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SEPSIS: RISK FACTORS IN PATIENTS ADMITTED TO A HOSPITAL IN TERESINA, PIAUI

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ABSTRACT

Objective: To analyze the epidemiological profile of patients with sepsis and the worsening factors in a university hospital. **Method:** This is an observational, cross-sectional, descriptive and retrospective study with medical records of patients who had a clinical diagnosis of sepsis. It was carried out at the University Hospital of the Universidade Federal do Piauí. Correlated "quick SOFA" score criteria - qSOFA (inpatient unit) and Sequential Organ Failure Assessment - SOFA (Intensive Care Unit), for sepsis. 209 records with sepsis were analyzed during January / 2018 to January / 2019. **Results:** The hospitalization profile was equivalent for both sexes with an average age of 60 years, average hospitalization time (64.5 days), and 57.9% of deaths. Hospitalizations in the intensive care unit were 32.5%, with vascular focus admission disease (27.3%) and neoplasms (22.5%); Urinary tract infection not associated with catheter-ITU-AC (23.4%) and Primary bloodstream infection-laboratory IPCS (17.7%), the microorganisms prevalent in *Klebsiella pneumoniae* (20.6%) and *Acinetobacter baumannii* (16.3%), respectively multidrug resistant (MDR), 79.1% and 85.3%. Associations of risk factors for worsening sepsis: age group and length of stay ($p = 0.0034$), MDR bacteria and length of stay ($p = 0.0001$), surgical procedure and neoplasia ($p = 0.0071$) and disease admission rate Infection and death ($p = 0.0246$). **Conclusion:** The risk factors for worsening sepsis and their associations have an interaction relationship, and lead to believe in the influence of health conditions and unfavorable outcomes for septic patients.

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INTRODUCTION

Sepsis is an acute picture of organ dysfunction to a host's unregulated response to an infection (1). Sepsis (2) is an expensive disease with a high fatality, being considered one of the major public health problems, and its incidence has increased over the past few years. Some clinical conditions are important in compromising the patient's immune response, which may increase the incidence of infections such as invasive procedures, aging, immunosuppression and the presence of the human immunodeficiency virus (HIV), the use of immunosuppressive and cytotoxic agents, malnutrition, alcoholism, diabetes mellitus, transplant procedures, and a greater number of infections by multi-resistant microorganisms to antibiotics.

In addition, it is considered that the length of hospital stay as a condition of worsening and the appearance of sepsis, this results from the evolution of more intensive treatment and the good prognosis of a patient with chronic diseases (3). Patients admitted to the Intensive Care Unit (ICU) are at high risk of developing septicemia. Taking into account that these patients may undergo invasive procedures that increase the risk, such as insertion of peripheral tubes, central venous catheters and tracheal ventilation (4). In the United States of America (USA), about 3% of hospitalized patients have sepsis and part of these are treated in Intensive Care Units (ICU) (5). In this sense, the importance of managed protocols that enable early diagnosis and treatment is emphasized, in order to obtain a high level of efficiency in care, impacting the survival of patients as well as reducing the length of hospital stay and morbidity and mortality rates (6). According to Lobo (7) and collaborators from the national registry, about 30% of adult

ICU beds in the country, with data from 190,999 hospitalized patients, between 2010 and 2016, in 638 ICUs from 349 public and private hospitals that were part of the "Brazilian ICUs" project, demonstrate a progressive increase in the number of sepsis cases in Brazilian Intensive Care Units, from 19.4% of the total hospitalizations in 2010 to 25.2% in 2016. A retrospective analysis of causes of death between 2002 and 2010 showed an increase in absolute numbers and proportions for sepsis of 9.77% in 2002 and 16.46% in 2010. Mortality rates increased by age were also found, being higher in the elderly. These data confirm the health problem that is sepsis in Brazil (8). The role of the Hospital Infection Control Commission (CCIH) is paramount in establishing an appropriate method of epidemiological surveillance, adapting criteria to the staff structure, the risk of assistance, measuring magnitude, severity, pragmatism of fees and costs (9,10,11, 12,13). Thus, the preparation of the study is based on the context of risk assessment of patients admitted to the hospital, taking into account the epidemiological data, the location of the bed upon admission, the existence of Infection Related to Health Care (HAI), caused by multiresistant bacteria to antimicrobials. The analysis of these criteria elucidates whether the association of these parameters leads to considering them as risk factors for sepsis.

MATERIALS AND METHODS

This is an observational, cross-sectional, descriptive and retrospective study with medical records of patients who had a clinical diagnosis of sepsis, in order to analyze the risk factors for worsening sepsis. It was carried out at the University Hospital of the Federal University of Piauí. It targets medical records of patients hospitalized with sepsis, in addition to the hospital infection notification forms, request for restricted antibiotics from the Health Surveillance, specifically the Hospital Infection Control Commission (CCIH). In data collection, an instrument was used containing variables in relation to the patient on his clinical-epidemiological profile (age, sex, basic disease type, hospital discharge and death); data on infection related to health care, length of stay and its evolution; pathogen data, antimicrobial resistance. In the period from January 2018 to January 2019, 5,784 patients were admitted to the University Hospital and 438 were diagnosed with Health Care-Related Infections (HAI). The interest of the work is the patients diagnosed with sepsis. The sample was identified according to the Sequential Organ Failure Assessment - SOFA criteria for patients admitted to the ICU and "quick SOFA" - qSOFA for patients admitted to the four hospitalization posts (1,2,3 and 4), thus 209 were selected hospitalizations, that is, all records with a clinical diagnosis of sepsis, from January 2018 to January 2019. Non-parametric significance tests were used for statistical analysis, Chi-square test or Fisher's exact test and measure of statistical significance, with a 95% confidence interval (95% CI) to assess the association between variables. The project was approved by the UFPI ethics committee with opinion number 2402435.

RESULTS

Table 1 shows the total sample, which consisted of 209 medical records of patients diagnosed with sepsis, of which 106 (50.7%) were female and 103 (49.3%) were male; the age group had an average of 60 years, ranging from 18 years to 89 years. The average number of days of hospitalization was

64.65 days with a longer period of 360 days. The number of hospitalizations that resulted in death was 121 (57.9%).

Table 1. Characterization of patients admitted with sepsis to a teaching hospital in Teresina (PI), 2019. N: 209

Variables	N	%	Mean	Min	Max	Std
Sex						
Feminine	106	50.7%				
Male	103	49.3%				
Age Range			60	18	89	15
≤24 years (young)	3	1.4%				
25- 59 years old (Adult)	91	43.5%				
≥60 years old (Elderly)	115	55.0%				
Length of Hospitalization			64.65	4.00	360.00	68.52
≤1 month	59	28.2%				
1- 6 Months	140	67.0%				
> 6 months	10	4.8%				
Death						
No	88	42.1%				
Yes	121	57.9%				

Table 2. Characterization of the place of admission, disease present at admission and medical specialty of inpatients with sepsis of a teaching hospital in Teresina (PI), 2019. N: 209

Variables	N	%
Place of stay		
Rank 1	32	15.3%
Rank 2	22	10.5%
Rank 3	46	22.0%
Rank 4	41	19.6%
ICU	68	32.5%
Diagnosis present at admission		
Hepatic	14	6.7%
Infection	18	8.6%
Neoplasm	47	22.5%
Pulmonary	8	3.8%
Trauma	20	9.6%
Vascular	57	27.3%
Others	45	21.5%
Clinic		
Cardiology	27	12.9%
General Physician	19	9.1%
Medical clinic	40	19.1%
Gastroenterologist	11	5.3%
Geriatrics	30	14.4%
Hematologist	11	5.3%
Oncology	24	11.5%
Others	47	22.5%
Surgical procedure		
Yes	126	60.28%
No	83	39.72%

Table 2 shows the places where patients were admitted, and in the ICU, the highest number of sepsis cases was 68 (32.5%), followed by hospitalization 3 with 46 (22.0%). The most prevalent HAIs were catheter-associated urinary tract infection (ITU-AC) 49 (23.4%), laboratory primary bloodstream infection (IPCS) with 37 (17.7%), ventilation-associated pneumonia (VAP) 33 (15.8%), pneumonia 31 (14.8%). Sample collections for microbiological examination were blood (blood culture) and urine (urine culture), both with 73 (34.9%) (Table 3). The bacteria with the highest prevalence of multiresistance to antimicrobials (MDR) were *Acinetobacter baumannii* 29 (85.3%), *Escherichia coli* 13 (81.3%) and *klebsiella pneumoniae* 34 (79.1%). Extremely multiresistant antimicrobial bacteria (XDR) was *Acinetobacter baumannii* 1 (2.94%) (Table 4).

Table 3. Characterization of the type of nosocomial infection, material collected and isolated microorganism from patients admitted with sepsis to a teaching hospital in Teresina (PI), 2019. N: 209

Variables	n	%
Type of IRAS		
IPCS Laboratory	37	17.7%
Deep ISC	1	0.5%
ISC-Clean	11	5.3%
ISC- Not Clean	12	5.7%
ITU-AC	49	23.4%
ITU-NAC	24	11.5%
Other IRAS	11	5.3%
PAV	33	15.8%
Pneumonia	31	14.8%
Collected material		
Blood culture	73	34.9%
Wound Secretion	8	3.8%
Surgical Wound Secretion	4	1.9%
Tracheal Secretion	42	20.1%
Uroculture	73	34.9%
Others	9	4.3%
Isolated microorganism		
Acinetobacter baumannii	34	16.3%
Candida albicans	27	12.9%
Escherichia coli	16	7.7%
Klebsiella pneumoniae	43	20.6%
Pseudomonas aeruginosa	33	15.8%
Staphylococcus aureus	15	7.2%
Others	41	19.6%

2019. N: 209.

Table 4. Sensitivity Profile for Antimicrobials for Multiresistant Bacteria according to the classification MDR, XDR and PDR. Teresina (PI), 2019. N: 209

<i>acinetobacter baumannii</i>	No MDR	%	MDR	%	XDR	%	PDR	%	TOTAL
<i>enterobacter spp</i>	4	11.76	29	85.3	1	2.94	0	0	34
<i>enterococcus spp</i>	4	26.67	11	73.3	0	0	0	0	15
<i>escherichia coli</i>	4	26.67	11	73.3	0	0	0	0	15
<i>klebsiella pneumoniae</i>	3	18.75	13	81.3	0	0	0	0	16
<i>morganella spp</i>	9	20.93	34	79.1	0	0	0	0	43
<i>proteus spp</i>	0	0	1	100	0	0	0	0	1
<i>provides rettgeri</i>	1	25	3	75	0	0	0	0	4
<i>pseudomonas aeruginosa</i>	0	0	1	100	0	0	0	0	1
<i>raoultella planticola</i>	18	54.55	15	45.5	0	0	0	0	33
<i>serratia marcescens</i>	1	100	0	0	0	0	0	0	1
<i>staphylococcus aureus</i>	1	50	1	50	0	0	0	0	2
<i>acinetobacter baumannii</i>	10	66.67	5	33.3	0	0	0	0	15
	55		124		1		0		

Legend: MDR - multidrug-resistant those that are not susceptible to at least one agent in three or more antimicrobial categories. XDR - Extensively drug-resistant as not susceptible to at least one agent in all, except two or less antimicrobial categories. PDR-Pandrug-resistant is defined as not susceptibility to all agents in all antimicrobial categories (ie, no agent tested as susceptible to that organism).

An association was found between MDR Bacteria and other risk factors, of which, length of stay ($p = 0.0001$), Death ($p = 0.003$). The analysis of the associations between the performance of the surgical procedure and other risk factors for sepsis was evidenced, there was an associative relationship with neoplasia-type disease ($p = 0.0071$). The association of the place of hospitalization and other factors of association, there was an associative relationship between age group ($p = 0.004$), length of hospital stay ($p = 0.0013$), Infection-like disease ($p = 0.0012$). The association of death and other factors of worsening of sepsis, evidenced an associative relationship between age group ($p = 0.0264$), MDR Bacteria ($p = 0.0036$), Infection Type Disease (0.0246).

DISCUSSION

The prevalence of sepsis at HU-UFPI was 3.61% in the period from January 2018 to January 2019. The average age group of 60 years, characterized as a risk factor for sepsis, in which there is an immunosenescence relationship that is characteristic of the reported age group, in which the

susceptibility to infectious diseases is greater, also observed in this study (14). Another study (15) emphasizes the nature of hospitalization of patients in a medical clinic (42.4%), with a prevalence of respiratory complications and kidney diseases in the diagnosis of ICU admission. In the present study, the medical clinic with 19.1% patients and geriatrics (14.4%), corroborating a large part of the diagnosis of sepsis for elderly patients, however, there is a dispersion of origin from other clinics, which suggests that IRAS for the diagnosis of sepsis is a general event of the hospital. The average length of stay is well above what was seen in the study (16) in which the length of stay was 27.2 days, in the study it was 64.5 days with a large number of patients hospitalized over 90 days, 60, 28% of all hospitalizations had at least one surgical intervention. Other authors (8) carried out a study from 2002 to 2010 and found 12.9% of deaths in Brazil were related to sepsis. The death rate in the present study was 57.9%. In studies (17,15), the death rate is 53.03% and 63.4%. Stratified the study by age groups, the death rate over 60 years was 76.52%, and the sample of patients aged 25 to 59 years was 64.83%, which may suggest an equivalent proportion of deaths in both groups.

When analyzing death and place of hospitalization, it is possible to observe that the inpatient posts had a death rate of 37.5% and in the ICU the fatal outcome for hospitalized patients was 100%. Admission diseases obtained scattered results in a wide range of etiologies, but we highlight vascular diseases with 27.3% and neoplasms with 22.5%. That corroborates with Moura et al. (2017), the main underlying diseases found in this study were pneumonia (PNM) (9.8%), polytrauma (6.7%), respiratory failure (4.6%), severe community aspiration pneumonia (CAP) and traumatic brain injury (TBI) (2.9%), pancreatitis (2.6%), COPD (2.3%). We emphasize, comorbidities are commonly exposed in several studies analyzed, so we consider it a limitation in our study, because the data source did not provide a regularity in the demonstration in the medical records. The authors report (15) that the origin of sepsis is related to HAI, in 50.2% of the patients studied. In this sense, the characterization of HAIs is a factor of high importance in the diagnosis of sepsis and is a risk factor when related to microorganisms resistant to antimicrobials, aggravating treatment.

Most HAIs of the type Urinary tract infection not associated with catheter-ITU-AC were found, characterized by urinary infection in the presence of a urinary device that, according to Brazil (9), had an incidence density with CVD (Bladder Catheter) of 4.70 / 1000 people / year, in Adult ICU, and IPCS Laboratory, which suggests bacteremia in a blood sample (blood culture). This IPCS is mandatory for all hospitals that have more than 10 ICU beds. However, it is worth mentioning that Pneumonia and VAP obtained 14.8% and 15.8% of the diagnoses associated with sepsis, according to the authors' research (17), are related to sepsis with an estimate of 43% and obtained considerable prevalence in the sample. , and for Brazil (8), the incidence density of VAP was 11.50, which is the highest of the HAIs in this study. Of the isolated microorganisms relevantly are Gram negative bacilli *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, which corroborates with the study (17) that about 20% of the isolated bacteria were Gram negative bacilli, and (15) that presented isolated Gram negative bacilli by 12.1%. And similarly with the notifications of microorganisms in the ICU of Brazilian hospitals, they obtained *Klebsiella pneumoniae* with 19%, *Acinetobacter baumannii* with 10.7%, *Pseudomonas aeruginosa* with 9.6% (9).

The classification of the bacteria resistance profile (18) is based on the strains of pathogenic bacteria most frequently found in healthcare, which provides us with an internationally comparable frequency, and these bacteria were analyzed in the study that presented themselves as Multidrug Resistant (MDR) were: *Staphylococcus aureus* (33.3%), *Enterococcus spp.* (73.3%), *Enterobacteriaceae* (*Enterobacter spp.* 73.3%, *Escherichia coli* 83.5%, *Klebsiella pneumoniae* 79.1%), *Pseudomonas aeruginosa* 45.5% and *Acinetobacter spp.* (85.3%) 40% of Brazilian bacterial isolates are *Klebsiella spp.* Resistant to carbapenems and 80% of isolates are *Acinetobacter spp.* In Brazilian patients with IPCS-type HAI (9). By associating risk factors for sepsis, length of stay, age group, type of underlying disease, antimicrobials with microbial resistance, multidrug-resistant bacteria (MDR), surgical procedure and place of hospitalization, and the outcome variable death, we analyzed whether these factors together have the strength to increase the prevalence of the disease in the sample. Thus, they were statistically placed in

relational evidence. It was evaluated that the age group and length of stay have an association ($p = 0.0034$), a major risk relationship between the patient's age and the increase in length of stay is suggested. Likewise, it is suggested that length of stay and MDR Bacteria ($p = 0.0001$), that the longer the length of stay, the greater the prevalence of multi-resistant bacteria, the length of stay increases the severity of septic disease, characterized by presence of multi-resistant bacteria to antimicrobials (17). Regarding the relationship between age group and the prevalence of trauma ($p = 0.01800$), it is evident that trauma can be associated with sepsis in an elderly patient. According to the authors Cardoso Junior and Silva (19) traumatized patients aged over 50 years diagnosed positively with sepsis (37.2%) died.

It is important to highlight the use of antimicrobials in the hospital environment and the association with a risk association factor with an emphasis on classes mostly described as broad spectrum and belonging to the MDR / XDR / PDR classification are related to the worsening of the clinical picture and treatment difficulty (17.18). The analysis of the association of antimicrobials to which the bacteria were resistant, suggested a relationship with length of hospital stay and found an association with Cefazolin (2nd generation cephalosporin) ($p = 0.010$), Cefoxitin (cephamycin) ($p = 0.026$), Cefazidime (cephalosporin 3rd generation) ($p = 0.007$), Ceftriaxone (3rd generation cephalosporin) ($p = 0.031$), Linezolid (oxazolidinones) ($p = 0.034$), Penicillin ($p = 0.029$) and Piperacillin + Tazobactam (antipsudomone penicillin + inhibitor betalactamase) ($p = 0.013$). The performance of a surgical procedure has an associative relationship with neoplasia-type disease ($p = 0.0071$), denotes a risk of sepsis in neoplastic patients when undergoing invasive procedures, which may be related to immunological integrity. In the study (17) there is a prevalence of 16.3% of patients with neoplasms, and according to Cortez (20) patients undergoing surgical procedures (60.4%), may be associated with disorders related to auto antibodies and micro events and macrovascular. The (location) hospitalization post was related to length of stay ($p = 0.0013$) and Infection-like Disease ($p = 0.0012$), which may suggest the risk of sepsis with prolonged hospital stay and whether underlying disease is infection.

What can suggest both a community infection and an HAI can progress to sepsis, even in highly sensitive bacteria. In another study, about 15.6% of patients were diagnosed at least once with an infection during the hospital stay (21). The lethality in the study carried out between 2002 and 2010 found an increase of 77.5%, and estimated at 3.5 deaths / 100,000 inhabitants per year (8). In a study by other authors, they reported the fatal outcome due to HAI in 34.5% of their sample (15). And the mortality associated with sepsis was particularly high in patients over 60 years of age in the present study. The death outcome was analyzed in association with the age group ($p = 0.0264$), which can statically suggest that there is an increased risk of sepsis with an unfavorable outcome for advanced age. The analysis of the associative relationship between Death and MDR Bacteria ($p = 0.0036$), corroborates how the risk factor Multiresistant Bacteria may suggest an increased risk of sepsis with an unfavorable outcome. The study at Hospital Universitário de Londrina Study with notification forms and medical records of adult patients found that half of the sample of patients with infection colonized by multi-resistant microorganisms (45.2%) evolved to death (16).

Conclusion

Sepsis is a pathology of global and multifactorial prevalence, forcing the public and private health care network to follow diagnostic and treatment parameters with characteristics of international comparability. Our study took into account the technique used by the body of professionals related to sepsis screening, which are the microbiology laboratory, the hospital infection control committee and the patient safety center. According to the objectives of our study, we can accentuate the seriousness of the situation of combating and controlling sepsis in the university hospital. We can attribute this severity to the hospital profile that occurs in the reception of critically ill patients, with chronic diseases, especially patients with neoplasms and of great social vulnerability of the entire hospital network in the Brazilian mid-north. The study demonstrated in its analysis that the sample of hospitalizations, the factors of aggravation of sepsis imply the presence of multidrug resistant bacteria with emphasis on the MDR / XDR / PDR classification, the use of antimicrobial therapy in which the bacteria have multidrug resistance, the range age above 60 years, prolonged hospital stay, the use of invasive devices, surgical procedures, the presence of neoplasia and infection as the underlying disease. The limitations of the study were the absence of an accurate sepsis diagnosis protocol, lack of information on comorbidities that should be referenced by primary care, in addition to the fact that the sepsis protocol developed by the patient safety sector at the university hospital is still it is not in operation and is not widespread in the institution. Therefore, intervention studies at the University Hospital are suggested, focusing on international recommendations to combat sepsis and septic shock. This includes the necessary participation of the entire hospital, academic and other associated actors for the implementation and maintenance of programs to prevent and combat sepsis.

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