THE IMPACT IN HOSPITALIZATIONS AND MORTALITY OF BLOODSTREAM INFECTION: A COHORT STUDY IN PATIENTS WITH HEMATOLOGIC NEOPLASM

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INTRODUCTION AND OBJECTIVES

Bloodstream infections (BSI) are life-threatening events, especially in patients with hematologic neoplasm (HN). In addition, these individuals are especially susceptible to BSI caused by the immunosuppression associated with the oncologic disease and its treatments such as chemotherapy, radiotherapy, corticosteroids use, and hematopoietic stem cell transplantation. Thus, the impact of BSI occurrence on hospitalization, cancer treatment delay and death in patients with HN is an important concern in public health. This statement must be especially true in resource-constrained countries, where healthcare associated infection rates are higher than in developed areas. However, the burden of BSI in this population has not been studied enough.

Thus, the objectives of the present study are:

- To describe the frequency of hospitalization due to BSIs in patients with HN;
- To describe BSI lethality and mortality in patients with HN
- To analyze the risk of death attributable to BSI.

This knowledge is essential to plan preventive measures.

METHODS

Study design and population: a cohort of patients with HN assisted in HCI/INCA from October/2012 to December/2015.

Inclusion criteria: patients with HN admitted to HCI during the study period. All admissions and BSI episodes of each patient were considered for further analysis.

Data collection: patients with positive blood culture (potential cases of BSI) are prospectively detected by laboratory-based surveillance performed by the Infection Control Section of HCI/INCA. The following data were collected by bedside evaluation and charts review using Magpi (Mobile data collector): epidemiological (gender, date of birth, address, place of admission, date of admission), clinical (baseline disease, presence of neutropenia, outcome in 30 days and date), and about the BSI episode (date, environment of acquisition, topography, detected microorganism and antimicrobial susceptibility test). Thereafter, any data needed will be collected through additional chart review and microbiology reports. Information about the number of admissions of patients with HN, the number of death among these admitted patients, gender and age of them were obtained from Technical and Logistic Support of INCA (http://intranet.inca.local/bipainel/indice/painel_analitico.asp).

Statistical analysis: proportions and medians were calculated for categorical and continuous variables, respectively. The frequency of hospitalization due to BSI, mortality, lethality, relative risk (RR) and attributed risk (AR) of death associated with BSI, 95% CI, and p value were calculated by Epi-info program **(Version 7.1.5.2; CDC).**

The frequency of hospitalization due to BSI: nº of hospitalized individuals due to BSI/nº of patients with hospitalized in HCI in the same period X 100.

Lethality: nº of deaths within 30 days after BSI/nº of BSI detected in the same period x 100.

Mortality: nº of death within 30 days after BSI/nº of patients hospitalized in the period x 100.

The risk of death attributable to BSI (AR): (incidence of death among patients with BSI admitted to HCI) – (incidence of death among in patients without BSI admitted to HCI in the study period.)

Microbiological procedures the cultures are being processed in the Clinical Microbiological Laboratory of HCI/INCA. The collection of blood samples for blood culture will be indicated and performed by the hospital's care team, according to a routine already established in HCI/INCA. Positive blood cultures are detected by automated method, BactecTM 9240 system (Becton Dickinson, Cockeysville, MD, EUA). Bacterial samples will be identified by Vitek2® automated system (BioMérieux Vitek Inc., Hazelwood, Mo., EUA). Complementary biochemical tests are performed according to protocol already established by the Laboratory. Antimicrobial susceptibility testing will be performed using the agar - diffusion method, according to The Clinical and Laboratory Standards Institute (CLSI) in force in the period.

PRELIMINARY RESULTS

Population and mortality

During the study period, 3,906 patients admissions occurred in HCI (1,372 and 2,534, in the pediatric and adults wards, respectively)**.** The overall mortality was 14.6% (n: 572 deaths): 12.6% (n: 320 deaths) in adults and 2.0% (n: 30 deaths) in pediatric patients. A total of 313 episodes of BSI occurred among 221 patients with HN during the study period, 132 (59.7%) were male and 89 (40.2%) female; with median age 37 years (range: 0 - 86). Of 3,906 admissions, 83 (2.1%) occurred due to BSI episodes. The mortality by BSI was 2.1% (n: 84 among 3,906 admissions). The BSI lethality was 26.8% (n:84 among 313 episodes of BSI).

The overall AR was 11.1% (95%CI:6.5–16.4). In pediatric patients, AR was 5.7% (95%IC:-0.14-11.6) and among adult AR was 22% (95%CI:16.7-29.9). These data are detailed in Table 1 and Graph.

Description of BSI episodes

Of 313 BSI episodes, 233 (74.3%) were detected in adult and 80 (25.5%) in pediatric patients. Most of the BSI episodes 183 (58.4%) occurred in patients with neutropenia. The topography of BSIs was: 178 (56.9%) primary, 64 (20.1%) secondary and 71 (22.6%) undetermined. Most of the BSI episodes were Hospital acquired 221 (70.6%). Most of the BSI were caused by Gram-negative bacteria (n: 200, 63.8%); the most isolated microorganisms were *Klebsiella pneumoniae* 46 (14.6%) and *Staphylococcus aureus* 23 (7.3%). 30 (9.5%) episodes were polymicrobial, 46 (14.6%) BSI episodes were caused by multidrug resistant agents. These data are detailed in Table 2.

Table1. Description of attributable risk (AR) and relative risk (RR) for death due to bloodstream infection (BSI) in patients with hematological neoplasm admitted to HCI/INCA.

Patient	Variable, n (%)	Total of admissions	Alive	Death	RR (95% CI)	AR* (95% CI)	p value
All ages		3906	3334	572			
	BSI, yes	313	229 (7.0)	84 (13.8)	1.9 (1.6-2.4)	13.2 (8.2-18.2)	<0.0001
Adult		2534	2213	321			
	BSI, yes	234	155 (7.0)	78 (24.3)	3.1 (2.5-3.9)	22.9 (16.7-29.19)	<0.0001
Children		1372	1341	30			
	BSI, yes	79	73 (5.4)	6 (20.0)	4.1 (1.7-9.7)	5.7 (0.1-11.6)	0.006
Adult patients							
Male		1488	1325	163			
	BSI, yes	140	101 (7.6)	39 (23.9)	3.0 (2.2-4.1)	18.7 (11.1-26.30)	<0.0001
Female		1046	888	158			
	BSI, yes	93	54 (6.1)	39 (24.7)	3.3 (2.5-4.5)	29.5 (19.2-39.7)	<0.0001
Pediatric patients							
Male		918	897	21			
	BSI, yes	46	41 (4.5)	5 (25.0)	6.3 (2.4-16.6)	9.1 (0.1-18.2)	0.002
Female		454	444	10			
	BSI, yes	33	32 (7.2)	1 (10.0)	1.4 (0.18-10.8)	0.8 (5.1-6.9)	0.53

Note.95% CI: confidence interval of 95%

Graphic. Incidence of death and attributable risk (AR) for death due to bloodstream infection stratified by gender and age.

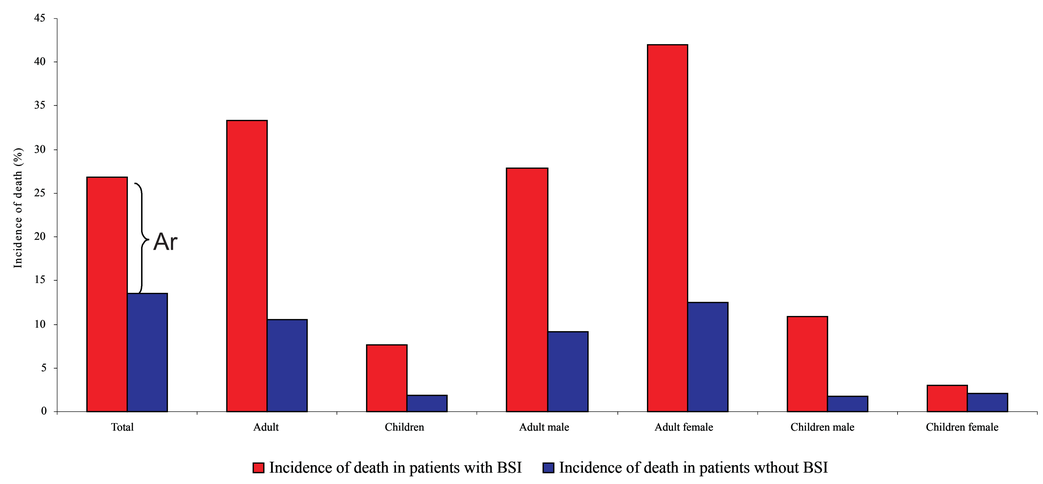

Table 2: Epidemiological, clinical and microbiological characteristics of bloodstream infections (BSI) in patients with hematological neoplasm admired to HCI/INCA.

Variable, n (%)*	Total n: 313	Pediatric patient n: 79	Adult patient n: 234
Ages in years, median (range)	37 (0-86)	10 (0-19)	47 (20-86)
Males	187 (59.7)	46 (58.2)	141 (60.3)
Type of cancer			
Acute leukemia	174 (55.6)	51 (64.6)	123 (52.6)
Chronic leukemia	9 (2.9)	0	9 (3.8)
Lymphomas	102 (32.6)	28 (35.4)	74 (31.6)
Multiple myeloma	22 (7.0)	0	22 (9.4)
Myelodysplasia	5 (1.6)	0	5 (2.1)
Neutropenia	184 (58.8)	49 (62.0)	135 (57.7)
Topography of BSI			
Primary	178 (56.9)	59 (74.7)	119 (50.9)
Long-term central venous catheter			
Semi-implantable	118 (37.7)	46 (58.2)	72 (30.8)
Totally implantable	10 (3.2)	2 (2.5)	8 (3.4)
With peripheral insertion	3 (1.0)	3 (3.8)	0
Short-term venous catheter	29 (9.3)	8 (10.1)	21 (9.0)
Others	19 (6.1)	0	19 (8.1)
Secondary	64 (20.4)	6 (7.6)	58 (24.8)
Intestinal	22 (7.0)	2 (2.5)	20 (8.5)
Pneumonia	13 (4.2)	3 (3.8)	10 (4.3)
Others	30 (9.6)	2 (2.5)	28 (12.0)
Undetermined.	71 (22.7)	14 (17.7)	57 (24.4)
Type of acquisition			
Healthcare associated	89 (28.4)	28 (35.4)	61 (26.1)
Hospital acquired	221 (70.6)	51 (64.6)	170 (72.6)
Community acquired	2 (0.6)	0	2 (0.9)
Undetermined	3 (1.0)	0	3 (1.3)
Outcome			
30-day death	84 (26.8)	6 (7.6)	78 (33.3)
7-day death	44 (14.1)	3 (3.8)	41 (17.5)
Discharge within 30-day follow up	164 (52.4)	60 (75.9)	104 (44.4)
Remained hospitalized after 30-day follow up	56 (17.9)	11 (13.9)	45 (19.2)
Microbiological characteristics			
Agent	n:342	n88	n254
Polymicrobial	23 (7.3)	10 (12.7)	13 (5.6)
Gram-negative	198 (57.9)	45 (51.1)	153 (60.2)
Gram-positive	112 (32.7)	33 (37.5)	79 (31.1)
Fungi	32 (9.4)	10 (11.4)	22 (8.7)

Note.* except when differently indicated beside the variable.

PRELIMINARY CONCLUSION

- Among all admission of patients with HN, 2% was due to BSI.
- The mortality and lethality associated with BSI was 2.1% and 26.8%, respectively.
- Among all adult patients with HN admitted to HCI, 22.9% of the death occurrence could be attributable to BSI. Our data suggest that the the impact of BSI on mortality is higher among female (AR: 29.5%) patients than in male (AR: 18.7%).
- There was no evidence BSI occurrence impacts on mortality among pediatric patients with HN.

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