GMR
The Original

COMMON ORGANISM IN BLOOD CULTURE OF NEUTROPENIC PATIENTS

Dr. Maria Iqbal[1] , Dr. Ayaz Mir[2] , Dr. Khadija Bano[3] , Dr. Danyal Ahmed Ghani [3] , Dr. Tariq Satti[3] , Dr. Ayesha Iftikhar[3]

1. FCPS Fellow Hematology, Shifa International Hospital, Islamabad
2. Supervisor & Consultant Hematologist, Shifa International Hospital, Islamabad
3. Consultant Hematologist, Shifa International Hospital, Islamabad

[1] mariaiqbal1578@gmail.com
[2] khadija_doctor@yahoo.com
[3] danyal.ahmad.ghani@gmail.com
[3] tariq.mahmood@shifa.com.pk
[3] ayesha.iftikhar@shifa.com.pk
Corresponding Author:
Dr. Maria Iqbal - Email: mariaiqbal1578@gmail.com

Abstract

Background: Bloodstream infections (BSIs) are a significant complication of neutropenic patients, especially those receiving chemotherapy for malignant disorders. Rapid identification of the etiologic microorganisms is indispensable for the prompt administration of the proper antimicrobial agents and for improving the survival of the patient.
Objective: To determine the most frequent isolated microorganisms from blood cultures in neutropenic patients and to assess the concomitant antimicrobial resistance patterns and the clinical outcomes.
Methods: This prospective observational study was performed at the department of hematology and oncology, Shifa international hospital, Islamabad. Total of 300 patients aged ≥18 years who had febrile neutropenia and had at least 1 positive blood culture were included. Demographic data, clinical features, microbiological results, antimicrobial susceptibility profiles and clinical outcome were entered on a structured proforma. Data were analyzed by using the software SPSS v.31.0.
Results: Among 300 culture-positive neutropenic patients, 57.3% were male and 54.0% were admitted to hematology/oncology wards. Gram-negative organisms predominated (71.7%), followed by gram-positive (17.0%) and fungal isolates (11.3%). The most common pathogens were E. coli (21.7%), Klebsiella pneumoniae (15.3%), and Pseudomonas aeruginosa (9.7%). Multidrug resistance was observed in 37.3% of isolates and extensively drug-resistant organisms in 11.0%. Overall mortality was 17.0%. Patients who died had significantly lower ANC, longer duration of neutropenia, and delayed administration of appropriate antibiotics.
Conclusion: Gram-negative organisms remain the major cause of BSIs in neutropenic patients. Early detection of pathogens and surveillance of antimicrobial resistance patterns are needed to support empirical antibiotic treatment and enhance patient outcomes.

Keywords: Neutropenia, Bloodstream infection, Blood culture, Febrile neutropenia, Antimicrobial resistance.

INTRODUCTION

Neutropenia is a common and severe side effect of chemotherapy, especially in hematologic cancer patients, and is closely related to bloodstream infections (BSIs), sepsis, and death. Extensive and acute neutropenia impairs host defenses and opportunistic pathogens can cause invasive disease. The increasing clinical pressure of antimicrobial resistance (AMR), especially in Gram negative bacilli, has complicated choice of treatment regimens and undermined the efficacy of conventional empiric regimens. [1] The increasing clinical pressure of antimicrobial resistance (AMR), especially among Gram negative bacilli, has complicated choice of treatment regimens and challenged the effectiveness of standard empiric regimens.

Febrile neutropenia (FN)-related microbiological spectrum of BSIs has changed over time and differs based on geographical regions. This inconsistency is associated with variations in antibiotic use, prophylaxis, hospital ecology, and device usage, with increased resistance to third generation cephalosporin's and carbapenems being reported. 4, 5 These variations are associated with delays to proper therapy and adverse outcomes. Guidelines need to be adapted to local resistance rates and the viability of an escalation strategy versus a de escalation strategy in the resource limited setting.

Multicenter series of cases confirm Gram negative rods as the most common pathogens in FN and that a significant proportion of these organisms display multidrug resistance (MDR). [7], [8] MDR Gram negative BSIs are always associated with poor outcome, long term hospitalization, and intensive care unit (ICU) admission. [10], [11] Host factors include severity and duration of neutropenia Outside of microbiology, antimicrobial stewardship is a new FN management priority. Reassessment, early therapy narrowing when necessary, and carbapenem sparing are increasingly recommended to balance the objective of sufficient early coverage against the unwarranted broad spectrum use.[13] Pharmacokinetic variability of neutropenic patients, such as augmented clearance, may also undermine the exposure to drugs and long-term or continuous infusion strategies are essential in achieving therapeutic levels against resistant Gram negative microbes.

Taken together, these findings underscore the need to implement local surveillance to inform empiric antibiotic policies due to the geographic variability of causative organisms and resistance patterns, and the high morbidity of invasive fungal infections in cohorts of neutropenic patients.

The current research was designed to describe the distribution of organisms of neutropenic patients in a tertiary care oncology/hematology environment based on blood culture, to determine the trends in antimicrobial resistance, and to determine the clinical outcomes associated with the same. This study will use local data to inform empiric antibiotic selection, enhance stewardship practices and enhance survival in this high risk population.

MATERIALS AND METHODS

This is a pre-observational study that will be carried out at the Department of Hematology and Oncology, Shifa International Hospital, Islamabad, a tertiary care teaching hospital, between a period of six months that includes 25 June 2025 and 25 December 2026. All participants or legal guardians were informed of the study and provided informed consent (IRB # 168-25) Dated: 25 June 2025. Data were anonymized to ensure patient confidentiality.

Patients that were eligible were adults (aged 18 and above) receiving chemotherapy and experienced neutropenia and febrile episodes. Neutropenia was considered an absolute neutrophil count (ANC) of less than 500 cells/U or ANC of less than 1000 cells/U with an expected lowering to less than 500 cells/U. Febrile neutropenia was suggested as a single oral temperature of 38.3 or higher and/or a sustained temperature of 38.0 or higher at least 1 hour with neutropenia. To be included, there had to be at least one positive blood culture taken prior to or during 24 hours of empirical antibiotic therapy. Eligible patients included patients with hematologic malignancies or solid tumors undergoing chemotherapy. Blood cultures were taken through the peripheral venipuncture or central venous catheters with the use of aseptic technique.

Exclusion criteria were blood cultures that were suggestive of contamination without clinical correlation, improperly collected or transported samples, previous systemic antibiotic therapy within 48 hours without clinical suspicion of breakthrough infection, non bacteremic infections with negative cultures, recurrent bacteremia involving the same organism and lost to follow up before outcome could be assessed. Sampling was done consecutively and all the eligible patients who were within the period of study were involved. The single proportion formula was used to determine the sample size, with a prevalence of 50, confidence level of 95% (Z = 1.96) and margin of error of 5.7, which resulted in a sample size of 300 patients. Sequential sampling was used.

Automated systems were used to handle blood cultures in the hospital microbiology lab. ID of organisms was done using routine microbiological methods and susceptibility to antimicrobials was done based on Clinical and Laboratory Standards Institute (CLSI) guidelines. Mechanisms of resistance such as extended spectrum beta lactamase (ESBL), carbapenem resistance, methicillin resistant Staphylococcus aureus (MRSA), and vancomycin resistant enterococci (VRE) had been reported.

Clinical outcomes, antimicrobial therapy, neutrophil counts, clinical background, presence of central venous catheters, microbiological findings, demographic characteristics, and a structured proforma were used to record data prospectively. The severity of neutropenia was divided into mild (ANC 1000-1500 cells/ uL), moderate (ANC 500-999 cells/ uL), and severe (ANC <500 cells/ uL). The main finding was the most common organisms that were identified in blood cultures. The antimicrobial resistance profiles, risk factors of bloodstream infection, and clinical outcomes (intensive care unit admission and mortality) were included as the secondary outcomes.

To conduct statistical analysis, The Statistical Package of Social Sciences (SPSS) was used with version 16. Data were summarized using descriptive statistics, frequencies and percentages (n%) were used to summarize categorical variables, such as mortality outcome, gender, hospital unit, ANC severity, central venous catheter (CVC) presence, chemotherapy within 2 weeks, organism category, isolate susceptibility, empirical antibiotic regimen, septic shock, ICU admission following bloodstream infection (BSI), clinical non- To determine the difference between the mean of continuous variables between expired and survived groups, independent samples t-test was used. The Chi-square test of independence was used to assess associations between categorical variables and outcomes (mortality, septic shock, organ dysfunction, and ICU admission). Pearson correlation analysis was performed to assess the

correlation between continuous variables (ANC, duration of neutropenia, and time to appropriate antibiotics). Regression analysis was conducted of independent variables predicting mortality, septic shock with organ dysfunction and ICU admission (ANC severity, type of organism, neutropenia duration and time to suitable antibiotics). A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 300 neutropenic patients were enrolled in this study. Among them, 57.3% were men, and 42.7% were women, and most (78.0) were hospitalized in hematology/oncology wards and 22.0% in intensive care unit (ICU). The exposure to chemotherapy was high, with 80.7% undergoing treatment in the last 30 days and 40.0% in the last two weeks. The presence of central venous catheters was found in 40.0% of patients, with central venous catheters mostly peripherally inserted. Most cases (61.0 percent) had a moderate neutropenia, with mild (26.3 percent) and severe (12.7 percent) being the next most common. The most common underlying diagnosis was acute lymphoblastic leukemia (41.0) and acute myeloid leukemia (38.7), with the most common regimen being HCVAD (38.3%)

Table 1 Participant Characteristics and Clinical Profile (n = 300).

Variable	Category	n (%)
Gender	Female	128 (42.7)
	Male	172 (57.3)
Hospital Unit	Hematology/Oncology	234 (78.0)
	ICU	66 (22.0)
Neutropenic State	No	1 (0.3)
	Yes	299 (99.7)
Chemotherapy within 30 days	No	58 (19.3)
	Yes	242 (80.7)
Chemotherapy within 2 weeks	No	180 (60.0)
	Yes	120 (40.0)
Presence of CVC	No	180 (60.0)
	Yes	120 (40.0)
Type of CVC	PICC line	120 (40.0)
	No line	180 (60.0)
ANC Severity	Mild	79 (26.3)
	Moderate	183 (61.0)
	Severe	38 (12.7)

Microbiological analysis revealed a predominance of Gram-negative organisms (71.7%), followed by Gram-positive (17.0%) and fungal isolates (11.3%). The most frequent pathogens were Escherichia coli (21.7%), Klebsiella pneumoniae (15.3%), and Pseudomonas aeruginosa (9.7%). Other notable isolates included Serratia (7.7%), Salmonella typhi (4.3%), and extensively drug-resistant (XDR) Klebsiella (7.0%). Gram-positive organisms were mainly methicillin-resistant coagulase-negative staphylococci (MRSE, 9.0%) and Staphylococcus aureus (MRSA, 3.0%). Fungal isolates were predominantly Candida species (10.3%), with rare cases of mucormycosis. Polymicrobial infections occurred in 12.0% of patients, most often involving Pseudomonas or Acinetobacter(Table 2)(Figure 1)(Figure 2).

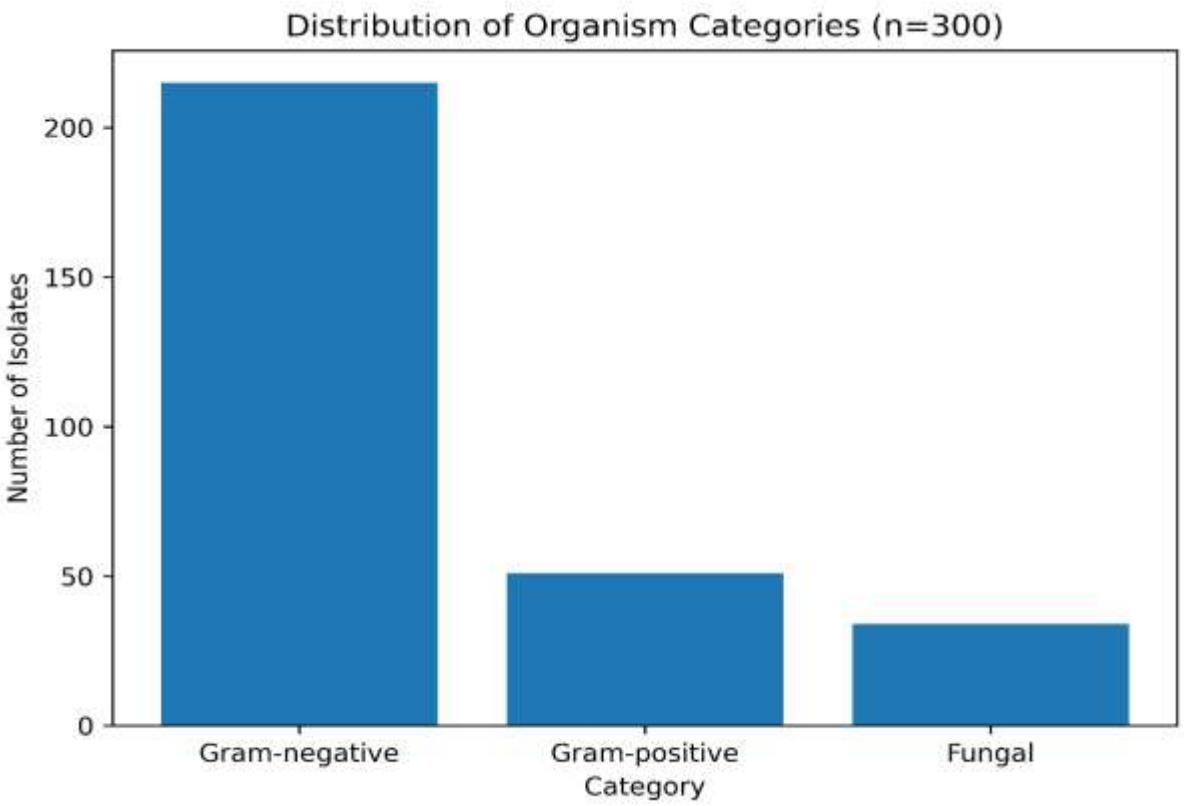

Figure 1. Distribution of organism categories.

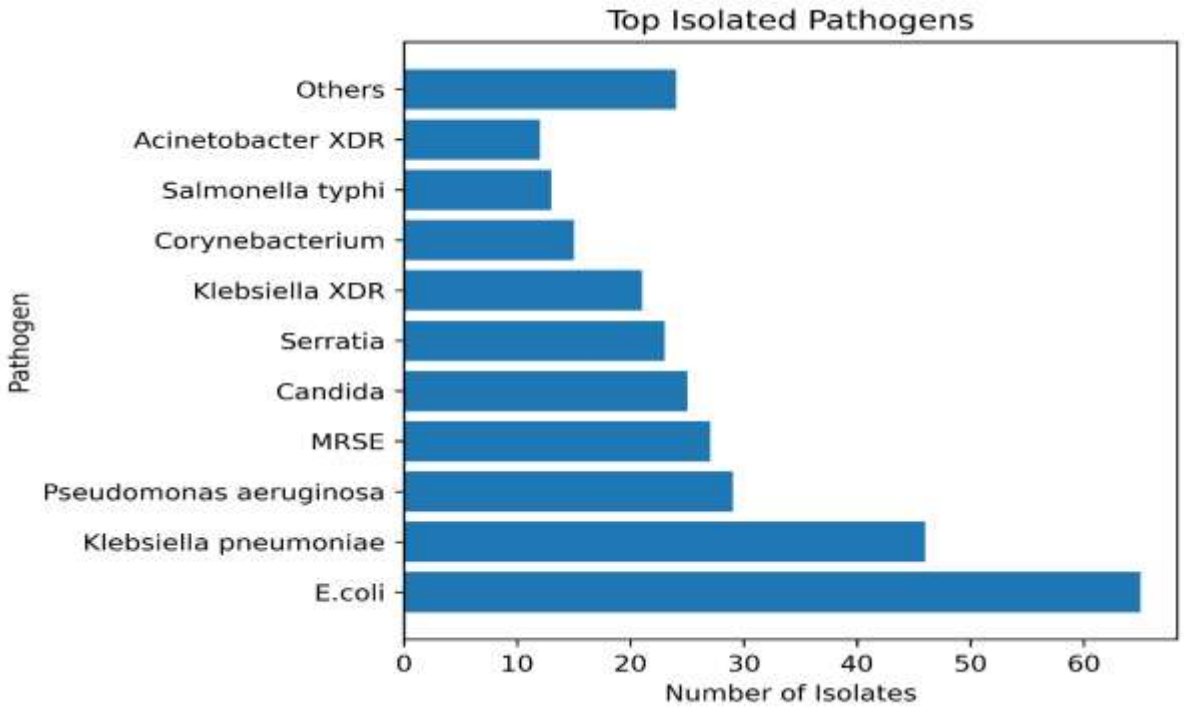

Figure 2. Frequency of isolated pathogens.

Table 2 Diagnosis, regimen, microbiology, susceptibility, and empirical therapy.

Variable	Category	n (%)
Diagnosis	ALL	123 (41.0)
	AML	116 (38.7)
	Aplastic anemia	15 (5.0)
	Solid	26 (8.7)
	Others (ALL B-cell, AML/MDS, Burkitt's, Dengue, DLBCL, Enteric fever, MM, Myeloid sarcoma, NHL-DLBCL, Primary CNS lymphoma)	20 (6.6)
Protocol/Regimen	HCVAD	115 (38.3)
	D3A7	59 (19.7)
	HIDAC	30 (10.0)
	No chemo	29 (9.7)
	HD MTX	22 (7.3)
	V3	21 (7.0)
	Others (ABVD, FLAG, FLAG+IDA, FLAG-ven, HIDAC+Ven+Dara+Bortezomib, Mini-HCVAD, MOPAD+Ven+Dara+Bortezomib, R-CHOP, VCD)	24 (8.0)
Organisms Category	Gram-negative	215 (71.7)
	Gram-positive	51 (17.0)
	Fungal	34 (11.3)
1st Isolate Organism		
Gram-negative	E. coli	65 (21.7)
	Klebsiella pneumonia	46 (15.3)
	Pseudomonas aeruginosa	29 (9.7)
	Serratia	23 (7.7)
	Klebsiella XDR	21 (7.0)
	Salmonella typhi	13 (4.3)
	Acinetobacter XDR	12 (4.0)
	Others (Stenotrophomonas)	6 (2.0)
Gram-positive	MRSE	27 (9.0)
	Corynebacterium	15 (5.0)

Variable	Category	n (%)
	MRSA	9 (3.0)
Fungal	Candida	31 (10.3)
	Mucor spp. (Mucormycosis)	3 (1.0)
2nd Isolate (Polymicrobial)	Single isolate	264 (88.0)
	Pseudomonas	13 (4.3)
	Acinetobacter	9 (3.0)
	Candida	5 (1.7)
	E. coli XDR	5 (1.7)
	Others (Enterococcus, MRSE)	4 (1.4)
1st Isolate Susceptibility	MDR	112 (37.3)
	Pan sensitive	95 (31.7)
	XDR	60 (20.0)
	Anti-fungal	33 (11.0)
2nd Isolate Susceptibility	Not susceptible (no organism)	264 (88.0)
	MDR	21 (7.0)
	XDR	10 (3.3)
	Antifungal	4 (1.3)
	Pan sensitive	1 (0.3)
Empirical Therapy Given	Meropenem	140 (46.7)
	Meropenem and vancomycin	59 (19.7)
	Vancomycin	101 (33.7)

Antimicrobial susceptibility testing demonstrated that 37.3% of first isolates were multidrug-resistant (MDR), 20.0% extensively drug-resistant (XDR), and 31.7% pan-sensitive. Among second isolates, MDR and XDR patterns were observed in 7.0% and 3.3% respectively. Empirical therapy most frequently included meropenem (46.7%), vancomycin (33.7%), or a combination of meropenem and vancomycin (19.7%). Despite broad empiric coverage, resistance rates indicated that many regimens were inadequate against prevailing pathogens.

Table 3: Organisms' comparisons: crosstabs with chi-square tests and ANOVA by organism category.

Comparison (Organisms' vs)	Statistic	df	P
Gender	0.377	2	.828
ANC severity	7.996	4	.017

Presence of CVC	2.217	2	.030
Chemo within 2 weeks	3.384	2	.018
Hospital unit	8.698	6	.191
1st isolate susceptibility	8.462	6	.006
Empirical rule given	5.444	8	.245
Mortality	5.594	2	.046

ANOVA and Tukey HSD homogeneous subset

Variable	Fungal (n=34)	Gram-negative (n=215)	Gram-positive (n=51)	F	P
ANC at time of blood C/S	386.85	398.21	399.20	0.070	.050
Duration of neutropenia	10.73	11.14	11.61	0.488	.048
Time to appropriate antibiotics	4.734	5.181	5.295	1.808	.041

Clinical outcomes highlighted significant morbidity. Septic shock developed in 32.0% of patients, organ dysfunction in 32.0%, and ICU admission post-BSI in 22.0%. Clinical non-response at 72 hours was observed in 60.0% of cases. Overall mortality was 17.0% (51/300), with infection-related deaths accounting for 15.7%. Patients who died had significantly lower ANC counts, longer duration of neutropenia, and delayed initiation of appropriate antibiotics compared to survivors (Table 3).

Table 4 Clinical Outcomes (n = 300)

Variable	Category	n (%)
Septic Shock	No	204 (68.0)
	Yes	96 (32.0)
ICU Admission Post BSI	No	234 (78.0)
	Yes	66 (22.0)
Clinical Non-Response at 72 Hours	No	120 (40.0)
	Yes	180 (60.0)
Organ Dysfunction	No	204 (68.0)
	Yes	96 (32.0)

Statistical analyses confirmed associations between organism category and ANC severity (p = .017), presence of central venous catheters (p = .030), chemotherapy within two weeks (p = .018), susceptibility profile (p = .006), and mortality (p = .046). ANOVA demonstrated differences across organism groups in ANC at the time of culture (p = .050), duration of neutropenia (p = .048), and time to appropriate antibiotics (p = .041). Regression modeling identified ANC severity, organism category, time to appropriate antibiotics, and neutropenia duration as independent predictors of mortality, explaining 42% of the variance. Severe neutropenia (OR = 2.3, p = .01) and presence of central venous catheters (OR = 1.9, p = .03) predicted Gram-positive infections, while prolonged neutropenia predicted fungal infections (OR = 1.12 per day, p = .02) (Table 4).

Further regression analyses showed that ANC severity, duration of neutropenia, and delayed antibiotic initiation independently predicted septic shock and organ dysfunction, accounting for 15.7% of the variance. Although ICU admission was associated with ANC severity, susceptibility profile, and organism category, regression modeling did not identify independent predictors. Overall, patients with severe neutropenia, MDR or XDR infections, and delayed antibiotic therapy were at greatest risk of adverse outcomes.

DISCUSSION

Bloodstream infections continue to be a significant source of morbidity and mortality among neutropenic hematologic malignancy patients. Gram negative organisms were the major cause of isolation in this prospective cohort and almost three quarters of isolates were Gram negative with Escherichia coli and Klebsiella pneumoniae as the most common pathogens. This finding is in agreement with recent international series whose Gram negative prevalence was 60-75 per cent in cases of febrile neutropenia.[16,18] The high rate of Gram negative bacteremia highlights the need to be concerned about the world on multidrug resistance and the outcome of clinical practice.

The mortality rate of this study was 17 and death related to the infection was 15.7. Adverse outcomes were highly correlated with such host factors as severe neutropenia, the long period of neutropenia, and the delay in the use of relevant antibiotics. These results align with previous reports that demonstrate the importance of host immunity and microbial resistance in prognosis.[19,20,21] Multidrug resistant Gram negative infections were specifically associated with poor survival, similar to high resistance environments in which carbapenem resistance and extended spectrum beta lactamase production greatly undermines empiric therapy.

Less common (11.3%), but related to longer neutropenia and slow initiation of antibiotic treatment were invasive fungal infections. Candida prevalence is in line with other hematology cohorts as invasive candidiasis is a major cause of death in patients with acute leukemia and prolonged neutropenia. These results support the relevance of antifungal prophylaxis in high risk groups.

Meropenem, vancomycin, or a combination of both was most commonly used in the empirical therapy of this cohort. Though it was widely covered, resistance rates showed that most regimens were not sufficient against the existing pathogens. This gap between the guideline recommendations and actual practice has been observed in other studies where empirical therapy fails to keep pace with the changing trends in resistance.[23] Antimicrobial stewardship programs are hence important in ensuring timely reviewing, minimization of therapy where necessary and judicious use of carbapenems to prevent further growth of resistance.[24]

Of interest was the relation between delayed initiation of antibiotics and mortality. Later patients who had been properly treated were much more likely to die, which supports the argument that every hour of delay in sepsis treatment risks the death of a patient.[25] This observation highlights the importance of strict compliance with sepsis bundles and the timely administration of empiric antibiotics to neutropenic fever. Moreover, the period of neutropenia alone was forecasting the occurrence of septic shock and organ dysfunction, which indicated the interaction of host susceptibility and pathogen virulence.[26]

The use of central venous catheters was prevalent, but the presence of this device did not have an independent mortality predictive value in this study. However, catheter related bloodstream infections are still a significant source of morbidity in neutropenic patients and this lack of association could be because of good catheter care practice or because of the presence of predominantly Gram negative pathogens which do not involve catheter care.

There are a number of limitations in the study. It is a single center study, so the results might not be applicable in other facilities with varying resistance profiles. Unculturable organisms could be missed by culture based methods, and identified by metagenomic methods. Short-term evaluation of outcomes was done without considering relapse or long term survival. Irrespective of these constraints, the prospective design, the large sample size, and the microbiological analysis, in detail, enhance the validity of findings.

In the future, there should be the incorporation of quick diagnostic methods like the use of molecular and metagenomic assays to enhance detection of pathogens and inform therapy. Empirical regimens should be configured to local resistance data, and strengthening antimicrobial stewardship programs are necessary. For high risk patients with prolonged neutropenia, antifungal prophylaxis should be considered. Inter-centre partnerships are required to help eliminate regional differences in resistance and outcomes, to facilitate larger-scale interventions to decrease mortality of neutropenic patients due to infections.

CONCLUSION

Gram-negative organisms are the major pathogens of bloodstream infections in neutropenic patients with a high burden of multidrug resistance. Mortality was strongly correlated with severe neutropenia and delays in appropriate antibiotic treatment. Continuous local microbiological patterns surveillance and enhanced antimicrobial stewardship are required to improve the outcome.

REFERENCES

1. Sandherr, M., Stemler, J., Schalk, E., Hattenhauer, T., Hentrich, M., Hertenstein, B., ... & Busch, E. (2025). 2024 update of the AGIHO guideline on diagnosis and empirical treatment of fever of unknown origin (FUO) in adult neutropenic patients with solid tumours and hematological malignancies. The Lancet Regional Health–Europe, 51. https://doi.org/10.1016/j.lanepe.2025.101214

2. Rabagliati, R., Salazar, G., Pérez-Lazo, G., Iturrieta, M. P., Portillo, D., Soria-Segarra, C., ... & Garcia, P. (2024, March). An emergent change in epidemiologic and microbiological characteristics of bloodstream infections in adults with febrile neutropenia resulting from chemotherapy for acute leukemia and lymphoma at reference centers in Chile, Ecuador, and Peru. In Open forum infectious diseases (Vol. 11, No. 3, p. ofae052). US: Oxford University Press. https://doi.org/10.1093/ofid/ofae052
3. Wang, S., Song, Y., Shi, N., Yin, D., Kang, J., Cai, W., & Duan, J. (2023). Characteristics, outcomes, and clinical indicators of bloodstream infections in neutropenic patients with hematological malignancies: a 7-year retrospective study. Infection and Drug Resistance, 4471-4487. https://doi.org/10.2147/IDR.S413454
4. Adekunle, M., Majaliwa, E., Reljic, T., Abebe, W., Assani, K., Atwiine, B., ... & Mukkada, S. (2025). Context-Informed Clinical Practice Guidelines for Fever With Neutropenia Management Among Sub-Saharan African Children With Cancer: A GRADE-Based Approach. JCO Global Oncology, 11, e2500215. https://doi.org/10.1200/GO-25-00215
5. Zimmer, A. J., Stohs, E., Meza, J., Arnold, C., Baddley, J. W., Chandrasekar, P., ... & Freifeld, A. G. (2022). Bloodstream infections in hematologic malignancy patients with fever and neutropenia: Are empirical antibiotic therapies in the United States still effective? Open Forum Infectious Diseases, 9(7). https://doi.org/10.1093/ofid/ofac240
6. Tajudeen, M., Phyo, T. P., Moh, P. A. M., Htar, S. T., Namitha, S., Eiei, P., ... & Griffith, D. (2025). Antibiotic Susceptibility Report of Bacteria Isolated From Blood Cultures of Neutropenic Sepsis Patients Undergoing Chemotherapy. Cureus, 17(6). https://doi.org/10.7759/cureus.85903
7. El Assaad, N., Azzi, A., Haddad, F., Lebbos, J., Haddad, E., Chehata, N., ... & Saliba, G. (2025). Febrile neutropenia in the Middle East and North Africa Region: trends, management, and outcomes (2000-2024) A systematic review. IJID regions, 16, 100682. https://doi.org/10.1016/j.ijregi.2025.100682
8. Janani, F., Azami, P., Sanani, M. G., & Bamneshin, K. (2024). Systematic review on epidemiology of Escherichia coli in bloodstream infection of patients undergoing hematopoietic stem cell transplantation. Germs, 14(1), 85. https://doi.org/10.18683/germs.2024.1420
9. Wang, S., Song, Y., Shi, N., Yin, D., Kang, J., Cai, W., & Duan, J. (2023). Characteristics, outcomes, and clinical indicators of bloodstream infections in neutropenic patients with hematological malignancies: a 7-year retrospective study. Infection and Drug Resistance, 4471-4487. https://doi.org/10.2147/IDR.S413454
10. Deng, S. M., Wei, W. J., Duan, T. J., & Jiang, Z. P. (2025). Risk factors and outcomes of bloodstream infection with multidrug-resistant bacteria in adult patients with acute leukemia. Journal of Infection and Public Health, 103088. https://doi.org/10.1016/j.jiph.2025.103088
11. Zhou, J., Sun, J., Lu, S., Han, X., He, J., Zhang, P., ... & Yu, Y. (2024). Clinical characteristics and prognosis of bloodstream infections with carbapenem-resistant Gram-negative organisms in patients with hematological malignancies: A multicenter case-control study in China. Journal of Infection, 89(6), 106331. https://doi.org/10.1016/j.jinf.2024.106331
12. Laporte-Amargos, J., Ulldemolins, M., Hernández-Mitre, M. P., Roberts, J. A., Rigo-Bonnin, R., Carmona-Torre, F., ... & Gudiol, C. (2025). Population pharmacokinetics and optimized dosing of piperacillin-tazobactam in hematological patients with febrile neutropenia. Antimicrobial Agents and Chemotherapy, 70(1), e01253-25. https://doi.org/10.1128/aac.01253-25
13. Sandherr, M., Stemler, J., Schalk, E., Hattenhauer, T., Hentrich, M., Hertenstein, B., ... & Busch, E. (2025). 2024 update of the AGIHO guideline on diagnosis and empirical treatment of fever of unknown origin (FUO) in adult neutropenic patients with solid tumours and hematological malignancies. The Lancet Regional Health–Europe, 51. https://doi.org/10.1016/j.lanepe.2025.101214
14. Cui, Y., Feng, X., Pan, L., Lin, Q., Wang, J., Zhen, S., ... & Feng, S. (2025). Antibiotic stewardship in hematological patients with Escherichia coli and Klebsiella pneumoniae bloodstream infections: evaluating short-course and carbapenem-sparing strategies. Annals of Clinical Microbiology and Antimicrobials, 24(1), 34. https://link.springer.com/article/10.1186/s12941-025-00801-y
15. Laporte-Amargos, J., Ulldemolins, M., Hernández-Mitre, M. P., Roberts, J. A., Rigo-Bonnin, R., Carmona-Torre, F., ... & Gudiol, C. (2025). Population pharmacokinetics and optimized dosing of piperacillin-tazobactam in hematological patients with febrile neutropenia. Antimicrobial Agents and Chemotherapy, 70(1), e01253-25.https://doi.org/10.1128/aac.01253-25
16. Rabagliati, R., Salazar, G., Pérez-Lazo, G., Iturrieta, M. P., Portillo, D., Soria-Segarra, C., ... & Garcia, P. (2024, March). An emergent change in epidemiologic and microbiological characteristics of bloodstream infections in adults with febrile neutropenia resulting from chemotherapy for acute leukemia and lymphoma at reference centers in Chile, Ecuador, and Peru. In Open forum infectious diseases (Vol. 11, No. 3, p. ofae052). US: Oxford University Press. https://doi.org/10.1093/ofid/ofae052

17. Wang, S., Song, Y., Shi, N., Yin, D., Kang, J., Cai, W., & Duan, J. (2023). Characteristics, outcomes, and clinical indicators of bloodstream infections in neutropenic patients with hematological malignancies: a 7-year retrospective study. Infection and Drug Resistance, 4471-4487. https://doi.org/10.2147/IDR.S413454
18. Zimmer, A. J., Stohs, E., Meza, J., Arnold, C., Baddley, J. W., Chandrasekar, P., ... & Freifeld, A. G. (2022). Bloodstream infections in hematologic malignancy patients with fever and neutropenia: Are empirical antibiotic therapies in the United States still effective? Open Forum Infectious Diseases, 9(7). https://doi.org/10.1093/ofid/ofac240
19. Mostaghim, A., Hashem, N. G., Pathan, S., & Han, A. (2025, February). P-2253. Epidemiology and Outcomes of Gram-Negative Bacteremia in a Diverse Immunocompromised Population. In Open Forum Infectious Diseases (Vol. 12, No. Supplement_1, pp. ofae631-2406). US: Oxford University Press. https://doi.org/10.1093/ofid/ofae631.2406
20. Ayaz, C. M., Hazırolan, G., Sancak, B., Hascelik, G., & Akova, M. (2022). Factors associated with gram-negative bacteremia and mortality in neutropenic patients with hematologic malignancies in a high-resistance setting. Infectious Diseases & Clinical Microbiology, 4(2), 87. https://doi.org/10.36519/idcm.2022.87
21. Mori, G., Diotallevi, S., Farina, F., Lolatto, R., Galli, L., Chiurlo, M., ... & Oltolini, C. (2024). High-risk neutropenic fever and invasive fungal diseases in patients with hematological malignancies. Microorganisms, 12(1), 117. https://doi.org/10.3390/microorganisms12010117
22. Arango, M., & Ramirez, I. C. (2025, February). P-2268. Candida tropicalis Invasive Infection in Febrile Neutropenia, a High Mortality Infection. In Open Forum Infectious Diseases (Vol. 12, No. Supplement_1, pp. ofae631-2421). US: Oxford University Press. https://doi.org/10.1093/ofid/ofae631.2421
23. Guillotin, F., Aubert, L., Benguerfi, S., Munoz Calahorro, R., Vennier, A., Boutoille, D., ... & Canet, E. (2025). Neutropenic sepsis and septic shock in ICU patients: A single-center experience over the last decade. PLoS One, 20(10), e0334511. https://doi.org/10.1371/journal.pone.0334511
24. Gretland, J., Sjømæling, S., Mosevoll, K. A., & Reikvam, H. (2025). Timing of antibiotic initiation in sepsis and neutropenic fever. Frontiers in Medicine, 12, 1597047. https://doi.org/10.3389/fmed.2025.1597047
25. Deng, S. M., Wei, W. J., Duan, T. J., & Jiang, Z. P. (2025). Risk factors and outcomes of bloodstream infection with multidrug-resistant bacteria in adult patients with acute leukemia. Journal of Infection and Public Health, 103088. https://doi.org/10.1016/j.jiph.2025.103088
26. Zhou, J., Sun, J., Lu, S., Han, X., He, J., Zhang, P., ... & Yu, Y. (2024). Clinical characteristics and prognosis of bloodstream infections with carbapenem-resistant Gram-negative organisms in patients with hematological malignancies: A multicenter case-control study in China. Journal of Infection, 89(6), 106331. DOI: https://doi.org/10.1016/j.jinf.2024.106331