JCOMS eISSN:2783-3127 https://journalofcoms.com

Journal of

Current Oncology and Medical Sciences

Vol. 4, No. 3

Original Free Access

Prevalence and clinical significance of saprophytic bacteria in bloodstream infections among cancer patients

Sheetal Goenka [1], Wanshisha Wanswett [1], Manisha Jain [1] *, Poonam Loomba [1], Abha Sharma [1], Shivani Tyagi [1]

[1] Department of Microbiology, GB Pant Institute of Medical Education and Research (GIPMER), Delhi, India

Abstract

Introduction: Bloodstream infections (BSIs) in cancer patients are associated with high morbidity and mortality. While common pathogens are well-studied, the role of saprophytic bacteria in BSIs among this population is less understood. To investigate the prevalence and clinical significance of saprophytic pathogens causing BSIs in cancer patients at a tertiary care center.

Materials and Methods: This retrospective study included all 200 consecutive adult cancer patients with suspected sepsis over four months. Blood cultures were processed on an automated BACTEC system. Subculture and identification were performed using standard microbiological techniques and the Vitek 2 system. Antimicrobial sensitivity was performed as per CLSI guidelines.

Results: The blood culture positivity in these patients was 79% (158/200). Of the 158 positive blood cultures, 10.1% (16/158) were saprophytic pathogens. These included *Enterococcus avium, Sphingomonas paucimobilis, Actinomyces meyeri, Kodamaea ohmeri, Elizabethkingia meningoseptica, Aeromonas hydrophila, Achromobacter xylosoxidans, Stenotrophomonas maltophilia, Pantoea dispersa,* and *Burkholderia pseudomallei*. The overall 30-day mortality rate for patients with saprophytic pathogen BSIs was 20%.

Conclusion: Saprophytic bacteria have gained recognition as possible human pathogens, especially in immunocompromised patients including cancer patients. Such high-risk patients should be put on empiric antibiotics to improve patient outcomes till the time clinical significance is established.

Keywords: Bloodstream infection, Saprophytic organism, Cancer patients

Corresponding Authors: Manisha Jain

✉ Email: manisha_jain29@yahoo.com

Receive: 2024.6.7, Accepted: 2024.9.17

Introduction

Bloodstream infections (BSIs) remain a significant cause of morbidity and mortality in cancer patients, with mortality rates ranging from 18% to 42% (1-3). It has been known for decades that the fundamental cause of the life-threatening organ damage seen in sepsis is not the direct result of the invading organisms but rather the host response to infection(1,2). Additionally, patients who survive sepsis endure long-term physical, psychological, and cognitive impairment, known as post-sepsis syndrome (3,4).

Blood culture remains the gold standard for diagnosing BSI. While common pathogens like *Klebsiella pneumoniae* and *Escherichia coli* are well-recognized in this setting, the role of saprophytic bacteria in causing BSIs among cancer patients is less understood(5-7).

The immunocompromised state of cancer patients, coupled with frequent hospitalizations and invasive procedures, creates a unique environment where typically non-pathogenic organisms can cause severe infections(8-12). A recurring challenge in clinical practice is distinguishing true pathogens from colonizers and contaminants in blood cultures. This study aimed to investigate the prevalence and clinical significance of saprophytic pathogens causing BSIs in cancer patients in a large tertiary care center

Material and methods

This retrospective study was carried out over four months, from January to April 2023 at one of the large tertiary care referral center. A total of 200 consecutive patients (age ≥ 18 years) with a confirmed diagnosis of cancer presenting with signs and symptoms of bloodstream infection were included in the study. Non-cancer patients or cancer patients with polymicrobial bloodstream infections or where the clinical significance of the isolate could not be determined were excluded from the study.

As a routine hospital protocol, venous blood was taken aseptically from patients clinically suspected of having bloodstream infections. The blood was inoculated aseptically into the automated blood culture bottle and incubated using the BACTEC system. Once flagged positive, the blood culture bottles (PBC) were processed using standard microbiological techniques. Briefly, direct gram staining was done from PBC along with subculture on blood agar and MacConkey agar. The plates were incubated at 37°C, and the next day growth was observed. The colonies were identified by colony characteristics, gram stain, and biochemical reactions. Identification was confirmed by the Vitek 2 system (Biomerieux, France). Antimicrobial susceptibility testing was carried out by the Vitex 2 system as well as manually using the disk diffusion method and the antibiotics tested were chosen either from the CLSI guidelines or the available literature where CLSI guidelines was not available.

Statistical Analysis: Descriptive statistics were used to summarize patient demographics and clinical characteristics. Categorical variables were presented as frequencies and percentages. Continuous variables were expressed as means and ranges. Fisher's exact test was used to compare mortality rates between groups. A p-value <0.05 was considered statistically significant. All analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY).

Data Collection and Analysis: Clinical data including patient demographics, cancer type, presenting symptoms, and treatment outcomes were collected from medical records. The frequency of saprophytic pathogens was calculated as a percentage of total isolates.

The data for this study were collected as part of routine clinical care and were fully anonymized. It is essential to highlight that all patient data were de-identified to maintain confidentiality. Personal identifiers were removed prior to data analysis, and no identifiable information was used in the study. This approach ensured compliance with patient privacy regulations and ethical standards. There was no ethical consideration regarding the study.

Results

Out of 200 patients, 60 (30%) were female and 140 (70%) were male. The mean age was 52 years (range: 18-75 years). The most common cancer types were colorectal (25%), lung (20%), and hematological malignancies (15%) as shown in Figure 1.

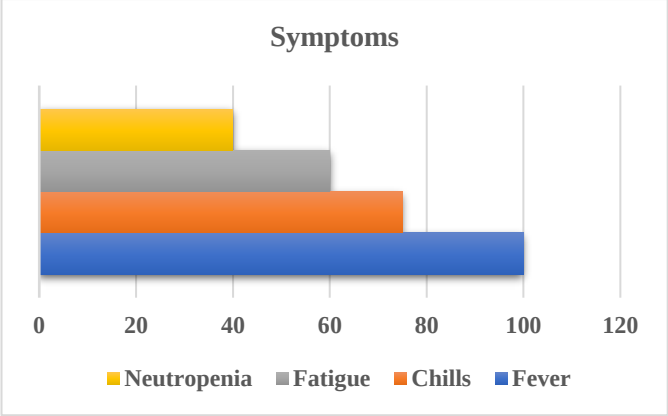

Figure 1. Symptoms prevalence.

A total of 158 organisms were isolated from 200 patients, indicating a culture positivity rate of 79%. Common pathogens such as *Klebsiella pneumoniae, Acinetobacter baumannii, Escherichia coli, Enterococcus spp, and Staphylococcus aureus accounted for 142 (89.9%) of isolates, while 16 (10.1%) isolates were identified as saprophytic pathogens. This included Enterococcus avium, Sphingomonas paucimobilis, Actinomyces meyeri, Kodamaea ohmeri, Elizabethkingia meningoseptica, Aeromonas hydrophila, Achromobacter xylosoxidans, Stenotrophomonas maltophilia, Pantoea dispersa, Burkholderia pseudomallei* as shown in table 1.

The most common presenting symptoms were fever (100%), chills (75%), and fatigue (60%). Neutropenia was present in 40% of cases. The overall 30-day mortality rate for patients with saprophytic pathogen BSIs was 20%, compared to 18% for those with common pathogens (p=0.42, Fisher's exact test) (Figure 2).

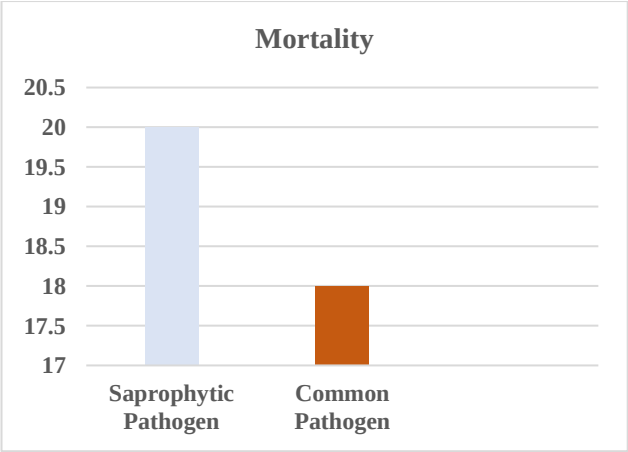

Figure 2. Mortality Rate.

Table 1. Demographic and Clinical Characteristics of Patients with Saprophytic Pathogen BSIs.

Pathogen	Number of Cases	Mortality Rate (%)
Enterococcus avium	1	0
Sphingomonas paucimobilis	2	50
Actinomyces meyeri	1	0
Kodamaea ohmeri	1	100
Elizabethkingia meningoseptica	2	0
Aeromonas hydrophila	2	0
Achromobacter xylosoxidans	2	0
Stenotrophomonas maltophilia	2	0
Pantoea dispersa	1	0
Burkholderia pseudomallei	2	50

Enterococcus avium (7-12)
A 60-year-old male with metastatic colon cancer on chemotherapy presented with fever, lethargy, and unresponsiveness. Blood tests showed leukopenia and thrombocytopenia with elevated lactate levels. Blood cultures revealed *Enterococcus avium*, sensitive to ampicillin, vancomycin, and linezolid, but resistant to high-level gentamicin, ciprofloxacin, levofloxacin, and erythromycin. Vancomycin was administered, resulting in clinical improvement and resolution of fever over 7 days. *Enterococcus avium* is a rare pathogen in humans, often found in birds, and requires prompt diagnosis and treatment, especially in immunocompromised patients.

Sphingomonas paucimobilis (13-17)
Case 1: A 37-year-old male with metastatic pancreatic cancer had a fever and chills. *Sphingomonas paucimobilis*, sensitive to ciprofloxacin, ceftazidime, ceftriaxone, meropenem, and imipenem, was isolated from blood cultures. Treatment with ceftriaxone led to clinical improvement and sterile follow-up cultures.

Case 2: A 20-year-old male with meningioma presented with fever and headache. Blood culture grew *Sphingomonas paucimobilis*, sensitive to ceftazidime and ceftriaxone but resistant to ciprofloxacin, meropenem, and imipenem. The patient succumbed to septicemia despite ceftriaxone treatment.

Actinomyces meyeri (18-19)
A 46-year-old woman with cervical cancer on chemotherapy presented with fever and hypotension. Blood culture initially showed no growth but later identified *Actinomyces meyeri.* Sensitive to penicillin, ciprofloxacin, and amoxicillin-clavulanic acid, she was treated with penicillin but left the hospital against medical advice after 3 days of worsening condition. *Actinomyces meyeri* is a rare pathogen, typically part of polymicrobial infections, and is often underdiagnosed.

Kodamaea ohmeri (20-22)
A 28-year-old male with colorectal adenocarcinoma and traumatic pancreatic injury presented with abdominal distention, poor appetite, and weight loss. Kodamaea ohmeri, sensitive to amphotericin B, itraconazole, and voriconazole but resistant to fluconazole, was isolated. Despite voriconazole therapy, the patient's condition deteriorated rapidly, leading to death. *Kodamaea ohmeri* is an emerging opportunistic pathogen with high mortality rates.

Elizabethkingia meningoseptica (23-24)
Case 1: A 58-year-old male with meningioma had a fever and weakness. Elizabethkingia meningoseptica, sensitive to ciprofloxacin, amikacin, and minocycline, was isolated. Ciprofloxacin treatment led to significant clinical improvement.

Case 2: A 63-year-old male with metastatic lung cancer had respiratory symptoms and fever. Blood culture grew *Elizabethkingia meningoseptica*, sensitive to ciprofloxacin and resistant to gentamicin. Ciprofloxacin treatment resolved symptoms and follow-up cultures were negative. *Elizabethkingia meningoseptica* is an emerging nosocomial pathogen often associated with high mortality in cancer patients.

Aeromonas hydrophila (25-26)
Case 1: A 62-year-old male with chronic lymphoid leukemia presented with fever and dizziness. *Aeromonas hydrophila*, sensitive to multiple antibiotics, was treated with meropenem, leading to symptom resolution.

Case 2: An HIV-positive patient with colorectal cancer and a recent leg injury presented with fever and elevated leukocytes. *Aeromonas hydrophila*, sensitive to multiple antibiotics including trimethoprim-sulfamethoxazole, was treated successfully. *Aeromonas hydrophila* is increasingly recognized as a significant pathogen in immunocompromised patients.

Achromobacter xylosoxidans (27-28)
Case 1: A 64-year-old male with colon cancer and a 58-year-old female with pancreatic cancer, both with type 2 diabetes, presented with fever and chills. *Achromobacter xylosoxidans*, sensitive to ciprofloxacin, was isolated. Both patients responded well to ciprofloxacin treatment. *Achromobacter xylosoxidans* can cause significant infections, particularly in immunocompromised individuals.

Stenotrophomonas maltophilia (29-30)
Case 1: A 67-year-old male with sigmoid adenocarcinoma had persistent fever and cough. *Stenotrophomonas maltophilia*, treated with trimethoprim-sulfamethoxazole and levofloxacin, showed clinical improvement.

Case 2: A 60-year-old male with glioblastoma presented with fever and altered mental status. *Stenotrophomonas maltophilia* was treated with trimethoprim-sulfamethoxazole and ceftazidime with gradual improvement. *Stenotrophomonas maltophilia* is challenging to diagnose and manage but responds well to trimethoprim-sulfamethoxazole.

Pantoea dispersa (31)
A 35-year-old chronic alcoholic with liver cirrhosis presented with abdominal pain, fever, and vomiting. *Pantoea dispersa*, sensitive to minocycline, was treated effectively, leading to the resolution of symptoms. *Pantoea dispersa*, while less virulent, can cause significant infections in immunocompromised individuals.

Burkholderia pseudomallei (32-34)
Case 1: A 57-year-old male with colon cancer improved significantly with imipenem therapy after isolation of *Burkholderia pseudomallei.*

Case 2: A 43-year-old female with pulmonary tuberculosis and ovarian cancer succumbed to septic shock despite aggressive treatment. *Burkholderia pseudomallei*, endemic to tropical regions, poses a high mortality risk and highlights the need for early detection and preventive measures.

This study shows that saprophytic pathogens account for a notable proportion of bloodstream infections in cancer patients, emphasizing the need for accurate identification and targeted treatment, particularly for high-mortality organisms like *Kodamaea ohmeri and Burkholderia pseudomallei*.

Discussion

Our study reveals that saprophytic pathogens account for a significant proportion (10.1%) of bloodstream infections (BSIs) in cancer patients, highlighting the importance of considering these organisms in the differential diagnosis of BSIs, especially in immunocompromised hosts. This finding is consistent with recent literature that has increasingly recognized the role of opportunistic pathogens in causing severe infections in vulnerable populations (1,2).

The prevalence of saprophytic pathogens in our study (10.1%) is slightly higher than that reported by Rega et al (6), who found a 7.5% prevalence of unusual bacterial isolates in BSIs among Ethiopian cancer patients (3). This difference might be attributed to variations in geographical location, patient population, or improvements in diagnostic techniques. Our findings underscore the need for clinicians to maintain a high index of suspicion for atypical pathogens in cancer patients presenting with signs of BSI.

Of particular note was the isolation of *Kodamaea ohmeri* and *Burkholderia pseudomallei*, both associated with high mortality rates. *K. ohmeri*, once considered a benign organism, has emerged as an opportunistic pathogen capable of causing invasive infections in immunocompromised individuals (4). Similarly, *B. pseudomallei*, the causative agent of melioidosis, is increasingly recognized as a significant threat to immunocompromised patients, particularly in endemic regions (5). These findings align with recent global surveillance data that highlight the growing importance of emerging pathogens in healthcare-associated infections (6).

Our statistical analysis revealed no significant difference in 30-day mortality rates between patients with saprophytic pathogen BSIs and those with common pathogens (20% vs. 18%, p=0.42). This finding is intriguing and contrasts with some previous studies that have reported higher mortality rates associated with unusual pathogens (7,8).

The successful treatment of some cases with targeted antimicrobial therapy in our study demonstrates the importance of prompt and accurate identification of these pathogens. This observation is supported by recent literature emphasizing the critical role of rapid diagnostics and appropriate antimicrobial stewardship in managing BSIs, particularly those caused by unusual pathogens (9,10)

Our study also highlights the challenges in distinguishing true pathogens from colonizers or contaminants, particularly in the case of saprophytic organisms. This dilemma is well-recognized in clinical microbiology and emphasizes the need for careful interpretation of blood culture results in the context of the patient's clinical presentation (13,14). The implementation of clinical decision support systems and machine learning algorithms shows promise in aiding clinicians in this complex decision-making process (15).

The high rate of neutropenia (40%) observed in our cohort of cancer patients with BSIs is consistent with previous studies and underscores the vulnerability of this population to opportunistic infections (16,17). Recent research has focused on strategies to prevent and manage infections in neutropenic cancer patients, including the use of prophylactic antimicrobials and immunomodulatory agents (18,19). Our findings support the need for tailored approaches to infection prevention and management in this high-risk group.

While our study provides valuable insights into the prevalence and clinical significance of saprophytic pathogens in cancer-associated BSIs, it has several limitations. As a single-center study with a relatively small sample size, particularly for saprophytic pathogen infections, the statistical power of our comparisons is limited. This may have prevented us from detecting significant differences in outcomes between groups. Additionally, the short duration of the

study precluded analysis of seasonal variations in pathogen distribution and potential confounding factors that may influence patient outcomes. These limitations highlight the need for larger, multi-center studies with longer follow-up periods to more comprehensively characterize the epidemiology and clinical impact of saprophytic pathogen BSIs in cancer patients.

Despite these limitations, our study contributes to the growing body of evidence highlighting the importance of saprophytic pathogens in BSIs among cancer patients. The findings underscore the need for heightened awareness among clinicians, improved diagnostic strategies, and tailored antimicrobial approaches for managing these infections. Future research should focus on developing rapid diagnostic tools specifically targeted at identifying unusual pathogens, as well as exploring novel therapeutic strategies for managing infections caused by these emerging organisms**.**

Conclusion

Our study demonstrates that saprophytic pathogens account for a significant proportion (10.1%) of BSIs in cancer patients, with no statistically significant difference in mortality rates compared to common pathogens(1-6,25). These findings underscore the importance of considering these organisms in the differential diagnosis of BSIs, especially in immunocompromised hosts. Further large-scale, multicenter studies are needed to better understand the epidemiology and clinical impact of saprophytic pathogen BSIs in cancer patients.

In the present study, the patients were started on early empiric therapy and almost 75% of the patients responded to the treatment. The response to treatment in the present study reiterates that the presence of saprophytic bacteria from cases of BSI should not be ignored in cancer patients. It would be worthwhile to start the patient on early empiric treatment till the time a repeat blood culture is sent for confirmation of the clinical significance of these isolates. Raising awareness among healthcare providers about the potential for such infections is crucial to ensure timely diagnosis and intervention.

Author contribution

ShG: Conceptualization, Data curation, Formal analysis, Methodology, Software, Validation, Visualization, Writing original draft, Writing review & editing. **WW:** Writing review & editing, Resources, Software, Data curation, Methodology, Project administration, Software, Validation. **MJ:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing original draft, Writing review & editing. **PL:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources. **Ash:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision. **ShT:** Investigation, administration.

Conflict of interest

The authors declare that they have no competing interests.

Funding

There is no funding agency involved in this research.

Ethical approval

This is a retrospective study and there is no ethical consideration related to paper. The data for this study was collected as part of routine clinical care and was fully anonymized. All patient data were de-identified to maintain confidentiality. Personal identifiers were removed prior to data analysis, and no identifiable information was used in the study. This approach ensures compliance with patient privacy regulations and ethical standards.

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