A RETROSPECTIVE STUDY ON THE INCIDENCE OF CHEMOTHERAPY-INDUCED NEUTROPENIA AMONG CANCER PATIENTS

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Abstract

In a tertiary care institution, a retrospective study was done on chemotherapy-induced neutropenia in cancer patients to determine oncologist practise trends in the incidence of chemotherapy-induced neutropenia during September 2021 to March 2022, at the oncology department with a validated questionnaire. The primary goal is to assess the patient-specific risk factors. Patient-specific risk factors validated include age, gender, type of cancer, diagnosis, and comorbidities. Cancer is one of the leading causes of death worldwide, the treatment of cancer is complex, and one such complication is CIN. Neutropenia is a low neutrophil count. This report outlines CIN: Neutropenia is classified by count. This study found 63 severe, 75 moderate, and 86 mild cases of neutropenia. There were 223 patients, 65 men and 158 women. With increasing age, the risks of neutropenia increased, with 19% of total cases reported in age 70 and beyond and 4% in age 1-10. Depending on adjuvant chemotherapy (11%), consolidated chemo (1%), and oral metronomic (1%). Haematological, breast, and ovarian cancers accounted for 29%, 26%, and 11% of cases respectively, but other cancers accounted for 57%. The study helped to identify risk factors of neutropenia and the efficacy of CSF in neutropenia as well as pharmacist intervention in addressing cancer patients.

Keywords

Chemotherapy induced neutropenia, Pegfilgrastim, G-CSF.

Introduction

Neutropenia is a fatal and common complication of chemotherapy caused due to administration of anti-neoplastic drugs. Febrile neutropenia is an emergency condition, which if not treated, might ultimately lead to the death of the patient. Side effects are associated with life-threatening infections, whose incidence is to be marked and treatment options are to be looked at. Hence a study was carried on determining the incidence of chemotherapy-induced neutropenia among cancer patients.

Background of the study

The previous study on the incidence of chemotherapy-induced neutropenia among cancer patients was done by several authors and gave some fruitful messages to carry out this work. Injection of pegfilgrastim is just similarly obliging just as filgrastim (7gms/d) for the management of neutropenic patients who had sessions of chemotherapy, neutropenia was taken note. It was seen that a pegfilgrastim 100 μ g/kg per session was as obliging as an infusion of filgrastim 7 μ g/kg/d in complications and its severities¹. A review that deciphered the rehashed beginning of chemotherapy-instigated neutropenia factors in breast cancer patient also rehashed beginning of neutropenia in 1 of 3 bosom disease patients had shown neutropenia while on chemotherapy².

The neutropenic rates were consistent with pegfilgrastim. No new ADRs were noticed. G-CSF stoppage was not normal but rather seemed to expand the rehashed beginning of neutropenia³. Another review which sees (G-CSF) fit by malignant growth type, which recommended G-CSF treatment, for each cycle. when the hazard of neutropenia is more than 20 %, the rehashed beginning of neutropenia among patients who halted pegfilgrastim prophylaxis. Patients who didn't take G-CSF, neutropenia contrasted by routine, these regimens have high risk of nuetropenia⁴. There was a study found that included grown-up patients with NHL who got (CHOP±R). Among patients 265 years, Grade ³/₄ neutropenia, decreased RDI, and part delays were conventional in both age social gatherings, however, patients 265 years had a higher speed of survival of neutropenia lessens⁵. The expansion of rituximab to G-CSFupheld portion thick Cleave is practical. Starter information proposes the achievability of portion thick chemotherapy for NHL with the once per cycle G-CSF, pegfilgrastim. Portion thick chemotherapy with G-CSF support created g clinical results in both more youthful and more seasoned. Stage 3 preliminaries of portion thick Hack in addition to rituximab show a similar impact⁶. In old patients, G-CSF worked on the RDI of Cleave. However, this didn't give for better general endurance⁷.

Various investigations distinguished decreased RDI, including expanded age; a 28-day schedule; CSF was regularly in the chemotherapy cycle. More established patients, overweight patients, and those getting three-drug blends or 28-day plans. Because of such dangerous elements, models ought to be capable of the specific use of strong measures to convey the full portion of chemotherapy⁸. Rituximab-containing regimens are viable and very much endured, even in pre-treated patients with reoccurring B-cell NHL⁹.

Aim

The main aim of the study is to determine the Incidence of Chemotherapy Induced Neutropenia Among cancer patients.

Objectives

This retrospective study aims to assess chemotherapy-induced neutropenia in cancer patients. First, examine patient-specific risk factors. Age, gender, and cancer type are patient-specific risk factors. Determine how oncologists manage chemotherapy-induced neutropenia. G-effectiveness CSF in neutropenic patients.

Method

The study was carried out in a tertiary care hospital, in Hyderabad for a period of 6 months duration from September 2021 to March 2022. Using the validated data collection form and patient informed consent form a total of 223 cases were collected.

Study criteria

All patients admitted to the oncology ward were included and patients admitted for daycare chemotherapy were also included in this study by choosing the age groups: 3 yrs. to 83 yrs., Both the genders and all types of cancers. Infant below 3 years, COVID19 patients, and pregnant and lactating women were excluded from the study as per the Institutional review board approval.

Study instruments

Patient medical records, Previous medical records, Prescription charts, Progress charts and Laboratory data of patients were used for the study.

Study procedure

A tertiary hospital's oncology ward hosted the trial. 223 patients with chemotherapyinduced neutropenia were included in this retrospective analysis.

Data collection

Age, sex, complaints, medical history, and ID. We collected lab testing and medication information. Neutrophil count following chemotherapy cycles, drug regimens, duration of neutropenia and number of chemo cycles, comorbidities, diagnosis, and management were collected.

Data collection procedure

Data documentation form: This patient documentation form includes the following information: Case details were collected using a validated standard form. The IRB verified and approved the patient consent form.

Results

A total of 223 patient data were collected, from a tertiary hospital. The study includes 65 male patients and 158 female patients. The data obtained was used to formulate the result.

Mean age	No. o	f X ²	Y ²	XY
	patients			
5	11	25	121	55
15	14	225	196	210
25	23	625	529	575
35	27	1225	729	945
45	30	2025	900	1350
55	35	3025	1225	1925
65	40	4225	1600	2600
75	44	5625	1936	3300
$\Sigma x = 320$	Σy= 224	$\Sigma x^2 = 16767$	Σy ² =7236	Σxy=1096
				0

The successive increase in the no. of cases reported with the increasing age groups. Linear Regression on Age Distribution



The Linear Regression on Age Distribution.

The comparison of the no. of male and female cases, reported in successive age groups. In the age group 71-80 years, the incidence of cancer among males and females is shown maximum, reported as 13 and 31.



Age And Gender Distribution

The distribution of cancer patients based on age and gender. This figure illustrates that the 70 and above age group has the highest number of cancer patients i.e., 13 males and 31 females. While age group 01-10 years has the lowest number of cancer patients i.e., 4 males and 5 females.

The rate of distribution on type of cancer based on number of patients:

The different types of cancers reported, as per the no. of patients. Maximum no. of cases was reported for haematological cancer i.e., 65(29%) followed by Breast Cancer i.e., 59(26%), Ovarian Cancer i.e., 24(10%), Lung Cancer i.e., 15(6%), Stomach Cancer i.e., 7(3%), Liver Cancer i.e., 6(2.6%), Kidney Cancer i.e., 5(2.2%). The number of patients undergoing other cancers is 42(18%).

The incidence of different types of cancers in the number of patients. According to this study, haematological cancer was seen the most i.e., in 65 patients followed by breast cancer is the second most common i.e., in 59 patients.

Chemotherapy sessions	No. Of patients attended
	chemotherapy sessions
Cycle 1	143
>Cycle 1	80

The rate of distribution on the number of chemotherapy sessions attended by the patients

The above table shows the rate of distribution of Chemotherapy sessions based on the number of patients who attended Chemotherapy sessions. In this study, Chemotherapy Cycle 1 was seen to be the most i.e., 143(64%) Cancer patients attended. While 80(36%) of Cancer patients attended more than 1 Chemotherapy session. Patients that attended Chemotherapy sessions more than 1 time are 80.

Type of chemo	Number of patients		
Adjuvant chemo	135		
Neoadjuvant chemo	32		
Induction chemo	29		
Palliative chemo	21		
Maintenance chemo	4		
Consolidation chemo	1		
Oral metronic chemo	1		

The rate of distribution on type of chemotherapy based on number of cancer patients

The table represents the treatment approach for cancer i.e., the type of chemotherapies, as depicted. Among these, CIN was observed more in adjuvant chemotherapy with an incidence of 11% and the least were seen for consolidation chemotherapy and oral metronic chemotherapy -0.45%.

The rate of distribution of type of chemotherapy is based on the number of cancer patients.

The treatment approach of cancer i.e., the type of chemotherapies, as depicted. Among these, CIN was observed more in adjuvant chemotherapy with an incidence of (135)11%, and the least was seen for consolidation chemotherapy and oral metronic chemotherapy (1) -0.45%. The rate of appearance of neutropenia in number of patients

The classification of neutropenia shows the maximum number of patients had severe neutropenia i.e., 86. Moderate neutropenia was seen in 75 patients and mild neutropenia was seen in 63 patients.



The Rate of Appearance of Neutropenia in the Number of Patients Based on Absolute

Neutrophil Count

The classification of absolute neutrophil count is based on Severe, Moderate and Mild neutropenia occurrence in cancer patients. Among them, 86 patients showed <200-500 cells/mm³ neutrophils, exhibiting Severe Neutropenia followed by 75 patients who showed

600-1000 cells/mm³ neutrophils exhibiting Moderate Neutropenia and 63 patients showing 1100-1500 cells/mm³ neutrophils exhibiting Mild Neutropenia.

The rate of appearance of neutropenia among cancer patients based on grades:

The rate of appearance of Neutropenia in cancer patients is based on grades. Grade 4 Neutropenia was observed to have occurred in most of the patients i.e.,86 which marks as Severe Neutropenia followed by Grade 3 i.e.,75 then Grade 2 i.e.,63.



The Rate of Appearance of Neutropenia Among Cancer Patients Based on Grades.

The classification of Neutropenia among cancer patients based on grades. According to this study, Grade 4CIN was most prevalently seen in 86 patients, followed by Grade 3 CIN in 75 patients then Grade 2 CIN in 63 patients.

AGE	GROUP	MALE	FEMALE	X 1 ²	X 2 ²
(Years)					
1-10		4	7	16	49
11-20		4	10	16	100
21-30		7	15	49	75
31-40		7	20	49	400
41-50		9	21	81	441
51-60		9	26	81	676
61-70		12	28	144	784
71-80		13	31	169	961
		$\Sigma x_1 = 65$	Σx ₂ =158	$\Sigma x_1^2 = 605$	$\Sigma x_2^2 = 3,485$

T-Test on Age and Gender Distribution Based on Number of Cancer Patients:

The calculated 't' value for the mean of the number of cases in both gender is greater than the tabulated 't' value. The difference between the number of cases in both gender means is significant. The null hypothesis states that the number of cases in both genders means is rejected at p < 0.01. Therefore, the number of cases is significantly high in females than in males.

Discussion

The occurrence of neutropenia cancer patients has been reported as common toxicity of chemotherapy. The study targets Haematological, Breast, and Ovarian cancer primarily among which the maximum cases of neutropenia due to chemo was reported in Haematological (29%) followed by Breast (26%), Ovarian Cancer (10.75%), Lungs (6.7%), Stomach (3%), liver (3), Kidney (2.8) while other cancers reported 42% of cases. The maximum of CIN in patients was majorly reported in the age group 71 (19%) and above, while the minimum was seen in 1-10 Years old patients (4%). Among males and females, the study shows that Neutropenia was reported more in females - 158 cases, while male patients were – 65 of total 223 Cases. The incidence of CIN in patients was majorly reported in the first cycle of chemo. Depending upon Neutrophil count severity of neutropenia was established, and the statistics are as follows:

Severe [ANC 200-500 CELLS/MCU] – 39%

Moderate [ANC 600-1000] - 34%

Mild [ANC 1100-1500] – 28%

The Treatment approach for cancer (Type of Chemo) is *Adjuvant, Neoadjuvant, Induction, Palliative, Maintenance, Consolidation and Oral metronic*, among these CIN, was observed more in Adjuvant Chemotherapy with an incidence of 11% and least incidence was equally reported in consolidation Chemo and Oral metronic – 0.45%.

Conclusion

Cancer is one of the leading causes of death worldwide, the treatment of cancer is complex, and one such complication is CIN. Neutropenia is a low count of a type of WBC – Neutrophil. This study gives an overview of CIN. Neutropenia can be categorized into 3 depending on the count. In this study we noticed – Severe neutropenia cases were 63, Moderate were 75 and mild were 86. A total of 223 patients were recorded, among which male patients were 65 and female patients we 158. From the data a fashion was established with increasing age, the chances of neutropenia accelerated, about 19% of total cases were reported in the last age group pf the study, i.e., 70 and Above, Least No. of cases were seen in age 1-10 only 4%. Depending Upon the extent of cancer and severity, the type of chemo that resulted in more cases of neutropenia was adjuvant chemotherapy (11%), consolidated chemo and oral metronic resulted in 1% of cases. Primarily, haematological, breast and ovarian cancer were seen with incidences of 29%, 26% and 11% respectively however other cancers in the study comprised about 57% of cases cumulatively. The study aids to identify risk factors of neutropenia and the efficacy of G-CSF in neutropenia as well as pharmacist intervention in addressing cancer patients.

References

- Holmes FA, Jones SE, O'Shaughnessy J, Vukelja S, George T, Savin M, Richards D, Glaspy J, Meza L, Cohen G, Dhami M, Budman DR, Hackett J, Brassard M, Yang BB, Liang BC. Comparable efficacy and safety profiles of once-per-cycle pegfilgrastim and daily injection filgrastim in chemotherapy-induced neutropenia: a multicenter dose-finding study in women with breast cancer. Ann Oncol. 2002 Jun;13(6):903-9. doi: 10.1093/annonc/mdf130. PMID: 12123336.)
- Lustberg MB. Management of neutropenia in cancer patients. Clin Adv Hematol Oncol. 2012 Dec;10(12):825-6. PMID: 23271355; PMCID: PMC4059501.
- Varughese T, Joseph J, Menon R. Efficacy of Jackfruit365[™] Green Jackfruit Flour Fortified Diet on Pegfilgrastim to Prevent Chemotherapy-Induced Leukopenia, Irrespective of Tumor Type or Drugs Used-A Retrospective Study. Biomolecules. 2020 Feb;10(2): E218. DOI: 10.3390/biom10020218. PMID: 32024271; PMCID: PMC7072368.
- Mehta HM, Malandra M, Corey SJ. G-CSF and GM-CSF in Neutropenia. J Immunol. 2015 Aug 15;195(4):1341-9. doi: 10.4049/jimmunol.1500861. PMID: 26254266; PMCID: PMC4741374.
- Pettengell R, Johnsen HE, Lugtenburg PJ, Silvestre AS, Dührsen U, Rossi FG, Schwenkglenks M, Bendall K, Szabo Z, Jaeger U. Impact of febrile neutropenia on R-CHOP chemotherapy delivery and hospitalizations among patients with diffuse large Bcell lymphoma. Support Care Cancer. 2012 Mar;20(3):647-52. doi: 10.1007/s00520-011-1306-6. Epub 2011 Nov 20. Erratum in: Support Care Cancer. 2013 Feb;21(2):653. Johnson, Hans E [corrected to Johnsen, Hans E]. PMID: 22101611; PMCID: PMC3271211.
- Dotan E, Aggarwal C, Smith MR. Impact of Rituximab (Rituxan) on the Treatment of B-Cell Non-Hodgkin's Lymphoma. P T. 2010 Mar;35(3):148-57. PMID: 20442809; PMCID: PMC2844047.
- Hopman RK, DiPersio JF. Advances in stem cell mobilization. Blood Rev. 2014 Jan;28(1):31-40. doi: 10.1016/j.blre.2014.01.001. Epub 2014 Jan 14. PMID: 24476957; PMCID: PMC4068706.
- Bennett CL, Djulbegovic B, Norris LB, Armitage JO. Colony-stimulating factors for febrile neutropenia during cancer therapy. N Engl J Med. 2013 Mar 21;368(12):1131-9. doi: 10.1056/NEJMct1210890. Erratum in: N Engl J Med. 2013 Jul 18;369(3):293. Dosage error in article text. PMID: 23514290; PMCID: PMC3947590.

 Huang et al. Expenditure and fnancial burden for the diagnosis and treatment of colorectal cancer in China: a hospital-based, multicenter, cross-sectional survey, Chin J Cancer (2017) 36:41 DOI 10.1186/s40880-017-0209-4.