Source, microbiological profile and mortality associated with bloodstream infections in adult patients with onco-hematological disease assisted at HCI/INCA

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INTRODUCTION

Bloodstream infection (BSI) is an important cause of hospitalization and death in patients with onco-hematological disease (OHD).[1-3] These patients are especially susceptible to BSI due to the immunosuppression inherent to OHD and its treatment, besides other risk factors.[4-6] The presence of infection may delay cancer therapy, and thus interfere with its prognosis.[6] Knowledge about epidemiological, clinical and microbiological characteristics of BSI occurrence is extremely important to guide interventions to reduce the social impact of these events in patients with neoplasm. In view of this context, the following questions motivated this study: what are the anatomical origins, microbiological profile and mortality associated with BSI in adult patients with OHD assisted in HCI/INCA?

OBJECTIVE

To describe the environmental of acquisition, anatomical origin, microbiological profile and mortality associated with BSI in adult patients with OHD assisted in HCI/INCA.

METHODS

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

Population: patients 18 years old or older with OHD assisted in HCI/INCA.

Inclusion criteria: patients with OHD and BSI assisted in HCI during the study period. The first BSI episode of each patient was included only.

Exclusion criteria: patients without sufficient data for analysis will be excluded.

Dynamics of data collection: patients with positive blood cultures (potential cases of BSI) have been prospectively detected by Laboratory-based surveillance since September 2012. These patients had epidemiological, clinical and microbiological data collected using Magpi (Mobile Data Collection) by bedside evaluation and records review. During this evaluation, patients were classified as presenting true or false BSI (contamination of blood specimen with commensal microbiota of skin). Follow-up period was from the date of BSI detection to 30 days after.

The following information was obtained:

- Demographic: gender, date of birth, place of admission, date of admission;
- Clinical: baseline disease, presence of neutropenia, clinical outcome within 30 days after BSI and date;
- About BSI episode: date of positive blood culture, environment of acquisition (community acquired, hospital acquired or health care associated), anatomical origin of BSI (primary or secondary);
- Microbiological: agent and antimicrobial susceptibility.

Collection of blood specimens and microbiological analysis: the indication of blood culture (BC) for investigation of infectious event was made by the HCI care team. The collection of blood samples was done according to protocol already established in HCI by Infection Control Section (ICS). All cultures were processed in the Laboratory of Clinical Microbiology HCI/INCA. Detection of positive culture was done by automated system BactecTM 9240 (Becton Dickinson, Cockeysville, MD, USA). Bacterial isolates identification and antimicrobial susceptibility test were performed by the Vitek2® automated system (BioMérieux Vitek Inc., Hazelwood, Mo., USA), as recommended by the manufacturer. Complementary biochemical tests were performed according to protocol already established by the LMC/INCA. The antimicrobial susceptibility test was done by the disk-diffusion method in Agar, according to The Clinical and Laboratory Standards Institute (CLSI). The Minimum Inhibitory Concentration was done by dilution test (Etest® ,BioMérieux Vitek Inc., Hazelwood, Mo., USA).

Primary outcome: death within 30 days after BSI detection.

Data storage and analysis: proportions, mean or median were calculated for categorical and continuous variables, respectively. The data were analyzed by the Excel program.

PRELIMINARY RESULTS

Among 837 patients, median age was 61 years (Inter-quartile rage, IQR: 18 - 94), males were predominant (n = 528, 63.1%). The most frequent type of cancer observed was solid tumors (n = 555, 66.3%). Neutropenia was present in 161 (19.2%) patients. 30-day and 7-day mortality were 40.4% (n = 338) and 25.2% (n = 211), respectively. These data are shown in **Table 1**.

Table 1 - Epidemiological and clinical characteristics of 837 patients at the time of bloodstream infection (BSI) diagnosis

Variable n (%) *	Number	Frequency (%)
Gender, male	528	63.1
Age, median in years (IQR)	61 (18 - 94)	
Length of hospital stay until BSI, median in days (IQR)**	13 (0 - 214)	
Time from BSI to admission, median in days (IQR)***	0 (-7 - 3)	
Type of neoplasm	837	
Solid	555	66.3
Hematologic	282	33.7
Neutropenia[a]	161	19.2
Clinical outcome at 30-day follow up		
Descharged	295	35.2
Remainded hospitalized	174	20.8
Death	338	40.4
Death ≤ 7 days	211	25.2

Note - * Except when indicated next to the variable; IQR: interquartile range; ** Calculated for hospital acquired infection, ***Calculated for healthcare associated and community acquired infection; [a]absolute number of neutrophils <500 cells / mm3.

Regarding the environment of acquisition, most (n = 416, 49.7%) of the 837 BSI episodes were hospital acquired. A total of 466 (55.7%) episodes were secondary to an extravascular site of infection: 157 (18.8%) were related to gastrointestinal/intraabdominal infections, 134 (16%) to pneumonia, 105 (12.5%) urinary tract infections and 11 (1.3%) related to mucositis. Among primary BSIs (n = 216, 25.8%), those associated with short-term central venous catheters were prevalent (n = 70, 8.4%). These data are detailed in **Table 2.**

A total of 897 microorganisms were isolated among 837 BSI episodes. Gram-negative microorganisms (n = 535, 59.6%) were the most commonly found agents. The overall prevalence of multidrug resistant organisms was 8.9%, as seen in **Table 2.**

Table 2 - Epidemiological and microbiological characteristics of 837 bloodstream infections episodes detected among 837 patients with onco-hematological disease

Variable	Number	Frequency (%)
Epidemiological characteristics, n:837 episodes		
Environmental acquisition		
Hospital acquired	416	49.7
Community acquired	260	31.1
Healthcare associated	157	18.8
Undetermined	4	0.5
Topographic origin		
Secondary	466	55.7
Gastrointestinal/intraabdominal	157	18.8
Pneumonia	134	16.0
Urinary tract	105	12.5
Mucositis	11	1.3
Others	59	7.0
Primary	216	25.8
Long-term central venous catheter	86	10.3
Semi-implantable	56	6.7
Totally implantable	27	3.2
Peripheral insertion	3	0.3
Short-term central venous catheter	70	8.4
Hemodialysis catheter	19	2.3
Peripheral venous catheter	3	0.3
Endocarditis	4	0.5
Others	5	0.6
Undefined	29	3.5
Undetermined	155	18.5
Microbiological characteristics, n:897 agents		
Gram-negative	535	59.6
Gram-positive	311	34.7
Fungi	50	5.6
Undetermined	1	0.1
Polymicrobial	59	7.0
Gram-negative +Gram-negative	29	3.5
Gram-negative + Gram-positive	19	2.3
Gram-positive + Gram-positive	8	0.9
Gram-negative + Gram-negative + Gram-negative	1	0.1
Gram-negative + fungi	1	0.1
Fungi + fungi	1	0.1
Multidrug resistant	80	8.9

The most frequent Gram-negative isolated was *Escherichia coli* (n = 180, 20%), followed by *Klebsiella pneumoniae* (n = 95, 10.6%) and *Pseudomonas aeruginosa* (n = 93, 10.4%). Among Gram-positive microorganisms, *Streptococcus* spp (n = 104, 11.6%) was predominant. *Candida tropicalis* and *C. parapsilosis* prevailed among the fungemias. Data detailed on **Table 3**.

Table 3 - Frequency of microorganisms and prevalence of multidrug resistant agents in 897 isolates from 837 episodes of bloodstream infection in patients with onco-hematological disease

MICROORGANISM	Number	Frequency (%)
Gram-negative	535	59.6
Escherichia coli	180	20
Klebsiella pneumoniae	95	10.6
Pseudomonas aeruginosa	93	10.4
Enterobacter cloacae	22	2.4
Acinetobacter baumannii	15	1.7
Others	130	14.5
Gram-negative multidrug resistant	60	6.7
Cephalosporin resistant Enterobacteriaceae*	20	2.2
Carbapenems resistant Enterobacteriaceae	22	2.5
Polymyxin resistant Enterobacteriaceae	0	0
Carbapenems resistant *Acinetobacter baumannii*	7	0.8
Carbapenems resistant *Pseudomonas aeruginosa*	11	1.2
Polymyxin resistant *Acinetobacter baumannii*	0	0
Polymyxin resistant *Pseudomonas aeruginosa*	0	0
Gram-positive	311	34.7
Streptococcus spp	104	11.6
Staphylococcus aureus	75	8.4
Coagulase-negative *Staphylococcus*	71	7.9
S. epidermidis	36	4
S. haemolyticus	21	2.3
S. capitis	6	0.7
S. hominis	3	0.3
S. lugdunensis	3	0.3
S. warneri	1	0.1
S. saprophyticus	1	0.1
Others	61	6.8
Gram-positive multidrug resistant	20	2.2
Methicillin-resistant *S. aureus*	14	1.5
Penicillin-resistant *Streptococcus* spp	6	0.7
Vancomycin resistant *Enterococcus* spp	0	0
Fungi	50	5.6
C. tropicalis	13	1.5
C. parapsilosis	13	1.5
C. albicans	8	0.9
C. glabrata	7	0.8
C. krusei	3	0.3
C. famata	1	0.1
C. dubliniensis	1	0.1
Others	4	0.4

Note - * 3rd / 4th cephalosporin generation.

PRELIMINARY CONCLUSION

- Mortality associated with BSI was extremely high, 40%.
- Not surprising, most of the BSI episodes were acquired during hospitalization.
- Gastrointestinal/intraabdominal infections seem to have an important impact on the occurrence of BSI in this population, suggesting this extravascular site of infection should be diagnosed and treated early.
- Gram-negative microorganisms, specifically *E. coli*, were the most frequent agents detected. This finding is differently from other studies showing predominance of Gram-positive agents such as coagulase-negative *Staphylococcus*. We believe this difference can be explained by the elevated frequency of BSI secondary to gastrointestinal/intraabdominal infection found.

Further analyzes: anatomical origin and microbiological profile of BSI among patients with solid and hematological neoplasms will be compared.

REFERENCES

1. FREIFELD AG, BOW EJ, SEPKOWITZ KA, BOECKH MJ, ITO JI, MULLEN CA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010. Update by the Infectious Diseases Society of America. Clin Infect Dis 2011; 52:427–31.

2. TUMBARELLO M, SPANU T, CAIRA M, TRECARICHI EM, LAURENTI L, MONTUORI E, FIANCHI L, LEONE F, FADDA G, CAUDA R et al. Factors associated with mortality in bacteremic patients with hematologic malignancies. Diagn Microbiol Infect Dis 2009; 64:320-326.

3. VELASCO, E., et al. Bloodstream infection surveillance in a cancer centre: a prospective look at clinical microbiology aspects. Clinical microbiology and infection 2004, 10(6): 542-549.

4. DONNELLY, J. PETER; BLIJLEVENS, NICOLEM. A.; VAN DER VELDEN, WALTER J. F. M. Infections in the Immunocompromised Host:General Principles. In: MANDELL GL, DOUGLAS RG, BENNETT JE DOLIN. Principles and practice of infectious diseases. Philadelphia: elsevier, 2015. Cap.309, p.3384-3394.

5. WISPLINGHOFF H, SEIFERT H, WENZEL RP, EDMOND MB. Current trends in the epidemiology of nosocomial bloodstream infections in patients with haematological malignancies and solid neoplasms in hospitals in the United States. Clin Infect Dis 2003; 36:1103-1110.

6. ANATOLIOTAKI M. et al. Bloodstream Infections in Patients with Solid Tumors: Associated Factors, Microbial Spectrum and Outcome. Infection 2004;32: 65–71.

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