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Frequency of Chemotherapy Induced Febrile Neutropenia

Hussain S[1], Hassan SUI[2*], Muteaullah A[3], Khan F[3] and Ahmad B[5]

[1]Specialist Registrar, Medical Oncology Unit Hayatabad Medical Complex Peshawar, Pakistan

[2]Postgraduate Trainee, Medical Oncology Unit Hayatabad Medical Complex Peshawar, Pakistan

[3]Postgraduate Trainee, Medical Unit Hayatabad Medical Complex Peshawar, Pakistan

[*]Corresponding author:

Dr. Sani Ul Hassan (MBBS, FCPS-I), Postgraduate Trainee, Medical Oncology Unit Hayatabad Medical Complex Peshawar, Pakistan, Tel: +92-321-9087290; E-mail: saniulhassan173@gmail.com

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1. Abstract

1.1. Objective: To determine the frequency of chemotherapy induced febrile neutropenia at oncology unit, Hayatabad Medical Complex, Peshawar

1.2. Materials and Methods: A total of 202 patients with solid organ or hematological malignancy were included in the study and assessed for chemotherapy induced neutropenia.

1.3. Study Design: Cross sectional (Descriptive) study

1.4. Setting: Medical Oncology Department Hayatabad Medical Complex Peshawar Pakistan.

1.5. Duration of Study: 1-6-2021 to 31-12-2021.

1.6. Results: Age range of patients varies between 5-50 years, with a mean age of 22.4 ± 11.3 years. Out of total 136 (67.3%) patients were male and 66 (32.7%) were female. Patients were followup in outpatient department for 12 months. A total of 61 (30.2%) patients were subject to high risk, 103 (51%) intermediate risk and 38 (18.8%) patients were subject to low risk of neutropenia regime of chemotherapy. Out of 202 154 (76.2%) patients having hematological malignancies, while solid organ tumour were found in 48 (23.8%) of patients. Febrile neutropenia was recorded in 68 (33.7%) of patients, while 134 (66.3%) of patients didn't gone through this condition. We stratified febrile neutropenia with chemotherapy regime and type of tumor.

1.7. Conclusion: Febrile neutropenia is a common problem in our local population with subjected to chemotherapy for solid organ or hematological malignancy and significantly common in patients with high risk of chemotherapy regime. More studies are required to develop association of its risk factors which lead to febrile neutropenia, its control and its effect on efficacy of chemotherapy.

2. Introduction

Febrile neutropenia (FN) is a serious complication of cancer chemotherapy that can lead to delays in treatment and necessary dose reductions of chemotherapy, which compromise treatment efficacy [1]. Approximately 1% of patients with cancer receiving chemotherapy develop febrile neutropenia (FN), which contributes to morbidity and mortality, and imposes substantial burdens on healthcare resource use for management of this affected population [2]. Neutropenia is characterized by a reduction in neutrophils below normal counts, usually occurring within 7 to 12 days following cancer chemotherapy [3]. It is diagnosed with a blood test that confirms an absolute neutrophil count (ANC) of less than 500 cells per microliter following cytotoxic chemotherapy, or by an ANC expected to decrease to less than 500 cells per microliter within 48 hours [4]. Due to reduced levels of neutrophils in circulation, patients with neutropenia may have an impaired ability to fight infections. Hence, even a minor infection for patients with neutropenia may become very serious. It is crucial to monitor patients for signs and symptoms of infection, which may present as fever, chills, or sweats [5]. Neutropenia may be accompanied by fever originating from an underlying infection. Fever may be the sole indicator of an underlying infection in patients with chemotherapy-induced neutropenia; other signs and symptoms of inflammation may be absent [6]. Patients with neutropenia thus must be assessed for risk of severe infection immediately at presentation of fever. Febrile neutropenia is defined by an oral temperature greater than 101ºF from a single reading or an oral temperature of at least 100.4ºF sustained over a 1-hour period or reported from 2 consecutive readings in a 2-hour period [7]. There is a clear relationship between the severity of neutropaenia (which directly influences the incidence of febrile neutropenia) and the intensity of chemo-

therapy. Currently, the different regimens are classified as producing a high risk (>20%), an intermediate risk (10%-20%) or a low risk (<10%) of febrile neutropenia [8]. In one study Chemotherapy induced neutropenia occurred in 147 (50.5%) patients over 378 (23.4%) chemotherapy cycles. Febrile neutropenia occurred in 20 (6.9%) patients over 25 (1.5%) cycles [9]. Another study revealed that febrile neutropenia (FN) episodes occurred more frequently in patients with solid tumors (57%) than those suffering from hematological malignancies and were associated more with Gram-negative bacteria infections (56.25%). However, the morality level between the two types of patient was not significantly different (14% vs. 12.5%) [10].

The present study is designed to determine the frequency of chemotherapy induced febrile neutropenia in patients receiving cancer chemotherapy at our hospital. The idea behind doing this study came into our mind by doing through literature search and observing the febrile neutropenia being the most common and most neglected problem in cancer chemotherapy patients. Moreover, the exact burden of febrile neutropenia is not known in our population due to lack of local evidence and if not treated in time, it has adverse consequences in addition to other effects of chemotherapy itself. This study will give us local magnitude of the problem and based upon results of this study, we will be able to suggest future research and policy recommendations for the control of febrile neutropenia with chemotherapy.

3. Materials and Methods

3.1. Study Design: Cross sectional (Descriptive) study

3.2. Setting: Oncology Department, Hayatabad Medical Complex, Peshawar.

3.3. Duration of Study: 1-6-2020 to 31-5-2021.

3.4. Sample Size: Sample size is 202 patients

3.5. Sample Technique: Non probability consecutive sampling

3.6. Inclusion Criteria:

- All newly diagnosed patients of any type of cancer scheduled for chemotherapy.
- Patients presenting with sudden onset of fever of more than 99^{O}F.
- Either gender
- Age group between 5 to 50 years

3.7. Exclusion Criteria

- Chronic liver disease diagnosed by history and medical records.
- History of blood transfusions in the last three months.
- History of any type of bleeding of any amount in the last three months.

4. Results

The study was conducted at Medical Oncology Department Hayatabad Medical Complex Peshawar on 202 patients subjected to chemotherapy for hematological or solid organ malignancies. Age range of patients varies between 5-50 years, with a mean age of 22.4 $\pm$ 11.3 years. Out of total 136 (67.3%) patients were male and 66 (32.7%) were female. Patients were follow up in OPD from 3- 12 months' period. Mean follow up period was 7.3 $\pm$ 2.6. A total of 61 (30.2%) patients were subject to high risk, 103 (51%) intermediate risk and 38 (18.8%) patients were subject to low risk of neutropenia regime of chemotherapy (Table 1). Out of 202 154 (76.2%) patients having hematological malignancies, while solid organ tumour were found in 48 (23.8%) of patients (Table 2). Febrile neutropenia was recorded in 68 (33.7%) of patients, while 134 (66.3%) of patients didn't gone through this condition. We stratified febrile neutropenia with chemotherapy regime and type of tumor (Table 3).

Table 1: Type of Chemotherapy Regime (N=202)

Chemotherapy Regime	Frequency	Percent
High risk	61	30.2
Intermediate risk	103	51
Low risk	38	18.8
Total	202	100

Table 2: Type of Malignancy (N=202)

Type of Malignant Tumor	Frequency	Percent
Solid organ	48	23.8
Hematological	154	76.2
Total	202	100

Table 3: Chemotherapy Regime and Type of Tumour Stratification

Chemotherapy Regime	Febrile Neutropenia		P value
	Yes	No	
High risk	35(57.4%)	26 (42.6%)	< 0.001
Intermediate risk	28 (27.2%)	75 (72.8%)	
Low risk	5 (13.2%)	33 (86.8%)	
Total	68 (33.7%)	134 (66.3%)	
Type of tumor	Febrile Neutropenia		
	Yes	No	0.179
Solid organ	20 (41.7%)	28 (58.3%)	
Hematological	48 (31.2%)	106 (68.8%)	
Total	68 (33.7%)	134 (66.3%)	

5. Discussion

Chemotherapy induced neutropenia may be more of a problem in the safe management of chemotherapy as outpatient chemotherapy

is performed more frequently. Chemotherapy induced neutropenia is a known source of major stress for physicians and patients. Febrile neutropenia is a serious clinical problem [11]. In many cases G-CSFs are administered to patients with malignancy to prevent such events. International guidelines for the use of G-CSF include the ASCO recommendations update 2006, the EORTC guideline 2010, and the NCCN guideline update 2011 [12]. Although these guidelines differ from each other slightly, including the definition or risk factors of febrile neutropenia, the clinical benefits of G-CSF use are evident in specific chemotherapy, with a threshold rate of febrile neutropenia of 20%. Identification of risk factors for febrile neutropenia may be important for the safe management of chemotherapy-induced neutropenia without the unnecessary use of G-CSFs. In our study chemotherapy induced neutropenia occurred in 33.7% of patients. The reported incidence of chemotherapy induced neutropenia varies widely. Smith et al reported chemotherapy induced neutropenia in 6–50% of patients depending on the cancer type, disease staging, patient functional status, and chemotherapy regimen [13]. Laskey et al reported that chemotherapy-induced neutropenia was observed in 43% of patients with ovarian cancer during primary chemotherapy l [14]. Shama et al reported febrile neutropenia in 12% patients with epithelial ovarian cancer during first line adjuvant chemotherapy and concluded that the rate of febrile neutropenia was higher than reported previously [15]. Laskey et al reported febrile neutropenia in 7% of patients with ovarian cancer during primary chemotherapy. In these reports febrile neutropenia occurred frequently in early cycles particularly after cycle 1. Okera et al reported that 50% of all episodes of febrile neutropenia occurred at or near the initiation of chemotherapy courses (cycles 1 and 2) in patients with solid tumors. Shama et al reported that 60% of febrile neutropenia cases occurred after cycle 1 in patients receiving first line adjuvant chemotherapy for epithelial ovarian cancer. In G-CSF guidelines such as the ASCO recommendations update 2006, the EORTC guideline 2010, and the NCCN guideline update 2011, poor performance status was not clearly identified as a risk factor for febrile neutropenia [16]. The National Chemotherapy Advisory Group (NCAG) recommendation ensures that patients receive antibiotics within 1 h of presentation (door-to needle) [17]. Mc Meekin et al reported that the source of fever was unexplained by examination or cultures in 56% of episodes in patients with gynecologic oncology [18]. Shama et al reported positive cultures in 47% of patients receiving first line adjuvant chemotherapy for epithelial ovarian cancer.

The development of myelosuppression during chemotherapy is influenced by the demographics of the patients (age, gender, and comorbidities), cancer types, stages, and characteristics of the chemotherapy regimen used. Higher incidence of chemotherapy induced febrile neutropenia (CIFN) was exhibited in the age group > 32 years. There is a clear relationship between the severity of neutropaenia (which directly influences the incidence of febrile neutropenia) and the intensity of chemotherapy. Currently, the different regimens are classified as producing a high risk (>20%), an intermediate risk (10%-20%) or a low risk (<10%) of febrile neutropenia. The causative organisms including either bacteria, fungi or viruses. The bacteria Gram positive (currently dominating) and Gram negative (Dominant in the 1970s), are usually the main microorganisms responsible for febrile neutropenia and cause complicated infections. Although the morbidity and mortality rates of febrile neutropenia have decreased over the years due to use of proper antibiotic treatment, preventive measures and use the standard risk management plan as per guidelines but it is still one of oncological emergency. Febrile neutropenia is responsible for considerable morbidity as 20%-30% of patient's present complications that require in hospital management with an overall in hospital mortality of 10% [19].

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 [20]. 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. Febrile neutropenia was found to be present in 30.9% of males and 39.4% of female patients in our study which was insignificant (p-value=0.230).

6. Conclusion

Febrile neutropenia is a common problem in our local population with subjected to chemotherapy for solid organ or hematological malignancy and is significantly common in patients with high risk of chemotherapy regime. More studies are required to develop association of its risk factors which lead to febrile neutropenia, its control and effect on efficacy of chemotherapy.

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