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

Javeria Ali¹, Reena Kumari²*, Ahsan Ali Siddiqui³, Maryam Nasir⁴, Samurna Sabir⁵, Shahzain Hasan⁶, Muhammad Asim Khan⁷ and Adnan Anwar⁸

¹House Officer, PNS Shifa Hospital, Karachi, Pakistan
²Resident Medical Oncology, Oncology Ward, Jinnah hospital, Pakistan
³Public Health, Specialist Family Medicine, Ministry of Health, Riyadh, Pakistan
⁴Medical Officer, Paediatrics, Agha Khan University Hospital, Pakistan
⁵Medical Officer, Dow University of Health Sciences, Pakistan
⁶Medical Officer, Hamdard University Hospital, Pakistan
⁷Medical Officer, Ziauddin Medical University, Pakistan
⁸Assistant Professor, Al Tibri Medical College Karachi, Pakistan

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 °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±20.68/mm3 and females had total leukocyte count 2862.36±1970.80 cells/cum, neutrophil count 38.56±21.87/mm³ which is significantly different among two groups (p-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-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 ≥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°C or two consecutive readings of >38.0°C for 2 h and an absolute neutrophil count (ANC) of <0.5 × 10⁹/l, or expected to fall <0.5 × 10⁹/l’ [5]. They are the most numerous
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, duanorubicin, alkyl ting agents like cyclophophamide, dacarbazine and micro tubular inhibitors like docitexal, paditezal, vincristine, vinblastine, steroids like prednison and other agents like cisplatin, asparaginase and etoposide. Patients who had co-morbid 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, chemotheraphy protocol, number of days of chemotherapy, haemoglobin, total leucocyte 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 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 leucocyte count of 2076.30±1207.72 cells/cum, neutrophil count of 29.91±20.68/mm³, monocytes of 7.16±7.28/mm³, absolute neutrophil count of 785.50±989.59/mm³ 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 leucocyte count 2862.36±1970.80 cells/mm³, neutrophil count 38.56±21.87/mm³, monocytes 9.03±9.78/mm³, absolute neutrophil count 1367.58±1408.94/mm³ and duration of chemotherapy 10.42±2.79 days. There was a significant difference (p-value<0.05) in weight, height, monocyte count, total leucocyte 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 chemotherapy regimen (Table 2, Figure 2). The difference in frequency of febrile neutropenia between two genders was insignificant (p-value=0.080).

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

Table 1: Descriptive statistics of chemotherapeutic patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n=168)</th>
<th>Group 2 (n=148)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.90±14.90</td>
<td>42.35±13.17</td>
<td>0.069</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.51±12.63</td>
<td>54.50±10.62</td>
<td>0.042</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.89±9.95</td>
<td>153.79±8.29</td>
<td>0.017</td>
</tr>
<tr>
<td>Body Surface Area (m²)</td>
<td>1.62±0.19</td>
<td>1.51±0.16</td>
<td>0.003</td>
</tr>
<tr>
<td>Hemoglobin (mg/dl)</td>
<td>9.51±1.88</td>
<td>9.89±1.68</td>
<td>0.250</td>
</tr>
<tr>
<td>Platelets (mm³)</td>
<td>144454.09±106076.47</td>
<td>190087.83±120316.52</td>
<td>0.365</td>
</tr>
<tr>
<td>Total Leucocyte Count (/mm³)</td>
<td>2076.30±1207.72</td>
<td>2862.36±1970.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>29.91±20.68</td>
<td>38.56±21.87</td>
<td>0.121</td>
</tr>
<tr>
<td>Monocytes (%)</td>
<td>7.16±2.88</td>
<td>9.03±9.78</td>
<td>0.029</td>
</tr>
<tr>
<td>Absolute Neutrophil Count (mm³)</td>
<td>785.50±989.59</td>
<td>1367.58±1408.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.76±0.33</td>
<td>0.77±0.42</td>
<td>0.916</td>
</tr>
<tr>
<td>Chemotherapy (days)</td>
<td>1.09±3.56</td>
<td>10.42±2.79</td>
<td>0.056</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1  n(%)</th>
<th>Group 2  n(%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile Neutropenia</td>
<td>Yes  96(57.1%)</td>
<td>70(47.3%)</td>
<td>0.080</td>
</tr>
<tr>
<td></td>
<td>No   72(42.9%)</td>
<td>78(52.3%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>168(100%)</td>
<td>148(100%)</td>
<td></td>
</tr>
</tbody>
</table>

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

Figure 2: Febrile neutropenia in different groups

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 leucocyte count 6.90x10⁹/mm³ (3.8-19.5x10⁹/mm³) and absolute neutrophil count 4.3x10⁹/mm³ (1.6-17.0x10⁹/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 <2.0x10³/mm³ [24]. In our study, males had total leukocyte count 2076.30±1207.72x10⁹/mm³, neutrophil count 29.91±20.68/mm³ and females had total leukocyte count 2862.36±1970.80x10⁹/mm³, neutrophil count 38.56±21.87/mm³ 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 females in our study which was insignificant (p-value=0.80).

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.

References

20. Tahwar V, Nirni SS, Mallawarapu KM, Ramkumar A, Sinha N. Safety and tolerability of Peg-grafeel™, a pegfilgrastim, for the prophylactic treatment of chemotherapy-induced neutropenia and...


