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Evaluation of hematological side effects during chemotherapy in a tertiary care hospital

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Abstract
Objective: The study is aimed to evaluate the hematological side effects during chemotherapy in a tertiary care hospital.
Materials and Methods: This study was a Prospective observational study. The study was conducted at the Oncology Department of Muthoot Healthcare Hospital Pvt Ltd., Kozhencherry, Pathanamthitta, Kerala. A sample size of 200 cancer patients undergoing chemotherapy in the hospital was selected. All subjects were provided with a brief introduction regarding the study and the confidentiality of the data. Relevant information was collected according to the approved pre-designed data collection form. Haematological parameters of the subject was collected to evaluate the myelosuppression.
Result: During the study period around 200 cancer patients were found to be admitted in oncology department. The study revealed that all subjects showed haematological side effects. After analyzing the haematological side effects i.e., leukopenia, neutropenia, anemia, thrombocytopenia and lymphocytopenia post tenth day of five cycles of chemotherapy, Grade 1 anemia was found to be more frequent and its incidence increases with chemotherapy whereas other haematological side effects remained at very minimal levels.
Conclusion: Cancer is a major concern of current society. By using Common Terminology Criteria for Adverse Events (CTCAE) grade 1 anemia was the most frequently reported haematological side effects. In this study, the effective management of myelosuppression by providing supportive measures like GCSF, whole blood transfusion helped in maintaining the blood counts within normal limits.

Keywords: cancer, chemotherapy, myelosuppression, hematological side effects, anemia

1. Introduction

Cancer is the second leading cause of death globally after cardiovascular diseases. Cancer patients generally have a poor prognosis in developing countries, including India, because of relatively low cancer awareness and late diagnosis when compared to patients in developing countries [1]. Chemotherapy involves the use of drugs to destroy cancer cells. It works by destroying cancer cells that grow rapidly [2]. Unfortunately, chemotherapy also affects normal cells that grow rapidly, such as blood cells forming in the bone marrow, cells in the hair follicles or cells in the mouth and intestines [3]. The most common dose-limiting side effect of the majority of chemotherapeutic drugs is myelosuppression which has the potential for infectious and hemorrhagic complications[4]. Proliferating progenitor cells that produce the mature red and white blood cells and platelets found in the peripheral circulation are destroyed due to the destructive effect of chemotherapy. The individual's blood cell count is decreased as immature cells in the marrow are destroyed and preexisting mature cells are eliminated [5]. Chemotherapy-inducedneutropenia is a common complication and is one of the major dose-limiting toxicities in cancer treatment. It is associated with increased mortality, morbidity and treatment costs. Therefore, neutropenia is a clinically relevant problem that affects the patient's quality of life [6]. Colony-stimulating factors (CSFs) reduce the incidence, duration, and severity of chemotherapy-induced neutropenia, and associated complications by promoting hematopoietic recovery after chemotherapy. Pegfilgrastim was approved by the U.S. Food and Drug Administration (FDA) in January 2002 to decrease the incidence of infection, as manifested by neutropenic patients receiving myelosuppressive anticancer drugs. Single subcutaneous (SC) injection of 6 mg administered once per chemotherapy cycle is the recommended dosage of pegfilgrastim. It should not be administered in the period between 14 days before and 24 hours after administration of cytotoxic chemotherapy because of the potential for an increase in sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy [7]. Anemia is common in patients with cancer and is a frequent complication of myelosuppressive chemotherapy. The severity of anemia depends on the extent of disease and the intensity of treatment. Repeated cycles of chemotherapy may impair erythropoiesis. The symptoms of anemia can reduce Quality Of Life (QOL). The management of anemia resulting from myelosuppressive chemotherapy depends on its severity. Treatment options include RBC transfusion, epoetin alfa administration, or its combination [8]. Thrombocytopenia is a common problem in patients with cancer. It can result from chemotherapy or radiation therapy, or from the cancer itself. Thrombocytopenia creates a number of problems in the treatment of a cancer patient. Clinicians have varied responses to thrombocytopenia in a cancer patient. More effective regimens with thrombocytopenic toxicity may be avoided. One method is to reduce the dose intensity of chemotherapy or radiation. For some patients, treatment of the underlying cause of thrombocytopenia may work. Platelet transfusion is a readily available treatment [9].

The Common Terminology Criteria for Adverse Events is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term. The CTCAE displays Grades 1 through 5 with unique descriptions of severity for each AE based on this general guideline.

- Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age- appropriate instrumental Activities of Daily Living (ADL).
- Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL.
- Grade 4: Life-threatening consequences; urgent intervention indicated.
- Grade 5: Death related to AE. (Death is not appropriate for some AEs and therefore is not an option.) [10]

Table 1: Ctcae Grading For Haematologic Adverse Events [14].

Hematologic AE	Grade 1	Grade 2	Grade 3	Grade 4
Anemia (Hb level)	<LLN-10g/dL	<10-8g/dL	<8-6.5g/dL	<6.5g/dl
Thrombocytopenia (platelet count)	<LLN- 75,000/µL	<75,000- 50,000/µL	<50,000-25,000 /µL	<25,000/µL
Lymphopenia (lymphocyte count)	<LLN -800/ µL	<800- 500/µL	<500-200/µL	<200/µL
Neutropenia (ANC)	<LLN- 1,500/µL	<1,500-1,000/µL	<1,000-500/µL	<500/µL
Leukopenia (total WBC count)	<LLN- 3000/µL	<3,000-2,000/µL	<2,000-1,000/µL	<1,000/µL

AE= adverse event; ANC= absolute neutrophil count; LLN= lower limit of normal; WBC= white blood count

In our study, we used the above CTCAE to assess the incidence of anemia, neutropenia, leukopenia, throm bocytopenia and lymphocytopenia after chemotherapy.

2. Methodology

The study was a Prospective observational study which was conducted at the Oncology

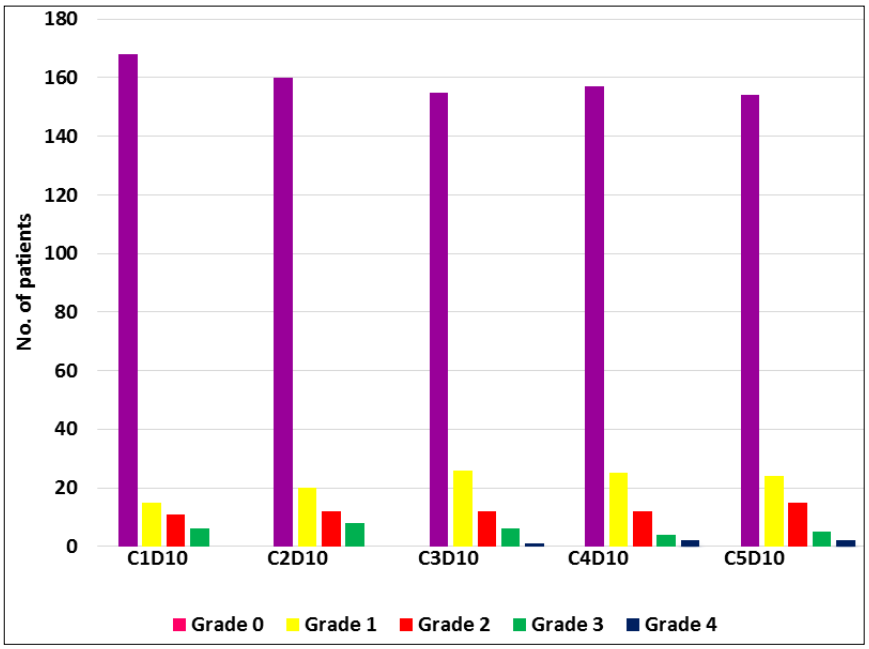
Department of a tertiary care hospital Pvt Ltd., Kozhencherry, Pathanamthitta, Kerala after obtaining the approval from the Institutional Ethical Committee of the hospital. Study period was 6 months and was done in 200 cancer patients undergoing chemotherapy in the hospital during this period. Patients between the age group of 18-90, both gender, IP and OP patients undergoing chemotherapy was chosen for the study. The data were collected from inpatient prescription records at the hospital in a specially designed data collection form. Each prescription was critically studied for the patient's demographic details such as patient's name, age, gender, etc. Name of the drug, dose, dosage form, frequency, duration were noted. All subjects were provided with a brief introduction regarding the study and the confidentiality of the data.

A written Informed Consent printed in their understandable language was obtained from the patient or care-giver, if the subject was unable to give the same. Haematological parameters of the subject was individually collected to evaluate the myelosuppression.

3. Result

Table 2: Grading of Haematological Side Effects

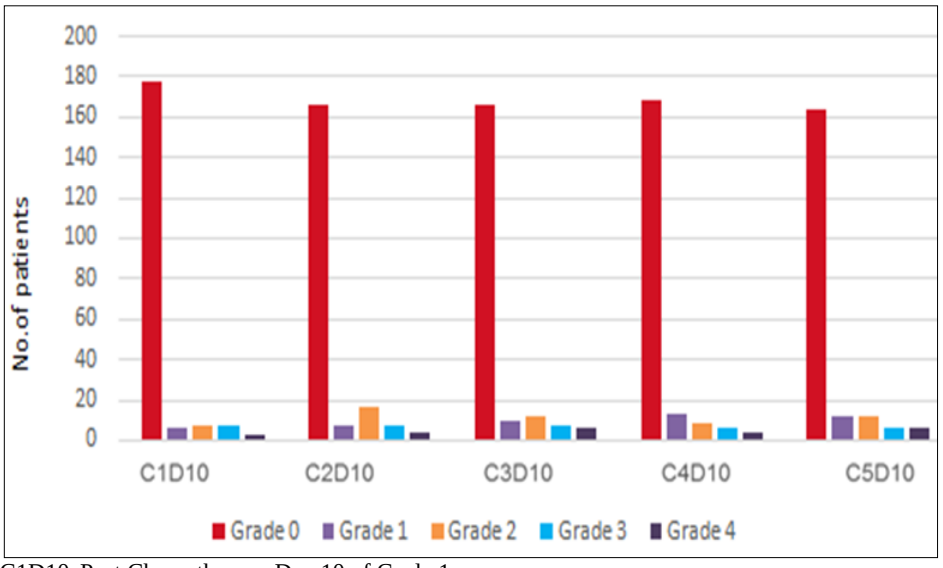
Sl. No	Conditions	Grading	C1d10	C2d10	C3d10	C4d10	C5D10
1	Leukopenia	Grade 0	168	160	155	157	154
		Grade 1	15	20	26	25	24
		Grade 2	11	12	12	12	15
		Grade 3	6	8	6	4	5
		Grade 4	0	0	1	2	2
2	Neutropenia	Grade 0	178	167	166	169	164
		Grade 1	6	7	9	13	12
		Grade 2	7	16	12	8	12
		Grade 3	7	7	7	6	6
		Grade 4	2	3	6	4	6
3	Anemia	Grade 0	40	37	65	41	49
		Grade 1	85	85	88	93	101
		Grade 2	64	56	37	53	41
		Grade 3	10	19	9	13	9
		Grade 4	1	3	1	0	0
4	Thrombocytopenia	Grade 0	163	150	158	146	147
		Grade 1	35	43	40	48	49
		Grade 2	0	4	2	3	2
		Grade 3	1	1	0	2	2
		Grade 4	1	2	0	1	0
5	Lymphocytopenia	Grade 0	158	156	154	82	80
		Grade 1	16	17	19	38	32
		Grade 2	18	19	18	46	53
		Grade 3	7	6	5	30	30
		Grade 4	1	2	4	4	5



C1D10 -Post Chemotherapy Day10 of Cycle 1
C2D10 - Post Chemotherapy Day 10 of Cycle 2
C3D10 - Post Chemotherapy Day10 of Cycle 3
C4D10 - Post Chemotherapy Day 10 of Cycle 4
C5D10 - POST Chemotherapy Day 10 of Cycle 5

Fig 1: Grading of Leukopenia

Among 200 study subjects enrolled, leukopenia on post tenth day of chemotherapy was found to be: In cycle 1 grade0 is more frequent (84%) followed by grade1 (7.5%), grade 2 (5.5), grade 3 (3%), grade 4 (0%).
In cycle 2 grade 0 is more prominent (80 %) preceded by grade 1(10%), grade 2 (6%), Grade 3(4%), grade 4(0%).
In cycle3 grade0 is more recurrent (77.5%) trailed by grade1 (13%), grade 2 (6%), grade 3(3%), grade 4 (0.5%).
In cycle 4 grade 0 is more frequent (78.5%) followed by grade 1 (12.5%), grade 2(6%), grade 3(2%), grade 4(1%).
In cycle 5 grade 0 is more prominent (77%) preceded by grade 1(12%), grade 2 (7.5%), 3(2.5%), grade 4(1%).



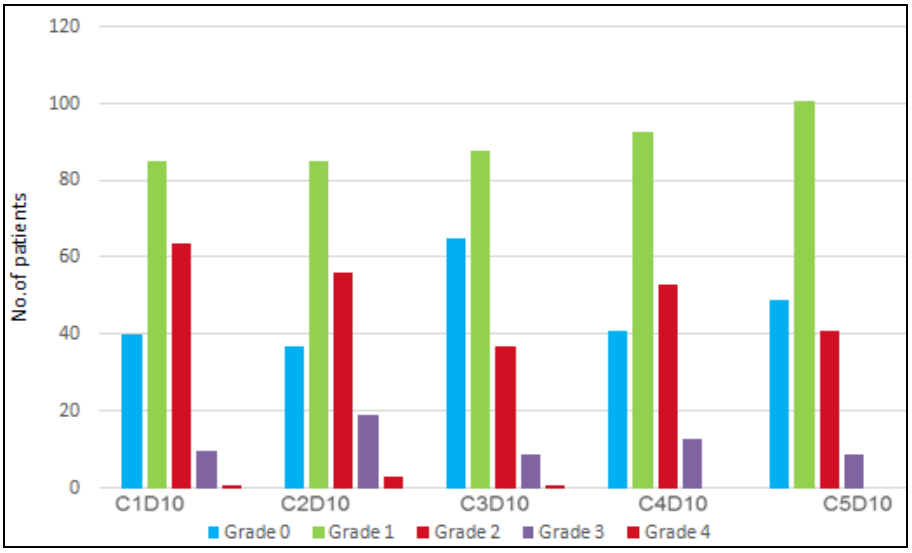
C1D10- Post Chemotherapy Day 10 of Cycle 1
C2D10- Post Chemotherapy Day 10 of Cycle 2
C3D10- Post Chemotherapy Day10 of Cycle 3
C4D10- Post Chemotherapy Day 10 of Cycle 4
C5D10- Post Chemotherapy Day 10 of Cycle5

Fig 2: Grading of Neutropenia

Among 200 study subjects enrolled, neutropenia on post tenth day of chemotherapy was found to be: In cycle 1 grade 0 is more prominent (89%) followed by grade 1 (3%), grade2 (3.5%), grade 3(3.5%) grade 4 (1%)
In cycle 2 grade 0 is more prominent (83.5%) preceded by grade1 (3.5%), grade 2 (8%), grade 3(3.5%), grade 4(1.5%).
In cycle 3 grade 0 is more frequent (83%) followed by grade 1 (4.5%), grade 2(6%), grade 3(3.5%), grade 4(3%).

In cycle 4 grade 0 is more frequent (84.5%) followed by grade 1 (6.5%), grade 2(2%), grade 3 (3%), grade 4 (2%).

In cycle 5 grade 0 is more frequent (82%) followed by grade 1(6%), grade 2(6%), grade 3(3%), grade 4(3%).



C1D10- POST CHEMOTHERAPY DAY 10 OF CYCLE 1
C2D10- POST CHEMOTHERAPY DAY 10 OF CYCLE 2
C3D10- POST CHEMOTHERAPY DAY10 OF CYCLE 3
C4D10- POST CHEMOTHERAPY DAY 10 OF CYCLE 4
C5D10- POST CHEMOTHERAPY DAY 10 OF CYCLE5

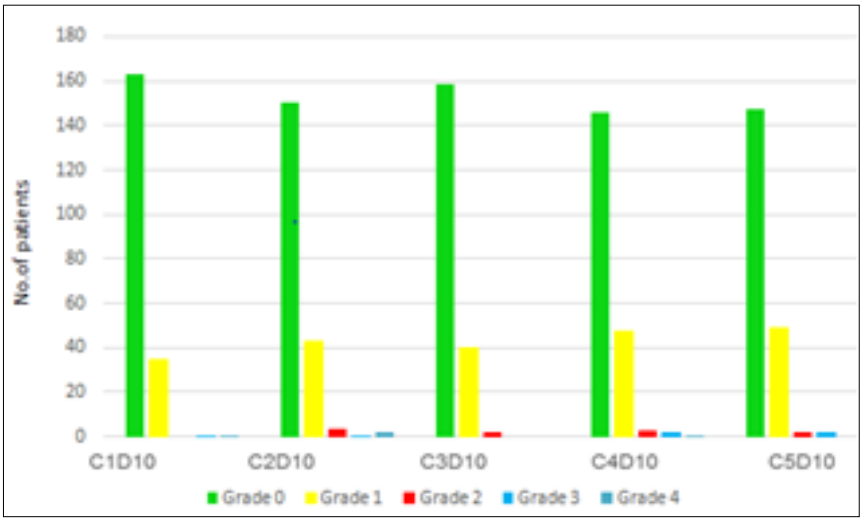
Fig 3: Grading of anemia

Among 200 study subjects enrolled, anemia on post tenth day of chemotherapy was found to be: In cycle 1 grade 1 is more frequent (42.5%), followed by grade 0(20%), grade 2 (32%), grade 3 (5%), grade 4(0.5%) In cycle 2 grade 1 is more frequent (42.5%),followed by grade 0 (18.5%),grade 2 (28%),grade 3 (9.5%),grade 4 (1.5 %).

In cycle 3 grade 1 is more frequent (44%), followed by grade 0 (32.5%), grade 2(18.5%), grade 3 (4.5%), grade 4(0.5%).

In cycle 4 grade 1 is more frequent (46.5%), followed by grade 0 (20.5%), grade 2(26.5%), grade 3 (6.5%), grade 4(0%).

In cycle 5 grade 1 is more frequent (50.5%), followed by grade 0(24.5%), grade 2 (20.5%), grade 3 (4.5%), grade 4 (0%).

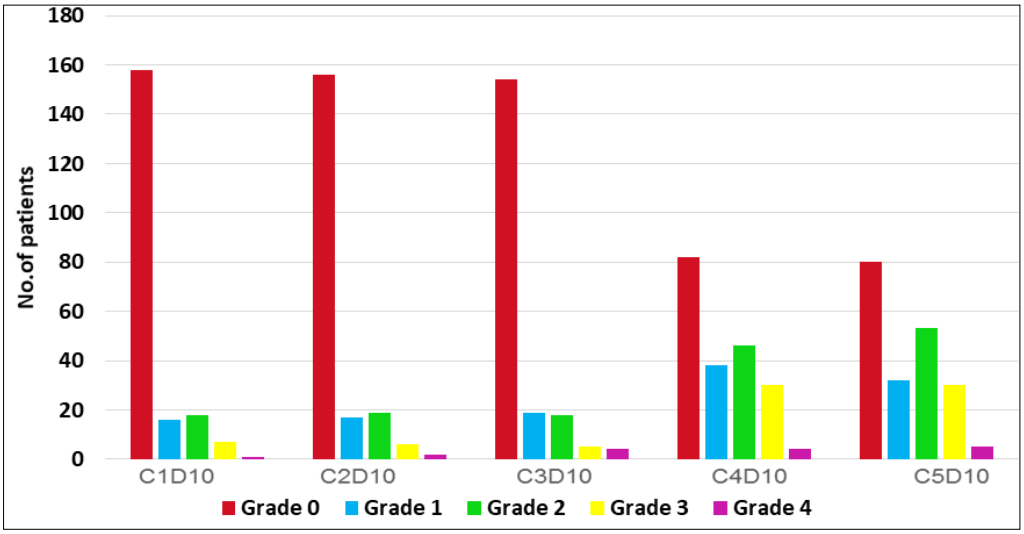


C1D10- Post Chemotherapy day 10 OF CYCLE 1
C2D10- Post Chemotherapy Day 10 OF CYCLE 2
C3D10- Post Chemotherapy Day10 OF CYCLE 3
C4D10- Post Chemotherapy Day 10 OF CYCLE 4
C5D10- Post Chemotherapy Day 10 OF CYCLE5

Graph 4: Grading of Thrombocytopenia

Among 200 study subjects enrolled, thrombocytopenia on post tenth day of chemotherapy was found to be: In cycle 1 grade 0(81.5%) is more frequent, followed by grade 1 (17.7%), grade 2(0%), grade 3(0.5%), grade 4(0.5%). In cycle 2 grade 0 (75%) is more frequent, followed by grade 1 (21.5%), grade 2(2%), grade 3(0.5%), grade 4(1%).In cycle 3 grade 0 (79%) is more frequent, followed by grade 1(20%), grade 2(1%)In cycle 4 grade 0 (73%) is more

frequent, followed by grade 1(24%), grade 2(1.5), grade 3(1%), grade 4(0.5%) In cycle 5 grade 0(73.5%) is more frequent, followed by grade 1(24.5), grade 2(1%), grade 3 (1%)



C1D10-Post Chemotherapy Day 10 OF CYCLE 1
C2D10-Post Chemotherapy Day 10 OF CYCLE 2
C3D10-Post Chemotherapy Day10 OF CYCLE 3
C4D10-Post Chemotherapy Day 10 OF CYCLE 4
C5D10-Post Chemotherapy Day 10 OF CYCLE5

Graph 5: Grading of Lymphocytopenia

Among 200 study subjects enrolled, lymphocytopenia on post tenth day of chemotherapy was found to be:
In cycle 1 grade 0 (79%) is more frequent, followed by grade 1(8%), grade 2 (9%), grade 3(3.5%), grade 4 (0.5%)
In cycle 2 grade 0 (78%) is more frequent followed by grade 2 (9.5%), grade 1 (8.5%), grade 3 (3%), grade 4(1%)
In cycle 3 grade 0 (77%) is more frequent followed by grade 1(9.5%), grade 2 (9%), grade 3 (2.5%), grade 4(2%)
In cycle 4 grade 0 (41%) is more frequent followed by grade 2(23%), grade 1 (19%), grade 3 (15%), grade 4(2%)
In cycle 5 grade 0(40%) is more frequent followed by grade 2 (26.5), grade 1 (16%), grade 3 (15%), grade 4 (2.5%)

4. Discussion

Cancer is one of the major health issue which has a great impact on society. Many treatment options are available, including chemotherapy, radiation therapy, immunotherapy, surgery. Wide range of potent chemotherapeutic agents are now available for the treatment of cancer. These potent cytotoxic drugs act on both cancerous cells and healthy living cells. It makes the healthy living cells vulnerable to the cytotoxic action of anticancer drugs.

Evaluation of Haematological Side Effects

From 200 subjects enrolled in the study all subjects showed haematological side effects. After analyzing the haematological side effects i.e., leukopenia, neutropenia, anemia, thrombocytopenia and lymphocytopenia post tenth day of five cycles of chemotherapy, Grade 1 anemia was found to be more frequent whereas other haematological side effects remained at very minimal levels. Most of the patients did not experience leukopenia, neutropenia, thrombocytopenia and lymphocytopenia as a result of the use of granulocyte colony stimulating factor (GCSF-filgrastim and pegfilgrastim) and other supportive measures. Anemia is frequent in cancer patients and its incidence Increases with chemotherapy. According to Xu H *et al.*, [11] 58% of the study population have grade 1 anemia. This results strongly agree with our study. Higher frequency of anemia can be due to the fact that chemotherapy affects all rapidly dividing cells, particularly sensitive erythroid progenitor cells in a process known eryptosis. Eryptosis and resultant erythrocyte deficiency contribute to anemia.

5. Conclusion

By using Common Terminology Criteria for Adverse Events (CTCAE) grade 1 anemia was the most frequently reported haematological side effects. In this study, the effective management of myelosuppression by providing supportive measures like GCSF, whole blood transfusion helped in maintaining the blood counts within normal limits.

Limitations

- Lack of patient compliance in filling the questionnaire.
- Due to the short period of time, follow up could not be done.
- Difficulty to differentiate myelosuppression caused due to chemotherapy and cancer.

6. Acknowledgement

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Conflict of interest

The Author(s) declare(s) that they have no conflicts of interest to disclose.

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Authors' Contributions
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