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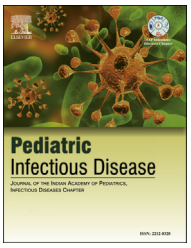

Original Article

Febrile neutropenia in pediatric cancer patients: Experience from a tertiary health care facility of Pakistan

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ABSTRACT

Aims: Pediatric cancer patients with febrile neutropenia (FN) have an increased risk of infectious complications and mortality.

Methods: This study was a retrospective analysis of pediatric cancer patients with FN.

Results: Out of 872 episodes of FN, 559 (64.1%) were males and 313 (35.9%) females. The mean age was 5.32 ± 4.07 years. ALL (67.7%) was the most common diagnosis followed by AML (12.2%), lymphoma (9.9%) and solid tumors (5.8%). Age < 5 year (Odd Ratio = 1.5; $p = 0.043$), AML (OR = 1.8; $p = 0.019$), patients who received chemotherapy within 2 week of FN (OR = 1.9; $p = 0.007$), absolute neutrophil count < 50/cm (OR = 1.5; $p < 0.041$), platelets count < 50,000/cm (OR = 1.5; $p < 0.027$), fungal infection (OR = 15.6; $p < 0.001$), and pneumonia were identified as risk factors associated with development of prolonged FN in pediatric cancer patients. A total of 25 (2.9%) patients required PICU admission and 12 (1.4%) patients expired. Both variables, PICU admission (9% Vs 2%; OR = 5.4; $p < 0.001$) and mortality rate (5.2% Vs 0.8%; OR = 8.1; $p < 0.001$) were statistically significant in patients with prolonged FN versus FN respectively.

Conclusion: Prospective studies in large cooperative trials may be beneficial in evaluating these risk factors further.

1. Introduction

There have been major advances in the treatment and outcomes of childhood cancer over the last few decades. Improved outcomes have largely been achieved by aggressive treatment of childhood cancers including systemic antineoplastic and radiation therapy that have secondary effects on a variety of normal cells including hematopoietic elements of the bone marrow.[1] Chemotherapy induced neutropenia is a common complication which renders children extremely vulnerable to life threatening infections. Epidemiological

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studies have demonstrated a high incidence of sepsis in paediatrics cancer patients. Rates up to 12.8% and 17.4% in children aged 1–9 years and 10–19 years respectively, have been reported making febrile neutropenia (FN) a worrying and serious complication in childhood cancer treatment.[1,2]

In recent years, several studies from developed countries have evaluated the risk factors for bacteremia or poor outcomes among patients with cancer and helped to establish the current guidelines for the treatment of FN.[3–5] However, despite major advances in understanding, established guidelines and recommendations for the treatment of FN, children remain extremely vulnerable to life threatening infections. This contributes to a significant morbidity and mortality in pediatric patients with cancer.[1,6,7]

Mortality associated with FN ranges from 2 to 6% in children.[8,9] Considering that the overall mortality rate for FN episodes was 10% a decade ago the current 2–4% rate indicates a significant improvement in management resulting in a favorable impact. Nevertheless this mortality rate still remains substantial, warranting further improvement.

The single most important advancement in oncology supportive care leading to an improved survival has been the prompt initiation of empirical antibacterial antibiotics when the neutropenic patient becomes febrile. Before this approach was instituted in the early 1970s, the mortality rate from gram-negative infections, approached 80%, but with the widespread use of effective empirical antibiotics, the overall mortality rate has significantly declined.[10] Recently the Infectious Diseases Society of America has published general guidelines for use of antimicrobial agents in neutropenic patients with unexplained fever.[11]

Many studies from developed countries have reported the importance of prompt management of FN. However, reports from the developing countries are lacking and no published reports are available in Pakistan. Thus this study was carried out to identify the burden of febrile neutropenia and describe the demographic, clinical feature, laboratory data and management outcomes of febrile neutropenia in pediatric cancer patients at tertiary health care center of Pakistan.

2. Material and methods

2.1. Study design and setting

This is a retrospective study analyzing the clinical data of all children admitted with or who developed febrile neutropenia in the pediatric oncology unit at the Aga Khan University Hospital (AKUH) in Karachi, Pakistan from January 2011 to December 2012.

2.2. Patient population and definition

Patients one month to 15 years of age, who were admitted to the pediatric oncology ward from January 2011 to December 2012 with diagnosis of febrile neutropenia (FN) were included. For definition the Fever and Neutropenia Guideline of Infectious Diseases Society of America (IDSA) were followed.[12] Fever was defined as a single oral temperature of >38.3 °C or a temperature of >38.0° sustained over a 1-h period on more than one occasion in a 24-h period. Neutropenia was defined as an absolute neutrophil count (ANC) of less than 500/mm^3.

2.3. Data collection

All patients who had diagnosis codes for both neoplastic disease (International Classification of Diseases, 9th revision, clinical modification [ICD-9-CM] code 140–239) and febrile neutropenia, and were 15 years of age or younger were identified by using health information management system and included in the analysis. For those patients who had more than one admission for febrile neutropenia, each admission was counted as separate case. The primary outcomes of this analysis were pediatric intensive care unit (PICU) admission and mortality. Relevant covariates data were collected including demographic features, type of malignancy, phase of chemotherapy, clinical features at presentation, duration of symptoms, presentation location (Emergency department, clinic, or inpatient ward), initial laboratory findings including total white blood cell (WBC) count, ANC, and platelet count; microbiological data, antibiotic(s) used, radiological finding (if applicable) and outcomes data. All patients were treated as in patients following the International Pediatric Fever and Neutropenia Guideline.[13]

2.4. Statistical analysis

The data was analyzed by using SPSS version 20.0 (IBM, Chicago, USA) was used. Summary statistics were used to describe the cohort. Results were presented as mean and standard deviation for continuous variables and frequency and percentage for categorical variables. Data was stratified in two groups to identify the mortality associated risk factors in pediatric oncology patients with febrile neutropenia. A p-value of <0.05 was considered statistically significant.

2.5. Ethical approval

The study was approved by the Ethical Review Board (ERB) of Aga Khan University, Karachi.

3. Results

The total number of admissions in the pediatric oncology unit during the study period was 2516 and a total admission with febrile neutropenia was 918 (36.5%). Forty-six cases were excluded from the study because of noncompliance and/or missing data. Out of 872 available febrile neutropenic patients for analysis, 737 (84.5%) had febrile neutropenia of less than 5 days versus 135 (15.5%) patients with prolonged febrile neutropenia (FN > 5 days). Febrile neutropenia and PFN admission rate among all pediatric oncology patients was 34.7% and 5.3% respectively.

Demographic features, clinical characteristics of the patients and their hospitalizations are presented in Table 1. The mean age of the study population was 5.32 (±SD 4.07) years. There were 559 (64.1%) males and 313 (35.9%) females, with male: female ratio 1:1.8. The emergency room was the most