Original Article

Association Between Rectal Bacterial Colonization and Bloodstream Infections During Paediatric Haematopoietic Stem Cell Transplantation at A Tertiary Care Center

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Abstract

Background: Bloodstream infections (BSIs) remain a major cause of morbidity and mortality in paediatric haematopoietic stem cell transplantation (HSCT) recipients. Gastrointestinal colonization by multidrug-resistant (MDR) organisms has increasingly been recognized as an important reservoir for invasive infections during neutropenia and mucosal barrier injury. This study evaluated the prevalence and spectrum of bacteria colonizing the GIT and to see any association between rectal colonisation and BSI. **Material and Methods:** A retrospective cohort study was conducted among 100 paediatric patients who had undergone HSCT. Serial rectal swabs were obtained at admission and at Weeks 2, 4, 6, and 8 post-transplantations. Blood culture findings obtained during the same period were analyzed. Rectal colonization patterns, Enterococcus and vancomycin-resistant Enterococcus (VRE) trends, bloodstream infection profiles, and concordance between rectal and bloodstream isolates were evaluated. Descriptive and comparative analyses were performed using available statistical methods. **Results:** Overall bloodstream infection (BSI) incidence was 23%, with the highest incidence occurring during the first two weeks post-transplant (17%) and declining thereafter, with no BSI detected by Week 8. Early BSIs were predominantly caused by Klebsiella spp., Escherichia coli, Pseudomonas spp., and staphylococcal species, while Acinetobacter spp. emerged during later phases. Rectal colonization demonstrated progressive predominance of Enterococcus spp. and resistant Enterobacteriaceae during the transplant course. Enterococcus colonization increased significantly from 7% at baseline to 32% at Week 8 ($p < 0.001$), with vancomycin-resistant Enterococcus emerging at Week 4 and peaking at 30%. No patient with a negative rectal swab developed bloodstream infection, although the association between concurrent rectal colonization and BSI didn't reach statistical significance ($\chi^2=1.59$, $p=0.207$). A significant association was observed between underlying diagnosis and occurrence of BSI ($\chi^2=15.30$, $p=0.018$). **Conclusion:** Progressive intestinal colonization with resistant organisms occurs during paediatric HSCT and appears closely associated with subsequent bloodstream infections. Although concurrent colonization-BSI association was not statistically significant, rectal swab sterility strongly predicted absence of bacteraemia. Surveillance rectal cultures may therefore provide clinically useful information for infection-risk stratification and empirical antimicrobial decision-making in paediatric HSCT recipients.

Keywords: Paediatric Haematopoietic stem cell transplantation, bloodstream infection, rectal colonization, MDR organisms, vancomycin-resistant Enterococcus, antimicrobial resistance.

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Introduction

Bloodstream infections (BSIs) are among the most important infectious complications encountered during haematopoietic stem cell transplantation (HSCT), particularly in paediatric recipients undergoing prolonged neutropenia, intensive immunosuppression, and mucosal barrier injury.[1,2] In spite of advances in supportive care, infection control, and antimicrobial therapy, BSIs continue to contribute substantially to transplant-related morbidity, prolonged hospitalization, intensive care utilization, and mortality.[3,4]

The gastrointestinal tract plays a crucial role in the pathogenesis of bloodstream infections during HSCT. Conditioning chemotherapy, broad-spectrum antibiotics, disruption of commensal microbiota, and mucosal injury facilitate intestinal dysbiosis and translocation of pathogenic organisms into the bloodstream.[5,6] So many literatures have demonstrated that gut domination by resistant Enterobacteriaceae or Enterococcus species may precede invasive bloodstream infections in HSCT recipients.[7,8]

However, data regarding longitudinal colonization dynamics and colonization-BSI association in paediatric HSCT recipients from low- and middle-income settings remain limited. Understanding

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local epidemiological patterns is essential for antimicrobial stewardship, infection prevention strategies, and optimization of empirical therapy.

The present study was undertaken to evaluate the association between rectal bacterial colonization and bloodstream infections during paediatric HSCT at a tertiary care center. The study specifically aimed to assess temporal patterns of rectal colonization, characterize organisms causing bloodstream infections, determine concordance between rectal and blood culture isolates, and evaluate the contribution of resistant organisms including VRE.

Aim and objectives

To assess temporal pattern of rectal colonization and evaluate any association between rectal bacterial colonization and bloodstream infections in paediatric patients undergoing haematopoietic stem cell transplantation at a tertiary care center.

Materials and Methods

Study Design and Setting: This retrospective cohort study was conducted in the Bone Marrow Transplant Unit, Department of Paediatrics, at Super Specialty Hospital, M.G.M. Medical College, Indore.

Study Population: A total of 100 paediatric patients who had undergone HSCT in the last five years were included in this study. Patients with complete serial rectal swab and blood culture data during the transplant course were analyzed.

Sample Size and Sampling: The study included all paediatric patients who underwent haematopoietic stem cell transplantation (HSCT) at the study center during the preceding five-year period and fulfilled the eligibility criteria. A total of 100 patients with complete serial rectal swab surveillance and blood culture data during the transplant course were enrolled. As this was a retrospective cohort study, a consecutive sampling method was employed, wherein all eligible patients available in the institutional HSCT database during the study period were included to minimize selection bias and ensure representative sampling of the transplant population.

Inclusion Criteria: Paediatric patients who had undergone HSCT within last 5 years with available serial rectal swab and blood culture data during the transplant period.

Exclusion Criteria: Patients with incomplete microbiological records or inadequate follow-up during the transplant course.

Study Procedure and Data Collection: Demographic and clinical details of all eligible patients were collected from their medical records. The information included the patient's name, age, sex, and residential address along with contact details. Additional data on socioeconomic status and educational background were recorded to provide context on the patient population. Clinical parameters such as the primary disease diagnosis, type of donor for hematopoietic stem cell transplantation, and number of siblings were noted.

Serial rectal swabs were obtained at: Admission, Week 2, Week 4, Week 6, and Week 8 post-transplantation. Blood culture data obtained during corresponding time periods were recorded and analyzed.

Microbiological Analysis: Rectal swabs and blood cultures were processed according to standard microbiological protocols. Organisms were identified using conventional microbiological methods. Antimicrobial susceptibility testing was performed according to institutional laboratory standards.

Organisms were categorized based on resistance profiles into: Pan-sensitive, ESBL-producing, Carbapenem-resistant, and Pan-resistant organisms. Enterococcus isolates were additionally assessed for vancomycin resistance.

Definitions

- Rectal colonization: isolation of pathogenic bacteria from rectal swab cultures.
- Bloodstream infection (BSI): positive blood culture with clinically significant bacterial pathogen.

Statistical Analysis: Data were entered in Microsoft excel and analyzed using SPSS 25.0 trial version. Descriptive statistical analysis was performed, continuous data were expressed in terms of mean and standard deviation. Categorical data were expressed in terms of frequencies and percentages. Chi-square test and Fisher's exact test were used wherever applicable. A p-value <0.05 was considered statistically significant.

Results

Table 1: Baseline demographic and transplant characteristics of study participants

Variable	Categories	Frequency (%)
Age	<5 years	25 (25.0)
	5-10 years	41 (41.0)
	>10years	34 (34.0)
Mean Age	8.96 ± 4.34	
sex	Male	71 (71.0)
	Female	29 (29.0)
Indication for HSCT	Thalassemia	59 (59.0)
	Aplastic Anaemia	23 (23.0)
	Leukemia	7 (7.0)
	Others	11 (11.0)
Type of transplant	Allogeneic BMT	96 (96.0)
	Autologous BMT	4 (4.0)

The mean age of the cohort was 8.96 ± 4.34 years, with a male predominance. Thalassaemia was the most common (59%) underlying diagnosis, followed by aplastic anaemia/bone marrow failure syndromes and

leukaemia/myelodysplastic syndrome.

Most patients (96%) underwent allogeneic transplantation. Serial rectal surveillance cultures and blood cultures were available at predefined intervals throughout the transplant course.

Table 2: Temporal pattern of rectal bacterial colonization during HSCT

Organism	Admission n (%)	Week 2 n (%)	Week 4 n (%)	Week 6 n (%)	Week 8 n (%)
Klebsiella spp.	13 (13.0)	23 (23.0)	17 (17.0)	38 (38.0)	23 (23.0)
Escherichia coli	65 (65.0)	22 (38.0)	44 (44.0)	44 (44.0)	30 (30.0)
Enterococcus spp.	7 (7.0)	22 (22.0)	30 (30.0)	10 (10.0)	32 (32.0)
Other Gram-negative bacilli	3 (3.0)	11 (11.0)	5 (5.0)	0 (0)	2 (2.0)
No growth (sterile)	12 (12.0)	6 (6.0)	4 (4.0)	8 (8.0)	13 (13.0)
Total culture-positive	88 (88.0)	94 (94.0)	96 (96.0)	92 (92.0)	87 (87.0)

Rectal colonization remained consistently high throughout the transplantation period, with culture positivity exceeding 85% at all surveillance time points. A progressive ecological shift in intestinal flora was observed during the transplant course.

Gram-negative bacilli, particularly Klebsiella spp. and Escherichia coli, predominated during the early transplant period. Over time, increasing enterococcal dominance and emergence of resistant organisms were noted.

Enterococcus colonization increased significantly from 7% at admission to 32% by Week 8 ($\chi^2 = 29.36$, $p < 0.001$), demonstrating progressive intestinal dysbiosis during HSCT.

Table 3: Emergence of antimicrobial resistance patterns among rectal isolates

Resistance Pattern	Admission (%)	Week 2 (%)	Week 4 (%)	Week 6 (%)	Week 8 (%)
ESBL-producing isolates	63 (71.6)	60 (15.9)	75 (78.1)	74 (80.4)	55 (63.2)
Carbapenem-resistant isolates	14 (15.9)	25 (26.6)	17 (17.7)	18 (19.6)	28 (32.2)
Pan-sensitive isolates	11 (12.5)	7 (7.4)	2 (2.1)	0 (0)	4 (4.6)
Pan-resistant isolates	0 (0)	2 (2.1)	2 (2.1)	0 (0)	0 (0)
Vancomycin-sensitive	7(100.0)	19(86.4)	14(46.7)	5(50.0)	14(43.8)
VRE isolates	0(0)	0(0)	9(30.0)	2(20.0)	3(9.4)
Total	88 (100.0)	94 (100.0)	96 (100.0)	92 (100.0)	87 (100.0)

ESBL-producing organisms predominated at all surveillance points, while carbapenem-resistant isolates increased progressively over time.

Pan-sensitive organisms steadily declined and were absent by Week 6, indicating increasing antimicrobial selective pressure during hospitalization and antibiotic exposure.

Table 4: Distribution of bloodstream infections during the transplant course

Organism	Week 2 n (%)	Week 4 n (%)	Week 6 n (%)	Week 8 n (%)
Klebsiella spp.	6 (6.0)	0 (0)	0 (0)	0
Escherichia coli	3 (3.0)	3 (3.0)	0 (0)	0
Pseudomonas spp.	2 (2.0)	0 (0)	0 (0)	0
Staphylococcus spp.	3 (3.0)	3 (3.0)	0 (0)	0
Coagulase-negative staphylococci	3 (3.0)	0 (0)	0 (0)	0
Acinetobacter spp.	0	0	6 (6.0)	0
Total BC- positive	17 (17.0)	6 (6.0)	6 (6.0)	0 (0)

Overall bloodstream infection (BSI) incidence was 23%. The majority of BSIs occurred during the early post-transplant period, particularly within the first two weeks after transplantation.

The incidence of BSI progressively declined over time, with no bloodstream infections documented by Week 8.

Gram-negative organisms predominated among bloodstream isolates. Klebsiella spp. represented the commonest pathogen during the initial post-transplant period, followed by Escherichia coli. Late-onset infections included Acinetobacter spp., suggesting possible nosocomial acquisition.

Table 5: Association between rectal colonization and bloodstream infection

Time Point	Rectal Swab	Bloodstream Infection Yes n (%)	Bloodstream Infection No n (%)	Total n (%)	χ^2 / p-value
Week 2	Positive	17 (19.3)	71 (80.7)	88 (100)	1.592 / 0.207
	Negative	0 (0)	12 (100)	12 (100)	
Week 4	Positive	6 (6.3)	90 (93.7)	96 (100)	0.312 / 0.576
	Negative	0 (0)	4 (100)	4 (100)	
Week 6	Positive	6 (6.5)	86 (93.5)	92 (100)	0.001 / 0.974
	Negative	0 (0)	8 (100)	8 (100)	
Week 8	Positive	0 (0)	87 (100)	87 (100)	Not applicable
	Negative	0 (0)	13 (100)	13 (100)	

Table 6: Distribution of bloodstream infections according to underlying diagnosis

Underlying Diagnosis	Patients with BSI n (%)	No BSI n (%)	Total N (%)
Leukaemia/MDS	4 (57.1)	3 (42.9)	7 (100.0)
Thalassaemia	14 (23.7)	45 (76.3)	59 (100.0)
Aplastic anaemia/BMF	3 (13.0)	20 (87.0)	23 (100.0)
Chronic granulomatous disease (CGD)	1 (100.0)	0	1 (100.0)
Hodgkin lymphoma	0	5 (100.0)	5 (100.0)
Sickle cell disease	0	4 (100.0)	4 (100.0)
Other	1 (100.0)	0	1 (100.0)
Total	23 (23.0)	77 (77.0)	100 (100.0)

A statistically significant association was observed between primary diagnosis and occurrence of bloodstream infection ($\chi^2 = 15.30$, df = 6, p = 0.018).

Patients with leukaemia/myelodysplastic syndrome demonstrated the highest proportion of bloodstream infection, whereas no BSI episodes were observed among patients with Hodgkin lymphoma or sickle cell disease.

Discussion

The current study evaluated the relationship between gastrointestinal bacterial colonization and bloodstream infections (BSIs) in paediatric haematopoietic stem cell transplantation (HSCT) recipients using serial rectal surveillance cultures. The observations demonstrated progressive intestinal colonization with resistant organisms during transplantation, high prevalence of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae, emergence of vancomycin-resistant Enterococcus (VRE), and a clinically relevant association between rectal colonization status and bloodstream infection risk.

The overall BSI incidence of 23% observed in the present study is comparable to rates previously reported among paediatric HSCT recipients. Perez P et al. (2020) reported bloodstream infection rates ranging between 20-30% in paediatric transplant cohorts, especially during the early neutropenic period.[15] The predominance of BSIs during the first two weeks after transplantation in this study likely corresponds to the phase of profound neutropenia, mucosal barrier injury, and maximal exposure to broad-spectrum antimicrobial agents. Similar findings have been described by Tomblyn M et al. (2009) and Mikulska M et al. (2012), who also identified the immediate post-transplant period as the phase of greatest infectious vulnerability in HSCT recipients.[3,4]

Klebsiella spp. and Escherichia coli predominated both as rectal colonizers and bloodstream isolates, supporting the concept of gastrointestinal translocation as a major mechanism underlying bacteraemia during HSCT. Taur Y and Pamer EG (2013) described how chemotherapy-induced intestinal mucosal disruption facilitates microbial translocation from the gut lumen into the systemic circulation.[5] Similarly, Jenq RR et al. (2015) highlighted the importance of intestinal microbiota alterations in influencing infectious complications following transplantation.[6] Also, Kelly MS et al. (2019), using genomic sequencing techniques, demonstrated close genetic relatedness between rectal and bloodstream isolates in paediatric HSCT recipients, thereby strongly supporting the gut reservoir hypothesis.[7]

A progressive increase in Enterococcus colonization and emergence of VRE was observed during the transplant course. This phenomenon likely indicates profound ecological disruption induced by chemotherapy, prolonged hospitalization, and selective antibiotic pressure. Taur Y et al. (2012) observed that intestinal domination by Enterococcus species is associated with increased risk of subsequent invasive infection and adverse transplant outcomes.[8] Likewise, Vaitkute G et al. (2022) identified enterococcal dominance as a marker of intestinal dysbiosis and reduced microbial diversity in paediatric HSCT recipients.[16] Despite substantial enterococcal colonization in the present cohort, no Enterococcus bloodstream infections were documented. Comparable findings have been reported by Krawiec KM et al. (2022), suggesting that colonization alone may not invariably progress to invasive disease and that additional host and microbial factors likely influence progression to bacteraemia.[17]

One of the most clinically important finding in the present study was that no patient with a negative rectal swab developed bloodstream infection during the surveillance period. Although statistical significance was not demonstrated, likely because of limited sample size and structural zeros, the apparent negative predictive value of rectal swab sterility was 100%.

Previous literature has consistently emphasized the gastrointestinal tract as a major reservoir for bloodstream pathogens in immunocompromised hosts. A study by Severyn CJ et al. (2021) demonstrated that pathogenic gut colonization frequently precedes bloodstream infection among paediatric HSCT recipients.[18] Likewise, Kelly MS et al. (2019) reported that intestinal domination by pathogenic organisms preceded bloodstream infections by a median duration of approximately 17 days.[7] Therefore, the lack of statistically significant concurrent association observed in the present study may reflect a temporal delay between colonization and subsequent bloodstream invasion rather than absence of biological association.

The progressive increase in ESBL-producing and carbapenem-resistant organisms observed during transplantation is particularly concerning. Girmenia C et al. (2015) highlighted the growing burden of carbapenem-resistant Klebsiella pneumoniae infections among stem cell transplant recipients and highlighted their association with poor outcomes.[9] Alike, Satlin MJ et al. (2013) described the emergence of carbapenem-resistant Enterobacteriaceae as a major threat in patients with haematological malignancies and HSCT recipients.[10] The gradual disappearance of pan-sensitive organisms and increasing carbapenem resistance in the present study likely reflect the cumulative selective pressure imposed by prolonged

hospitalization, repeated antibiotic exposure, and immunosuppression.

The significant association between primary diagnosis and bloodstream infection risk observed in this study is also noteworthy. Patients with leukaemia and myelodysplastic syndrome demonstrated the highest BSI burden, likely attributable to prior chemotherapy exposure, prolonged immunosuppression, recurrent neutropenia, and severe mucosal injury. Study by Weber D et al. (2016) similarly observed that patients receiving intensive chemotherapy exhibit marked intestinal microbiota disruption and increased infectious complications during transplantation.[19] In contrast, the absence of bloodstream infection among Hodgkin lymphoma patients in the current study may reflect lower cumulative immunosuppressive exposure and the predominance of autologous transplantation in this subgroup. Recent microbiome-based investigations have further strengthened the relationship between intestinal dysbiosis and bloodstream infection in HSCT recipients. Vaitkute G et al. (2022) stated that Enterococcus- and Enterobacteriaceae-dominated microbial communities were associated with adverse clinical outcomes following paediatric HSCT.[16] Corcione S et al. (2025) further found that ESBL colonization significantly alters gut microbiota composition during allogeneic transplantation.[20] Similarly, Gao Q et al. (2025) reported reduced microbial diversity and increased abundance of pathogenic organisms among paediatric HSCT recipients who subsequently developed bloodstream infections.[21]

The findings of the present study have important clinical implications. Serial surveillance rectal cultures may facilitate infection-risk stratification and support individualized empirical antimicrobial therapy in paediatric HSCT recipients. Early identification of resistant colonizers could help antimicrobial stewardship programs, optimize empirical antibiotic selection, and strengthen infection prevention strategies, particularly in tertiary care centers with high multidrug-resistant organism burden.

Strengths and Limitations

The study's strengths include longitudinal serial surveillance of rectal colonization during HSCT, comprehensive assessment of bloodstream infections, and detailed evaluation of multidrug-resistant organisms and VRE patterns in a paediatric transplant cohort. Inclusion of all eligible patients over a 5-year period using consecutive sampling reduced selection bias.

The study is limited by its retrospective single-center design, which restricts causal inference and generalizability. Molecular typing to establish strain-level concordance between rectal and bloodstream isolates was not performed, and detailed data on antibiotic exposure, neutropenia duration, graft-versus-host disease, and transplant outcomes were unavailable.

Conclusion

Progressive intestinal colonization with resistant Gram-negative organisms and Enterococcus species occurs during paediatric HSCT and appears closely associated with bloodstream infection dynamics. Although concurrent statistical association between rectal colonization and bacteraemia was not found, absence of bloodstream infection among rectal swab-negative patients suggests potential clinical utility of surveillance rectal cultures as predictive tools.

The increasing prevalence of ESBL-producing organisms, carbapenem resistance, and VRE underscores the urgent need for antimicrobial stewardship and infection control interventions in paediatric transplant units. Prospective multicentric studies incorporating molecular typing and microbiome analysis are required to further define the predictive role of intestinal colonization in HSCT-related bloodstream infections.

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Conflicts of interest

There are no conflicts of interest.

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