



## BLOODSTREAM INFECTIONS IN HOSPITALIZED PATIENTS IN CRITICAL CARE UNITS FROM A BRAZILIAN PUBLIC HOSPITAL

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### ABSTRACT

**Objective:** To describe the epidemiology of bloodstream infections (BI) in adult hospitalized in critical care units of a teaching hospital. **Methods:** This is an epidemiological study, using descriptive and quantitative approaches, done through the analysis of patient records between August 2015 and July 2016. **Results:** Among the 56 hospital-acquired infections, 42 were primary bloodstream infections related to central venous catheter (CVC). The most prevalent bacterium was oxacillin-resistant coagulase-negative *Staphylococcus*. Patients who developed blood infections presented average age of 50.57 years, with male dominance and the main associated comorbidity was high blood pressure. The average hospital stay was of 41.31 days. **Conclusions:** The results showed high prevalence of BI related to CVC, suggesting the need for improvement in the implementation of measures for the prevention and control of these infections.

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### INTRODUCTION

Individuals hospitalized in health institutions are exposed to a wide variety of pathogenic microorganisms, especially in Intensive Care Units (ICUs), where invasive procedures are usual. Hospital infections (HI), defined as any infection acquired after hospitalization and occurring during

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hospitalization or after discharge, related to hospitalization or hospital procedures, have a great impact on morbidity and mortality of adult and elderly population, as well as expenses on diagnostic and therapeutic procedures (Oliveira, 2010; Agência Nacional de Vigilância Sanitária, 1998). Among all types of HI, the bloodstream infections (BI) have multifactorial pathophysiology complications, and is frequent in hospitalized patients. The main cause of BI is the use of intravascular devices, mainly the central venous catheter (CVC). A Brazilian study analyzed 68 cases of BI associated with use of CVC, and found a high mortality rate (47.8%)

(Rocha, 2012). To obtain the diagnosis of BI, it's necessary analyze clinical parameters associated with the confirmation of positive blood culture, isolation of the etiological agent and determination of resistance profile (Agência Nacional de Vigilância Sanitária, 2013). It's important to note that blood culture may be subject to changes due to several factors, such as positive results of contamination in the collection procedure, causing incorrect use of antibiotics and consequently multiresistant bacterial, factors that culminate in the prolongation of hospitalization time and increasing hospital costs (Alahmadi *et al.*, 2011). Infections occurring in the ICUs are the most severe, because health assistance is provided to dependent patients. These infections are associated with the clinical severity of patients, invasive procedures (CVC, bladder catheter and mechanical ventilation), the use of immunosuppressant, longer hospitalization, colonization by resistant microorganisms and mistaken antimicrobial prescription. Furthermore, the BI agents and the antimicrobial susceptibility profile are variable and may be associated with the hospital environmental and the patient's hospitalization sector (Barros *et al.*, 2012; Chien *et al.*, 2009). Search the clinical and socioeconomic profile of patients with BI and epidemiological variables of this type of infection, can be positive for understanding the increased occurrence of BI in ICU, risk factors and necessary actions to prevent them, as well as to help health professionals in the implementation of specific care, such as premature diagnosis, rational use of antimicrobials, reducing empirical treatment and mortality (Parenti *et al.*, 2013). Thus, the objective of this study was to describe the epidemiology of BI occurring in adult patients hospitalized in the ICUs of a public hospital in Minas Gerais State, Brazil.

## MATERIALS AND METHODS

### Type of study, place of study and ethical considerations:

This is an epidemiological study of retrospective approach, quantitative and descriptive, done in the adult ICU (ICU-A) and coronary ICU (ICU-C) sectors of the Clinical Hospital of Federal University of Triangulo Mineiro (HC-UFTM), Uberaba City, Minas Gerais State - Brazil, from August 2015 to July 2016. This hospital has extensive regional importance, providing services for 27 cities of macro region of the southern Triangulo Mineiro, and offering high complexity care, currently has 295 hospital beds. This work was approved under Research Ethical Committee number 922.429 of UFTM.

**Procedure of data collect:** Data were collected through the analysis of patient's clinical charts. To obtain the information about microbial growth, a sociodemographic and clinical form was developed with independent variables, such: sex, age, hospitalization time, comorbidities, microorganism and your antibiotic sensitivity profile and clinical evolution, and also dependent variables: presence of HI, primary infection of the bloodstream (1BI), secondary infection of the bloodstream (2BI) or bloodstream community infection. The blood samples were preceded by a request from the attending physician. Blood culture was performed using automated equipment, model BACTEC 924010. The antimicrobial susceptibility profile was performed by disk diffusion technique<sup>11</sup>. Antimicrobials were tested according to the availability of hospital.

**Inclusion and exclusion criteria:** Inclusion criteria was positive blood cultures of patients admitted to the ICU-A during the study period, and excluded blood cultures from

samples obtained through central venous catheter. The BI, whether 1BI or 2BI and also community infections, were classified according to the diagnostic criteria of health care-related infections (Agência Nacional de Vigilância Sanitária, 2013). The laboratories criteria for confirmed of BI were based on the patient's clinical manifestations (for example: fever, tremors, oliguria, hypotension) and these symptoms weren't related to infection at another site associated with two or more blood cultures (at different blood sample with maximum 48h) and also, one or more positive blood cultures collected from peripheral venous access peripheral.

**Calculation of sample size and statistical analysis:** The sample size calculation considered a sampling error of 5% and a 95% confidence level, resulting in the minimum number of 75 patients to be analyzed with internal consistency statistic. The database was created, validated by double typing, using the statistical program Statistical Package for the Social Sciences Version 16.0 (IBM SPSS®) for statistical analyses. The descriptive simple analyzes were conducted: frequency distribution, percentages and averages.

## RESULTS AND DISCUSSION

A total of 79 positive blood cultures were analyzed, 63 (79.7%) collected from ICU-A patients and 16 (20.3%) from ICU-C patients.

**Table 1. Sociodemographic and clinical characteristics of critically ill patients with bloodstream infection. Uberaba City, August 2015 to July 2016**

Characteristics	n (%)
<b>Gender</b>	
Female	26 (38.8)
Male	41 (61.2)
<b>Age Range (years)</b>	
14 – 30	12 (17.9)
31 – 50	21 (31.3)
51 – 70	20 (29.9)
≥ 71	14 (20.9)
<b>Comorbidities</b>	
Systemic Arterial Hypertension	30 (44.8)
Cardiac diseases	23 (34.3)
Diabetes Mellitus	20 (29.8)
Chronic Renal Insufficiency	3 (4.5)
Cancer	3 (4.5)
AIDS*	3 (4.5)
Malnutrition	2 (3.0)
<b>Hospitalization Stay (days)</b>	
3 - 15	17 (25.4)
16 - 30	21 (31.3)
31 - 45	11 (16.4)
46 - 60	4 (6.0)
≥ 61	14 (20.9)
<b>Outcome</b>	
Discharge	33 (49.2)
Death	32 (47.8)
Transfer to another service	2 (3.0)

**Table 2. Distribution of hospital bloodstream infections. Uberaba, August 2015 to July 2016.**

Infection Focus	n (%)
<b>1BI</b>	
Central venous catheter	42 (75.0)
Peripheral venous catheter	4 (7.1)
<b>2BI</b>	
Abdominal	4 (7.1)
Urinary	3 (5.4)
Cutaneous	1 (1.8)
Pulmonary	1 (1.8)
Neurological	1 (1.8)
Total	56 (100)

1BI: primary infection of the bloodstream; 2BI: secondary infection of the bloodstream

**Table 3. Distribution of microorganisms causing hospital bloodstream infection. Uberaba, August 2015 to July 2016.**

Microorganisms	n (%)
<b>Gram-positive Cocci</b>	
<i>Staphylococcus coagulase negative</i> (CNS)	20 (34.5)
<i>Staphylococcus aureus</i>	3 (5.2)
<i>Enterococcus faecalis</i>	2 (3.4)
<i>Enterococcus faecium</i>	1 (1.7)
<b>Gram-negative Bacilli</b>	
<i>Acinetobacterbaumani</i>	13 (22.4)
<i>Escherichia coli</i>	6 (10.4)
<i>Klebsiellapneumoniae</i>	6 (10.4)
<i>Pseudomonas aeruginosa</i>	4 (6.9)
<i>Pseudomonas sp.</i>	2 (3.4)
<i>Citrobacterfreundii</i>	1 (1.7)
<b>Total</b>	<b>58 (100)</b>

Among the samples, 12 (15.2%) were considered contaminated samples, while 67 were classified as BI, with 11 (16.4%) considered as community infection and 56 (83.6%) nosocomial infections. From the 56 BI of hospital origin, 46 (82.1%) are 1BI and 10 (17.9%) are 2BI. The collected samples were obtained from 67 patients, because eight patients had more than one episode of infection. According to The American Society of Microbiology, acceptable levels of sample contamination are around 1 to 3%, with a tolerance threshold of 5%, but can be greater than that in emergency and pediatric units (García, 2011). A study done in João Pessoa City – Paraíba State, Brazil, with critically ill patients at a university hospital, reported 11% of contamination from the collected material (Albernaz *et al.*, 2013), similar to the present study. Another recently published study in Greece showed that among 120 septic episodes recovered, 20 were true bacteremia's while in the remaining 100 episodes coagulase-negative *Staphylococcus* (CNS) were isolated and characterized as contaminants (Papadimitriou *et al.*, 2016).

The reduction of false positive results in blood cultures leads to positive impacts, as this could avoid running additional tests, reduces the risk of adverse events related to the unnecessary use of antimicrobials and shortens the length of hospitalization, causing a significant reduction in financial expenses of health institutions (Harding *et al.*, 2013). The incidence of laboratory confirmed cases of BI by blood cultures was 79.1% in the ICU-A and 20.9% in the ICU-C during the period evaluated. The difference in the percentage between the two intensive care units for tells that similar exposure risk may not occur, since in the adult ICU of the HC-UFTM the hospitalized patients are more severe and with longer hospitalization time, while the coronary ICU admits, principally, patients with heart disease, which allows shorter hospitalization time and, consequently, a lower risk of developing HI. A Brazilian study that evaluated 1,879 ICU patients showed that 282 of them were affected by HI; among them, BI ranked third with 14.4% of the cases (Machado *et al.*, 2011). Table 1 represents the characterization of patients who developed BI, with predominance of males (61.2%). The average age was 50.57 years, ranging from 14 to 93 years. Contrasting results were found in a study conducted in Brasília, where 54.4% of the 68 patients with critical heart failure were male, but with a average age of 72.2 years (Rocha, 2012). Another study done in the general ICU of a hospital in Salvador, 144 patients were evaluated: 29 (20.1%) with SBI, 55.2% were male and average age was 73.1 ± 14.6 years (Juncal *et al.*, 2011).

There are associations between extremes of age and increased risk of mortality related to BI – ages over 65 years consist in considerable risk factor for mortality in BI (Son *et al.*, 2010). The American study concluded that the average age of patients with BI increased from 57.4 to 60.8 years in 22 years (Martin *et al.*, 2003). The BI characteristics observed in our study may possibly be related to the greater exposure of men in the economically active age group to automobile-related accidents that are responsible for 26.5% of deaths in Brazil, a fact that explains the average age found in this study<sup>20</sup>. There are those stating that higher patterns of anti-inflammatory mediators and hormonal inequalities between the sexes are the alleged causes of greater incidence of BI and worse outcome in males in the present study (Martin *et al.*, 2003; Ministério da Saúde, 2011; Todeschini, 2011).

The most frequent comorbidities in the studied patients were Systemic Arterial Hypertension (SAH) (44.8%), Cardiac Diseases (34.3%), and Diabetes Mellitus (DM) (29.8%). These findings were similar to those found in a study performed at a school hospital in the Southern Region of Santa Catarina, where DM (18.3%), Cardiac Diseases (16.9%) and SAH (14.46%) were the most prevalent comorbidities (Farias *et al.*, 2013; Schuetz *et al.*, 2011; Silveira, 2014). Contrasting with our findings, a study in a public hospital ICU of Fortaleza State listed as more common comorbidities Malignant Neoplasms (30.4%), SAH (19.6%), Cardiac Diseases (15.2%), DM (17.4%) and Renal Insufficiency (17.4%) (Marra *et al.*, 2011). The presence of chronic diseases may worsen the health status of patients with CHF and has a significant role in the therapeutic preference of the medical team (Faria *et al.*, 2011; Marra *et al.*, 2011). Regarding the hospitalization time, the average hospitalization was 41.3 days. In this study, the total hospitalization period was evaluated, not only in the ICUs. A study performed in a hospital in Ribeirão Preto City, São Paulo State, the average length of hospital stay was 36.4 days and the average length of ICU stay was 13.1 days (Marra *et al.*, 2011), a result similar to this study.

An international investigation showed that survivors of BI had a longer stay in the ICU, confirming the negative impact of BI on the length of hospital stay (Santana *et al.*, 2008). In the present study, discharges from hospital occurred in 49.2% and mortality reached 47.8% of ICU patients. A study performed at the hospital of Uberlândia City, Minas Gerais State, showed mortality rate of 38.1% in patients with BI (Faria *et al.*, 2011). Another Brazilian study found that adult patients with BI had 40% mortality, without relating it as the cause of death (Marra *et al.*, 2011), similar to the present study. The high mortality found in this study can be explained by the severe state of the patients admitted to the various sectors of HC-UFTM. It is important to emphasize that the mortality rate described in this investigation is not related to the deaths that occurred in the ICUs, but to the final outcome of these patients who presented BI. In the critical units evaluated, there were 42 cases (75%) of 1BI related to the CVC, followed by 4 cases (7.1%) of 1BI related to the peripheral venous catheter (Table 2). A study done in a university hospital in Minas Gerais State detected 69.1% of 1BI in its findings (Faria *et al.*, 2011), similar to that found in the present study. A multi-center study involving ICU from 9 Spanish hospitals with 1,366 patients and 2,101 CVC confirmed 66 episodes of 1BI related to CVC (Garnacho-Montero *et al.*, 2008). Another study evaluating 83 records of patients with central venous catheter and 1BI association, had laboratory confirmation of sepsis in 49.4% of the cases

(Todeschini *et al.*, 2011). A study involving 55 ICU from eight countries, determined that IBI associated to the central venous catheter was the second highest risk of HI, behind only of pneumonia associated with mechanical ventilation (Harding, 2013; Brezolin *et al.*, 2014). The frequency of 2BI was 10 cases (17.9%) in relation to the total BIo bserved in this study. The main primary sites of 2BI were abdominal (7.1%) and urinary (5.4%). In a study conducted in a school hospital in Minas Gerais State, Brazil, the frequency of 2BI was 46.7%, with microbiological diagnosis confirmation in 57.1% of the cases and the primary infection foci were pulmonary, gastrointestinal and surgical, not corroborating with the findings of this study (Carvalho *et al.*, 2010). Another study done in the school hospital of Itajubá, Minas Gerais State, focused mainly on BI in the respiratory tract (Baracho *et al.*, 2011). The distribution of the microorganisms that cause hospital BI is described in Table 3. Of the 56 blood cultures, two presented growth of more than one species of bacteria, one had two species of Gram-negative, while the other one had one Gram-negative and one Gram-positive simultaneously, totaling 58 microorganisms.

CNS was the most prevalent pathogen in both ICU with 34.5% (n=20), followed by *Acinetobacter baumannii* 22.4% (n=13), *Escherichia coli* 10.4% and *Klebsiella pneumoniae* 10.4%. Corroborating with our results, a study done in an ICU of a school hospital in Goiânia, the most prevalent Gram-positive bacterium was CNS (23.5%) and Gram-negative bacilli were *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Escherichia coli* (Baracho *et al.*, 2011). CNS were also the most frequently bacteria isolated in blood cultures (58.5%) in another study, followed by *Klebsiella pneumoniae* non-ESBL (12.2%) and ESBL-producing (7.3%) (Faria *et al.*, 2011). A Brazilian study group carried out a 3-year investigation in 16 Brazilian hospitals, finding that Gram-negative organisms were responsible for 58.5% of BI and Gram-positive bacteria for 35.4%, while CNS were responsible for 12, 6%<sup>26</sup>. Possibly, the differences in the research regarding the microbiological profile of BI may be due to the different colonization of ICU by microorganisms resistant to the antimicrobial treatment employed in those hospital institutions. CNS make up the micro biota of the skin and mucous membranes, and represent an important infectious agent mainly for the critically ill, immunocompromised, extreme age groups, such as low birth weight infants and those with some underlying disease. The increase in invasive procedures, among which is the use of intravascular catheters, has favored the appearance of important infections caused by these microorganisms (Machado, 2011; Juncal *et al.*, 2011; Son *et al.*, 2010; Martin *et al.*, 2003). The analysis of the resistance and sensitivity profile of the CNS detected in blood cultures, showed that 60.0% were resistant to oxacillin. The sensitivity profile of these bacteria to Vancomycin was tested only in 20% of the blood cultures that presented CNS causing BI, and none was resistant to this antibiotic. A study evaluating 125 positive blood cultures of critically ill patients in Portugal found that all CNS were susceptible to vancomycin, 100% were resistant to penicillin and 80% were resistant to oxacillin (Garcez, 2012). Regarding resistance and sensitivity profile of *Acinetobacter baumannii* to carbapenems, a high level of resistance to these antibiotics was observed, with 81.8% resistance to Imipenem and 83.3% to Meropenem. The sensitivity profile to Polymixin B was tested in 84.6% of blood cultures and 100% of them were sensitive to this drug. Different Brazilian studies have corroborated these results,

which is a cause for concern, since carbapenems are antibiotics used in severe infections that presented therapeutic failure to other antimicrobials due to bacterial resistance.

## Conclusion

It was possible to trace the sociodemographic and clinical profile of the critical patients presenting BI, which was predominantly male, with a mature age group and associated comorbidities, such as hypertension, heart disease and DM. The average hospital stay was 41.3 days and 47.8% of these patients died. The majority of the positive blood cultures represented infection of the blood of hospital origin and in more than half of the cases there was prevalence of the IBI related to the CVC. The 2BI had a primary focus mainly on the abdominal and urinary sites. The most frequently isolated pathogen causing BI in blood cultures was CNS with resistance to oxacillin and sensitivity to vancomycin. After this epidemiological diagnosis, longitudinal and clinical studies of an analytical approach need to be performed so that associations and epidemiological correlations can support decision-making of health professionals regarding adult care in ICUs, as well as related actions for the prevention of infectious events such as BI.

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