

CLINICAL IMPACT OF CHEMOTHERAPY ON BLOOD CELL PARAMETERS IN KASHMIR CANCER PATIENTS

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DOI: <https://doi.org/10.5281/zenodo.17670732>

How to cite this Article: Zeeqad Zehra*, Dr. Pankaj Kaul, K.S. Rana. (2025). CLINICAL IMPACT OF CHEMOTHERAPY ON BLOOD CELL PARAMETERS IN KASHMIR CANCER PATIENTS. European Journal of Biomedical and Pharmaceutical Sciences, 12(11), 317–326.

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Article Received on 21/09/2025

Article Revised on 11/10/2025

Article Published on 01/11/2025

ABSTRACT

Cancer treatments continue to be the backbone of cancer care, but the harmful side effect of chemotherapy is systemic harm to the bone marrow and can cause myelosuppression that can result in anemia, neutropenia and thrombocytopenia. Myelosuppression is one of the most common and dangerous adverse reactions to cancer treatment; it often results in treatment interruptions, dose reduction, and an increase in morbidity and mortality. This study investigated the long-term effects of chemotherapy on the hematologic profile of patients who received cancer treatment in the Kashmir region and identified the frequency, severity, and factors that contribute to chemotherapy induced cytopenias. The study involved serial analysis of complete blood counts taken at different times during treatment to identify changes in the hematologic parameters, including Red Blood Cell Indices, Hemoglobin Concentration, White Blood Cells, Neutrophils, and Platelets. The chemotherapeutic drugs evaluated for their hematologic toxicity included the commonly used chemotherapeutic drug classes, i.e., Alkylating Agents, Antimetabolites, Platinum Compounds, Anthracyclines, and Taxanes. The study found that the occurrence of chemotherapy-induced myelosuppression was both high and regimen-dependent with nadir values typically being observed between days 7-14 of each cycle of treatment. Neutropenia was identified as the earliest and clinically most relevant cytopenia due to its association with febrile neutropenia and the subsequent development of infections, while anemia and thrombocytopenia were identified as contributing to patient fatigue, transfusion dependency, and bleeding risks, respectively. The degree of cytopenia was found to be influenced by the patients' pre-treatment bone marrow reserve, nutritional status, tumor type, and total cumulative exposure to chemotherapy. The use of supportive therapies such as G-CSF therapy and blood product transfusions was variable based upon the clinical requirements and availability of resources, indicating the need for the establishment of regionally appropriate management protocols.

KEYWORDS: Chemotherapy-induced cytopenias, Haematological toxicity, Myelosuppression, Cancer patients, Kashmir region.

1. INTRODUCTION

Chemotherapy has been at the core of treating malignant conditions for many years; however, it can also be harmful to other areas of the body, especially the hematopoietic system, which is responsible for producing all the blood cells that we need to live.

Chemotherapy is known to cause myelosuppression (a decrease in the bone marrow's ability to make new blood cells), which is caused by the damage to both the bone marrow stem cells and stromal cells from chemotherapy. As a result of myelosuppression, patients experience problems with haematopoiesis (the process of making

blood cells), reduced immune function, problems with delivering oxygen throughout the body and problems with the coagulation of blood.^[1] In addition to the above-mentioned haematologic side effects, they are among the most common dose limiting toxicities seen with chemotherapy and may lead to delays in treatments, reduction in doses of chemotherapy, the need for hospitalizations and an increase in mortality.^[2] It is very important to understand how the hematologic system is affected by chemotherapy so that the intensity of treatment can remain high while providing better outcomes for the patient.

Alkylating agents, antimetabolites, platinum compounds, anthracyclines, and taxanes all interfere with either the replication of DNA in rapidly dividing hematopoietic progenitors or the formation of microtubules and, therefore, suppress cell proliferation in a lineage-independent manner.^[3] These actions produce predictable nadirs usually occurring between days 7 to day 14 after each cycle of chemotherapy, and the degree of recovery depends on the regimen, previous treatments, and the host factors. The clinical impact of CIC is very important because the risk of developing febrile neutropenia (FN) and subsequent sepsis increases with neutropenia, the risk of fatigue and requirement for transfusions increases with anemia, and the risk of bleeding increases with thrombocytopenia.^[4] According to international guidelines, the use of risk adapted prophylaxis with granulocyte-colony stimulating factors (G-CSFs) should be considered when the risk of FN greater than 20% based on the specific chemotherapy regimen, in addition to using validated algorithms for managing acute complications.^[5]

India's cancer burden will continue to grow over the next decade, and according to the National Cancer Registry Programme (NCRP/ICMR) there will be an increase in the incidence of cancers up to the mid-2020s (ESMO Clinical Practice Guidelines, 2019). Emerging studies have shown unique demographics, environmental exposures, and barriers to healthcare within the Kashmir Valley, indicating a need for regionally-based data regarding tolerance to chemotherapy and hematologic toxicities to direct local practice and policy (NCCN, 2020).

The degree to which chemotherapy affects the hematologic system varies significantly based on the chemotherapy regimen, the number of chemotherapy cycles administered, the tumor type, the baseline marrow reserve, nutritional status, and concurrent therapies.^[7] Although predictive models for the occurrence of chemotherapy induced cytopenias and prophylactic strategies such as G-CSF or thrombopoietin receptor agonist exist, the effectiveness of these strategies in resource limited regions such as Kashmir has not been well documented. Local data will provide a framework to balance the efficacy, cost, and safety of supportive care plans.

With this context, the primary purpose of the current study was to examine longitudinal changes in hematologic parameters in cancer patients undergoing chemotherapy in the Kashmir region. Specifically, the study measured the incidence and severity of cytopenias as related to chemotherapy cycle and regimen, identified the predictors of hematologic risk that would be relevant to the clinical practice of the region, and provided actionable data to support refinement of supportive care pathways, direction for development of transfusion and prophylaxis policies, and improvement of the selection of chemotherapeutic regimens for the Kashmiri patient population.^[8]

This paper is divided into four main sections. Section 2 reviews existing literature regarding chemotherapy-induced hematologic toxicities, including the mechanisms underlying them, their clinical relevance, and their management. Section 3 describes the methodology of the study, including the study design, the population of patients studied, the criteria for inclusion and exclusion of patients, the methods of collecting data, the instruments utilized, and the statistical methods used to assess the changes in the hematologic parameters of the patients undergoing chemotherapy. Section 4 provides the results of the study, including demographic and baseline characteristics, the sequential changes in the hematologic parameters of the patients, the incidence and grades of hematologic toxicities experienced by the patients, and the frequency of supportive care measures implemented. Section 5 discusses the results obtained in the study in relation to those previously reported in the literature, emphasizes the clinical implications of the study, and considers possible reasons for the variability in the hematologic responses and the patterns of toxicities observed in the study population. Section 6 summarizes the findings of the study, emphasizes their clinical relevance, and indicates the necessity for region-specific approaches to mitigate chemotherapy-induced hematologic toxicities.

2. BACKGROUND

Chemotherapy is one of the major treatments used to cure a wide variety of cancers. It works by using cytotoxic drugs, which are designed to kill the rapidly growing malignant cells. However, cytotoxic drugs will also kill other rapidly growing normal tissues, notably those involved in the hematopoietic system, where blood cells are produced (NCCN Guidelines, 2022). Hematologic toxicity, which includes alterations in counts of red blood cells (RBC), white blood cells (WBC), platelets and haemoglobin levels, is one of the most common and clinically important adverse effects of chemotherapy. Thus, an understanding of these toxicities is essential to prevent treatment-related morbidities, provide appropriate supportive care and ensure patient safety.

Chemotherapy induced bone marrow damage leading to reduced RBC counts and haemoglobin concentration is

referred to as chemotherapy-induced anaemia. Agents such as alkylating drugs (cyclophosphamide), antimetabolites (methotrexate), and platinum-based drugs (cisplatin) either directly damage mature erythrocytes or inhibit hematopoietic stem cell proliferation. Clinical manifestations include fatigue, weakness, pallor, and diminished tolerance to exercise. Treatment strategies include erythropoiesis-stimulating agents (ESAs), iron supplements and red blood cell (RBC) transfusions. Regular measurement of haemoglobin levels is essential to quickly diagnose and manage anaemia to maintain adequate oxygen delivery capacity.

WBC especially neutrophils, are critical for the defense mechanisms against infection. Cytotoxic chemotherapy drugs (fluorouracil, 5-FU, doxorubicin, and paclitaxel) can decrease leukopoiesis, leading to decreased WBC and neutrophil counts (leukopenia and neutropenia) and increasing the risk of infections. A significant complication in oncology is febrile neutropenia, which is caused by the increased risk of infection. Use of granulocyte-colony stimulating factors (G-CSFs) to preventively and therapeutically decrease the risk of infection and allow continuation of full-dose chemotherapy regimens.

Platelets are important for haemostasis, and thrombocytopenia secondary to chemotherapy can lead to bleeding, bruising, and abnormal prolongation of coagulation time. Impaired megakaryocyte function and platelet production by drugs (carboplatin, cyclophosphamide, and vincristine) can cause severe thrombocytopenia. Platelet transfusions or thrombopoiesis-stimulating agents may be required to restore haemostasis. Therefore, it is crucial to continuously monitor platelet counts to evaluate hemorrhagic risk during chemotherapy.

Hematologic toxicity from chemotherapy correlates with the dose and frequency of the chemotherapeutic regimen. Increasing or decreasing the dose of chemotherapy, or extending the interval between cycles will extend the period of hematologic toxicity, and delay the rate of hematologic recovery. Patient's general health status, and comorbidities can affect inter-cycle recovery. As a result, dose reduction, delaying a cycle, and administering growth factor support to facilitate the administration of chemotherapy while minimizing toxicity.

Neutropenia due to chemotherapy (CIN) is considered the most dangerous and potentially fatal complication of cytotoxic chemotherapy, since patients are at high risk of developing febrile neutropenia (FN) and sepsis. Granulocyte colony-stimulating factors (G-CSFs) like filgrastim and pegfilgrastim have reduced the incidence and duration of neutropenia, thus improving survival rates.^[11] More recent studies including large scale trials of mecapegfilgrastim, demonstrate the safety and

efficacy of G-CSF primary prophylaxis.^[12] Also, newer agents, such as trilaciclib—a CDK4/6 inhibitor—have demonstrated their potential in preventing multilineage myelosuppression when administered prior to chemotherapy, indicating a shift towards the active prevention of myeloprotection.^[13]

Another common debilitating toxicity of chemotherapy is chemotherapy-induced anaemia (CIA) that impacts both tolerance of treatment and quality of life. Erythropoiesis-stimulating agents (ESAs), such as epoetin alfa and darbepoetin alfa, increase haemoglobin levels and reduce transfusion dependency, although caution should be exercised due to potential thromboembolic and tumor-related risks. Recent studies emphasize the need to address concomitant iron deficiency via intravenous iron supplementation in order to enhance ESA response and diminish transfusion dependency. Additionally, CIA has been strongly correlated with fatigue and poor physical performance; therefore, correction of CIA has been found to improve overall well-being of patients.^[14]

Thrombocytopenia associated with agents such as carboplatin, gemcitabine and cisplatin increases bleeding risk and requires dose reduction or transfusion support. The development of thrombopoietin receptor agonists (TPO-RAs) such as romiplostim and eltrombopag offer new therapeutic options. TPO-RAs stimulate platelet production and have been shown to reduce transfusion dependency in patients with cancer.^[15]

3. MATERIALS AND METHODS

3.1.1. Equipment and Instruments Used

A number of laboratory apparatuses and analytical tools were employed in this investigation to provide an accurate assessment of the haematology data collected from the subjects. The haematology analysers provided all necessary blood counts and haematological analyses that are required to assess the blood. A variety of laboratory tools and supplies were utilised during the venous collection process to collect blood samples through the use of sterilized syringe barrels and needles, vacutainer tubes and various other consumables (i.e., alcohol swab, gauze pad, etc.) to ensure an aseptic environment. Blood samples that had been collected were then refrigerated under controlled temperature conditions to help prevent deterioration of the samples prior to their analysis. All laboratory glassware (test tubes, pipettes, etc.) used in the collection, processing, and preparation of the blood samples was standard laboratory materials.

3.1.2. Study Design, Population, Inclusion and Exclusion Criteria

The research methodology used a prospective cohort study model that was carried out during multiple chemotherapy cycles. Cancer patients were followed prospectively for all subsequent treatment cycles from commencement of chemotherapy, assessing

haematological parameters at defined points in time both before and after each cycle to assess temporal trends. The study group consisted of 100 cancer patients representing a variety of ages, enrolled from a number of different health care facilities and hospitals. Participants included adults between the ages of 15 and 75 years old with either solid tumors or hematologic cancers undergoing chemotherapy as a component of their treatment plan. All participants were asked to give their informed consent for participation and were free of previous histories of hematologic disorders of significant severity (i.e. aplastic anemia, myelodysplasia). Patients with other serious comorbid conditions (i.e., advanced cardiovascular disease, liver disease, kidney disease) as well as pregnant or lactating women and individuals who are not undergoing chemotherapy (i.e. radiation therapy) were also excluded from the study in order to ensure the reliability and validity of haematology assessments.

3.1.3. Sampling Technique and Sample Collection and Processing

To recruit cancer patients in order to gather data on their hematologic responses to chemotherapy, a convenience sampling method was used to identify participants who were visiting an oncology clinic or hospital. An attempt was made to select participants from the oncology population who would be representative of the greater cancer patient population so that the results could be generalized. Samples of blood were obtained from participants at two specific times prior to the start of chemotherapy and after each chemotherapy cycle, at predetermined intervals; these time frames allowed for monitoring of hematologic response to chemotherapy. Using sterile Vacutainer needles, venous blood was taken with strict adherence to aseptic techniques to minimize the potential for contamination and to maintain the integrity of the blood samples. Blood samples were analyzed using automated hematologic analyzers to measure key hematologic variables such as red blood cell (RBC) counts, white blood cell (WBC) counts, platelet counts and hemoglobin (Hb) concentrations. These analyses provided consistent and accurate data, which enabled comparisons of the hematologic status of participants throughout the course of the chemotherapy regimen.

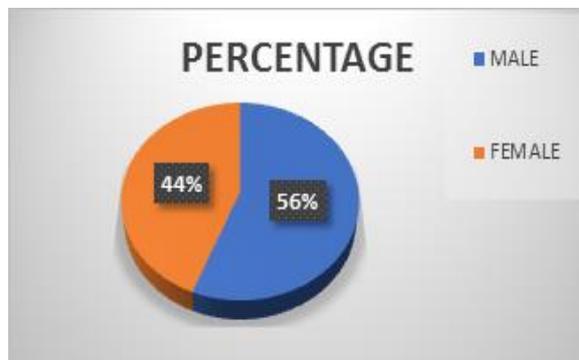
3.1.4. Statistical Analysis

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS, version XX) or equivalent statistical software. Descriptive statistics, including mean, standard deviation, median, and interquartile range, were used to summarize patient demographics and baseline haematological parameters. Comparative analyses were performed using paired t-tests to compare pre- and post-chemotherapy haematological parameters within the same patients, while the Wilcoxon signed-rank test was applied for non-parametric data. Analysis of variance (ANOVA) with repeated measures, or Friedman's test for non-parametric variables, was employed to evaluate changes across

multiple chemotherapy cycles. Correlation analyses using Pearson's or Spearman's methods were conducted to assess the relationships between chemotherapy dosage, number of cycles, and the extent of haematological toxicity. The Chi-square test was utilized to determine associations between categorical variables, such as chemotherapy drug type and the presence of severe haematological toxicity. Additionally, multivariate regression analyses were performed to identify independent predictors of chemotherapy-induced haematological toxicity, considering variables such as age, sex, cancer type, chemotherapy regimen, and comorbidities. A p-value of less than 0.05 was considered statistically significant for all analyses.

4. RESULTS

To recruit cancer patients in order to gather data on their hematologic responses to chemotherapy, a convenience sampling method was used to identify participants who were visiting an oncology clinic or hospital. An attempt was made to select participants from the oncology population who would be representative of the greater cancer patient population so that the results could be generalized. Samples of blood were obtained from participants at two specific times prior to the start of chemotherapy and after each chemotherapy cycle, at predetermined intervals; these time frames allowed for monitoring of hematologic response to chemotherapy. Using sterile Vacutainer needles, venous blood was taken with strict adherence to aseptic techniques to minimize the potential for contamination and to maintain the integrity of the blood samples. Blood samples were analyzed using automated hematologic analyzers to measure key hematologic variables such as red blood cell (RBC) counts, white blood cell (WBC) counts, platelet counts and hemoglobin (Hb) concentrations. These analyses provided consistent and accurate data, which enabled comparisons of the hematologic status of participants throughout the course of the chemotherapy regimen.



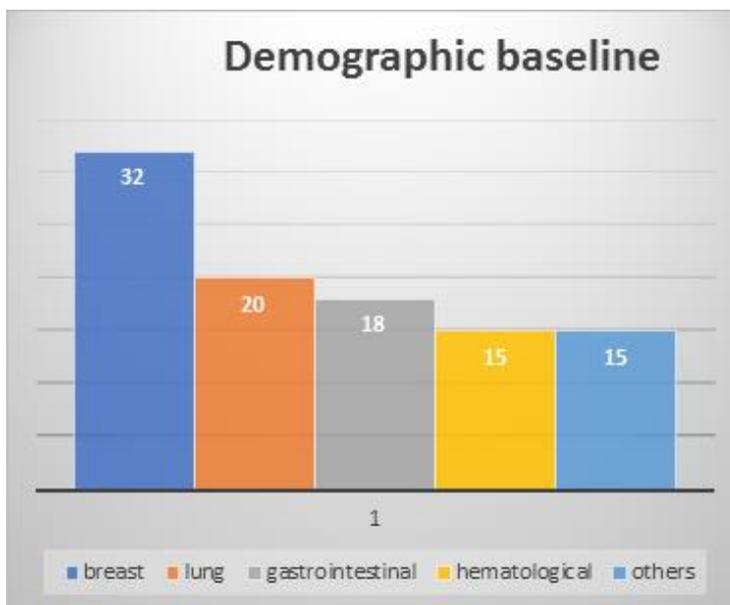
Graph 1: Demographic Chart Based on Gender.

Interpretation

Most of the patients were middle-aged and slightly more male than female; breast cancer was the most common malignancy among all malignancies seen in the study group.

Table 1: Baseline Demographic Characteristics of Patients (n=100).

Variable	Frequency (%) / Mean \pm SD
Age (years)	48.6 \pm 12.3
Gender (Male/Female)	56 (56%) / 44 (44%)
Cancer Type	
Breast	32 (32%)
Lung	20 (20%)
Gastrointestinal	18 (18%)
Haematological	15 (15%)
Others	15 (15%)
ECOG Performance Status (0–2)	1.4 \pm 0.6
Mean BMI (kg/m ²)	24.1 \pm 3.2

**Graph 2: Demographic characteristics of Cancer patients.****Table 2: Baseline Haematological Parameters Prior to Chemotherapy.**

Parameter	Mean \pm SD	Reference Range
Haemoglobin (g/dL)	12.4 \pm 1.8	12–16
WBC ($\times 10^9/L$)	7.2 \pm 2.1	4–11
Platelets ($\times 10^9/L$)	248 \pm 65	150–400
Neutrophils (%)	62 \pm 8	50–70
Lymphocytes (%)	28 \pm 7	20–40

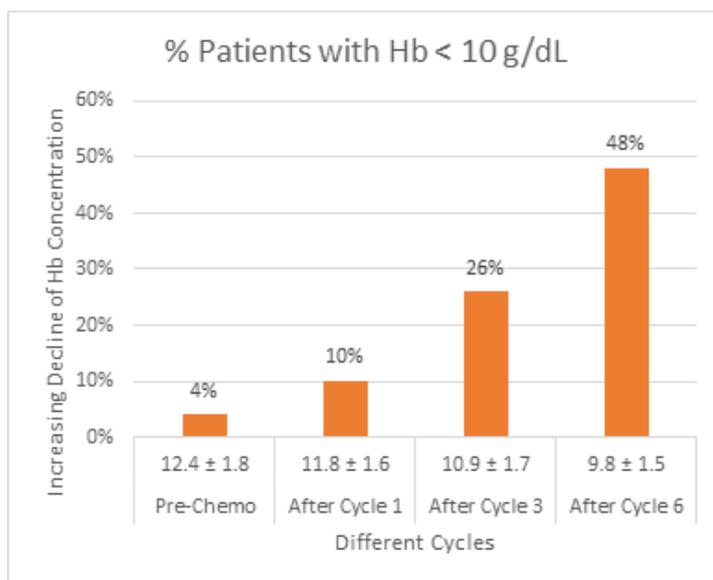
Interpretation

Prior to the onset of chemotherapy, baseline values in nearly all cases were near normal; thus, the study group's demographic and clinical parameters were relatively consistent. The study group's relative consistency in

terms of both demographic and clinical parameters provides a reliable base from which to assess subsequent hematologic effects of chemotherapy throughout each cycle.

Table 3: Haemoglobin Trends During Chemotherapy Cycles.

Cycle	Mean Hb (g/dL) \pm SD	% Patients with Hb < 10 g/dL
Pre-Chemo	12.4 \pm 1.8	4%
After Cycle 1	11.8 \pm 1.6	10%
After Cycle 3	10.9 \pm 1.7	26%
After Cycle 6	9.8 \pm 1.5	48%



Graph 3: Haemoglobin decline across chemotherapy cycles.

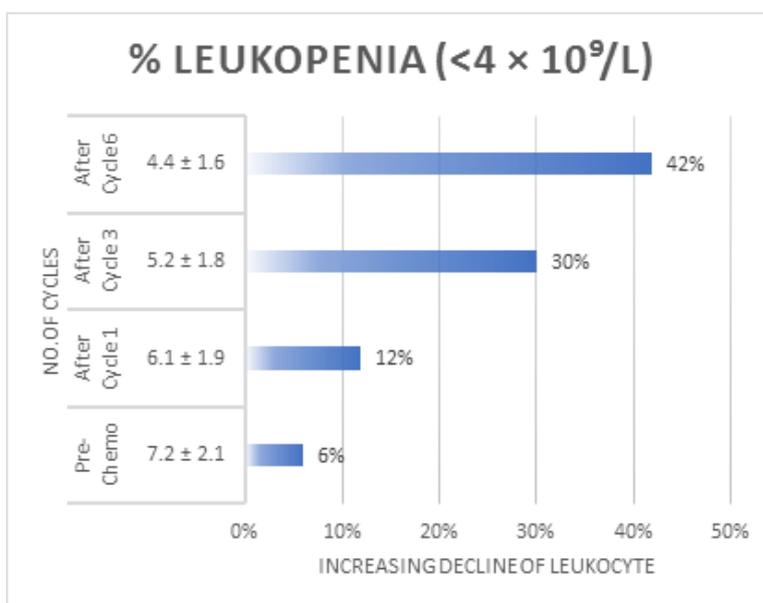
Interpretation

Haemoglobin levels were shown to be progressively reduced through each subsequent round of chemotherapy; and almost 50% of the patients developed

anaemia due to chemotherapy at or before the end of the sixth round of chemotherapy. This trend demonstrates an accumulative haematologic (blood) effect of chemotherapy on erythropoiesis.

Table 4: White Blood Cell Count Trends During Chemotherapy.

Cycle	Mean WBC ($\times 10^9/L$) \pm SD	% Leukopenia ($< 4 \times 10^9/L$)
Pre-Chemo	7.2 \pm 2.1	6%
After Cycle 1	6.1 \pm 1.9	12%
After Cycle 3	5.2 \pm 1.8	30%
After Cycle 6	4.4 \pm 1.6	42%



Graph 4: White blood cell decline along different chemotherapy cycles.

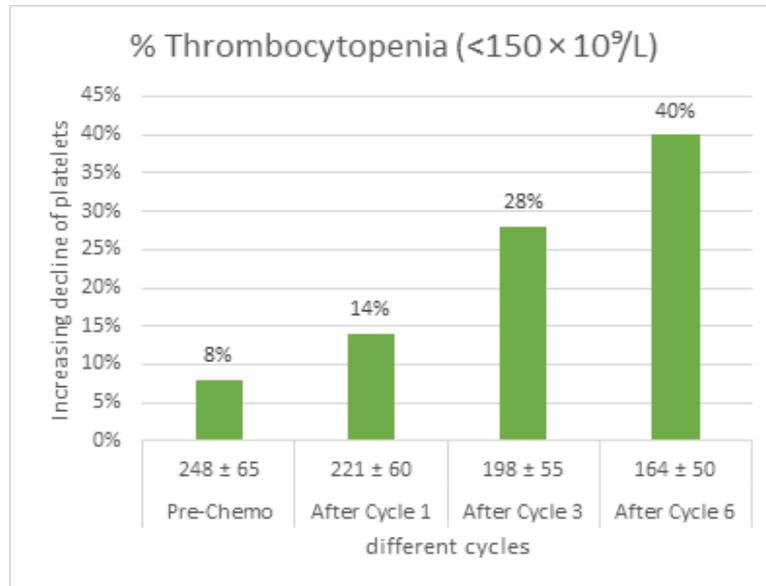
Interpretation

The WBC counts showed a statistically significant decline in WBC counts from cycle to cycle of chemotherapy. Leukopenia occurred in approximately

42% of patients by the end of the sixth round of chemotherapy. The trend shows that there is a significant myelosuppressive effect of chemotherapy on white blood cells.

Table 5: Platelet Count Variations During Chemotherapy.

Cycle	Mean Platelets ($\times 10^9/L$) \pm SD	% Thrombocytopenia ($<150 \times 10^9/L$)
Pre-Chemo	248 \pm 65	8%
After Cycle 1	221 \pm 60	14%
After Cycle 3	198 \pm 55	28%
After Cycle 6	164 \pm 50	40%

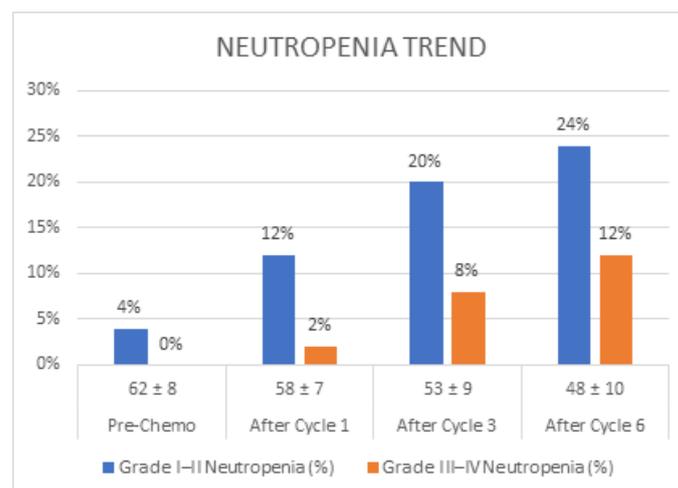
**Graph 5: Thrombocyte decline during chemotherapy cycles.****Interpretation**

The administration of chemotherapy resulted in a continuous reduction in platelet count that led to thrombocytopenia in approximately one-third of the patient population, and an additional one-third of the

patients fell below the previously established safe threshold for platelet count. These results suggest that the cumulative myelosuppressive effect of chemotherapy has a significant impact on the production of platelets.

Table 6: Neutropenia Incidence During Chemotherapy.

Cycle	Mean Neutrophil (%) \pm SD	Grade I-II Neutropenia (%)	Grade III-IV Neutropenia (%)
Pre-Chemo	62 \pm 8	4%	0%
After Cycle 1	58 \pm 7	12%	2%
After Cycle 3	53 \pm 9	20%	8%
After Cycle 6	48 \pm 10	24%	12%

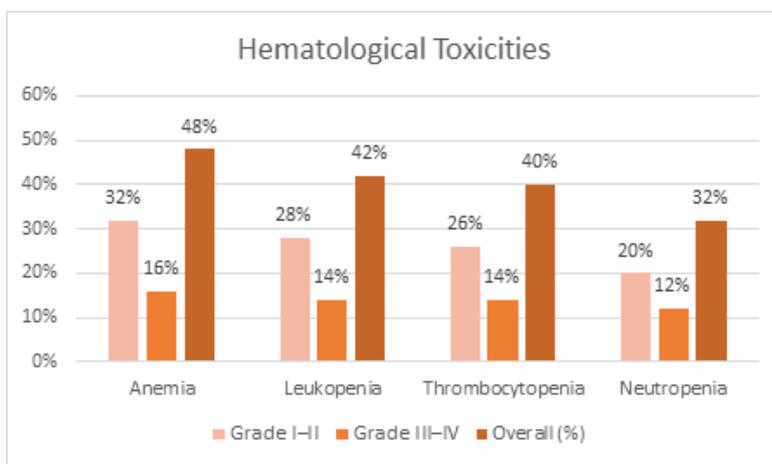
**Graph 6: Neutrophil reduction trend in different chemotherapy cycles.**

Interpretation

There were significant concerns about the risk of infectious complications due to the high number of patients who experienced Grade III-IV neutropenia after their sixth chemotherapy cycle. The severity of this event is underscored by the fact that there are no effective treatments available to prevent or treat the complications of neutropenia, other than providing intensive monitoring and prophylaxis to reduce the risks associated with infection.

Table 7: Frequency of Haematological Toxicities by WHO Grade.

Toxicity	Grade I-II	Grade III-IV	Overall (%)
Anaemia	32%	16%	48%
Leukopenia	28%	14%	42%
Thrombocytopenia	26%	14%	40%
Neutropenia	20%	12%	32%



Graph 7: Different Haematological toxicities.

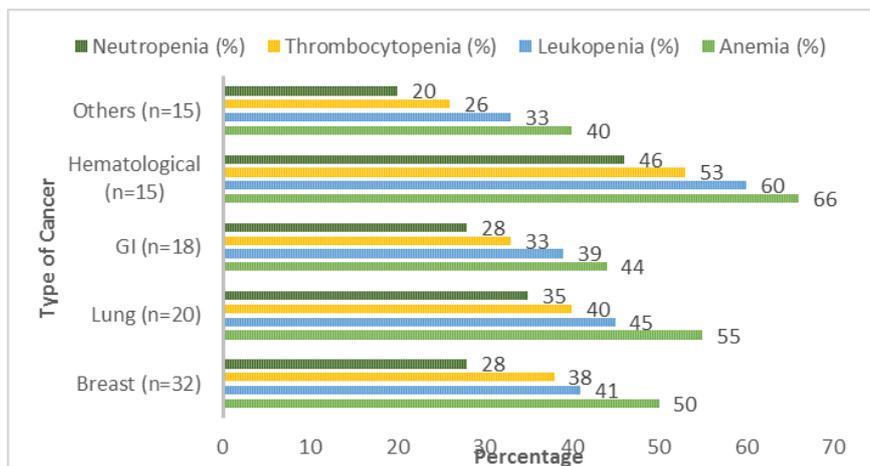
Interpretation

Anemia and leukopenia were identified as the two most common hematologic adverse events, with the majority of patients experiencing these conditions at the grade 3 or higher level. The prevalence of anemia and leukopenia

among patients receiving chemotherapy indicates the profound myelosuppressive effects of chemotherapy and the importance of establishing and maintaining close hematologic surveillance of patients receiving this type of treatment.

Table 8: Comparison of Haematological Toxicities Across Cancer Types.

Cancer Type	Anaemia (%)	Leukopenia (%)	Thrombocytopenia (%)	Neutropenia (%)
Breast (n=32)	50	41	38	28
Lung (n=20)	55	45	40	35
GI (n=18)	44	39	33	28
Haematological (n=15)	66	60	53	46
Others (n=15)	40	33	26	20
Total %	51	43	38	31



Graph 8: Distribution of toxicities across cancer types.

Interpretation

Those suffering from Haematologic Malignancies were significantly affected by hematologic toxicities than all other subgroups of cancer (solid tumor), which indicates that their bone marrow is more vulnerable as well as susceptible to chemotherapy induced myelosuppression.

Table 9: Supportive Interventions Required During Chemotherapy.

Intervention	Frequency (%)
Blood transfusions	22 (22%)
Platelet transfusions	10 (10%)
G-CSF administration	18 (18%)
Hospitalization for febrile neutropenia	8 (8%)

Interpretation

Therefore, a significant number of patients required supportive care interventions, which highlights the severity of the clinical impact that chemotherapy induced hematologic toxicities have on a patient's health status, and the need for active management strategies to minimize adverse effects of treatments.

5. CONCLUSION

This current study examined the influence of chemotherapy on the hematologic health of cancer patients from the Kashmir area. The current study demonstrated a progressive reduction of several critical hematologic values (e.g., hemoglobin, WBCs, neutrophils, platelets) throughout successive chemotherapy regimens. Anemia and Leukopenia were the most common side effects noted during this study, with a large percentage of patients experiencing severe toxicity. Neutropenia and Thrombocytopenia were found to be significant complications as well. The study further illustrated the varying degrees of marrow sensitivity between different cancer types; specifically, patients diagnosed with hematologic malignancies showed increased susceptibility to myelosuppression compared to those diagnosed with solid tumors.

These study findings demonstrate that myelosuppression due to chemotherapy continues to represent one of the major challenges to patient management, and the need for various forms of supportive care (i.e., blood transfusions, G-CSF, hospitalizations for febrile neutropenia). These findings illustrate the necessity of monitoring patient hematologic status on an ongoing basis, the identification of cytopenias at their earliest point in time, and the implementation of both preventative and therapeutic measures designed to reduce morbidity and allow continued uninterrupted chemotherapy.

Overall, regionalized approaches to minimizing hematologic toxicities through preventive care, optimal scheduling of chemotherapy regimens, and evidence-based supportive care will be important to the overall

safety and efficacy of chemotherapy among cancer patients from Kashmir.

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