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Changing epidemiology of bloodstream infections associated with central venous catheters in patients after stem cell transplantation: increasing frequency of identification of Gram-negative pathogens

Anis Raddaoui
https://orcid.org/0000-0003-0293-9735
Laboratory Department, National Bone Marrow Transplant Center, Tunisia
Tunis El Manar University
https://ror.org/029cgt552
Corresponding author: anis.raddaoui@yahoo.fr

Khaoula Mezzi
https://orcid.org/0009-0000-9840-2283
Laboratory Department, National Bone Marrow Transplant Center, Tunisia
Tunis El Manar University
https://ror.org/029cgt552

Dorra Belloumi
https://orcid.org/0000-0003-0030-5528
Hematology and Transplant Department, National Bone Marrow Transplant Center, Tunisia

Siwar Frigui
https://orcid.org/0009-0003-5675-7969
Laboratory Department, National Bone Marrow Transplant Center, Tunisia
Tunis El Manar University
https://ror.org/029cgt552

Tarek Ben Othmen
–
Hematology and Transplant Department, National Bone Marrow Transplant Center, Tunisia

Nour Abdejlil
–
Hematology and Transplant Department, National Bone Marrow Transplant Center, Tunisia

Yosra Chebbi
–
Laboratory Department, National Bone Marrow Transplant Center, Tunisia
Tunis El Manar University
https://ror.org/029cgt552

Wafa Achour
https://orcid.org/0000-0002-7245-9190
Laboratory Department, National Bone Marrow Transplant Center, Tunisia
Tunis El Manar University
https://ror.org/029cgt552

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ABSTRACT

Introduction. The frequent use of central venous catheters (CVC) in haematopoietic stem cell (HSC) transplant patients exposes them to a high risk of catheter-related bloodstream infections (CRBSI). The aim of

this study was to estimate the prevalence of CRBSI in HSC transplant patients and to describe their clinical and bacteriological characteristics.
Material and methods. A retrospective study (January 2011-December 2022) including 60 episodes of CRBSI occurring in the pre- or post-HSC transplant period in 56 patients was conducted in the Haematology and Transplant Department of the National Bone Marrow Transplant Centre.
Results. The prevalence of CRBSI was 4.9%. The median time between CVC placement and CRBSI was nine days. Gram-negative bacilli (GNB) CRBSI (N=33, 55%) were more frequent than gram-positive cocci (GPC) CRBSI (N=27, 45), with a GNB/GPC ratio of less than one before 2019, rising to two between 2019 and 2022. First-line antibiotic therapy was based mainly on Piperacillin-tazobactam (60%). Removal of the CVC was indicated in 51% of cases. Mortality associated with CRBSI was 0.32% (4/1217).
Conclusions. The increase in CRBSI prevalence and the high rate of antibiotic resistance highlight the need for heightened awareness, ongoing training for healthcare staff, and judicious antibiotic use.

Introduction

Central venous catheters (CVC) are essential for providing central venous access in hematopoietic stem cell (HSC) transplant patients, facilitating the administration of various treatments (chemotherapy, antibiotic therapy, parenteral nutrition, hydration, and blood product transfusions).

Patients receiving HSC transplants are profoundly immunocompromised, due to the underlying disease, intensive chemotherapy protocols or the transplant itself [1]. The presence of CVC in this particular population exposes them to a high risk of catheter-related bloodstream infections (CRBSI) [2,3]. This complication prolongs hospital stay and increases graft-related morbidity and mortality.

Gram-positive cocci (GPC), particularly staphylococci, are the most commonly implicated pathogens in CRBSI [1]. However, recent years have seen an increase in Gram-negative bacilli (GNB) in several onco-hematology studies, along with the emergence of resistant bacteria [4].

Recent data on the epidemiology and bacteriological profile of CRBSI are not available at the National Bone Marrow Transplant Center (NBMTC), the referral center of HSC allograft in Tunisia.

The aims of this study were to determine the overall prevalence of CRBSI in HSCT recipients and to describe their clinical and bacteriological features.

Material and methods

Patients

This retrospective study was conducted over a 12-year period, (January 2011 to December 2022) within the Hematology Department at the NBMTC. The Hematology ward comprised a transplant unit with eight laminar flow cabins, alongside a general hematology unit containing 10 conventional rooms. Throughout the study period, the center performed an annual average of 44 HLA-matched sibling allografts and 57 autografts.

In this study, we included all patients hospitalized in the transplant and hematology units for HSC transplantation (autologous or allogeneic) or for post-transplant complications, who had at least one confirmed episode of CRBSI in the pre- or post-transplant period. A confirmed episode of CRBSI is defined by the presence of the same microorganism in the central blood cultures (CVC-BC) and the peripheral blood cultures (PBC) with a differential time to positivity (DTP) between them > 2 hours (CVC-BC being positive earlier than PBC), or a positive culture from the tip of the CVC with at least 10^3 CFU/ml according to Brun-Buisson, and at least one positive PBC with the same bacteria [2,3]. Patients who experienced an episode of bacteremia with a DTP between CVC-BC and PBC of less than 120 minutes, or a bacterial count of < 10^3 CFU/ml in the CVC, were not included in the study, even if there

were signs of local infection at the CVC insertion site. Patients with incomplete medical records were excluded from the study.

The patients admitted for Allogeneic hematopoietic stem cell transplant (AHSCT) were hospitalized in laminar flow cabins with strict implementation of hygiene measures to prevent the transmission of infectious agents. Those admitted for autologous transplant (AT) or post-AHSCT complications were hospitalized in the conventional sector in individual rooms. Moreover, Systematic microbiological screening was routinely performed in all patients at admission and then weekly until discharge. Screening included rectal swabs (or stool cultures) and urine cultures for the detection of multidrug-resistant bacteria. In addition, weekly swabs of the catheter exit site and hub were performed to detect catheter colonization.

During hospitalization for autologous or allogeneic HSCT, no systemic fluoroquinolone prophylaxis was prescribed. In cases of febrile neutropenia without specific clinical signs, empirical therapy combined piperacillin–tazobactam with amikacin, or fluoroquinolones in patients with renal impairment or multiple myeloma. A glycopeptide was added after 72 hours in case of poor clinical response, particularly with CVC-related inflammation or grade 4 mucositis. If fever persisted, antifungal therapy was initiated. Antibiotic regimens were subsequently adjusted according to microbiological results and clinical evolution. In severe infections or when risk factors for extended spectrum beta-lactamases-producing bacteria were present, imipenem was indicated, while colistin, fosfomycin, and tigecycline were reserved for septic shock, uncontrolled sepsis, or carbapenem-resistant bacteria infections.

Central venous catheter

The CVCs used were double-lumen polyurethane catheters, latex-free and not impregnated with antibiotics or antiseptic agents. A CVC was inserted in all patients hospitalized for NBMTC, as well as in some patients readmitted for post-transplant complications requiring central venous access. Catheter placement was performed under strict aseptic conditions in the operating room of the NBMTC, using anatomical landmarks rather than ultrasound guidance, and positioned either in the subclavian vein or the internal jugular vein. Catheter position was confirmed by standard chest radiography. The femoral vein was used in emergency situations or in patients with a platelet count < 50,000/mm³. A transparent film dressing allowed daily visual inspection of the insertion site. The dressing was changed weekly in the absence of local inflammation, and daily in case of inflammation or for femoral CVCs. The entire tube connected to the CVC was replaced weekly. Microbiological sampling was systematically performed by swabbing the insertion site and the catheter hub.

Once removed, the distal tip of the CVC was immediately placed in a sterile tube and sent to the laboratory ward of the NBMTC.

CVC became eligible for CRBSI starting from the 3rd day after it was placed until the day after it was removed [5].

Blood cultures

Blood cultures were collected from both a peripheral vein and the CVC whenever patients presented with fever. In addition, for patients receiving corticosteroid therapy, blood cultures were systematically performed every other day as part of the routine monitoring protocol, regardless of the presence or absence of fever. CVC-BC and PBC were performed simultaneously (within ≤ 10 minutes), in strict compliance with aseptic techniques and labeling procedures, while ensuring that equal blood volumes were collected in each culture bottle. The samples were then transported to the laboratory for processing.

Microbiological study

CVC-BC, PBC and the tip of the CVC were analyzed at the laboratory ward of the NBMTC according to the French guidelines "Référentiel en Microbiologie Médicale (Rémic 6.1) [6]. Bacterial identification was done using conventionnel methods. Antibiotic susceptibility testing was performed according to the French CA-SFM guidelines

Statistical study

The results were analyzed using SPSS software version 22.0 and Excel software 2016. Frequencies were calculated for qualitative variables. For quantitative variables, means, medians, and extreme values were determined. The trend over time of CRBSI and antibiotic resistance rates was studied

using the Spearman rank correlation coefficient (Rs). The chi-square test was used for comparison. The significance threshold (p) was set at 0.05.

Results

During the study period, 60 episodes of CRBSI were identified in 56 patients out of 1217 HSC transplant recipients, with a prevalence of 4.9%.

Patients' characteristics

Patients with CRBSI had a sex ratio Man/women equal to 1.07 and a median age of 38 years (5–64 years). Among the 56 patients, 29 (52%) had received an AHSCT, and 27 (48%) had undergone AT. Patients with CRBSI were mainly suffering from acute leukemia (29%) (n = 16/56) and aplastic anemia (16%) (n = 9/56) (see **Table 1**).

Epidemiological study

CRBSI was more frequent after AHSCT (5.4%) (n = 29/531) than after AT (3.9%) (n = 27/686), but the difference was not statistically significant (p = 0.23). The median time from HSC transplant to CRBSI was 7 days (day-9 – 625 days). CRBSI occurred within the first 100 days after HSC transplant in 92% of cases (n = 55/60), and 72% of episodes (n = 43/60) took place within the first 30 days following the transplant. The prevalence of CRBSI was higher in patients with aplastic anemia (8%) (n = 9/112) and those with acute myeloblastic leukemia (6.2%) (n = 11/177).

The prevalence of CRBSI increased during the study period, rising from 3.6% (2011–2014), to 4.7% (2015–2018), and to 5.5% between 2019 and 2022. A statistically significant increase was observed during the study period (Rs = 1, p < 0.05).

CVC's characteristics

During our study all the CVC used were double light, latex-free, and not impregnated with antibiotics or antiseptic agents and the most frequently used site for CVC insertion was the subclavian vein (75%, n = 45), followed by the femoral vein

Table 1. Characteristics of Patients with Central Venous Catheter-Related bloodstream infections.

	Total number (n = 56)	Allograft patients (n = 29)	Autograft patients (n = 27)
Median age in years (range)	38 [5–64]	30 [5–52]	51 [18–64]
Children and adolescents < 18 years	5 (9%)	5 (17%)	-
Adults	51 (91%)	24 (83%)	27 (100%)
Sex ratio (M/F) *	1,07	1,4	0,8
Hematologic malignancy**			
AA	9 (16%)	9 (31%)	-
AML	11 (20%)	11 (38%)	-
ALL	5 (9%)	5 (18%)	-
CML	1 (2%)	1 (3%)	-
MDS	1 (2%)	1 (3%)	-
Lymphoma	13 (23%)	2 (7%)	11 (41%)
MM	16 (28%)	-	16 (59%)
Disease status before transplant			
Complete remission	35 (62%)	18 (62%)	17 (63%)
Other: (Partial remission / Failure / Progression)	11 (20%)	1 (3%)	10 (37%)
Not applicable***	10 (18%)	10 (34%)	-
Type of conditioning			
With TBI****	4 (7%)	4 (14%)	-
Chemotherapy without adjunctive treatment	52 (93%)	25 (86%)	27 (100%)
Post-transplant complications			
Conditioning-induced aplasia (ANC < 500/mm³)	44 78%	20 70%	24 89%
Graft-versus-host disease	-	9 31%	-
Corticosteroid therapy	10 18%	9 31%	1 4%

*M – Male; F – Female; **AA – Aplastic anemia; AML – Acute myeloid leukemia; ALL – Acute lymphoblastic leukemia; CML – Chronic myeloid leukemia; MDS – Myelodysplastic syndrome; MM – Multiple myeloma; *** – Not applicable for aplastic anemia and MDS without excess blasts; ****TBI – Total body irradiation.

(13%, n = 8) and the internal jugular vein (12%, n = 7). The CVC was essentially used for chemotherapy administration, accounting for 88% (n = 53/60).

Among the 60 episodes of CRBSI, three (5%) were associated with mechanical complications related to the placement of CVC: one hematoma, one catheter malposition, and one hemopneumothorax. Catheter-related venous thrombosis was documented in seven episodes (12%).

The median duration of catheterization before the onset of CRBSI is 9 days, with most cases (63%) developing within the first 10 days following CVC placement.

Colonization of the CVC by the same pathogen responsible for CRBSI was observed in 13% of cases (n = 8).

Clinical presentation

Among the 60 CRBSI episodes, 67% (40/60) presented with fever, while local signs were noted in 32% (19/60). Fever as the sole manifestation occurred in 25% of episodes (15/60). Four episodes (7%) were asymptomatic; all four patients were receiving corticosteroid therapy, and the bacteremia was detected through routine blood cultures. Sepsis developed in 5% of episodes (3/60) and septic shock in 13% (8/60)

Bacteriological study

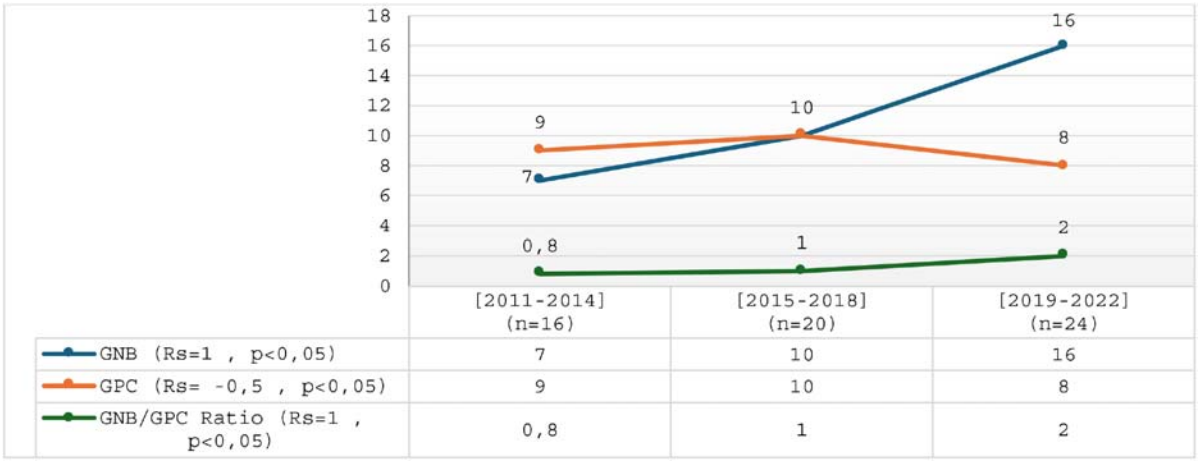
The GNB (n = 33, 55%) were more frequently implicated in CRBSI than the GPC (n = 27, 45%). The GNB/GPC ratio was 1.22. The GNB were predominantly represented by the *Enterobacterales* (n = 19, 32%), with a predominance of *Klebsiella pneumoniae* (n = 10, 17%) and *Enterobacter cloacae* (n = 3, 5%). The GPC were dominated by coagulase-negative staphylococci (CNS) (n = 20, 33%), especially *Staphylococcus epidermidis* (n = 15, 25%).

The GNB/GPC ratio was less than 1 before 2019 in favor of staphylococci. However, from 2019 to 2022, the ratio reached a value of two in favor of the *Enterobacterales* (see **Figure 1**).

Among the 19 strains of the *Enterobacterales* implicated in CRBSI episodes, 10 were resistant to piperacillin + tazobactam (PTZ), and amikacin (antibiotics commonly prescribed as first-line treatment for patients with febrile neutropenia) (see **Figure 2**).

Pseudomonas spp. (n = 7) showed resistance to piperacillin–tazobactam in three isolates, ceftazidime in two, and aztreonam in three. One isolate was resistant to meropenem and another to amikacin. Two isolates were resistant to ciprofloxacin. All three *Acinetobacter baumannii* isolates involved in CRBSI were resistant to piperacillin–tazobactam, ceftazidime, ciprofloxacin, and amikacin; two of these were also resistant to imipenem. No isolates displayed resistance to colistin.

Of the four strains of *Stenotrophomonas maltophilia*, two were resistant to ceftazidime, one to ticarcillin- acid clavulanic, and one to trimethoprim-sulfamethoxazole. All these strains were susceptible to levofloxacin.

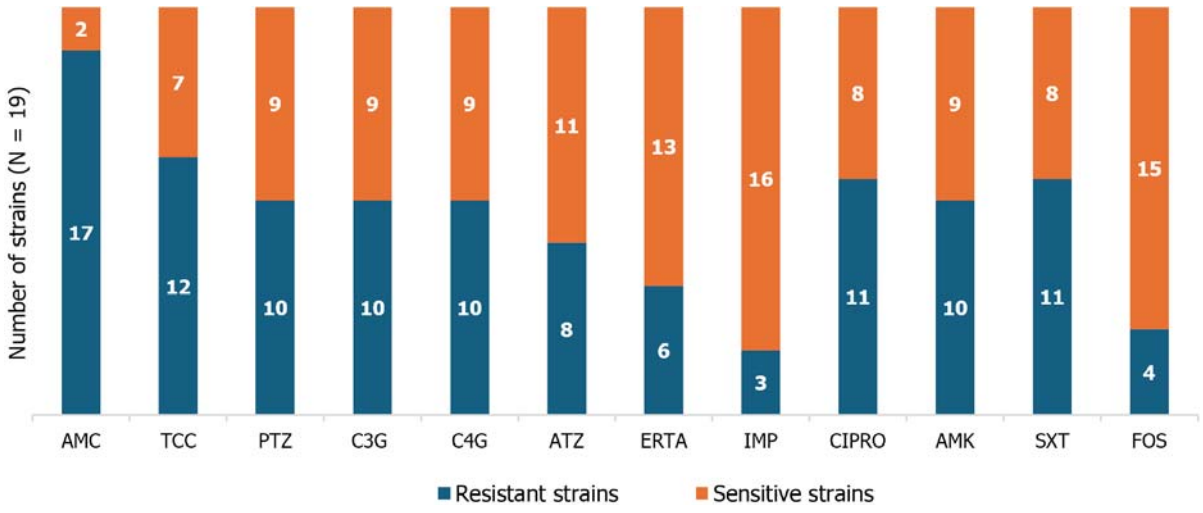


	[2011-2014] (n=16)	[2015-2018] (n=20)	[2019-2022] (n=24)
GNB (Rs=1 , p<0,05)	7	10	16
GPC (Rs= -0,5 , p<0,05)	9	10	8
GNB/GPC Ratio (Rs=1 , p<0,05)	0,8	1	2

Figure 1. Trends over time in the main bacteria responsible for central venous catheter-related bloodstream infections in haematopoietic stem cell transplant patients.

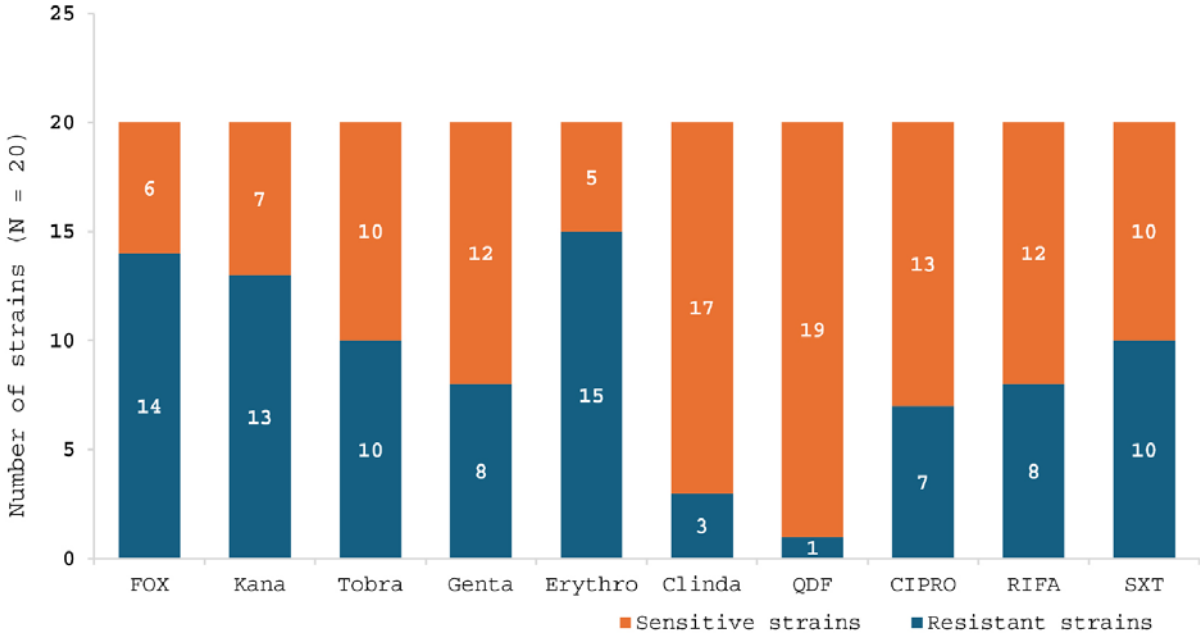
The CNS strains (n = 20) were resistant to methicillin in 14 cases. (see **Figure 3**). The methicillin-resistant strains were all sensitive to glycopeptides, except for one strain of *Staphylococcus haemolyticus* which was resistant to teicoplanin but susceptible to vancomycin. Of the five strains of *Staphylococcus aureus*, only one was resistant to meticillin and sensitive to other antibiotics.

Moreover, among patients with catheter-related bloodstream infections, 12 (20%) had concurrent pulmonary aspergillosis and five (8%) had simultaneous fungemi.



AMC – Amoxicillin-clavulanic acid; TCC – Ticarcillin-clavulanic acid; PTZ – Piperacillin-tazobactam; C3G – 3rd generation cephalosporins; C4G – 4th generation cephalosporins; ATZ – Aztreonam; ERTA – Ertapenem; IMP – imipenem; CIPRO – ciprofloxacin; SXT – Trimethoprim-sulfamethoxazole; AMK – Amikacin; FOS – Fosfomycin.

Figure 2. Antibiotic resistance in *Enterobacterales* responsible for central venous catheter-related bloodstream infections in haematopoietic stem cell transplant patients.



Fox – Cefoxitin; Kana – Kanamycin; Tobra – Tobramycin; Genta – Gentamicin; Erythro – Erythromycin; Clinda – Clindamycin; QDF – quinupristin-dalfopristin; CIPRO – Ciprofloxacin; RIFA – Rifampicin; SXT – trimethoprim-sulfamethoxazole.

Figure 3. Antibiotic resistance in coagulase-negative staphylococci responsible for central venous catheter-related bloodstream infections in haematopoietic stem cell transplant patients.

Treatment

First-line antibiotic therapy was essentially based on dual therapy in 58% of cases (n = 30) and monotherapy in 27% of cases (n = 14). It was empirical in 92% of cases (n = 48). The most commonly prescribed drugs were PTZ in 60% of cases (n = 31), followed by imipenem in 31% of cases (n = 16), amikacin in 31% of cases (n = 16), and ciprofloxacin in 29% of cases (n = 15). First-line antibiotic therapy was appropriate in 58% of cases (n = 30).

Second-line antibiotic therapy was indicated in 56% of cases (n = 29). It was indicated in 42% of cases (n = 22) for inappropriate first-line antibiotic therapy, in 12% of cases (n = 6) for persistent or aggravating symptoms despite appropriate first-line antibiotic therapy, and in only one case for a toxic complication (drug allergy). It was essentially based on dual therapy in 66% (n = 19) and triple therapy in 34% (n = 10). For episodes of GNB-CRBSI, second-line antibiotic therapy was required in 15 episodes (45%), most commonly involving imipenem (n = 8), amikacin (n = 6), and colistin (n = 5). Similarly, second-line therapy was necessary in 14 GPC-CRBSI episodes (52%), with teicoplanin utilized in all 14 cases.

CVC removal was indicated in 31 episodes (51%): *S. aureus* (n = 5), *Pseudomonas sp* (n = 6), GNB other than *Pseudomonas sp* (n = 10) and CRBSI with worsening of symptoms on appropriate antibiotic therapy (n = 10).

Evolution and mortality

Overall mortality directly attributable to CRBSI in our cohort was 4/56 (7.1%), representing 0.32% (4/1,217) of HSC transplant recipients.

Discussion

CRBSI are relatively common among HSCT recipients with CVC, particularly in the first 100 days post-transplant. The epidemiological profile of this bacteremia is constantly evolving.

In our study, the prevalence of CRBSI among HSCT patients was 4.9%, similar to that reported in a previous study conducted in a Chinese intensive care unit [7]. However, it was lower than the prevalence observed in a retrospective study conducted in a HSC transplant unit in the United States, between July 2012 and July 2016, where the CRBSI prevalence was 9% [8]. It was also lower than the prevalence observed in patients undergoing AHSCT (22%) in Pakistan, between 2004 and 2012 [9]. Furthermore, a five-year study in pediatric onco-hematology reported a higher prevalence of CRBSIs (14.6%), with a higher frequency in patients hospitalized post-HSCT [10]. The prevalence of CRBSI in cancer patients is highly dependent on the population studied (transplant patients, neutropenic patients), the environment, CVC handling and the definitions used. As a result of the wide variability of studies, the reported rate of CRBSI in literature varies between 9% and 80% [8]. Furthermore, CRBSI rates may vary according to the type of study (prospective or retrospective approach): prospective studies, with control measures such as daily monitoring of the insertion site, tend to reduce infections, whereas retrospective studies generally do not offer this level of control [3,11].

Our study period saw a notable increase in CRBSI episodes. In contrast, research from a pediatric oncology unit in Washington demonstrated that a massive reduction is possible; they slashed CRBSI rates by over 50% (from 1.89 to 0.73 per 1,000 central line days). Their success relied on three pillars: forming a multidisciplinary team, emulating High-Reliability Organizations, and enforcing strict, ongoing vigilance [12]. Alain et al found that the prevalence of CRBSI in intensive care remained stable, at 0.99 in 2007 and 0.55 in 2016 (per 1,000 catheter days) [13]. The increase in CRBSI in our study may be attributed to the population's exposure to more intensive chemotherapy protocols and severe immunosuppression, along with prolonged and repeated use of antibiotics, which altered the bacteria environment and led to more harmful and resistant bacteria, particularly GNB.

The subclavian vein was the preferred site for CVC insertion, reflecting practitioners' preferences due to patient comfort and a relatively lower risk of infection compared to the internal jugular and femoral sites [14–16]. The CRBSI in our study were mainly at the site of insertion in the subclavian vein, which seemed to be associated with its frequent use rather than a higher risk of infection and colonization. All the CVC used were dual-lumen, not antibiotic or antiseptic-impregnated. Multilumen CVC carried a higher risk of bacterial colonization and infection compared to single-lu-

men CVC [14,17]. Some studies suggest that antibiotic or antiseptic-impregnated CVC reduce the risk of infection due to their effectiveness against biofilms and their broad-spectrum bactericidal action [14,18].

The median duration of catheterization before the development of CRBSI is 9 days, with the majority of cases (63%) occurring within the first 10 days after CVC placement, a period when extraluminal contamination from the skin is predominant [18].

The bacteriological profile of CRBSI in HSC transplant patients was dominated by GNB, particularly *Enterobacterales*, including *K. pneumoniae*. These findings were similar to those reported in other studies. Yokota et al demonstrated that GNB were the most implicated in CRBSI (49%), with a predominance of *Klebsiella spp.* (30% of GNB) [19]. Similarly, Agrawal et al found in their study of cancer patients (January 2017- June 2018) that GNB were the predominant pathogens, accounting for 72.6% of the microorganisms responsible for CRBSI [20]. Furthermore, a study conducted in a Chinese onco-hematology unit (2013 – 2020) reported that 57% of CRBSI were caused by GNB, with a predominance of *K. pneumoniae* [21].

However, some studies have shown a predominance of CNS among GPC. A Japanese study involving patients with hematological malignancies and solid tumors, revealed that 58.1% of CRBSI (2012- 2015) were caused by GPC, of which 31.9% were CNS [1]. Similarly, See et al found that 57.5% of CRBSI in oncology (2009–2012) were due to GPC, with CNS being the most frequently identified (16.9%), led by *S. epidermidis* [22].

The variability in the bacteriological profile from one study to another seems to be influenced by several factors, such as patient characteristics, the type of intravenous product (parenteral nutrition or chemotherapy), and the composition of the environmental microflora. Aseptic measures and protocols applied in each department may also explain the diversity of germs responsible for CRBSI [23,24].

The evolution of the bacteriological profile and the inversion of the BGN/CGP ratio in favor of BGN during our study has been reported in several studies [3]. Improved care and preventive measures have reduced CRBSI caused by GPC, in particular *S. aureus*. This change may also be explained by modifications in the management of neutropenic patients with haematological malignancies: in particular, the discontinuation of fluoroquinolone prophylaxis in some institutions [25].

The *Enterobacterales* involved in CRBSI (n = 19) were resistant to cephalosporins (third- and fourth-generation), ciprofloxacin, and amikacin in more than half of the cases. Additionally, six strains belonging to *K. pneumoniae* species were resistant to carbapenems. The rates of antibiotic resistance were higher than those described by See et al for *Enterobacterales* responsible for CRBSI in oncology. In fact, the rate of resistance to third-generation cephalosporins did not exceed 20% in *Klebsiella sp* and *Escherichia coli,* and 36% in *Enterobacter sp*, and the rate of resistance to carbapenems was less than 5% in all three species [22]. In France in 2019, 69 strains of *Enterobacterales* were responsible for CRBSI in haematology. The prevalence of C3G resistance was 23%, with variations depending on the species 42% for *Enterobacter cloacae*, 40% for *K. pneumoniae* and 7% for *E. coli*. Resistance to carbapenems was 3%. It has only been described in *E. cloacae* [26].

Among the 20 strains of CNS, 14 were resistant to methicillin. Several studies have revealed a rise in CNS resistance to methicillin, aminoglycosides, fluoroquinolones, and macrolides [27].

The frequent use of PTZ, imipenem and amikacin in empirical treatment of CRBSI in our study was justified in this particular population (neutropenic and immunocompromised patients). The empirical use of imipenem is explained by the relatively high rate of Extended-Spectrum Beta-Lactamase -producing Enterobacterales at the NBMTC (unpublished data).

In second-line antibiotic therapy, teicoplanin was the most commonly used antibiotic for CGP-CRBSI, considering the high prevalence of methicillin-resistant Staphylococcus strains in our study. The emergence of multidrug-resistant bacteria and the still reliable efficacy of imipenem (relatively low resistance to carbapenems in GNB responsible for CRBSI) justify the frequent use of this molecule in synergy with amikacin during second-line antibiotic therapy for GNB CRBSI.

The German Society of Haematology and Oncology recommends CVC removal in patients with CRBSI whenever possible. However, in patients with severe thrombocytopenia with limited venous access, such as those included in our study, the risk of reinserting the CVC should be

carefully weighed against the risk of deterioration and prolongation of infection [3].

Removal of the CVC formed part of the therapeutic strategy for CRBSI in 51% of cases, based on microbiological documentation or in the face of an unfavorable evolution of CRBSI episodes. However, according to IDSA guidelines, CVC removal is recommended in certain situations: severe clinical presentation, persistent bacteremia despite appropriate antimicrobial treatment for 72 hours, or infections caused by specific pathogens such as *S. aureus, P. aeruginosa*, fungi or mycobacteria [28,29].

In our study, the evolution of CRBSI was favorable with antibiotic therapy in most cases, which was consistent with other studies [8,9]. This low rate could be explained by early diagnosis and rapid, appropriate antibiotic therapy.

Prevention

The risk of developing CRBSI in HSC transplant recipients depends mainly on the management of CVC. It was possible to reduce the rate of CRBSI after the implementation of a set of measures comprising five components: Hand hygiene, maximum barrier precautions, disinfection of the insertion site with chlorhexidine, avoidance of femoral site and removal of unnecessary CVC. In 2009, these recommendations were included in the international guidelines for HSC transplant recipients [30,31].

Limitations of this Study

The authors acknowledge several limitations. This retrospective, single-center study may limit the generalizability of our findings. The sample size was modest (60 episodes), which reduces statistical power for subgroup analyses. Moreover, the long study period (2011–2022) encompasses changes in diagnostic methods and clinical practice that could have affected case detection and management.

Conclusion

In conclusion HSC transplant patients are a population at high risk of infection, particularly from CRBSI. The rise in the prevalence of CRBSI and the change in the bacteriological profile of CRBSI to BGN, with the emergence of increasingly resistant strains, underline the importance of ongoing control of these infections and the implementation of a strategy to combat them.

Abbreviations

AHSCT – allogeneic hematopoietic stem cell transplant
AT – autologous transplant
CNS – coagulase-negative staphylococci
CRBSI – catheter-related bloodstream infections
CVC – central venous catheters
CVC-BC – central venous catheters blood cultures
C3G – third-generation cephalosporins
DTP – differential time to positivity
GNB – gram-negative bacilli
GPC – gram-positive cocci
HSCT – hematopoietic stem cell transplant
HSC – Hematopoietic stem cell
NBMTC – National Bone Marrow Transplant Center
PBC – peripheral blood cultures
PTZ – piperacillin + tazobactam

Declarations and statements

Author contributions
Anis Raddaoui and Khaoula Mezzi: study design, laboratory experiments, data analysis and interpretation, preparation of the first draft of the manuscript; Siwar Frigui: participation in data analysis and interpretation; Yosra Chebbi and Dorra Belloumi: scientific supervision, study design, data analysis and interpretation, manuscript revision; Tarek Ben Othmen, Nour Abdejlil: expert consultation; Wafa Achour: scientific supervision, expert consultation, revision and final approval of the manuscript.

Ethical approval
Not required. Clinical data was collected anonymously and confidentially. As the bacterial strains were analyzed anonymously the study was exempted from Human Research Committee approval according to the regulations of the Local Medical Ethical Committee of the National Bone Marrow Transplant Centre of Tunis, Tunisia.

Conflict of interest statement
The authors declare no conflict of interest.

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