

Pattern of Blood Culture Positivity and Associated Clinical Characteristics in Febrile Neutropenic Patients: A Cross-Sectional Study

*Rahman M,¹ Sultana R,² Pinki SN,³ Azad MK,⁴ Hassan MK,⁵ Sharmeen Lipi SS⁶

Abstract

Background: Febrile neutropenia constitutes a medical emergency due to the heightened risk of bloodstream infection and rapid clinical deterioration. Patterns of causative organisms vary across institutions, underscoring the importance of local epidemiological data to guide empirical therapy.

Objective: This study aimed to determine the pattern of blood culture positivity and its association with clinical characteristics among febrile neutropenic adults.

Methods: This cross-sectional study included 50 adult patients with documented febrile neutropenia admitted to a Tertiary Hospital from October 2022 to September 2023. Blood samples were obtained under aseptic conditions and processed for aerobic culture. Clinical and hematologic parameters were recorded using a structured data sheet. Statistical analysis was conducted using SPSS, with significance set at $p < 0.05$.

Results: Blood cultures were positive in 15 patients (30%). Gram-positive bacteria accounted for 53.3% of isolates, with *Staphylococcus epidermidis* being the most frequent pathogen. Gram-negative organisms represented 46.7% of isolates, predominantly *Pseudomonas aeruginosa*. No significant associations were observed between culture positivity and age, gender, fever duration, temperature, hemoglobin, WBC, ANC, platelet count, or ESR. Patients receiving chemotherapy showed no significant difference in positivity rate compared to those not receiving chemotherapy. All Gram-positive isolates were fully sensitive to vancomycin and linezolid, whereas Gram-negative isolates showed inconsistent susceptibility patterns to carbapenems and antipseudomonal antibiotics.

Conclusion: In febrile neutropenic patients, Gram-positive bacteria were the leading cause of bloodstream infections, although Gram-negative pathogens continued to play a significant clinical role. These findings highlight the need for institution-specific surveillance to guide empirical antibiotic therapy.

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1. *Dr. Mizanur Rahman, Associate Professor (In Situ), Department of Medicine, Shaheed Syed Nazrul Islam Medical College Hospital, Kishoreganj, Bangladesh. mizan59dmc@yahoo.com
2. Dr. Rebeka Sultana, Junior Consultant (CC), Directorate General Health Services (OSD), Bangladesh Medical University, Dhaka, Bangladesh.
3. Dr. Sumaiya Nousheen Pinki, Lecturer, Department of Pharmacology, Holy Family Medical College and Hospital, Dhaka, Bangladesh
4. Dr. Md. Abul Kalam Azad, Pro Vice Chancellor (Administration), Bangladesh Medical University (BMU), Dhaka, Bangladesh
5. Dr. Md. Kamrul Hassan, Associate Consultant, Department of Hematology, Ahsania Mission Cancer and General Hospital, Dhaka, Bangladesh
6. Dr. Shahnaz Sharmeen Lipi, Assistant Professor, Department of Microbiology, Shaheed Syed Nazrul Islam Medical College, Kishoreganj, Bangladesh

*For correspondence

Introduction

Febrile neutropenia remains a critical clinical emergency in patients with hematologic malignancies and other immunocompromising conditions, given its strong association with rapid clinical deterioration and the risk of life-threatening bloodstream infections. Neutrophils constitute the primary effector cells of innate immunity, and reductions in absolute neutrophil count (ANC) markedly impair host defense mechanisms, facilitating microbial invasion and hematogenous dissemination.¹ In neutropenic patients, fever frequently serves as the first—and at times the sole—clinical indicator of infection, since a diminished inflammatory response can obscure the usual signs that facilitate early recognition.² As a result, prompt recognition and empiric initiation of broad-spectrum antimicrobials remain central to management, aimed at reducing morbidity and mortality associated with sepsis and bacteremia.^{3,4}

Historically, Gram-negative organisms such as *Pseudomonas aeruginosa* dominated bloodstream infections in neutropenic populations, frequently resulting in fulminant sepsis and high fatality rates.⁵ From the late 1970s, a worldwide shift in the epidemiology of infections became evident, with Gram-positive bacteria increasingly predominating. This change has been linked to clinical practices such as the widespread use of central venous catheters, prophylactic fluoroquinolone therapy directed against Gram-negative organisms, and chemotherapy-related mucositis that promotes translocation of resident Gram-positive flora.^{6,7} Similar patterns were reported in major surveillance studies, such as those conducted by the EORTC and U.S. multicenter groups, in which Gram-positive cocci constituted over 60% of bloodstream isolates during febrile neutropenic episodes.^{8,9} Despite this shift, Gram-negative organisms remain clinically

significant due to their association with rapid progression to septic shock, multidrug resistance, and higher mortality.¹⁰

Local microbiological patterns are vital for guiding empiric antimicrobial therapy. International guidelines emphasize that empirical regimens should be tailored to regional pathogen distribution and susceptibility profiles, particularly in low-resource settings where microbiological infrastructure and antimicrobial stewardship practices vary considerably.³ In many developing countries, Gram-negative predominance persists, while in others, both Gram-positive and Gram-negative organisms contribute substantially to febrile neutropenic infections.¹¹ Variability in cancer types, chemotherapy protocols, infection control practices, and antibiotic accessibility contributes to these differences.

Understanding blood culture positivity patterns also provides insight into clinical predictors of infection severity. Factors such as duration of fever, hematologic parameters, and exposure to prior antibiotics may influence culture yield and the spectrum of isolated organisms. Several studies have explored associations between patient characteristics and bacteremia, though findings remain inconsistent, underscoring the need for localized evidence.¹² Prior antibiotic use, in particular, may suppress bacterial growth and reduce culture positivity, potentially delaying targeted therapy.¹³

Against the backdrop of the clinical urgency of febrile neutropenia and the need for institution-based epidemiological data to inform empiric therapy, this study examines patterns of blood culture positivity and accompanying clinical characteristics in febrile neutropenic adults treated at a tertiary hospital. By examining the distribution of Gram-positive and Gram-negative pathogens,

as well as demographic, hematologic, and clinical correlates of culture positivity, the study aims to offer context-specific insights essential for optimizing management strategies. This localized evidence base may support the development of empiric antibiotic policies aligned with prevailing pathogen profiles, ultimately improving outcomes for immunocompromised patients.

Methods

This cross-sectional observational study was carried out in the Department of Internal Medicine at Shaheed Syed Nazrul Islam Medical College Hospital, Kishoreganj, Bangladesh, over a twelve-month period from October 2022 to September 2023. Fifty adult patients fulfilling the eligibility criteria for febrile neutropenia were enrolled. The target population consisted of hospitalized adults presenting with documented fever and neutropenia, irrespective of underlying hematologic diagnosis.

Sample Selection

Inclusion Criteria

- Adults aged >18 years
- Documented fever ($\geq 38.3^{\circ}\text{C}$ once or $\geq 38.0^{\circ}\text{C}$ for >1 hour)
- Absolute neutrophil count (ANC) $< 1500/\mu\text{L}$

Exclusion Criteria

- Neutropenia attributable to viral infections

Data Collection Procedure

Data were collected using a structured, pre-tested data sheet. After obtaining informed written consent, clinical history, physical examination findings, and laboratory parameters were recorded. Blood specimens for culture were collected under strict aseptic conditions, usually from the antecubital vein, with 10 mL of blood inoculated into aerobic culture bottles. Samples were transported promptly to laboratory facilities equipped with incubators, and aerobic cultures were

processed on standard microbiological media, including blood agar, chocolate agar, and MacConkey agar. Isolates were identified through colony morphology and Gram staining. Antibiotic susceptibility testing followed standard disc diffusion methods. Clinical variables—including age, temperature, duration of fever, hematologic indices, and prior antibiotic exposure—were documented concurrently. All data were verified to ensure accuracy, internal consistency, and completeness.

Ethical Considerations

Confidentiality and anonymity were strictly maintained. No personal identifiers were disclosed in study documentation. Written informed consent was obtained from all participants. The study adhered to institutional ethical guidelines and standard biomedical research ethics, including respect for autonomy, beneficence, and nonmaleficence.

Statistical Analysis

Data were analyzed using SPSS version 15. Descriptive statistics were presented as mean \pm SD for continuous variables and frequencies or percentages for categorical variables. Associations between blood culture results and clinical parameters were analyzed using chi-square and Student's t-tests, with $p < 0.05$ indicating statistical significance.

Results

Among 50 febrile neutropenic patients, blood cultures were positive in 15 cases (30%) and negative in 35 (70%). Age distribution varied with underlying disease, though no significant association with culture positivity was observed. Blood culture positivity occurred in 37% of females and 25% of males, without statistical significance. The pattern of positive cultures across underlying hematologic diagnoses showed no significant variation ($p = 0.926$). Clinical parameters—including

temperature, duration of fever, hemoglobin, WBC, ANC, platelet count, and ESR—did not differ significantly between culture-positive and culture-negative groups. Chemotherapy exposure also showed no

significant association with culture positivity ($p = 0.415$). These findings indicate that culture positivity was not linked to demographic or routine clinical parameters.

Table I: Age distribution of patients

Diagnosis	Age distribution			Total
	18-34	35-50	>50	
AML	9	6	6	21
ALL	10	2	3	15
CML	0	0	1	1
CLL	0	0	1	1
MM	0	0	1	1
Aplastic Anaemia	2	0	0	2
Lymphoma	0	0	3	3
MDS	0	0	6	6
Total	21	8	21	50

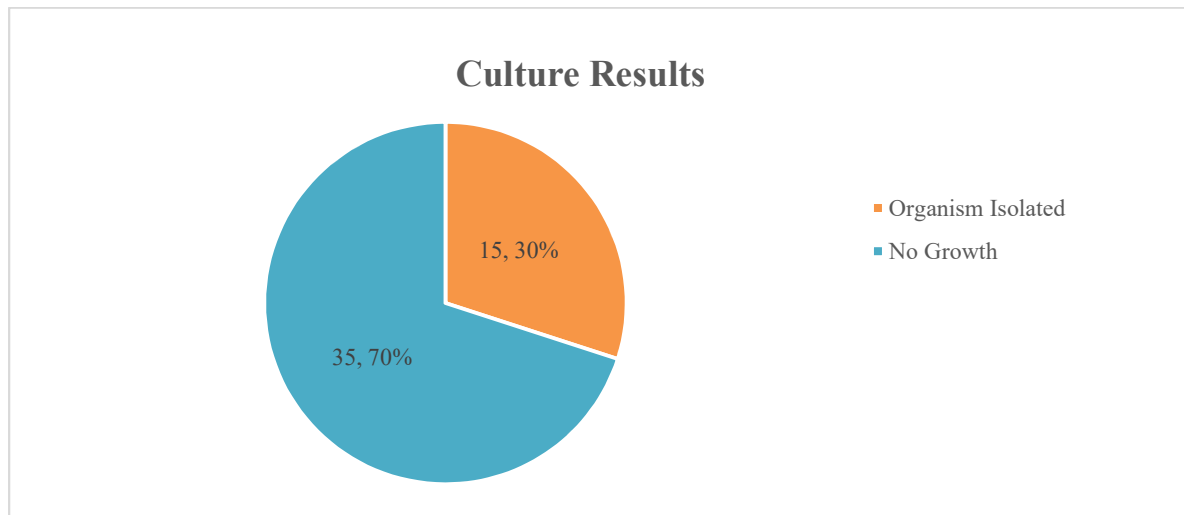


Figure 1. Culture results of febrile neutropenic patients

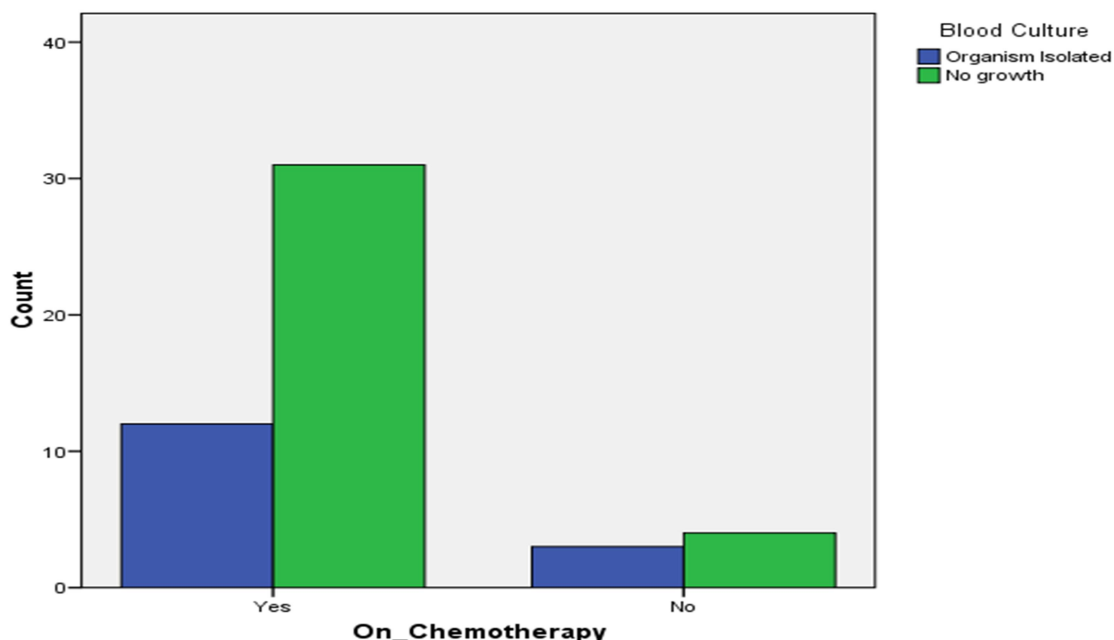


Figure 2. Result of Blood Culture in a febrile neutropenic patient receiving chemotherapy

Table II: Frequency of underlying causes of neutropenia based on blood culture results

	Positive, No. (%)	Negative, No. (%)	Total	P value
AML	6 (28.5)	15 (71.5)	21	0.926
ALL	5 (33.0)	10 (67.0)	15	0.926
MDS	2 (33.0)	4 (67.0)	6	0.926
CML	0 (0.0)	1 (100.0)	1	0.926
CLL	0 (0.0)	1 (100.0)	1	0.926
Lymphoma	1(33.0)	2 (67.0)	3	0.926
MM	0 (0.0)	1 (100.0)	1	0.926
Aplastic anaemia	1 (50.0)	1 (50.0)	2	0.926
Total	15 (30.0)	35 (70.0)	50	

Table III: Comparison of characteristics of patients based on blood culture results

Parameter	Positive Blood Culture Mean \pm SD	Negative Blood Culture Mean \pm SD	P value
Age (Years)	36.7 \pm 18.9	44.6 \pm 18.7	0.18
Oral T ($^{\circ}$ F)	102.6 \pm 1.2	102.3 \pm .9	0.28
Duration of fever (Days)	2.9 \pm 1.0	2.91 \pm .9	0.94

Table IV: Hematologic characteristics based on the blood culture result

Parameter	Positive Blood Culture Mean \pm SD	Negative Blood Culture Mean \pm SD	P value
HB (mg/dl)	7.8 \pm 1.4	7.9 \pm 1.03	0.76
WBC (cell/ μ l)	1319.0 \pm 205.3	1311.4 \pm 249.7	0.93
ANC (cell/ μ l)	406.2 \pm 123.6	423.4 \pm 140.7	0.52
PLT $\times 10^9$ (L)	101.1 \pm 53.1	112.1 \pm 60.1	0.53
ESR (mm in 1 st h)	104.0 \pm 12.0	99.2 \pm 12.1	0.19

Discussion

The current study investigated blood culture positivity patterns and their clinical associations in adults with febrile neutropenia, aiming to characterize the spectrum of causative organisms and explore potential links with demographic or clinical factors. Of the 50 patients enrolled, 30% had positive blood cultures, a rate comparable to previous reports that have documented yields between 20% and 60% in similar patient populations.¹² The moderate detection rate underscores the complexity of diagnosing infections in neutropenic hosts, where prior antibiotic exposure, low bacterial load, or non-bacterial etiologies may limit culture positivity.

The other study, Gram-positive organisms represented the majority of isolates (53.3%), with *Staphylococcus epidermidis* emerging as the most common pathogen. This pattern is consistent with the epidemiological shifts described over the past decades, where Gram-positive cocci increasingly predominated due to widespread use of central venous catheters, mucosal barrier injury, and prophylactic antibiotics targeting Gram-negative flora.⁶ Earlier multicenter surveillance by the EORTC demonstrated a gradual but definitive transition from Gram-negative predominance in the 1970s to Gram-positive dominance by the 1990s, with Gram-positive bacteria accounting for nearly 70% of isolates in later cohorts.⁸ The findings of the present study mirror these global patterns, although the proportion of Gram-negative isolates remains substantial at 46.7%, reflecting a mixed epidemiology similar to reports from regions undergoing transitional antimicrobial use patterns.

Notably, *Pseudomonas aeruginosa* was among the most frequently isolated Gram-negative organisms. Its continued prominence is clinically significant given its association with

severe sepsis, rapid clinical progression, and multidrug resistance. Comparable observations have been reported by Butt et al. in Pakistan, who found *Pseudomonas* to be a leading Gram-negative pathogen in febrile neutropenic infections.¹⁴ The presence of extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* in the present cohort further echoes reports from other centers in developing countries where antimicrobial resistance is rising, posing challenges to empirical therapy.¹³

The antibiotic susceptibility patterns observed in this study offer additional insight for empirical management. All Gram-positive isolates were fully susceptible to vancomycin and linezolid, reflecting trends observed in both regional and international studies.¹² Moderate susceptibility to piperacillin-tazobactam (60%) and low susceptibility to ceftriaxone or ceftazidime (40%) suggest that β -lactam monotherapy may be insufficient for Gram-positive coverage in this setting. Among Gram-negative isolates, *Pseudomonas aeruginosa* showed 60% susceptibility to meropenem, imipenem, amikacin, and piperacillin-tazobactam. While these results indicate retained sensitivity to key antipseudomonal drugs, the 40% resistance rate underscores the need for careful antibiotic stewardship and regular surveillance. The detection of *E. coli* sensitive only to colistin is particularly concerning, reflecting the emergence of highly resistant strains reported in several recent studies.¹³

An important observation from this study is the absence of significant associations between culture positivity and patient characteristics such as age, gender, duration of fever, oral temperature, hemoglobin, white blood cell count, ANC, platelet count, or ESR. Meidani et al. similarly reported no significant demographic or hematologic predictors of bacteremia among febrile

neutropenic adults.¹² These findings suggest that clinical parameters alone are insufficient for predicting bloodstream infection, reinforcing the need for timely cultures and broad-spectrum empirical treatment upon presentation.

Additionally, prior chemotherapy did not significantly influence culture outcomes, paralleling observations from international studies noting that cytotoxic therapy predisposes patients to bacterial translocation but does not reliably predict infection severity.¹⁵ The trend toward higher positivity among patients without prior antibiotic exposure, although not statistically significant, is biologically plausible and consistent with evidence that pre-culture antibiotics can suppress growth and reduce culture yield.¹⁶

Overall, the findings reflect a microbial landscape characterized by mixed Gram-positive and Gram-negative organisms, significant resistance among certain isolates, and limited predictive value of routine clinical parameters. This underscores the importance of local epidemiological surveillance to inform empirical regimens. Considering that mortality rises rapidly with delays in initiating treatment, context-specific data such as these remain essential for optimizing patient outcomes.

Conclusion

Overall, bloodstream infections in febrile neutropenic patients were largely driven by Gram-positive organisms, although Gram-negative pathogens continued to represent a significant portion of cases. No clinical or demographic predictors reliably indicated bacteremia, underscoring its unpredictability in this patient population. Susceptibility patterns showed consistent activity of vancomycin and linezolid against gram-positive isolates, whereas gram-negative

organisms exhibited variable responsiveness. These findings highlight the need for ongoing local surveillance to inform empirical therapy and strengthen antimicrobial stewardship.

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