Section: Microbiology

Original Research Article

A STUDY ON BACTERIAL BLOODSTREAM INFECTIONS IN PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES AND THE USEFULNESS OF PROCALCITONIN AS AN EARLY DIAGNOSTIC MARKER IN A TERTIARY CARE HOSPITAL

B. Sree Bavai Malar[1], S. Swarna[2], K. Akila[3]

[1]Assistant Professor, Department of Microbiology, Government Medical College, Dindigul, Tamil Nadu, India.
[2]Associate Professor, Department of Microbiology, Government Virudhunagar Medical College, Virudhunagar, Tamil Nadu, India.
[3]Assistant Professor, Department of Microbiology, Government Medical College, Dindigul, Tamil Nadu, India.

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Corresponding Author:
Dr. B.Sree Bavai Malar,
Assistant Professor, Department of Microbiology, Government Medical College, Dindigul, Tamil Nadu, India.
Email: drbavai@gmail.com

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ABSTRACT

Background: Bloodstream infections (BSIs) are a major cause of morbidity and mortality in patients with haematological malignancies, particularly those with neutropenia. Early diagnosis remains challenging due to nonspecific clinical features and delayed blood culture results. Procalcitonin (PCT) has emerged as a promising biomarker for early detection of bacterial infections.

Materials and Methods: A prospective study was conducted from November 2014 to August 2015 at Government Rajaji Hospital, Madurai. A total of 106 patients with haematological malignancies and clinical suspicion of bloodstream infection were included. Blood cultures were performed using standard microbiological techniques. Antimicrobial susceptibility testing was done as per CLSI 2014 guidelines. Serum procalcitonin levels were measured using a semi-quantitative immunochromatographic assay.

Results: Out of 106 patients, 27 (25.47%) had culture-positive bloodstream infections. Gram-negative organisms (55.55%) predominated over Gram-positive organisms (44.44%). *Klebsiella pneumoniae* was the most common isolate (25.9%). ESBL production was observed in 7.4% of E. coli and 14.81% of Klebsiella species. Procalcitonin demonstrated a sensitivity of 85.1%, specificity of 97.5%, positive predictive value of 92%, and negative predictive value of 95% for diagnosing bloodstream infections.

Conclusion: Bloodstream infections remain common in patients with haematological malignancies, with Gram-negative organisms predominating. Procalcitonin is a valuable adjunctive biomarker for early diagnosis and may help guide timely initiation of antimicrobial therapy.

Keywords: Bloodstream infection, Haematological malignancy, Procalcitonin, Bacteremia, Neutropenia.

INTRODUCTION

Haematological malignancies comprise a heterogeneous group of cancers involving the blood, bone marrow, and lymphoid tissues, including leukemias, lymphomas, and plasma cell disorders.[1] Despite significant advances in chemotherapy, immunotherapy, and supportive care, infections remain a leading cause of morbidity and mortality in these patients.[2] Among infections, bacterial bloodstream infections (BSIs) are particularly serious due to their rapid progression and high fatality rate, especially in the presence of neutropenia.[3] Patients with haematological malignancies are highly susceptible to bloodstream infections because of multiple predisposing factors such as disease-induced immune dysfunction, chemotherapy-associated neutropenia, disruption of mucosal barriers, prolonged hospitalization, use of central venous catheters, and exposure to broad-spectrum antibiotics.[4] Neutropenia, defined as an absolute

neutrophil count of less than 500 cells/mm³, is the most important risk factor and significantly increases both the incidence and severity of bacterial infections.[5] In many cases, fever may be the only clinical manifestation, as classical signs of inflammation are often absent due to impaired immune responses.[6] Blood culture is considered the gold standard for the diagnosis of bacteremia; however, it has several limitations.[7] The time required for organism isolation and antimicrobial susceptibility testing can delay appropriate therapy.[8] Prior antibiotic use may result in false-negative cultures, while contamination with skin commensals can complicate interpretation. These limitations highlight the need for additional diagnostic tools that can aid in the early detection of bacterial bloodstream infections.[9]

The microbial spectrum of bloodstream infections in patients with haematological malignancies has evolved over time.[10] Earlier studies reported Gram-negative bacilli as the predominant pathogens, whereas later reports from many centers showed a shift toward Gram-positive organisms, attributed to the use of central venous catheters and antimicrobial prophylaxis. However, recent studies, particularly from developing countries, have demonstrated a resurgence of Gram-negative organisms, many of which exhibit multidrug resistance. This changing epidemiology underscores the importance of periodic surveillance of local pathogen distribution and antimicrobial susceptibility patterns to guide empirical therapy.[11,12] Procalcitonin (PCT), a precursor of the hormone calcitonin, has emerged as a promising biomarker for the early diagnosis of bacterial infections and sepsis.[13] Under normal conditions, serum procalcitonin levels are very low.[14] During systemic bacterial infections, procalcitonin is released into the circulation in response to bacterial endotoxins and inflammatory cytokines, resulting in a rapid rise in serum levels. Importantly, procalcitonin levels remain low in viral infections and most non-infectious inflammatory conditions, making it a more specific marker for bacterial infections compared to conventional markers such as C-reactive protein.[15,16] Several studies have demonstrated that procalcitonin is useful in predicting bacteremia, assessing severity of infection, and differentiating true infection from contamination in blood cultures.[17] In patients with haematological malignancies, procalcitonin may play a crucial role in early diagnosis, timely initiation of empirical antibiotics, and reduction of unnecessary antimicrobial use.[18] In this context, the present study was undertaken to evaluate the bacterial etiology and antimicrobial susceptibility patterns of bloodstream infections in patients with haematological malignancies and to assess the usefulness of procalcitonin as an early diagnostic marker in a tertiary care hospital.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted at Government Rajaji Hospital, a tertiary care teaching hospital attached to Madurai Medical College, Tamil Nadu, India. The study was carried out in collaboration with the Institute of Microbiology from November 2014 to August 2015.

Study Population

Patients of all age groups with a confirmed diagnosis of haematological malignancy admitted to the medical oncology ward and clinically suspected to have bloodstream infection were included in the study.

Inclusion and Exclusion Criteria

Patients were included if they had haematological malignancies and presented with fever (single oral temperature ≥38.3°C or ≥38.0°C persisting for more than one hour), neutropenia (absolute neutrophil count ≤500 cells/mm³), hypotension, or other clinical features suggestive of sepsis such as oliguria or altered mental status. Patients with malignancies other than haematological malignancies were excluded.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Madurai Medical College. Written informed consent was obtained from all patients or their legal guardians prior to sample collection.

Sample Collection

A total of 106 blood samples were collected. Under strict aseptic precautions, 5 ml of venous blood was collected and inoculated into 50 ml of Brain Heart Infusion broth for bacterial culture. An additional 2 ml of blood was collected in a plain vial for serum procalcitonin estimation. Serum was separated by centrifugation at 2000 rpm for 2 minutes.

Blood Culture and Bacterial Identification

Blood culture bottles were incubated at 37°C and monitored for turbidity. Positive broths were subcultured onto blood agar, MacConkey agar, and nutrient agar. Broths without visible growth were incubated for up to seven days before being reported as negative. Bacterial isolates were identified based on colony morphology, Gram staining, motility testing, and standard biochemical tests.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was performed using the Kirby–Bauer disc diffusion method on Mueller–Hinton agar. Results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines 2014. Methicillin resistance in *Staphylococcus aureus* and coagulase-negative staphylococci was detected using cefoxitin (30 µg) discs. Extended-spectrum β-lactamase (ESBL) production in Escherichia coli and Klebsiella species was detected using the combined disc method with cefotaxime and cefotaxime–clavulanic acid.

Procalcitonin Estimation

Serum procalcitonin levels were measured using the B·R·A·H·M·S PCT-Q immunochromatographic assay. Two hundred microliters of serum was applied to the test device, and results were read after 30 minutes by comparing band intensity with the reference chart. A procalcitonin level ≥2 ng/ml was considered indicative of systemic bacterial infection.

Statistical Analysis

Blood culture was considered the reference standard for diagnosis of bloodstream infection. Descriptive statistics were used to analyze data. The diagnostic performance of procalcitonin was assessed by calculating sensitivity, specificity, positive predictive value, and negative predictive value.

RESULTS

A total of 106 patients with haematological malignancies and clinical suspicion of bloodstream infection were included in the study. Blood culture and serum procalcitonin estimation were performed for all patients.

Distribution of Haematological Malignancies

Among the 106 patients studied, acute lymphoblastic leukemia (ALL) was the most common haematological malignancy accounting for 51.88%, followed by acute myeloid leukemia (AML) constituting 26.41% of cases. Other malignancies included chronic myeloid leukemia, lymphomas, chronic lymphocytic leukemia, and multiple myeloma. [Figure 1]

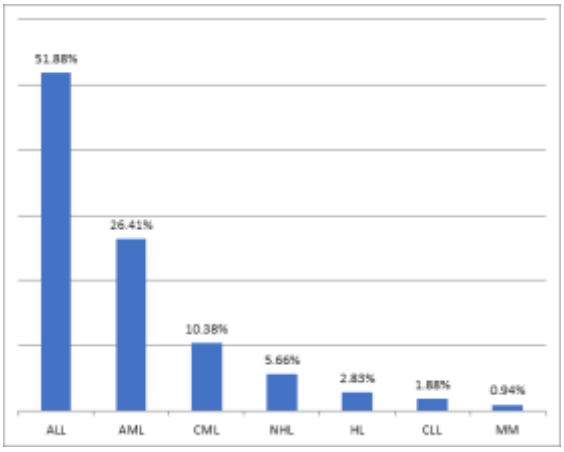

Figure 1: Haematological Malignancy in the Patients

Prevalence of Bloodstream Infections

Out of 106 blood cultures processed, 27 (25.47%) showed bacterial growth. Bloodstream infections were observed predominantly in patients with acute leukemias. No culture positivity was noted in patients with chronic leukemias, lymphomas, or multiple myeloma. [Table 1]

Gender Distribution of Bloodstream Infections

Among the 27 culture-positive cases, 19 (70%) were males and 8 (30%) were females, indicating a male predominance. [Figure 2]

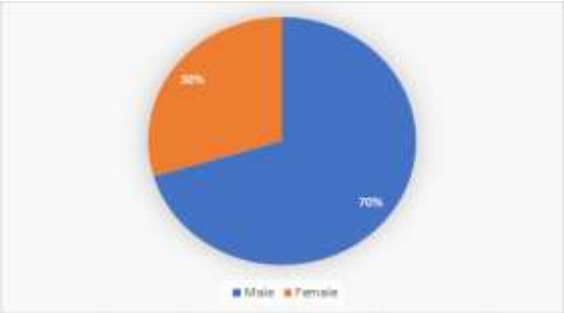

Figure 2: Gender Distribution of Bloodstream Infections (n = 27)

Age-wise Distribution

Bloodstream infections were nearly equally distributed between adults and children, with 52% occurring in adults and 48% in children. [Figure 3]

Figure 3: Age Distribution of Bloodstream Infections (n = 27)

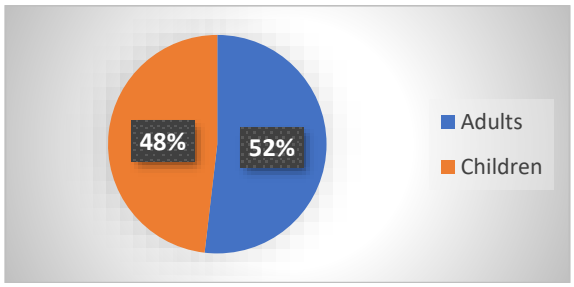

Figure 3: Age Distribution of Bloodstream Infections (n = 27)

Gram Reaction and Bacterial Etiology of Bloodstream Infections

Among the 27 culture-positive bloodstream infections, Gram-negative bacteria (56%) were isolated more frequently than Gram-positive bacteria (44%), as shown in Figure 4. Among the 27 bloodstream infection isolates, Klebsiella pneumoniae was the most frequently identified organism, accounting for 25.9% of cases, followed by coagulase-negative staphylococci (22.22%) and Staphylococcus aureus (18.51%). Klebsiella oxytoca and Escherichia coli each represented 11.11% of isolates, while Pseudomonas aeruginosa and Enterococcus spp. were less common, constituting 7.4% and 3.7%, respectively. Overall, Gram-negative bacteria were more prevalent than Gram-positive organisms, highlighting the predominance of Enterobacteriaceae in bloodstream infections. [Table 2]

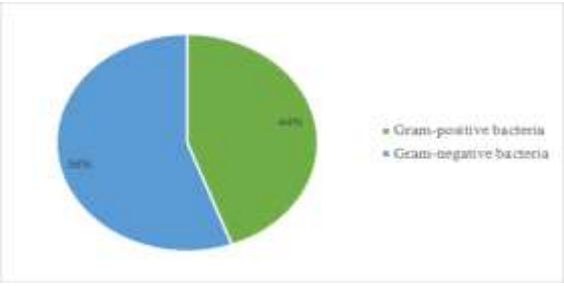

Figure 4: Distribution of Gram-positive and Gram-negative Isolates (n = 27)

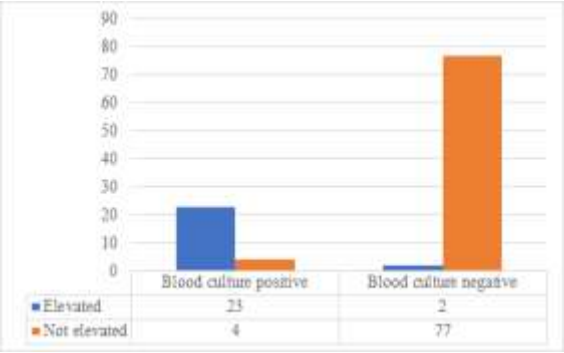

Figure 5: Comparison of Blood Culture Results and Procalcitonin Levels

Diagnostic Accuracy of Procalcitonin

Using blood culture as the reference standard for diagnosing bloodstream infections, serum procalcitonin demonstrated a high diagnostic accuracy. The sensitivity of procalcitonin was 85.1%, indicating its effectiveness in correctly identifying patients with bacteremia. The specificity was 97.5%, reflecting a low false-positive rate. The positive predictive value was 92%, while the negative predictive value was 95%, underscoring the utility of procalcitonin as a reliable biomarker for early detection of bacterial bloodstream infections in patients with haematological malignancies.

Table 1:

Malignancy	Blood cultures processed	Positive cultures	Percentage (%)
ALL	55	19	17.92
AML	28	8	7.55
CML	11	0	0
CLL	2	0	0
Hodgkin's lymphoma	3	0	0
Non-Hodgkin's lymphoma	6	0	0
Multiple myeloma	1	0	0
Total	**106**	**27**	**25.47**

Table 2: Bacterial Isolates from Bloodstream Infections (n = 27)

Organism	Number	Percentage (%)
Klebsiella pneumoniae	7	25.9
Klebsiella oxytoca	3	11.11
Staphylococcus aureus	5	18.51
Coagulase-negative staphylococci	6	22.22
Escherichia coli	3	11.11
Pseudomonas aeruginosa	2	7.4
Enterococcus spp.	1	3.7
Total	**27**	**100**

Antimicrobial Susceptibility Pattern

The antimicrobial susceptibility pattern of the bacterial isolates is summarized in Table 3. Among the antibiotics tested, gentamicin demonstrated the highest activity, with 74% of isolates being sensitive, followed by amikacin (62.96%) and ciprofloxacin (59.25%). Moderate sensitivity was observed with piperacillin–tazobactam (48.14%), while sensitivity to cefotaxime was comparatively low (37.03%). Notably, all isolates were resistant to ampicillin, indicating a high level of resistance to this antibiotic among bloodstream pathogens in the study population.

Table 3:

Antibiotic	Sensitive isolates	Percentage (%)
Gentamicin	20	74
Ciprofloxacin	16	59.25
Amikacin	17	62.96
Piperacillin–Tazobactam	13	48.14
Cefotaxime	10	37.03
Ampicillin	0	0

Distribution of MRSA, MRCoNS and ESBL Producers

The distribution of antimicrobial-resistant organisms is shown in Table 4. Methicillin resistance was detected in 3 (11.11%) isolates of Staphylococcus aureus, classifying them as methicillin-resistant S. aureus (MRSA). In addition, one (3.70%) coagulase-negative staphylococcal isolate was identified as methicillin-resistant (MRCoNS). Extended-spectrum β-lactamase (ESBL) production was observed in five Gram-negative isolates, including three Klebsiella pneumoniae, one Klebsiella oxytoca, and one Escherichia coli isolate, highlighting the presence of multidrug-resistant organisms among bloodstream infections.

Table 4: Distribution of Resistant Isolates (n = 27)

Organism	Resistance pattern	Number (%)
Staphylococcus aureus	MRSA	3 (11.11)
CoNS	MRCoNS	1 (3.70)
Escherichia coli	ESBL	1 (3.70)
Klebsiella pneumoniae	ESBL	3 (11.11)
Klebsiella oxytoca	ESBL	1 (3.70)

Serum Procalcitonin Levels

Serum procalcitonin levels among the study population are depicted in Table 5. Elevated procalcitonin levels (≥2 ng/ml), suggestive of systemic bacterial infection, were observed in 24 patients (22.63%). Among these, 14 patients (13.20%) had procalcitonin levels between 2 and <10 ng/ml, while 10 patients (9.43%) had markedly elevated levels (≥10 ng/ml), indicating a high likelihood of severe sepsis. The majority of patients (74.52%) had non-elevated procalcitonin levels.

Table 5: Serum Procalcitonin Levels in Study Population

Procalcitonin level	Number	Percentage (%)
Not elevated	79	74.52
<0.5 ng/ml	2	1.88
0.5–<2 ng/ml	1	0.94
2–<10 ng/ml	14	13.2
≥10 ng/ml	10	9.43

Correlation Between Blood Culture and Procalcitonin Levels

A strong correlation was observed between blood culture positivity and elevated serum procalcitonin levels (Figure 5). Among the 27 blood culture–positive cases, 23 patients showed elevated procalcitonin levels, whereas only 4 culture-positive patients had non-elevated procalcitonin. In contrast, among blood culture–negative patients, the majority (77 cases) had non-elevated procalcitonin levels, indicating good concordance between procalcitonin elevation and confirmed bacteremia.

DISCUSSION

Bloodstream infections remain a major cause of morbidity and mortality in patients with haematological malignancies, particularly in those undergoing intensive chemotherapy and experiencing prolonged neutropenia. Early diagnosis and appropriate antimicrobial therapy are critical for improving clinical outcomes. The present study evaluated the bacteriological profile, antimicrobial susceptibility pattern, and diagnostic utility of serum procalcitonin in patients with haematological malignancies suspected of having bloodstream infections. In the present study, bloodstream infections were documented in 25.47% of patients, which is comparable to rates reported in previous studies ranging from 20% to 40% among patients with haematological malignancies.[19,20] The majority of culture-positive cases were observed in patients with acute leukemias, particularly acute lymphoblastic leukemia and acute myeloid leukemia. This higher incidence may be attributed to profound and prolonged neutropenia, aggressive chemotherapy regimens, mucosal barrier injury, and frequent use of invasive devices in these patients.[21] A male predominance was observed among patients with bloodstream infections, similar to findings reported by other studies.[22] Bloodstream infections were almost equally distributed between adult and pediatric populations, indicating that age alone may not be a significant determinant of infection risk in haematological malignancies, but rather the degree of immunosuppression. Analysis of the bacterial spectrum revealed a predominance of Gram-negative organisms (55.56%) over Gram-positive organisms (44.44%). Although many studies from developed countries have reported a shift toward Gram-positive infections due to widespread use of central venous catheters and fluoroquinolone prophylaxis, several recent studies from developing countries, including India, have reported a resurgence of Gram-negative pathogens.[23,24] This trend is likely related to differences in infection control practices, antimicrobial usage patterns, and local epidemiology. Klebsiella species were the most common pathogens isolated in the present study, accounting for 37.01% of bloodstream infections. Similar findings have been reported by Gudiol et al. and Mehta et al., who identified Klebsiella pneumoniae as a major cause of bacteremia in neutropenic patients.[25,26] Among Gram-positive organisms, coagulase-negative staphylococci were the most frequently isolated, followed by Staphylococcus aureus. Coagulase-negative staphylococci are increasingly recognized as significant pathogens in immunocompromised patients, particularly in association with indwelling intravascular catheters.[27] The antimicrobial susceptibility pattern observed in this study is a cause for concern. While relatively good sensitivity was noted to gentamicin, amikacin, and ciprofloxacin, high resistance rates were observed against ampicillin and third-generation cephalosporins. Complete resistance to ampicillin highlights the limited utility of this agent for empirical therapy in this patient population. Similar resistance patterns have been reported in other Indian studies, reflecting

the growing problem of antimicrobial resistance among bloodstream pathogens.[28,29]

The detection of methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCoNS) further emphasizes the need for judicious use of antibiotics and adherence to infection control measures. Additionally, ESBL production was detected in five Gram-negative isolates, predominantly Klebsiella species. ESBL-producing organisms are associated with limited treatment options and poorer clinical outcomes, underscoring the importance of early detection and appropriate antimicrobial stewardship.[30] Serum procalcitonin levels were elevated (≥2 ng/ml) in 22.63% of patients. A strong correlation was observed between elevated procalcitonin levels and blood culture positivity. In the present study, 85.1% of culture-positive patients had elevated procalcitonin levels, while the majority of culture-negative patients had non-elevated levels. These findings are consistent with previous studies demonstrating the usefulness of procalcitonin as a biomarker for bacterial infections and sepsis in immunocompromised patients.[31] Procalcitonin showed a high sensitivity (85.1%) and specificity (97.5%) for diagnosing bloodstream infections when blood culture was used as the reference standard. The high negative predictive value (95%) suggests that a low procalcitonin level can reliably exclude bacteremia, potentially helping clinicians avoid unnecessary use of broad-spectrum antibiotics. This is particularly important in patients with haematological malignancies, where overuse of antibiotics contributes to antimicrobial resistance and adverse drug effects.[1,31] Despite its usefulness, procalcitonin should not be used in isolation. False-negative results may occur in localized infections or early stages of sepsis, and false-positive elevations may be seen in conditions such as severe tissue injury or major surgery. Therefore, procalcitonin should be interpreted in conjunction with clinical findings and microbiological data.[32]

Limitations

This study has several limitations. First, it was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Second, only culture-positive bloodstream infections were considered, potentially underestimating the true incidence of infections, especially in patients who received prior antibiotics. Third, molecular characterization of resistance genes was not performed, which could have provided more detailed insights into the mechanisms of antimicrobial resistance. Finally, procalcitonin levels were measured at a single time point, and serial measurements might have offered a better understanding of its dynamics in infection monitoring.

CONCLUSION

Bloodstream infections are a major cause of morbidity in patients with haematological malignancies, with Gram-negative bacteria, particularly Klebsiella species, being the predominant pathogens, while Gram-positive organisms such as coagulase-negative staphylococci and Staphylococcus aureus are also significant. High resistance rates to commonly used antibiotics, including ampicillin and cephalosporins, along with the presence of MRSA, MRCoNS, and ESBL-producing organisms, highlight the challenge of multidrug-resistant infections in this population. Serum procalcitonin demonstrated high sensitivity and specificity for early detection of bacterial bloodstream infections, supporting its role as a useful diagnostic biomarker. These findings underscore the importance of ongoing surveillance of antimicrobial susceptibility, rational use of antibiotics, and integration of biomarkers like procalcitonin to guide timely and targeted therapy, ultimately improving patient outcomes.

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