



# Antimicrobial agent prescription patterns for chemotherapy-induced febrile neutropenia in patients with hematological malignancies at Sultan Qaboos University Hospital, Oman

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## KEYWORDS

Neutropenia;  
Fever;  
Malignancy;  
Chemotherapy;  
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## Summary

**Objectives:** The aim of this study was to describe the antimicrobial prescription patterns of patients with hematological malignancies who developed febrile neutropenia (FN) at Sultan Qaboos University Hospital (SQUH) in Oman.

**Methods:** This was a retrospective observational study covering a period of 3 years (January 2007–February 2010). FN episodes were studied in patients with hematological malignancies in three different wards at SQUH.

**Results:** A total of 176 FN episodes were analyzed. Overall, 64% of the 107 patients studied experienced at least 2 episodes during the analysis period. Approximately, 69% of the febrile neutropenia episodes had severe neutropenia. The duration of neutropenia was less than 1 week in the majority of the episodes (57%). The mean duration of treatment was approximately 7 days, with no significant difference between specialties or different types of malignancies. Only 34 (19%) episodes had positive cultures, and most of these were from blood samples (30 episodes, 88%). The majority of isolates were gram-negative organisms (63%). The initial empirical treatment included monotherapy (37%), dual therapy (60%) and triple therapy (3%).

**Conclusions:** This study demonstrates that there is a large variation in the antimicrobial treatment of FN episodes in patients with hematological malignancies at SQUH. All chosen drugs were within international guideline recommendations.

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## Introduction

Infections due to neutropenia are common in patients with hematological malignancies receiving chemotherapy. Fever is usually the first and may be the only sign of infection in neutropenic patients. Neutropenia is defined as an absolute neutrophil count (ANC)  $<500$  cells/mm<sup>3</sup> or  $<1000$  cells/mm<sup>3</sup> that decreases to  $<500$  cells/mm<sup>3</sup> within 48 h [1]. The term febrile neutropenia (FN) describes the occurrence of fever (temperature  $\geq 38.3$  °C or  $>38.0$  °C for at least 1 h) in patients with neutropenia [1].

Cancer chemotherapy is the most common cause of FN. Studies have shown that up to 25% of patients treated with chemotherapy experience a FN episode, and the frequency of FN is higher in hematological malignancies [2]. The majority of neutropenic episodes occur within the first 14 days of chemotherapy [3]. FN is associated with significant morbidity, mortality and cost [4,2]. Morbidity is usually caused by infections during severe and prolonged episodes of neutropenia. Patients with FN are at risk of infection from all types of microbes including gram-positive and gram-negative bacteria, fungi and viruses. Because FN is a potentially life-threatening condition and as the progression of infection in neutropenic patients can be rapid, such patients should receive empirical antibiotic therapy immediately after blood cultures are obtained and before any other diagnostic procedures are performed.

The present study describes the pattern of antimicrobial therapy for FN in patients with hematological malignancies at Sultan Qaboos University Hospital (SQUH), Sultanate of Oman.

## Patients and methods

This study was a retrospective observational study of antimicrobial therapy for FN episodes in patients with hematological malignancies (leukemias, lymphomas and myelomas) from the adult hematology, pediatric hematology and adult oncology departments at SQUH, covering the period from January 2007 to February 2010. Neutropenia was defined as an absolute neutrophil count (ANC)  $<500$  cells/mm<sup>3</sup> or as an ANC  $<1000$  cells/mm<sup>3</sup> that decreased to  $<500$  cells/mm<sup>3</sup> within 48 h. Fever was defined as a single temperature reading  $\geq 38.3$  °C or a reading  $>38.0$  °C for at least 1 h. Oral temperatures were recorded for all patients. In addition, the axillary temperature was recorded for pediatric patients. The severity of neutropenia was classified as mild

(ANC between 1000 and 1500 cells/mm<sup>3</sup>), moderate (ANC between 500 and 1000 cells/mm<sup>3</sup>), severe (ANC less than 500 cells/mm<sup>3</sup>) or profound (ANC less than 100 cells/mm<sup>3</sup>) [5].

Data were collected for each FN episode. This included demographic data; the general profile of FN episodes, which included the onset of neutropenia; the absolute neutrophil count (ANC); the severity of neutropenia and degree/duration of fever; the details of antimicrobial therapy; blood, sputum and urine culture results; and the patient's outcome. The study was approved by the College of Medicine's research and ethics committee at SQU.

The data were coded and entered into the Statistical Package for the Social Sciences (SPSS) version 16, and the differences between groups were tested for statistical significance using the  $\chi^2$  test for categorical variables and Student's *t*-test for independent samples with continuous variables. A *p*-value  $<0.05$  was considered significant at the 95% confidence interval.

## Results

A total of 176 febrile neutropenic (FN) episodes were identified in 107 patients. The mean age of the patients was 22.5 years (SD  $\pm 20.8$  years), with 59 males (55.1%) and 48 females (44.9%). Leukemia was the main underlying malignancy occurring in 78.5% of these patients, with acute lymphocytic leukemia being the most common (51.4%). In addition, 18.7% and 2.8% of the patients had lymphoma or multiple myeloma, respectively. Sixty-nine patients (64.5%) suffered two FN episodes during the study period.

## Profile of febrile neutropenia episodes

Ninety-eight (55.5%) of the 176 episodes occurred in male patients, and the majority (83.0%) occurred in leukemic patients. The mean hospital stay for these episodes was 24.9 days (SD  $\pm 18.2$  days). The mean duration of hospital stay for episodes developed during a hospital stay was 34.3 days compared to 12.3 days for episodes that lead to admission (*p*-value  $<0.001$ ). Eighty-six episodes (49%) were treated in the Pediatric Hematology department, 77 (44%) in the Adult Hematology department and only 13 (7%) in the Adult Oncology department. The mean body temperature was 38.7 °C (range 38.3–40.4 °C) with a mean duration of 1.6 days (SD  $\pm 1.3$  days). The mean ANC was 309 cells/mm<sup>3</sup> (SD  $\pm 207$ ). Approximately 69%

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