional avaliou o perfil epidemiológico e as características dos pacientes com sepse, com o objetivo de analisar os fatores de risco relacionados com o aumento da mortalidade. A análise de risco de mortalidade foi realizada em duas partes. A primeira foi feita a partir do teste qui-quadrado de Pearson para determinar a associação entre as variáveis categóricas. Assim, apenas aquelas variáveis com valores de $p < 0,05$ foram incluídas no modelo de regressão logística final para neutralizar os efeitos das variáveis de confusão, para as quais valores de $p < 0,05$ foram considerados significativos. Os resultados deste estudo sugerem que o choque séptico e o uso de VMI e CVC são os fatores que merecem maior atenção em pacientes com sepse. Entretanto, entre eles, o VMI é o principal fator de risco de morte em pacientes com sepse em UTI. Variáveis como sexo, idade e comorbidades não inflacionaram a taxa de mortalidade dos pacientes estudados.

Palavras-chave: Sepse, Unidade de Terapia Intensiva, Epidemiologia, Fator de Risco.

1 INTRODUCTION

Sepsis is a potentially fatal clinical syndrome characterized by an abnormal response to infection associated with organic dysfunction. It is a relevant cause of admission to intensive care units (ICUs) and related to increased morbidity and mortality rates ⁽¹⁾. Septic shock is an even more worrying state with a mortality rate that can reach 40% ⁽²⁾.

According to the SPREAD and PROGRESS studies, the mortality rate of patients with sepsis in Brazil is 55.7% and 57.4%, respectively ⁽⁴⁾. These percentages are significantly higher than the 45% and 38.2% reported for developing and developed countries, respectively ⁽³⁾. However, the SPREAD study authors concluded that

inadequate treatment, delayed administration of antibiotics, high disease severity, and hospital infection are directly related to patient mortality ⁽⁴⁾.

In general, the risk factors that affect the prognosis of patients with sepsis depend on the clinical condition of each since it influences the response to the mechanism of damage to the body ⁽⁴⁾. The most significantly affected patients include those who are male, elderly, African-American, developing a pulmonary infection, have been hospitalized for a prolonged time, have preexisting comorbidities, and underwent invasive methods such as invasive mechanical ventilation (IMV), a bladder tube, and/or a central venous catheter (CVC) ^(5,6).

Given these facts, the clinical and epidemiological characteristics of sepsis must be highlighted to identify the main risk factors since its prevalence is increasing, especially in developing countries such as Brazil. However, the country lacks studies and research on this subject; therefore, accurate information on the profiles of ICU patients in Brazil can facilitate the process of early diagnosis, enable accurate therapeutic interventions that help prevent complications, and reduce morbidity and mortality rates ⁽⁷⁾. Thus, this study aimed to evaluate the epidemiological profile of adult ICU patients of Lauro Wanderley University Hospital (HULW) in the municipality of João Pessoa (PB) to determine the risk factors associated with increased mortality in patients with sepsis.

2 MATERIALS AND METHODS

The study was approved by the Ethics Committee on Human Medical Research of the Center for Health Sciences (number CAAE 89416618.5.0000.5188). The need to collect informed consent was waived by the Hospital Infection Control Commission due to the study's retrospective nature. The responsible researchers declare complying with the current standards expressed in Resolution 466 dated December 12, 2012 of the National Health Council/Ministry of Health. The collected data were kept confidential. The patients were not identified and their privacy was maintained without prejudice.

The study was performed in the adult ICU of HULW in PB, a teaching hospital of the Federal University of Paraíba that currently has a structure of 126 offices and 212 hospital beds, of which 27 are in the ICU.

This retrospective and observational methodological study evaluated the epidemiological profile and characteristics of patients with sepsis between January 2016 and December 2019, aiming to analyze the risk factors related to increased mortality. The

dependent variable of this study was the clinical outcome of patients admitted to the adult ICU of HULW. The independent variables were related to intrinsic and extrinsic factors such as sex, age, duration of hospitalization, main site of infection, and invasive procedures performed. The presence of comorbidities was defined as any chronic disease prior to ICU admission and evaluated as a prognostic factor.

Thus, the convenience sample of the study consisted of all patients admitted to the HULW ICU who met the established inclusion criteria. Patients of both sexes who were admitted to the adult ICU during the selected period and presented a diagnosis characterized as sepsis at the time of admission or during the hospitalization were included. Patients with incomplete records were excluded from the study.

The studied data were derived from hospital infection records that were completed and analyzed by the multidisciplinary team of the CCIH (Hospital Infection Control Commission) of HULW. These records were reviewed and those patients identified by the CCIH as having sepsis at the time of admission or during the hospitalization period were included.

The data were organized in Microsoft Excel. After checking for errors and inconsistencies, the analysis occurred in the Software Statistical Package for Social Sciences for Windows version 20.0. The descriptive statistical analysis of the results was performed using absolute and relative frequencies for categorical variables and the mean and standard or median deviation with a quartile interval for continuous variables according to the data symmetry, when appropriate.

The normality distribution of continuous variables was investigated using the Shapiro-Wilk test. At the end, the association between the independent variables and the occurrence of death was evaluated. The mortality risk analysis was performed in two parts. The first was made from Pearson's chi-square test to determine the association between categorical variables. Values of $p < 0.05$ were considered statistically significant. The odds ratio was calculated for risk estimation along with the 95% confidence interval. Thus, only those variables with p values < 0.05 were included in the final logistic regression model to neutralize the effects of the confounding variables, for which values of $p < 0.05$ were considered significant.

3 RESULTS

After the analysis of all notification forms completed by CCIH between January 2016 and December 2019, 253 patients (48.2% male, 51.4% female) were included in

the study. According to the Shapiro-Wilk test of the non-normally distributed data, the median age was 62 years (range, 15–98 years). The average length of stay in the ICU was 10 days (range, 1–118 days). The mortality rate was 54.1%.

Of the total number of patients, 45.5% were elderly (over 65 years of age; Table 1). IMV was used in 61.3% of the cases in the study. A CVC was used in 87.4% of the cases in this study. Of the study cohort, 69.4% and 30.6% were diagnosed with sepsis and septic shock, respectively (Table 2).

Table 1. Age group of patients admitted to the HULW ICU

Age Group	Frequency	%
Under 65 years old	127	50,2
65 years or older	106	41,9
Not informed	20	7,9
Total	253	100,0

Source: Hospital Infection Control Commission Committees (HICC), 2019/2020

* (%) Percentage

Table 2. Frequency of Invasive Mechanical Ventilation (IMV), Central Venous Catheter (CVC) and Sepsis in patients admitted to the HULW ICU.

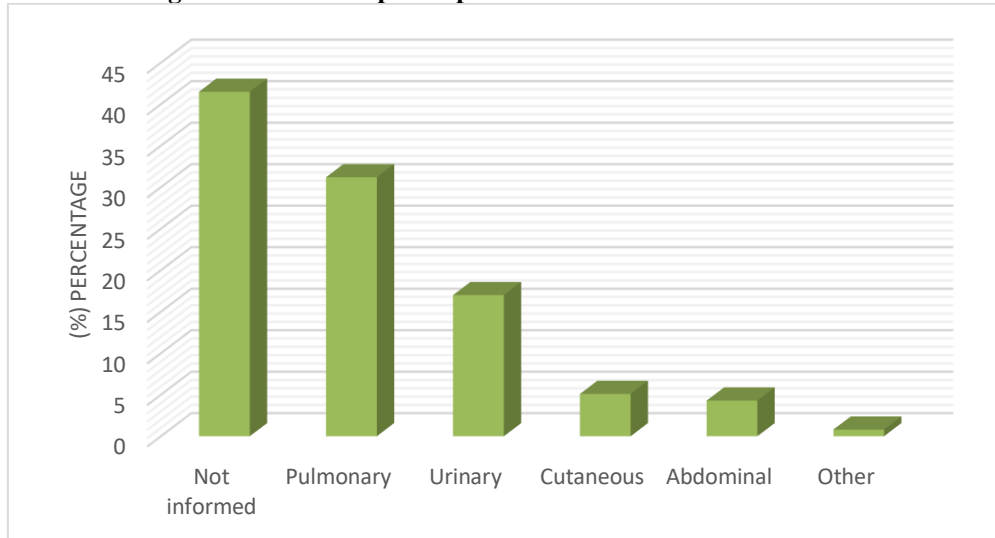
IMV	Frequency	%
No	98	38,7
Yes	155	61,3
Total	253	100,0
CVC	Frequency	%
No	32	12,6
Yes	221	87,4
Total	253	100,0
Septic shock	Frequency	%
No	175	69,2
Yes	77	30,4
Total	252	99,6

Source: Hospital Infection Control Commission Committees (HICC), 2019/2020

* (%) Percentage

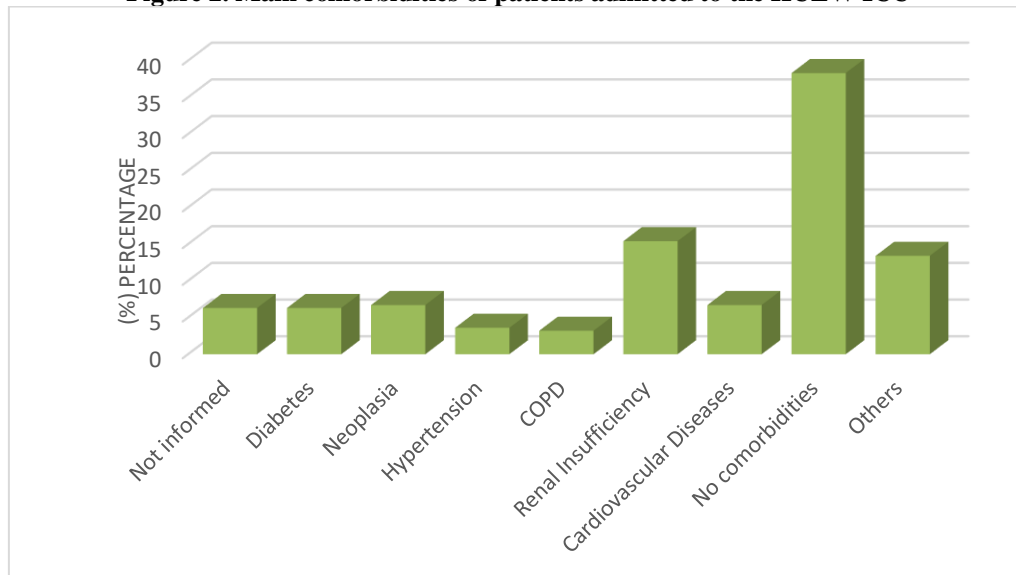
Regarding sepsis, patients with pulmonary sepsis prevailed (31.2%), followed by urinary sepsis (17%). In some patients (41.5%), the cause of the sepsis could not be determined (Figure 1). In the analysis, the majority of patients had no comorbidities, but those who did commonly had renal failure (15.4%) (Figure 2).

Figure 1. Focus of sepsis in patients admitted to the HULW ICU



Source: Hospital Infection Control Commission Committees (HICC), 2019/2020

Figure 2. Main comorbidities of patients admitted to the HULW ICU



Source: Hospital Infection Control Commission Committees (HICC), 2019/2020

*COPD: Chronic obstructive pulmonary disease

With the execution of the chi-square test, variables including sex, age, duration of hospitalization, presence of chronic diseases, or focus of sepsis were not significantly correlated with increased mortality with values of $p > 0.05$ (Table 3). Septic shock, the use of IMV, and the use of a CVC were significantly associated with increased mortality ($p < 0.05$) (Table 4). Thus, these three variables were included in the logistic regression analysis. Among them, only the use of IMV was identified as a risk factor for increased mortality in patients with sepsis ($p < 0.05$) (Table 5).

Table 3. Association of Variables, Sex, Age Group, ICU Stay Duration and Chronic Disease according to the Evolution of Patients Hospitalized in the ICU of HULW

Variables	Evolution				OR	CI (95%)	p-value
	Death		High				
	(N)	(%)	(N)	(%)			
Sex							
Male	62	55,9	49	44,1	1,177	0,693-1,998	0,547
Female	57	51,8	53	48,2			
Total	119	53,8	102	46,2	-	-	-
Age group (years)							
Under 65 years	54	47	61	53	1,632	0,931-2,859	0,086
65 years or older	52	59,1	36	40,9			
Total	106	52,2	97	47,8	-	-	-
ICU stay duration							
Less than 72 hours	20	64,5	11	35,5	0,661	0,299-1,463	0,305
More than 72 hours	95	54,6	79	45,4			
Total	115	56,1	90	43,9	-	-	-
Presence of Chronic Disease							
No	50	57,5	37	42,5	0,752	0,432-1,310	0,314
Yes	61	50,4	60	49,6			
Total	111	53,4	97	46,6	-	-	-

Hospital Infection Control Commission Committees (HICC), 2019/2020

- * (%) Percentage
- * (N)
- * (OD) Odds Ratio
- * (CI) Confidence Index
- * (p)

Table 4. Association of Variables: IMV, CVC, Sepsis and the Evolution of Patients Hospitalized in the HULW ICU

Variables	Evolution				OR	CI (95%)	p-value
	Death		Discharge				
	(N)	(%)	(N)	(%)			
IMV							
Yes	97	72,9	36	27,1	7,732	4,203-14,223	0,000
No	23	25,8	66	74,2			
Total	120	54,1	102	45,9	-	-	-
CVC							
Yes	111	57,5	82	42,5	3,008	1,303-6,946	0,008
No	9	31	20	69			
Total	120	54,1	102	45,9	-	-	-

Sepsis and Septic Shock							
Sepsis	72	48,3	77	51,7	2,139	1,190-3,843	0,010
Septic Shock	48	65,8	25	34,2			
Total	120	54,1	102	45,9	-	-	-

Source: Hospital Infection Control Commission Committees (HICC), 2019/2020

* (%) Percentage

* (N)

* (OD) Odds Ratio

* (CI) Confidence Index

* (p-value)

Table 5 - Final Model of Multivariate Analysis: IMV, CVC and Septic Shock.

Risk Factors	OR	IC 95%	p-value
IMV			
Yes	8,062	4,006-16,225	p< 0.001
No	-	-	-
Use of CVC			
Yes	0,711	0,263-1,917	p=0.500
No	-	-	-
Sepsis/Shock			
Septic Shock	1,826	0,945-3,529	p=0.073
Sepsis	-	-	-

Source: Hospital Infection Control Commission Committees (HICC), 2019/2020

* (%) Percentage

* (OD) Odds Ratio

* (CI) Confidence Index

* (p-value)

4 DISCUSSION

Among the study subjects, age above 65 years was not a risk factor for death. However, Barros *et al.* identified an association between this age group and a negative prognosis ⁽⁸⁾. Particularly in this study, men with sepsis of differing severities were the most affected and presented a higher mortality rate ⁽⁸⁾. However, in the present study, despite the prevalence of hospitalized women (51.4%), sex was not associated with a higher risk of death ⁽⁸⁾.

The most prevalent sepsis focus was pulmonary; however, it did not significantly influence a higher risk of mortality. Thus, in the city of São Paulo, Santos *et al.* showed that the pulmonary site has an increasing implication in the infectious process ⁽⁹⁾. In

addition, respiratory tract infection is the most common cause of sepsis, accounting for about half of all cases. Prado *et al.* reported that ventilator-associated pneumonia is a main factor associated with sepsis-related pulmonary disorders ⁽⁵⁾.

The mean length of stay of ICU patients was 10 days. It should be emphasized that patients admitted to the ICU are usually seriously ill, such as with septic shock, which is more likely to lead to death; therefore, a short hospital stay. In this context, it is noteworthy that the average ICU length of stay for sepsis is 7.1 days ⁽⁸⁾.

Barros *et al.* also used logistic regression to identify risk factors associated with higher mortality in patients with sepsis. Among them, comorbidities and hospitalization time were determinants of patient death. However, in this study, the existence of chronic diseases and the duration of hospitalization did not present significant results.

According to the implemented regression model, septic shock, although significant, was not a risk factor for death. These results were inconsistent with those reported in the integrative review by Luz Filho *et al.* that considered the scientific productions published in the last decade on risk factors for death among patients with sepsis ⁽¹⁰⁾. The study shows that the evolution of septic shock significantly affects patient mortality ⁽¹⁰⁾.

The use of invasive procedures such as CVC and IMV was significant. As some researchers claim, these two factors are associated with a high number of deaths of sepsis in the ICU. The more severe the sepsis, the greater the patient's exposure to invasive procedures ⁽⁸⁾. This statement corroborates the present study as observed after a logistic regression model in which the use of IMV (61.3% of cases) proved to be a risk factor for death. The use of IMV in patients with sepsis may improve their prognosis. However, if it cannot be performed correctly and safely, as it can cause serious complications. The vast majority of ICU patients require this type of IMV support since it increases the oxygen supply to the tissues and reduces the respiratory work of critically ill patients. Moreover, this measure is among the interventions recommended by the Surviving Sepsis Campaign guidelines ⁽¹¹⁾.

The use of CVC, although significant, was not a risk factor after logistic regression was applied, a finding that is inconsistent with that reported by Zanon *et al.*, whose observation of the use of a CVC was considered among the most worrisome risk factors for death ⁽¹²⁾. However, in cases of primary blood infection, the use of a CVC is a relevant risk factor for laboratory-confirmed sepsis. Rosenthal *et al.*, when surveying 55 ICUs in eight different countries, observed that blood infections associated with

CVC use (30%) were the highest risk factor for healthcare-related infections next to IMV-associated pneumonia ⁽¹³⁾. The analysis performed here revealed that the use of IMV in the HULW ICU was an important risk factor for death. Other risk factors commonly mentioned in recent studies, such as advanced age, male sex, septic shock, comorbidities, and CVC use were not statistically relevant in this study. However, these variables have significant relevance and are important in the literature as risk factors for death in cases of sepsis.

Nevertheless, studies are lacking related to the risk factors and worsening of sepsis among ICU patients worldwide, especially in Brazil. It is noteworthy that the evidenced data on this infection are extremely relevant because they can help in the elaboration and insertion of public policies, as well as increase our understanding of the characteristics of this infection ⁽⁸⁾. Although research in this area has intensified over the last decade, information on sepsis in Brazilian ICUs remain limited and insufficient ⁽⁵⁾.

5 CONCLUSION

This study's findings suggest that septic shock and IMV and CVC use are the factors that deserve greater attention in patients with sepsis. However, among them, IMV is the main risk factor for death in ICU patients with sepsis. Variables such as sex, age, and comorbidities did not inflate the death rate for the patients studied. The average ICU stay duration was 10 days, higher than the average in Brazil. In addition, a vast majority of patients undergo invasive treatment such as IMV and CVC use. Finally, among the analyzed patients, the main sepsis focus was pulmonary, with a high death rate.

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