

Febrile Neutropenia in Patients Receiving Chemotherapy; an observational study highlighting its association with haematological parameters on gender basis

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Received: June 13, 2018; Accepted: June 18, 2018; Published: June 22, 2018

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Abstract

Objective: This study was aimed to evaluate the frequency of febrile neutropenia between genders and find out its association with haematological parameters.

Methodology: This was an observational study conducted in the Oncology Department of Jinnah Postgraduate Medical Centre, Karachi Pakistan for 1 year. Data was collected using non-probability convenient sampling technique after taking informed consent from 316 patients diagnosed as having cancer on histopathology, undergoing treatment with chemotherapeutic agent and having neutropenia along with fever as a single oral temperature of $>38.3^{\circ}\text{C}$. Patients who had co-morbid conditions such as diabetes, heart disease, or psychiatric illness were excluded from this study. The variables recorded were age, gender, chemotherapy protocol, number of days of chemotherapy, haemoglobin, total leukocyte count, neutrophils, monocytes, platelets and creatinine. Patients were divided into 2 groups based on gender receiving the chemotherapeutic regimen, Group 1 consisted of male and Group 2 consisted of female patients. SPSS version 20.0 was used for data analysis. Chi-square test and t-test was used to assess the association. P-value was calculated to find association.

Results: The mean age of Group 1 patients was 41.90 ± 14.90 years while that of group 2 was 42.35 ± 13.17 years. In our study, males had total leukocyte count 2076.30 ± 1207.72 cells/cum, neutrophil count $29.91\pm 20.68/\text{mm}^3$ and females had total leukocyte count 2862.36 ± 1970.80 cells/cum, neutrophil count $38.56\pm 21.87/\text{mm}^3$ which is significantly different among two groups ($p\text{-value}<0.05$). Febrile neutropenia was found to be present in 96 (57.1%) of males and 70 (47.3%) of female patients in our study which was not statistically significant ($p\text{-value}=0.080$).

Conclusion: Our study showed that among male and female cancer patients on chemotherapy, more than half of males were found to have febrile neutropenia, while fewer females had febrile neutropenia. There was no significant difference in occurrence of febrile neutropenia between two genders.

Keywords: Febrile Neutropenia; Genders;

Introduction

Febrile neutropenia's one of the most prominent complication of cancer chemotherapy and leads to decreased efficacy of treatment due to reduction in dosage of chemotherapy. The mortality rate from febrile neutropenia remains on higher side [1]. In patients having solid tumours, the incidence of febrile neutropenia ranges from 10%-50% and is apparently $\geq 80\%$ in patients having haematological malignancies [2]. The

mortality associated with Febrile Neutropenia require prompt hospitalization and aggressive antimicrobial treatment [3]. In patients having Gram-negative and Gram-positive bacteremia, mortality rates of 18% and 5% have been stated respectively [4]. The definition of Febrile Neutropenia according to the European Society for Medical Oncology (ESMO) is: 'An oral temperature of $>38.5^{\circ}\text{C}$ or two consecutive readings of $>38.0^{\circ}\text{C}$ for 2 h and an absolute neutrophil count (ANC) of $<0.5 \times 10^9/\text{l}$, or expected to fall $<0.5 \times 10^9/\text{l}$ ' [5]. They are the most numerous

circulating white blood cells that are the first line of the defense for infections [6]. Several symptoms are related to neutropenia; and the occurrence of fever is typically because of an infection as the patients are immune-compromised and are more prone to progress to infections [7]. Neutrophils are the most frequently affected cells by chemotherapy acting on bone marrow and suppressing cell lineages [8]. The risk of infection as well as mortality increases as the severity and duration of neutropenia increases along with the persistence of fever wherein the duration of neutropenia is typically 7–10 days, with variations depending upon the type and strength of the chemotherapeutic regimen [9]. Febrile neutropenic patients have heterogeneous grouping; therefore, the development of the infection and outcome is related to individual patient factors such as age, tumour type and stage, previous hospitalizations, or severe comorbidities [10]. Neutropenic patients are prone to suffer from infections, with respiratory tract infection (35%–40%), bloodstream infections (15%–35%) and urinary tract infections (5%–15%) being most common [11]. Moreover, Febrile neutropenia commonly compromises the chemotherapeutic treatment being administered by necessitating a reduction in dose and/or interruption of treatment cycles, thereby directly affecting treatment efficacy, patient survival and quality of life [12]. Since it is common to develop febrile neutropenia during the initial cycles of chemotherapy, European and US guidelines recommend the use of colony stimulating growth factors in patients having >20% risk of developing febrile neutropenia [13,14]. Metastatic diseases are usually seen in elderly patients who have associated co-morbid conditions and hence poor performance status in comparison to the younger patients with less-severe disease. Treatment in the metastatic setting is often less aggressive, and alternative approaches to managing these toxicities such as the use of less myelosuppressive regimens or scheduled dose modifications in line of prophylaxis using colony-stimulating factors have been recommended in several literatures, especially when the intent of such care is palliative [15,16].

It is observed that there are variations of haematological parameters in normal individuals on gender basis. Therefore, this study was aimed to focus on genders of patients receiving chemotherapy and having febrile neutropenia. Purpose of this study was to determine the frequency of febrile neutropenia among genders so that an appropriate chemotherapeutic plan can be devised to manage the patients accordingly. This may help decrease mortality and morbidity in future.

Materials and Methods

This was an observational study conducted in the Oncology Department of Jinnah Postgraduate Medical Centre, Karachi Pakistan. The study was done for duration of 6 months from November 2017 till April 2018 by utilizing non-probability convenient sampling technique. The study comprised of a total of 316 patients after receiving informed consent. The Ethical approval was taken from Ethical Review Board of Jinnah Postgraduate Medical Centre.

Patients diagnosed as having cancer on histopathology, undergoing treatment with chemotherapeutic agent were included in this study. The different chemotherapeutic agents used were antibiotics like bleomycin, daunorubicin, alkylating agents like cyclophosphamide, dacarbazine and micro tubular inhibitors like docitaxel, paclitaxel, vincristine, vinblastine, steroids like prednisone and other agents like cisplatin, asparaginase and etoposide. Patients who had comorbid conditions such as diabetes, ischemic heart disease, or psychiatric illness and incomplete data were excluded from this study. The patients were divided into 2 groups based on gender receiving the chemotherapeutic regimen, Group 1 consisted of male patients (n=168) and Group 2, female patients (n=148). The variables including age, weight, height, gender and body surface area, type of cancer, chemotherapy protocol, number of days of chemotherapy, haemoglobin, total leukocyte count, neutrophils, monocytes, platelets and creatinine were recorded.

Data was analysed using SPSS version 20. Demographic and haematological variables were presented as mean, standard deviation. Qualitative data was expressed as frequency and percentages. T-test was applied to find significant difference between quantitative variables. Chi-square test was applied to find significant difference in febrile neutropenia between genders. P-value <0.05 was considered to be significant.

Results

Our study comprised of 316 patients in total, out of which Group 1 had 168 patients and Group 2 had 148 patients. The mean age of Group 1 patients was 41.90 ± 14.90 years while that of group 2 was 42.35 ± 13.17 years. Group 1 had mean weight of 59.51 ± 12.63 kg, mean height of 162.89 ± 9.95 cm, Haemoglobin level of 162.89 ± 9.95 gm/dl, platelet count of 144454.09 ± 106076.47 cells/cum, total leukocyte count of 2076.30 ± 1207.72 cells/cum, neutrophil count of $29.91 \pm 20.68/\text{mm}^3$, monocytes of $7.16 \pm 7.28/\text{mm}^3$, absolute neutrophil count of $785.50 \pm 989.59/\text{mm}^3$ and duration of chemotherapy was 10.98 ± 3.56 days. Group 2 had mean weight of 54.50 ± 10.82 kg, height of 153.79 ± 8.29 cm, Haemoglobin level 9.89 ± 1.68 gm/dl, platelet count 190087.83 ± 120316.52 cells/cum, total leukocyte count 2862.36 ± 1970.80 cells/ mm^3 , neutrophil count $38.56 \pm 21.87/\text{mm}^3$, monocytes $9.03 \pm 9.78/\text{mm}^3$, absolute neutrophil count $1367.58 \pm 1408.94/\text{mm}^3$ and duration of chemotherapy 10.42 ± 2.79 days. There was a significant difference (p-value <0.05) in weight, height, monocyte count, total leukocyte count and absolute neutrophil count between the two groups (Table 1). The most common type of carcinoma found in the patients on chemotherapy was carcinoma of breast observed in 72 (22.8%) and the least common was carcinoma of pancreas found in 10 (3.2%) of cases. (Figure 1) In group 1, more than half of the patients 96 (57.1%) had febrile neutropenia after chemotherapy, while in group 2, 78 (52.3%) patients were not having febrile neutropenia while on chemotherapy regimen (Table 2, Figure 2). The difference in frequency of febrile neutropenia between two genders was insignificant (p-value=0.080).

Table 1: Descriptive statistics of chemotherapeutic patients

Variable	Group 1 (n=168)	Group 2 (n=148)	P-Value
	Mean± SD	Mean± SD	
Age (years)	41.90±14.90	42.35±13.17	0.069
Weight (kg)	59.51±12.63	54.50±10.82	0.042
Height (cm)	162.89±9.95	153.79±8.29	0.017
Body Surface Area (m ²)	1.62±0.19	1.51±0.16	0.003
Hemoglobin (mg/dl)	9.51±1.88	9.89±1.68	0.250
Platelets (mm ³)	144454.09±106076.47	190087.83±120316.52	0.365
Total Leucocyte Count (/mm ³)	2076.30±1207.72	2862.36±1970.80	<0.001
Neutrophils (%)	29.91±20.68	38.56±21.87	0.121
Monocytes (%)	7.16±7.28	9.03±9.78	0.029
Absolute Neutrophil Count / (mm ³)	785.50±989.59	1367.58±1408.94	<0.001
Creatinine (mg/dl)	0.76±0.33	0.77±0.42	0.916
Chemotherapy (days)	10.98±3.56	10.42±2.79	0.056

Table 2: Frequency and percentage of patients on chemotherapy protocols based on gender

Variable		Group 1	Group 2	P-Value
		n(%)	n(%)	
Febrile Neutropenia	Yes	96(57.1%)	70(47.3%)	0.080
	No	72(42.9%)	78(52.3%)	
	Total	168(100%)	148(100%)	

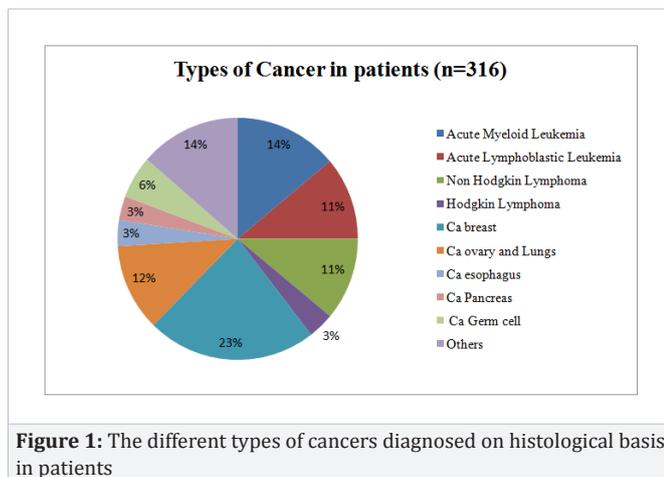


Figure 1: The different types of cancers diagnosed on histological basis in patients

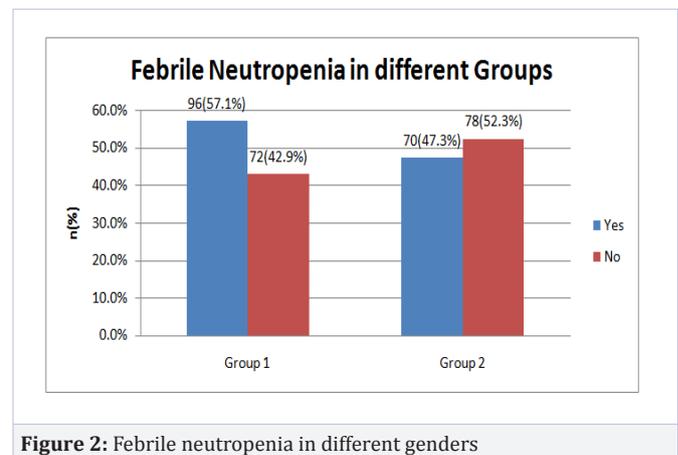


Figure 2: Febrile neutropenia in different genders

Discussion

In our study total 316 cancer patients receiving chemotherapeutic agents were divided into 2 groups depending on the gender of patients. In a study to determine febrile neutropenia, among the 215 patients who participated in that study, the mean age was reported to be 51.53 years [17]. In another study by Younus J et al, the mean age of febrile neutropenia patients was 61.5 years [18]. Patients aged 65 years or above were associated with greater (66%) chances of having febrile neutropenia after 1 cycle of chemotherapy [19]. In an Indian study to comprehend

safety and tolerability of febrile neutropenia treatment, the mean age was reported to be 54 years [20]. On the contrary in our study, the mean age of febrile neutropenia patients was reported to be 41.90±14.90 years in Group 1 patients and 42.35±13.17 years in Group 2, which is younger age than in the studies mentioned above.

In a study to identify patients at risk of developing febrile neutropenia, total leukocyte count 6.90x10⁹/mm³ (3.8-19.5x10⁹/mm³) and absolute neutrophil count 4.3 x10⁹/mm³ (1.6-17.0 x10⁹/mm³) pre-treatment were found to be at greater risk to encounter

episodes of febrile neutropenia [21]. After adjusting for age and cancer type, the most important independent risk factor in multi variant analysis were found to be prior chemotherapy, abnormal liver and renal function and low leukocyte count [22,23]. In another study, the risk factor for developing febrile neutropenia included advanced age, first cycle of chemotherapy and absolute neutrophil count $<2.0 \times 10^9/\text{mm}^3$ [24]. In our study, males had total leukocyte count $2076.30 \pm 1207.72 \times 10^9/\text{mm}^3$, neutrophil count $29.91 \pm 20.68/\text{mm}^3$ and females had total leukocyte count $2862.36 \pm 1970.80 \times 10^9/\text{mm}^3$, neutrophil count $38.56 \pm 21.87/\text{mm}^3$ which was significantly different among two groups (p -value < 0.05).

The studies done on non-Hodgkin lymphoma and small cell lung cancer patients have discovered that female gender is prone to develop febrile neutropenia or get admitted to hospital for management of febrile neutropenia [25,26]. In a study to determine occurrence of febrile neutropenia in patients receiving chemotherapy, the risk factors showed no significant difference (p -value = 0.931) between two genders [27]. Febrile neutropenia was found to be present in 96 (57.1%) of males and 70 (47.3%) of female patients in our study which was insignificant (p -value = 0.080).

This study is one of its kind in making an effort to determine the difference in occurrence of febrile neutropenia between two genders. However, the findings may have observer bias. Considering the observations of our study and to what extent febrile neutropenia may be consistent with the different chemotherapy regimens would be revealing to expedite more facts about the development of disease.

Conclusion

Our study predicted that among male and female cancer patients on chemotherapy, more than half of males were found to have febrile neutropenia, while less females had febrile neutropenia. There was no significant difference observed in frequency of febrile neutropenia between two genders. However, the neutrophil count and absolute neutrophil count in male and female febrile neutropenia patients had significant difference.

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