Clinical profile, treatment, and outcomes of febrile neutropenia in hematologic disorders: a look at 30-day mortality predictors

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Introduction

Febrile neutropenia is defined as a fever coinciding with a severely low absolute neutrophil count. Historically, gram-negative bacteria were the leading cause, but this has shifted to gram-positive organisms.. Factors like septic shock, impaired renal function, and pulmonary involvement predict poor patient outcomes. A significant concern is the limited data on febrile neutropenia in developing countries, especially given the increasing prevalence of resistant organisms in these regions. [1]

Aim

This study investigated the association between clinical profiles, treatment, and outcomes in patients with febrile neutropenia.

Methods

This retrospective observational cross-sectional study, conducted at Tikur Anbessa Specialized Hospital in Ethiopia, included all eligible patients aged 13 or older with acute leukemia, high-grade non-Hodgkin lymphoma, or aplastic anemia, experiencing their 'first' episode of febrile neutropenia. A census approach was employed, excluding individuals with incomplete medical charts or subsequent febrile neutropenia episodes. Data were systematically extracted using a structured questionnaire from medical charts, supplemented by information from the Health Management Information System (HMIS), the microbiology unit, and the hospital's Med Web intranet registry for comprehensive data collection and verification..

Table 5 Bi-variable and multivariable logistic regression analysis results of factors associated with death due to febrile neutropenia among hematologic malignancy patients with febrile neutropenia.

Variables	Death due to febrile neutropenia		AOR 95% CI
	Yes	No	
Medical ICU admission			
Yes	7 (70%)	3 (30%)	5.4 (1.2, 23.9) *
No	28 (23%)	94 (77%)	
Prior Episode of febrile neutropenia			
Yes	13 (52%)	12 (48%)	3.8 (1.44–10.16)
No	22 (20.6%)	85 (79.4%)	

Results

The study involved 132 patients with hematologic malignancy and febrile neutropenia (FN).

- Patient Demographics: Patients were primarily younger individuals (median age 25), with Acute Lymphoblastic Leukemia (ALL) being the most common underlying diagnosis.
- Prophylactic Antibiotic Use: High rates of prophylactic antibiotic use were observed among the patients.
- Microbial Culture Yield: Only 16.5% of microbial cultures yielded positive growth.
- Shifting Microbial Patterns:
  - A notable shift towards gram-positive cocci (GPC) was identified, with Coagulase-negative Staphylococcus being prominent.
  - Gram-negative bacilli (GNB), *Klebsiella pneumoniae* and *Escherichia coli*, remained significant pathogens.
- Factors Statistically Significant with 30-day-mortality in FN
  - Prior episodes of febrile neutropenia (p = 0.002)
  - Previous use of chemotherapy (p = 0.018)
  - WBC counts at the time of diagnosis (p = 0.033)
  - Chest CT scans suggestive of Invasive Aspergillosis (p = 0.00012)
  - Medical ICU admission during the febrile neutropenic episode (p = 0.04)
  - Independently Associated Factors (from Multivariable Analysis):
    - Admission at the Medical ICU (p = 0.04)
    - Prior episodes of febrile neutropenia (p = 0.002)

Discussion

This febrile neutropenia (FN) study revealed key insights into its epidemiology, patient characteristics, and evolving microbial patterns. It found FN predominantly in younger individuals, with a slight male majority, and a high incidence among patients with Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML).

Common infection sites included oral mucositis, the lower respiratory tract, and the gastrointestinal tract. Critically, a significant shift in microbial patterns was observed, with gram-positive cocci (52%), particularly coagulase-negative Staphylococcus, becoming predominant, although gram-negative bacilli (35%) like *Pseudomonas Aeruginosa* remained prevalent, and invasive aspergillosis was also noted in 9.1% of patients. These findings, largely consistent when compared to international studies, highlight the evolving epidemiology of FN, underscoring the need for targeted interventions in younger demographics, raising concerns about potential antibiotic resistance due to widespread prophylactic regimens. It also emphasizes the importance of tailoring treatment protocols based on specific patient characteristics and local microbial patterns in Africa.[2]

References

1. *Arega, B. et al. Microbial spectrum and drug-resistance profile of isolates causing bloodstream infections in febrile cancer patients at a referral hospital in addis ababa, Ethiopia. Infect. Drug Resist. 11, 1511–1519 (2018).*
2. *Al-Tawfiq, J. A. et al. Epid m.ol gy, ris sot c oj nf..ci n u p..u ni with febrile neutropenia: A ten-year longitudinal study J. 'n ect. 't ntic H altl 1^ (3, 3 4- .66 (2 19).*

Published on Nature's Scientific Reports: https://doi.org/10.1038/s41598-025-06787-z