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SCIENTIFIC ARTICLE - REVIEW ARTICLE

ETIOLOGIES OF BACTERIAL STRAINS ISOLATED FROM BLOOD CULTURES OF CANCER PEDIATRIC PATIENTS

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ABSTRACT

Introduction: Primary bloodstream infections (PBSIs) are serious adverse events, especially for vulnerable patients. Objectives: Data from pediatric ICUs indicate that PBSI cases are predominantly caused by coagulase-negative Staphylococcus, Staphylococcus aureus, Klebsiella pneumoniae complex, Serratia spp., and Pseudomonas aeruginosa. Of the total patients, 25 were neutropenic, and 5 were not. Methods: Data analysis showed that short-term catheters were more susceptible to PBSIs than long-term catheters. Results: The results indicated that the presence of onco-hematologic disease was a differentiating factor for positive blood cultures in neutropenic patients, where Staphylococcus epidermidis was the main agent identified among Gram-positive bacteria, and Klebsiella pneumoniae among Gram positive bacteria, which caused greater morbidity and mortality. Conclusions: Despite the limited evaluation of pathogenicity/virulence factors and the lack of investigation of antimicrobial resistance genes in the strains analyzed, it is considered that chemotherapy favors the translocation of intestinal bacteria. K. pneumoniae was the most frequent agent in PBSI cases, and probable changes may be due to colonization processes associated with the patients' multiple hospitalizations.

Keywords: Bloodstream infection, Staphylococcus sp, Klebsiella pneumoniae, Escherichia coli.

INTRODUCTION

In Brazil, cancer is the second leading cause of death in the pediatric population, and its treatment requires the use of central venous catheters (CVCs). These catheters are essential for the comprehensive treatment of these patients, with bloodstream infections being one of the main factors related to the loss of functionality of venous devices.[1] The rates of Primary Bloodstream Infections (PBSIs) also depend on the types of devices used and chosen for drug therapy.

Due to the subjectivity in the classification of PBSIs, the Brazilian Health Regulatory Agency (ANVISA) standardized the reporting of this infection across the country. Practically, PBSIs were divided into infections with a positive blood culture, corresponding to laboratory-confirmed primary bloodstream infections (LCPBSI), and infections characterized solely by clinical criteria, clinical primary bloodstream infections (CPBSI).[2]

Currently, although clinical primary bloodstream infections (CPBSIs) are not mandatory reportable infections in adult, pediatric, and neonatal Intensive Care Units (ICUs), they should be monitored and reported in these sectors within healthcare institutions.[3]

PBSIs are a global problem, especially for vulnerable patients such as pediatric patients, as they have specific characteristics that must be considered, including higher infection rates, increased susceptibility related to morbidity and mortality, and longer duration of infections.[4]

Hospitalized children with a cancer diagnosis are at a higher risk of acquiring infections, particularly hematological-oncological patients, who require longer hospitalization periods, may become colonized by hospital microbiota, and have less effective natural barriers due to the toxic effects of chemotherapy and immunosuppression caused by cancer. In most cases, infections are associated with the use of central venous catheters (CVCs).[5,6]

In this pediatric context, it is important to note that patients with hematological neoplasms are at a greater risk of acquiring PBSIs, as they are severely immunocompromised due to the underlying disease, anti-neoplastic therapy, and/or hematopoietic stem cell transplantation.[7] According to Ziegler Pellegrini and Safdar,[8] a meta-analysis study conducted in ICU patients suggested that PBSIs worsen the clinical course of hematological-oncological patients and contribute to overall mortality.

The diagnostic criteria for reporting PBSIs were updated in 2017. This update included a flowchart to facilitate the correct identification of the condition and, for the first time, added the concept of laboratory-confirmed primary bloodstream infection (LCPBSI) associated with mucosal barrier damage. This is due to mucositis associated with certain chemotherapy modalities or the occurrence of graft-versus-host disease, which, combined with neutropenia, can facilitate bacterial translocation, leading to bloodstream infection (BSI).[3]

One of the main characteristics of immunosuppressed patients undergoing cancer treatment is neutropenia.[9] This condition is characterized by a granulocyte count of fewer than 500 cells per cubic millimeter.[10] If this white blood cell count is accompanied by febrile episodes, with temperatures exceeding 38°C, it is considered that the patient has febrile neutropenia. The emergence of multidrug-resistant pathogens presents a significant challenge in treating immunosuppressed oncology patients and, in the pediatric context, is associated with an increase in infant mortality rates.[11]

Pediatric oncology patients have significantly reduced survival due to severe complications, with fever being the primary reason for seeking pediatric emergency services. Approximately 0.9% to 39% of febrile, non-neutropenic oncology patients are bacteremic, and about 7.3% of oncology patients admitted to emergency services have positive bacterial blood cultures. Factors that favor the development of sepsis include upper respiratory tract infections, neuroblastoma, other cancer diagnoses, and the use of central venous catheters.[12]

Bloodstream infections in neutropenic patients are primarily caused by coagulase-negative staphylococci (CNS), which readily acquire antimicrobial resistance genes in the hospital environment, complicating patient treatment. This resistance phenotype in S. epidermidis and S. haemolyticus isolated in hospital settings is common, with the percentage of oxacillin resistance around 80%. The role of these species as reservoirs for resistance genes is still under discussion; therefore, analyses and investigations should be conducted to guide hygiene measures, surveillance, and prevention in the hospital environment.[13]

Over time, the etiological agents of febrile neutropenia have changed. Gram-negative bacteria were of great importance in the etiology of this condition during the 1970s, while in the 1990s, Gram-positive bacteria, mainly those related to the Staphylococcus genus, were more commonly associated. More recently, there has been a noted predominance of Gram-negative microorganisms, particularly strains of Klebsiella spp. and E. coli. These epidemiological changes can be attributed to different approaches used in oncology patients, such as the prophylactic use of fluoroquinolones and the use of intravascular catheters. Additionally, the increase in the occurrence of severe mucositis associated with chemotherapy should not be overlooked.[11,14,15]

The identification of etiological agents of primary bloodstream infections (PBSIs) through the detection of bacterial rRNA 16S genes using Polymerase Chain Reaction (PCR) and microarray assays can significantly contribute to the speed of diagnosis. Molecular biology tools offer substantial benefits for the rapid and accurate diagnosis of etiological agents in PBSIs. However, implementing this methodology requires investment in resources that are not accessible to most healthcare institutions. We aim to describe the characteristics of pediatric patients with onco-hematological diseases in terms of age and sex (demographics), the presence of neutropenia, and the type of catheter (short or long-term); evaluate the association between catheter use in patients and the occurrence of primary bloodstream infection; identify bacterial species using phenotypic and molecular methods; and determine the antimicrobial susceptibility profile.

METHODS

Study Design and Variables

This is a descriptive retrospective study with a quantitative data approach, analyzing bacterial straims isolated from blood cultures of hospitalized pediatric patients from August 2015 to August 2016. The study site was the Pediatric Service of a Federal Hospital located in the municipality of Rio de Janeiro. This service consists of 10 clinical and surgical pediatric wards, each with 2 beds, 10 pediatric intensive care unit beds, and a pediatric hematology outpatient clinic, where consultations, laboratory tests, and chemotherapy administration are conducted. This research was carried out in collaboration with the Microbiology Laboratory of the aforementioned hospital, associated with the Department of Microbiology, Immunology, and Parasitology of the Faculty of Medical Sciences of the State University of Rio de Janeiro (DMIP-FCM-UERJ), where the bacterial strains were analyzed.

Sampling was conducted using a convenience approach, considering blood cultures from all pediatric patients during the period from August 2015 to August 2016, based on the following eligibility criteria: patients diagnosed with onco-hematological diseases who had blood cultures with microbial growth and considered to have an infection when two or more blood cultures showed growth of the same microorganism, provided that the patients did not have an identifiable infectious focus in another site (pulmonary, urinary, etc.) during the studied period. One sample per patient related to infection or colonization was included. Bacterial strains with an isolation interval of more than 14 days from the same patient were also included. The exclusion criteria were patients who had positive blood cultures but were related to secondary bloodstream infections, which would be those with positive blood cultures with identifiable infectious foci in another site (pulmonary, urinary, etc.).

Collection of bacterial strains isolated from blood cultures in the routine of the microbiology laboratory of the hospital institution.

The routine evaluation of patients with clinical suspicion of sepsis (clinical signs such as fever, tachycardia, hypotension, oliguria, among others), primary bloodstream infection, and those who, upon admission or during hospitalization, were experiencing febrile neutropenia includes the request for bacteriological tests by the clinical team of the hospital where the study was conducted. Thus, it is emphasized that both the request and the collection of blood for the analyzed blood cultures occur as standard clinical practice in the unit in question, regardless of the present study. The bacterial strains were forwarded and included in the Bacterial Collection of the Department of Microbiology, Immunology, and Parasitology (DMIP-UERJ). Data for registering these blood samples for cultures were obtained from the referral forms, which include information regarding patient characteristics, antimicrobial use, central venous catheter use, lock therapy in fully implanted catheters, neutropenia, abdominal symptoms, and the classification of IPCS based on the criteria defined by ANVISA.[3]

All bacterial samples were stored in a 10% skim milk solution (Skim Milk; Difco Laboratories, Detroit, Michigan, USA) containing 10% glycerol and maintained at -20°C until the tests were performed.

Bacterial Identification in the Clinical Laboratory

The bacterial samples underwent initial identification at the clinical laboratory using the VITEK® 2 System with software version 6.01 (bioMérieux, France). For the identification of Gram-positive and Gram-negative strains, the VITEK® 2 GP and GN cards (bioMérieux, France) were used, respectively. The probability of identification accuracy (confidence level) is categorized into four groups: excellent (96% to 99%), very good (93% to 95%), good (89% to 92%), and acceptable (85% to 88%).

Bacterial Identification by Mass Spectrometry

This stage of the work was conducted in collaboration with the Institute of Microbiology Professor Paulo de Góes at the Federal University of Rio de Janeiro (IMPG-UFRJ). All bacterial strains underwent identification confirmation through proteomic analysis, utilizing the Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS) technique. Using a wooden stick, a small sample of the colony isolated on Mueller Hinton agar (BD®, Heidelberg, Germany) was transferred to a well of a 96-well plate (Bruker Daltonik GMbH, Germany). To each well, an aliquot of 10 µL of alpha-cyano-4-hydroxycinnamic acid (CHCA - Bruker Daltonik GMbH, Germany) matrix was added and allowed to dry at room temperature.

Bacterial Identification by DNA Fragment Sequencing

For the species identification of an exigent microorganism that is rarely isolated in the routine of the studied hospital institution, the sequencing of the rDNA16S gene of the bacteria was employed. The sequencing of the amplification product was conducted in collaboration with the Fiocruz Network of Technological Platforms – Genomics in Rio de Janeiro, using the DYEnamic ET terminator kit (Amershambiosciences, São Paulo, Brazil). The reactions were carried out on the ABI 3730xL Sequencer. The sequences obtained were compared against sequences deposited in databases (NCBI) for bacterial identification.

Antimicrobial Susceptibility Testing

The strains had their antimicrobial susceptibility profiles obtained in the assistive laboratory using the automated VITEK® 2 System with software version 6.01 (bioMérieux, France).

For the Gram-positive strains, the VITEK® 2 AST-637 card (bioMérieux, France) was used. The following antimicrobials were analyzed: fusidic acid (AFS), ampicillin (AMP), benzylpenicillin (PEN), ciprofloxacin (CIP), clindamycin (CLIN), high-level streptomycin (HLR-ST), erythromycin (ERI), gentamicin (GEN), high-level gentamicin (HLR-GE), linezolid (LIN), moxifloxacin (MOX), norfloxacin (NOR), oxacillin (OXA), rifampicin (RIF), teicoplanin (TEC), tigecycline (TIG), and trimethoprim-sulfamethoxazole (SMX), vancomycin (VAN). For the Gram-negative strains, the VITEK® 2 AST-239 card (bioMérieux, France) was used. The following antimicrobials were analyzed: amikacin (AMI), ampicillin (AMP), ampicillin--sulbactam (APS), cefepime (CPM), cefoxitin (CFO), ceftazidime (CAZ), ceftriaxone (CRO), cefuroxime (CRX), ciprofloxacin (CIP), ertapenem (ERT), gentamicin (GEN), imipenem (IMP), meropenem (MER), piperacillin-tazobactam (PPT), and tigecycline (TIG).

Data Processing and Analysis

The data obtained were analyzed using a quantitative approach in light of descriptive statistics and tabulated using Microsoft Excel Office XP®. For continuous variables related to the patient, such as age range, microorganism profile, and resistance, absolute and relative frequency measures (percentage) were calculated. For associations, statistical significance (p) was assessed using the chi-square (χ^2) test, considering a significance level of 0.05.

Ethical Procedures

The study was submitted to the Research Ethics Committee and was approved with the following approval number: 4.502.848. CAAE: 41955320.4.0000.5259.

RESULTS

Patients

During the study (over the 12 months of data collection, from August 2015 to August 2016), 50 patients were included, of which 45 met the inclusion criteria established by the study. Five patients were excluded: one for being outside the age range, two because the clinical specimen was different from blood, and two for having secondary bloodstream infections. Of the total patients, 25 out of 45 (55.6%) had onco-hematological diseases, among which 20 out of 25 (80%) were neutropenic and 5 out of 25 (20%) were not neutropenic at the time of collection. Most onco-hematological patients were in the preschool age group, followed by school-age children and infants, respectively (Table 1).

Table 1. Distribution of pediatric onco-hematological patients with positive blood cultures according to age group, sex, and hospital ward

Age Group	Onco-hematological Patients				
	Female	Male	Pediatric ICU	Ward	Total
	n	n	n	n	n
0 to 28 days (neonatal)	0	0	0	0	0
>28 days to 2 years (infant)	1	2	0	3	3
3 to 6 years (preschool)	3	7	1	9	10
7 to 11 years (school-age)	2	6	2	6	8
12 to 18 years (adolescent)	2	2	1	3	4
Total	8	17	4	21	25

The majority of the onco-hematological patients, 10/25 (40%), were in the school-age group and were hospitalized in the pediatric ward. Males predominated in both patient groups. No statistical difference was found regarding the distribution of patients by age groups.

When associating the types of central catheters, classified as short-term (peripheral catheters and central catheters), which in pediatric patients (peripheral catheters) do not have a routine change, both must be continuously evaluated for the need for removal, hemodynamic monitoring, etc., and long--term (tunneled catheters that can remain implanted for months or even years, providing safe access for long-term therapies, such as for onco-hematological diseases, among others). Regarding the presence of CLABSI, as shown in Table 2, it was observed that patients with long-term catheters had a higher occurrence of CLABSI than those with short-term catheters among onco-hematological patients with neutropenia; however, the difference was not statistically significant. It is important to note that nine onco-hematological patients without neutropenia had two or more episodes of CLABSI (data not

Table 2. Association of Types of Catheters Inserted in Pediatric Onco-Hematological Patients with neutropenia regarding the presence of primary bloodstream infection.

Types of Catheter	PBI*	No PBI*	Total
	n	n	n
Short-Term	5	4	9
Long-Term	22	9	31
Total	27	13	40

*PBI: Primary bloodstream infection.

shown).

Bacterial Strains

In the identification of bacterial samples from oncology-hematology patients with neutropenia, 21 enterobacteria were isolated (11 K. pneumoniae, 7 E. coli, 3 E. cloacae), 2 P. aeruginosa, 1 Stenotrophomonas maltophilia, 1 Candida parapsilosis, and 3 Brevibacterium cellere. In oncology-hematology patients without neutropenia, bacterial species such as Campylobacter jejuni, Brevibacterium celere, and Pantoea sp. were isolated. The majority of bacterial species were derived from episodes of primary bloodstream infection (PBI), except for coagulase-negative staphylococci (CNS), where almost all were involved in non-PBI cases (Table 3). Only one episode of PBI was caused by CNS in a neutropenic patient (case 17, strains 47 - S. epidermidis in Table 4). In the blood cultures of patients (with or without neutropenia), we were able to detect species using unconventional identification methods, which do not correspond to "classical" pathogens, but may correspond to opportunists such as Corynebacterium sp., Sphingomonas paucimobilis, and Francisella tularensis (Table 4). However, Brevibacterium celere, a microorganism not associated with human infections, was isolated in blood cultures from 4 different patients (Table 5).

Bacterial Identification

Approximately three-quarters of the bacterial strains (54/79.4%) showed concordance in identification between the VITEK® 2 System, conducted at the originating laboratory, and MALDI-TOF MS, used as a confirmation instrument for the data. In the 12 cases of disagreement in identification, seven had scores above 2, indicating certainty in species identification, while five had scores between 1.7 and 1.99, relating to the level of confidence in genus (Table 5).

Table 3. Distribution of bacterial species and their antimicrobial resistance markers recovered from blood cultures of pediatric oncology-hematology patients with neutropenia.

Patient	Sample	Species	Episode of PBSI (P) / Contamination Episode (C)	Resistance Markers
1	9	*K. pneumoniae*	PBSI1	CIP-GEN-TIG-APS-CPM-CAZ-CRO-CRX*
2	2	*S. epidermidis*	C1	PEN-CIP-CLIN-ERI-MOX-NOR-OXA-RIF-
2	10	*K. pneumoniae*	PBSI1	MS
2	17****	*K. pneumoniae*	PBSI2	MS
3	14	*K. pneumoniae*	PBSI1	MS
5	113	*K. pneumoniae*	PBSI1	MS
7	38	*S. epidermidis*	C1	PEN-OXA*

7	59	*K. pneumoniae*	PBSI1	TIG-APS-CPM-CFO-CAZ-CRO-CRX-PPT*
7	38	*S. epidermidis*	C1	PEN-OXA*
7	80	*K. pneumoniae*	PBSI2	CIP-TIG-APS-CPM-CAZ-CRO-CRX*
8	53	*P. aeruginosa*	PBSI1	APS-CFO-CRO-CRX
8	60	*K. pneumoniae*	PBSI2	APS-CPM-CAZ-CRO-CRX-PPT*
8	62	*K. pneumoniae*	PBSI3	APS-CPM-CAZ-CRO-CRX-PPT*
8	79	*E. coli*	PBSI4	MS
8	68	*S. saprophyticus*	C1	PEN-OXA-SUT-AFS*
8	76	*K. pneumoniae*	PBSI5	APS-CPM-CAZ-CRO-CRX-PPT*
8	73	*K. pneumoniae*	PBSI6	MS
8	69	*C. parapsolosis*	PBSI7	-
11	16	*S. hominis*	-	C1
12	20	*S. epidermidis*	C1	PEN-ERI-OXA*
12	39	*S. epidermidis*	C2	PEN-ERI-OXA-TEC*
12	40	*S. epidermidis*	C3	PEN-ERI-OXA-TEC*
16	12	*B. celere*	C1	-
16	45	*B. celere*	PBSI1	-
16	37	*S. hominis*	-	C2
17	47	*S. epidermidis*	PBSI1	PEN-CLIN-ERI-OXA*
18	50	*S. hominis*	-	C1
18	51	*B. celere*	-	C2
19	130****	*S. hominis*	C1	PEN
23	103	*P. aeruginosa*	PBSI1	APS-CFO-CRO-CRX
23	91	*S. hominis*	-	C1
31	5	*S. maltophilia*	PBSI1	-
31	19	*E. coli*	-	-
34	1	*E. coli*	-	-
35	3	*E. coli*	-	-
37	132****	*E. coli*	-	IPCS1
38	58	*E. coli*	-	-
39	72	*E. coli*	-	-
48	30	*E. cloacae*	PBSI1	AMP-APS-CFO-CRX
48	33	*E. cloacae*	PBSI2	AMP-APS-CPM-CFO-CAZ-CRO-CRX-GEN*
48	56	*E. cloacae*	PBSI3	AMP-APS-CFO-CRX

*Resistance profile classified as multidrug-resistant; SCN: Coagulase-negative Staphylococcus; sample not analyzed. AMP: Ampicillin; AFS: Fusidic acid; APS: Ampicillin-Sulbactam; CAZ: Ceftazidime; CFO: Cefoxitin; CLIN: Clindamycin; CPM: Cefepime; CIP: Ciprofloxacin; CRO: Ceftriaxone; CRX: Cefuroxime; ERI: Erythromycin; ERT: Ertapenem; LIN: Linezolid; IMI: Imipenem; MER: Meropenem; MOX: Moxifloxacin; NOR: Norfloxacin; OXA: Oxacillin; PEN: Penicillin; PPT: Piperacillin-Tazobactam; RIF: Rifampicin; SUT: Sulfamethoxazole-Trimethoprim; TEC: Teicoplanin; TIG: Tigecycline; MS: Multisensitive sample; -: Antibiogram not standardized and not performed.

Table 4. Distribution of bacterial species and their antimicrobial resistance markers recovered from blood cultures of pediatric onco-hematological patients without neutropenia.

Patient	Sample	Species	Episode of PBSI (P) / Contamination Episode (C)	Resistance Markers
30	66	*S. aureus*	PBSI1	PEN-OXA*
32	8	*B. celere*	C1	-
41	134****	*C. jejunii*	PBSI1	-
42	54	*E. faecalis*	PBSI1	CLIN-HLR-G
47	26	*Pantoea*	PBSI1	-

Resistance profiles classified as multidrug-resistant; SCN: Coagulase-negative Staphylococcus; Sample not analyzed. CLIN: Clindamycin; GEN: Gentamicin; OXA: Oxacillin; PEN: Penicillin; -: antibiogram not standardized and not performed.

Table 5. Distribution of bacterial species and their antimicrobial resistance markers recovered from blood cultures of pediatric oncology-hematology patients without neutropenia.

Methods Applied in Bacterial Identification					
Pediatric Oncology-Hematology Patients with Neutropenia					
Patient	Sample	PBSI*/C**	VITEK® 2 System	MALDI-TOF MS (*score*)	16S rDNA Gene Sequencing
16	12	C1	**	*Brevibacterium celere* (2.049)	-
16	45	PBSI1	**	*Brevibacterium celere* (2.049)	-
18	51	C1	*Corynebacterium sp.*	*Brevibacterium celere* (2.049)	-
Oncology-Hematology Patients without Neutropenia					
Patient	Sample	PBSI/C	VITEK® 2 System	MALDI-TOF MS (*score*)	16S rDNA Gene Sequencing
32	8	C1	*Sphingomonas paucimobilis*	*Brevibacterium celere* (2.049)	-
41	134	PBSI1	*Francisella tularensis*	-	*Campilobacter jejuni*

* PBSI: Primary bloodstream infection; C: contamination in blood culture.

The bacterial strains 12 and 45 were not initially identified by the VITEK® 2 System but were identified as Brevibacterium celere using MALDI-TOF MS.

Antimicrobial Sensitivity Profile

For 22 samples, it was not possible to obtain a resistance profile to antimicrobials, as no resistance was observed in seven strains (K. pneumoniae n = 5; E. coli n = 2) to any of the tested antimicrobials. For 11 strains, there was no standardization for performing an antibiogram using the VITEK® 2 Sys-

tem (C. albicans n = 1, C. tropicalis n = 1, C. parapsilosis n = 1, Pantoea sp. n = 1, S. maltophilia n = 1, S. sanguinis n = 1, S. paucimobilis n = 1, and Brevibacterium celere n = 4). Additionally, for four strains, the viability of the microorganism was lost (C. jejuni n = 1, E. coli n = 2, and S. hominis n = 1). Different resistance profiles were observed in the bacterial strains, with the greatest diversity of profiles seen among SCN (14 profiles), K. pneumoniae (4 profiles), E. cloacae (4 profiles), and E. coli (4 profiles). Among the resistance profiles of SCN, approximately two-thirds exhibited markers that classified them as multidrug-resistant (resistant to OXA). All highlighted profiles in K. pneumoniae were multidrug-resistant (all resistant to cefepime and none resistant to imipenem). For E. cloacae, two profiles were resistant to CPM, while for E. coli, a single profile was classified as multidrug-resistant (resistant to CPM) (Table 3).

DISCUSSION

Studies show that among cancer patients, hematological diseases pose the highest risk for Primary Bloodstream Infection (PBSI) compared to patients with solid tumors, as well as for those with malignant hematological diseases such as leukemia and lymphoma.[6]

Neutropenia is the greatest independent risk factor for Primary Bloodstream Infection (PBSI), and patients with this infection have higher mortality rates compared to non-neutropenic patients. It is important to note that totally implanted catheters are inserted through surgical procedures, emphasizing the need for updates and reviews of routines, surveillance, training, and verification of preventive measures through insertion and maintenance bundles for Central Venous Catheters (CVCs), including hand hygiene and aseptic technique.[5,16]

A cross-sectional study conducted a retrospective analysis of Primary Bloodstream Infections (PBSI) in oncology-hematology patients with long-term venous catheters, showing that this device was associated with 68% of PBSI cases.[17] Indeed, oncology patients often use long-term central venous catheters for safe chemotherapy treatment, making them more susceptible to infection risks related to catheter care. Therefore, strict care in handling and infusing medications is necessary. This indicates that in the study unit, surveillance and preventive measures appear to be effective, and when these are not followed, the risk of PBSI may increase regardless of the type of catheter used.

Bloodstream infections associated with Ports are classified using the same criteria as those related to other central venous catheters. Although it is considered the device with the lowest risk compared to other venous catheters, frequent complications are encountered in some healthcare services. According to the IDSA and ANVISA guidelines, blood cultures should not be routinely collected from patients who do not show symptoms of Primary Bloodstream Infection (PBSI). In a retrospective study conducted at a pediatric oncology treatment institution, the main complications associated with this type of catheter were mechanical and infectious.[6]

This bacterial strains, due to being an exigent species for culture, was not recovered for further analysis, thus it was not possible to perform antimicrobial susceptibility testing.

Among the bacterial species isolated in this study, most were derived from episodes of PBSI. However, coagulase-negative staphylococci (CNS) species were mostly not associated with PBSI, except for one case of PBSI caused by CNS in a neutropenic patient. In contrast, Gram-positive bacteria predominated in blood cultures from patients with immunodeficiencies and other non-oncological and

non-hematological conditions.[4]

Özalp Gerçeker, Yardımcı, and Aydınok17 found coagulase-negative staphylococci (CNS) in 47.6% of oncological hematology patients, making it the most frequent species in bloodstream infections. Another study showed that in pediatric neutropenic patients, E. coli strains were the microorganisms most frequently observed.[18]

Gram-negative bacteria with a multidrug-resistant profile accounted for 40% of bacterial infection cases, with K. pneumoniae being the primary species associated, representing 66.6% of these cases. This bacterial species has been shown to pose a higher risk for admission to the Pediatric Intensive Care Unit and increased mortality in another study.[4] Our findings also contrast with those of Schonardie, Beck, and Rigatto, who noted that their results pertained exclusively to infections in neutropenic patients.[19] The authors identified the etiologies of bloodstream infections, detecting coagulase-negative staphylococci (CNS) as the most frequent agent (40.1%), with E. coli isolated more frequently (13.2%) than Klebsiella spp. (13.2).

In the present study, the isolation of multidrug-resistant Enterobacteriaceae was not prevalent; the prevalence of MDR Enterobacteriaceae was low, even when considering both infection agents and contaminating microorganisms. Among the resistance profiles observed among Staphylococcus spp., the phenotypic profile of multidrug resistance (resistance to oxacillin – MRSA and MRSE) was noted in nearly all bacterial strains. It is known that, in severe cases caused by oxacillin-resistant Staphylococcus spp., the most commonly adopted therapeutic option is vancomycin. However, a case has recently been reported in our country of a bloodstream infection caused by a vancomycin-resistant strain. The increasing number of reported infections caused by resistant Staphylococcus spp. in Brazil underscores the necessity for surveillance studies to help understand how these strains circulate in healthcare settings.[20,21] These infectious complications sometimes necessitate evaluating the potential need for intravenous device removal.[6]

Strains of Enterobacteriaceae isolated from blood cultures of neutropenic patients with onco-hematological diseases were analyzed, with the most prevalent species in this group being K. pneumoniae and E. coli, which are part of the intestinal microbiota. Klebsiella spp. samples were more prevalent, and this finding may be justified by the alteration of the microbiota in these patients due to multiple hospital visits and admissions related to their health condition. Intestinal colonization by K. pneumoniae is markedly associated with hospitalization.[22]

In total, we isolated 4 strains of K. pneumoniae and 1 strain of E. coli resistant to third-generation cephalosporins. Resistance to these antimicrobials is primarily related to the production of ESBL-type enzymes, with the most commonly associated genes worldwide, including in Brazil, being blaCTX-M and blaSHV.[23,24] A limitation of our study was the lack of investigation into the genetic mechanisms associated with this resistance. We did not search for the presence of these genes.

The evaluation of bacteremia in cancer patients should be considered and classified as PBSI according to the new criteria (breach of barrier and mucosa) recommended by national infection control classification guidelines. Therefore, this definition aims to identify bacteremias in this patient group related to the disruption of the mucosal barrier, promoting the translocation of gastrointestinal bacteria that are not directly associated with CVC infections.[5]

Infection rates are lower when using tunneled catheters with cuffs, totally implanted ports in subcutaneous tissue, peripherally inserted central catheters (PICC), and tunneled catheters without cuffs, compared to non-tunneled short-term catheters. PICCs have been frequently used in this patient group because they remain in place for a long time and have fewer complications related to infection compared to other catheters. Some studies in neonatology also show that central venous catheters present a lower risk of infection than peripheral ones in this population.[25]

The frequent use of catheters necessitates the routine evaluation of patients' clinical conditions and CVCs for diagnosing PBSI associated with these devices, with blood cultures being the most common test collected. Blood culture collection is widely used for diagnosing sepsis and PBSI. However, laboratory diagnosis in patients exhibiting signs and symptoms of PBSI caused by various bacterial species can be challenging, especially in neonates and children, requiring a combined assessment of clinical aspects and laboratory support. In many clinical situations, the positivity rate of blood cultures is low, often below 30%. Some patients may exhibit false-negative blood culture results due to prior antimicrobial use or the timing of blood collection when bacteremia is not present.[3]

CONCLUSION

Blood collection for blood cultures is particularly challenging in children, both due to clinical diagnostic issues and the necessary limitations on the volume and quantity of blood samples. In children with cancer, there is also a greater difficulty in determining whether microorganism isolations correspond to infections or are due to contamination. The occurrence of neutropenia, among other conditions that lead to immunosuppression, is associated with mucosal injuries, promoting bacterial translocation from the intestinal microbiota. Multiple hospitalizations resulting from remissions complicate matters since they lead to colonization by hospital strains of bacteria. Additionally, a major challenge is that hematological patients are more prone to infections by microorganisms that are not detectable by routine clinical microbiology, necessitating molecular biology methods for detection, which are not accessible to most healthcare institutions.

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