Mortality, source and microbiological profile of bloodstream infections in adult patients: a cohort study to compare patients with solid tumors and hematological neoplasms

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INTRODUCTION

Bloodstream infection (BSI) is an important cause of hospitalization and death in patients with solid tumors (ST) and hematological neoplasms (HN).[1-3] These patients are especially susceptible to BSI due to immunosuppression inherent in the to base disease, its treatment, and other risk factors.[4-6] In addition, 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 burden of these events in patients with neoplasm. Thus, the following questions motivated this study: what are the anatomical origins, microbiological profile and mortality associated with BSI according to the type of cancer in adult patients with ST and HN assisted in HCI/INCA?

OBJECTIVE

To compare type of acquisition, anatomical origin, microbiological profile and mortality associated with BSI between adult patients with ST and HN assisted in HCI/INCA.

METHODS

Study design: a cohort of patients with ST and HN and BSI, assisted in HCI/INCA from 10/01/2012 to 10/31/2017.

Population: patients with age >18 years with ST and HN assisted in HCI/INCA.

Inclusion criteria: patients with ST and HN and BSI assisted in HCI during the study period. All BSI episode of each patient were included.

Exclusion criteria: patients or BSI episodes without sufficient data for analysis.

Dynamics of cases detection and data collection: patient with positive blood cultures (potential cases of BSI) was prospectively detected by Laboratory-based surveillance. 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 until 30 days after.

The following information was obtained:

- Demographics: gender, date of birth, place of admission, date of admission;
- Clinical: baseline disease, presence of neutropenia, clinical outcome (death or not) 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.

Infection investigation and microbiological procedures

The investigation of infection by blood culture performance was a medical team decision. Two blood samples were obtained from at least two different venipuncture sites of each patient, according to recommendations of the Infection Control Section. In patients with suspected long-term catheter-associated infection, an additional blood sample was simultaneously taken through the respective vascular device. Each of two blood samples (20 mL per sample) was placed in an aerobic blood culture bottle (10 mL), anaerobic blood culture bottle (10 mL). An additional 5mL of blood was obtained when fungi infection was suspected and placed in a BACTEC MYCO/F Lytic blood culture bottle. All samples were processed at the Clinical Microbiology Laboratory of the hospital. The detection of microorganism growth was done by Bactec® 9240 system (Becton Dickinson, Cockeysville, MD, USA). Bacterial isolates were identified by the Vitek2® automated system (BioMérieux Vitek Inc., Hazelwood, Mo., USA). The antimicrobial susceptibility test was performed according to The Clinical and Laboratory Standards Institute recommendations at the moment.[7] Minimum Inhibitory Concentration was performed with E-test® (BioMérieux) strips, when indicated, according to the manufacturer's recommendations.

Statistical analysis

Categorical and continuous variables were described by proportions, means and medians, respectively. Chi-squared test or Fisher's exact test and Student's t-test or Mann-Whitney test were applied for categorical or continuous variables, as appropriate. Epidemiological, clinical and microbiological data were compared between patients with solid tumors and hematological neoplasms. Primary outcome described was death within 30 days after BSI detection. The *P* value <0.05 was considered statistically significant. Data were collected by using Magpi® (Advanced Mobile Data Collection) and analyzed by the Epi info 7.1.5.2 program.

RESULTS

Among 1351 patients included in the study, most had ST (n: 907, 67.14%). The median age was 63 years (IQR: 19 - 94) in patients with ST and 56 years (IQR: 19-89) in those with HN. Males were predominant (61, 44%) in both groups of neoplasms (ST, 62.73% vs. HN, 58.78%). These data are shown in **Table 1**.

Table 1. Epidemiological and clinical characteristics of 1351 patients at the time of diagnosis of bloodstream infection.

Variable, n (%) *	Total n:1351	Hematological neoplasms n: 444 (32.86)	Solid tumors n: 907 (67.14)	*P value*
Gender, male	830 (61.44)	261 (58.78)	569 (62.73)	0.18
Age, median in years (IQR)	61 (19 - 94)	56 (19 - 89)	63 (19 - 94)	<0.001

Note - * Except when indicated next to the variable; IQR: interqualtile range.

A total of 1651 BSI episodes occurred among 1351 patients. Most (54.51%) of them were hospital acquired, especially in patients with HN (63.17% vs. 49.32%; P<0.001). The proportion of BSI secondary to an extravascular site of infection was elevated (52.03%), mainly those with focus in gastrointestinal (40.78%) and respiratory (29.44%) sites. Primary BSI and BSI with undetermined focus occurred in 29.86% and 18.11% of the cases, respectively. Primary BSI was more frequent in patients with HN (42.81%; P <0.001), whereas secondary BSI was more common among those with ST (62.50%; P<0.001). Infections associated with long-term central venous catheters accounted for 55.09% (P<0.001) of the episodes in patients with HN and those associated with the short-term central venous catheters represented 47.37% (P<0.001) of the cases in individuals with ST. The presence of neutropenia was significant in the group with HN (39.10% vs. 6.5%; P<0.001). The overall mortality in 30 days was extremely high (39.07%), and statistically significant among those with ST (42.34% vs. 33.60%; P<0.01). Polymicrobial infections accounted for 10.72% of the cases. These results are detailed in **Table 2**.

Table 2. Epidemiological, clinical and microbiological characteristics of the 1651 episodes of bloodstream infection.

Variable, n (%)	Total n: 1651	Hematological neoplasms n: 619 (37.49)	Solid tumors n: 1032 (62.51)	*P value*
Type of acquisition				
Hospital acquired	900 (54.51)	391 (63.17)	509 (49.32)	<0.001
Community acquired	406 (24.59)	112 (18.09)	294 (28.49)	<0.001
Healthcare associated in INCA	328 (19.87)	114 (18.42)	214 (20.74)	0.28
Healthcare associated another hospital	8 (0.48)	1 (0.16)	7 (0.68)	0.27
Undetermined	9 (0.55)	1 (0.16)	8 (0.78)	0.17
Topographic origin				
Secondary	859 (52.03)	214 (34.57)	645 (62.50)	<0.001
Abdominal infections	325 (37.83)	62 (28.97)	263 (40.78)	0.003
Respiratory tract infections	233 (27.12)	63 (29.44)	170 (26.36)	0.43
Urinary tract infections	194 (22.58)	49 (22.90)	145 (22.48)	0.98
Soft parts infections	94 (10.94)	36 (16.82)	58 (8.99)	0.002
Others infections	13 (1.51)	4 (1.87)	9 (1.40)	0.75
Primary	493 (29.86)	265 (42.81)	228 (22.09)	<0.001
Long-term central venous catheter	203 (41.18)	146 (55.09)	57 (25.00)	<0.001
Semi-implantable	126 (25.56)	121 (45.66)	5 (2.19)	<0.001
Totally implantable	65 (13.18)	22 (8.30)	43 (18.86)	<0.001
Peripheral insertion	12 (2.43)	3 (1.13)	9 (3.95)	0.08
Short-term central venous catheter	183 (37.12)	75 (28.30)	108 (47.37)	<0.001
Hemodialysis catheter	42 (8.52)	11 (4.15)	31 (13.60)	<0.001
Peripheral venous catheter	3 (0.61)	2 (0.75)	1 (0.44)	1.00
Others	14 (2.84)	7 (2.64)	7 (3.07)	0.99
Undefined	48 (9.74)	24 (9.06)	24 (10.53)	0.69
Undetermined	299 (18.11)	140 (22.62)	159 (15.41)	<0.001
Neutropenia[a]	309 (18.72)	242 (39.10)	67 (6.49)	<0.001
Neutrophils <100 cells/mm^3	222 (13.45)	196 (31.66)	26 (2.52)	<0.001
Length of hospital stay until BSI, median in days (IQR)[b]	15 (-6 - 222)	16 (0 - 178)	14 (-6 - 222)	0.08
Time from BSI to hospital admission, median in days (IQR)[c]				
In community acquired	0 (-10 - 5)	0 (-6 - 4)	0 (-10 - 5)	0.47
In healthcare associated	0 (-6 - 3)	0 (-3 - 3)	0 (-6 - 3)	0.78
Clinical outcome at 30-day follow up				
Death	645 (39.07)	208 (33.60)	437 (42.34)	<0.001
7-day death	378 (58.60)	106 (50.96)	272 (62.24)	0.01
Descharged	585 (35.43)	259 (41.84)	326 (31.59)	<0.001
Remainded hospitalized	367 (22.23)	138 (22.29)	229 (22.19)	0.99
Was not hospitalized	51 (3.09)	13 (2.10)	38 (3.68)	0.10
Unknown	3 (0.18)	1 (0.16)	2 (0.19)	1.00
Monomicrobial bloodstream infections	1474 (89.28)	551 (89.01)	923 (89.44)	0.85
Polymicrobial bloodstream infections	177 (10.72)	68 (10.99)	109 (10.56)	0.85

[a]Absolute number of neutrophils <500 cells/mm^3; IQR: interquartile range; [b]Calculated for hospital acquired infection; [c]Calculated for healthcare associated and community acquired infection.

A total of 1848 microorganisms were isolated from 1651 BSI episodes. Gram-negative bacilli (GNB) were the major agents isolated among the episodes, in both groups. The occurrence of infections caused by Escherichia coli (20.47% vs 16.55%, *P*: 0.04) and *Pseudomonas aeruginosa* (7.89% vs. 12.52%, *P*: 0.002) were significant among the episodes detected in patients with ST and HN, respectively. *Streptococcus* spp. (11.45% vs.7.48%, *P*: 0.01) was important in those with ST. The overall frequency of multidrug resistant microorganisms was 18.94%, with significant occurrence among patients with HN (23.31% vs. 16.31%; *P*<0.001). Mainly, carbapenem resistant Enterobacteriaceae and *P. aeruginosa* were elevated (*P*<0.001) among these BSI episodes. Data detailed in **Table 3.**

Table 3. Frequency of 1848 microorganisms and multidrug resistant agents isolated from 1651 episodes of bloodstream infection.

Variable, n (%)	Total n: 1848	Hematological neoplasms 695 (37.61)	Solid tumors 1153 (62.39)	*P* value
Gram-negative	1088 (58.87)	408 (58.71)	680 (58.98)	0.95
Escherichia coli	351 (18.99)	115 (16.55)	236 (20.47)	0.04
Klebsiella pneumoniae	207 (11.20)	83 (11.94)	124 (10.75)	0.48
Pseudomonas aeruginosa	178 (9.63)	87 (12.52)	91 (7.89)	0.002
Proteus mirabilis	48 (2.60)	12 (1.73)	36 (3.12)	0.09
Enterobacter cloacae	45 (2.44)	16 (2.30)	29 (2.52)	0.90
Acinetobacter baumannii	43 (2.33)	22 (3.17)	21 (1.82)	0.09
Serratia marcenscens	42 (2.27)	14 (2.01)	28 (2.43)	0.68
Morganella morganii	24 (1.30)	7 (1.01)	17 (1.47)	0.52
Others	150 (8.12)	52 (7.48)	98 (8.50)	0.49
Gram-positive	642 (34.74)	232 (33.38)	410 (35.56)	0.37
Streptococcus spp	184 (9.96)	52 (7.48)	132 (11.45)	0.01
Coagulase-negative *Staphylococcus*	178 (9.63)	75 (10.79)	103 (8.93)	0.22
S. epidermidis	96 (5.19)	38 (5.47)	58 (5.03)	0.76
S. haemolyticus	38 (2.06)	19 (2.73)	19 (1.65)	0.15
S. hominis	21 (1.14)	10 (1.44)	11 (0.95)	0.47
S. capitis	14 (0.76)	3 (0.43)	11 (0.95)	0.33
Others	9 (0.49)	5 (0.72)	4 (0.35)	0.31
Staphylococcus aureus	146 (7.90)	47 (6.76)	99 (8.59)	0.19
Enterococcus spp	92 (4.98)	41 (5.90)	51 (4.42)	0.19
Others	42 (2.27)	17 (2.45)	25 (2.17)	0.82
Fungi	117 (6.33)	54 (7.77)	63 (5.46)	0.06
C. tropicalis	29 (1.57)	13 (1.87)	16 (1.39)	0.54
C. parapsilosis	29 (1.57)	14 (2.01)	15 (1.30)	0.32
C. albicans	20 (1.08)	5 (0.72)	15 (1.30)	0.35
C. krusei	7 (0.38)	3 (0.43)	4 (0.35)	1.00
C. glabrata	8 (0.43)	0 (0)	8 (0.69)	0.03
Others	24 (1.30)	19 (2.73)	5 (0.43)	<0.001
Unidentified bacteria	1 (0.05)	1 (0.14)	0 (0)	0.38
Multidrug resistant Microorganisms	n: 350 (18.94)	162 (23.31)	188 (16.31)	<0.001
Gram-negative	267 (14.45)	130 (18.71)	137 (11.88)	<0.001
Cephalosporin resistant Enterobacteriaceae*	87 (4.71)	39 (5.61)	48 (4.16)	0.19
Carbapenems resistant Enterobacteriaceae	62 (3.35)	38 (5.47)	24 (2.08)	<0.001
Cefoxitin resistant Enterobacteriaceae	61 (3.30)	16 (2.30)	45 (3.90)	0.08
Polymyxin resistant Enterobacteriaceae	1 (0.05)	1 (0.14)	0 (0)	0.38
Carbapenems resistant *Pseudomonas aeruginosa*	33 (1.79)	23 (3.31)	10 (0.87)	<0.001
Carbapenems resistant *Acinetobacter baumannii*	22 (1.19)	13 (1.87)	9 (0.78)	0.06
Bactrim resistant *Stenotrophomonas maltophilia*	1 (0.05)	0 (0)	1 (0.09)	1.00
Gram-positive	67 (3.63)	24 (3.45)	43 (3.73)	0.86
Methicillin-resistant *S. aureus*	42 (2.27)	10 (1.44)	32 (2.78)	0.09
Penicillin-resistant *Streptococcus spp*	19 (1.03)	10 (1.44)	9 (0.78)	0.26
Vancomycin resistant *Enterococcus spp*	6 (0.32)	4 (0.58)	2 (0.17)	0.21
Fungi	16 (0.87)	8 (1.15)	8 (0.69)	0.44
Fluconazol-resistant *Candida spp*	16 (0.87)	8 (1.15)	8 (0.69)	0.44

Note - * 3rd/4th cephalosporin generation.

DISCUSSION AND CONCLUSIONS

- Early mortality (up to 7 days) and late mortality (up to 30 days) were significantly higher in patients with ST.
- Not surprising, most of the BSI episodes were acquired during hospitalization.
- BSI secondary to an extravascular focus of infection were more frequent, principally among patients with ST.
- Gastrointestinal and respiratory infections were important focus of BSI in this population, suggesting these sites of infection should be diagnosed and treated promptly.
- Primary infections were representative in the BSI episodes occurred among patients with HN, especially those associated with long-term central venous catheter.
- The presence of neutropenia was significantly higher among BSI episodes occurred in patients with HN.
- GNB, specifically *E. coli*, were the most frequent agents detected. This finding is different from other studies showing a predominance of Gram-positive agents, such as Coagulase-negative *Staphylococcus*. We believe this difference can be explained by the high frequency of BSI secondary to the abdominal infections found.

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