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Research Article

Association Between Chemotherapy Regimens and Neutropenia Severity Among Cancer Patients: A Cross-Sectional Study

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Abstract

Chemotherapy-induced neutropenia (CIN) is a prevalent and potentially severe complication in cancer patients, significantly increasing the risk of infection, treatment delays, and overall morbidity. Despite its clinical importance, there is a paucity of data regarding the patterns and severity of neutropenia in relation to specific chemotherapy regimens in diverse oncology settings. A cross-sectional study was conducted involving 98 cancer patients diagnosed with neutropenia following chemotherapy at three oncology centers in Iraq. The data were collected retrospectively from the patients' medical records and included demographic characteristics, the number of chemotherapy cycles at the onset of neutropenia, the severity of neutropenia, the status of chemotherapy continuation, and the specific treatment regimens administered. The association between chemotherapy regimens and severity of neutropenia was analyzed using chi-square tests. The majority of patients were female (68.4%) and over 50 years of age (75.5%). Hematological malignancies were predominant (81%). Neutropenia was most frequently observed during the second cycle of chemotherapy (47%) and was typically of moderate severity (68.4%). Notwithstanding the occurrence of neutropenia, the administration of chemotherapy was pursued in 70.5% of cases. The most frequently observed association between the regimen and neutropenia was the Hodgkin lymphoma protocol (doxorubicin, bleomycin, vinblastine, and dacarbazine), which accounted for 14.3% of cases and exhibited a significant association with the severity of neutropenia ($p = 0.012$). Furthermore, the analysis revealed statistically significant associations between specific regimens and both acute lymphoblastic leukemia ($p = 0.031$) and non-Hodgkin lymphoma ($p = 0.044$). This study underscores the critical need for regimen-specific risk assessment and individualized management strategies for neutropenia in cancer patients. The identification of high-risk regimens can inform proactive monitoring and supportive interventions, with the aim of minimizing complications and optimizing treatment continuity.

Keywords: *Neutropenia, Chemotherapy, Hematological Malignancy, Oncology, Supportive Care.*

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Introduction

Neutropenia, a condition characterized by a reduced absolute neutrophil count, is one of the most frequent and clinically significant adverse effects observed in cancer patients undergoing cytotoxic chemotherapy (Fioredda et al., 2023). Neutrophils, a vital component of the innate immune response, play a central role in the body's first line of defense against bacterial and fungal infections. A decrease in neutrophil levels, specifically an absolute neutrophil count (ANC) of less than 1,500 cells/mm³, results in immune system compromise. This, in turn, leads to an increased susceptibility to infections and complicates the patient's treatment trajectory. Chemotherapy-induced neutropenia (CIN) has been shown to predispose patients to opportunistic infections and to significantly disrupt treatment continuity by necessitating reductions in dosage, delays in subsequent chemotherapy cycles, or complete cessation of treatment. These disruptions can result in suboptimal treatment outcomes, disease progression, increased hospitalization, and elevated cancer-related mortality rates (Boccia et al., 2022).

The severity of neutropenia is commonly categorized as mild (absolute neutrophil count [ANC] 1,000–1,500 cells/mm³), moderate (500–1,000 cells/mm³), or severe (<500 cells/mm³). Febrile neutropenia, a life-threatening complication involving fever and neutropenia, is the most urgent clinical manifestation. In such cases, immediate medical intervention is imperative, typically involving the administration of empirical broad-spectrum antibiotics and hematopoietic growth factors such as granulocyte-colony stimulating factor (G-CSF) to stimulate neutrophil production and reduce the duration and severity of neutropenia (Min & Byeon, 2025). The economic burden associated with CIN and febrile neutropenia (FN) is substantial. Numerous studies have highlighted increased rates of emergency department visits, intensive care unit admissions, and extended inpatient stays, especially in resource-limited settings where timely interventions may be delayed.

A multitude of interconnected factors contribute to an individual patient's risk of developing neutropenia during chemotherapy. These include patient characteristics such as age, gender, nutritional status, baseline bone marrow function, and co-existing comorbidities, as well as treatment-specific variables like chemotherapy dosage, combination of agents used, and treatment intensity. Genetic predispositions affecting drug metabolism pathways and bone marrow sensitivity also play a critical role in modulating individual susceptibility to neutropenia. For instance, elderly patients are particularly vulnerable due to decreased bone marrow reserve and altered pharmacokinetics of chemotherapeutic agents. Similarly, female patients and those with low body surface area have been shown to experience higher rates of CIN (Neesanun, 2022). Furthermore, the specific type of malignancy has been observed to exert a substantial influence on the risk of developing neutropenia. Hematological malignancies, which require more aggressive and myelosuppressive chemotherapy protocols, are typically associated with a higher incidence of both neutropenia and febrile neutropenia (FN) compared to solid tumors.

A mounting body of research has evidenced that patients diagnosed with hematologic cancers, most notably those with leukemias and lymphomas, demonstrate an elevated propensity to encounter severe and protracted instances of neutropenia, a consequence of both disease-related marrow involvement and the intensive nature of their treatment regimens (Jia et al., 2024). Furthermore, age has been identified as a consistent predictor, with older adults demonstrating a higher propensity for neutropenia and poorer outcomes when complications such as febrile neutropenia (FN) arise. However, despite these known associations, considerable gaps persist in the literature concerning the real-world patterns of chemotherapy use, timing and severity of neutropenia episodes, and clinical management practices across different healthcare settings, especially in developing countries.

In a multitude of low- and middle-income countries (LMICs), including Iraq, the prevalence of cancer is increasing. However, there is a paucity of comprehensive data regarding treatment-related complications, such as neutropenia. The dearth of structured national registries and the variability in treatment protocols across oncology centers further complicate efforts to assess and compare outcomes. Furthermore, the majority of extant studies are characterized by several limitations. Specifically, these studies are either single-center, narrowly focused on specific cancers such as breast or lung cancer, or lack the capacity to differentiate between neutropenia grades or chemotherapy cycles. These limitations, in turn, result in a restriction of the applicability of these studies for informing clinical guidelines. There is an urgent need for context-specific data that reflect the diversity of patient populations, cancer types, and chemotherapy regimens in use.

Therefore, the objective of this study is to address these critical knowledge gaps by analyzing the clinical and demographic characteristics associated with chemotherapy-induced neutropenia among cancer patients across three major oncology centers in Iraq. The objective of this research is to provide valuable insights that can inform personalized risk stratification strategies and evidence-based interventions to improve patient outcomes. To this end, the research examines the distribution of neutropenia severity, the timing of its onset across chemotherapy cycles, and its association

with specific treatment regimens (Bakirtas et al., 2022). The study's findings offer a valuable contribution to the field of oncology by enhancing the understanding of the epidemiology of neutropenia within the regional context. Furthermore, the study supports the development of standardized monitoring and management protocols, which are tailored to high-risk subgroups, thereby facilitating more effective treatment and management of patients.

Methods

Study Design and Setting

The present study employed a cross-sectional design to investigate the relationship between chemotherapy regimens and the severity of neutropenia in cancer patients. The research was carried out at three major oncology centers in Iraq: the Oncology Teaching Hospital, Al-Amal National Hospital, and the Hematology and Transplant Center (HTC). These centers were purposively selected due to their status as national referral institutions, their capacity to provide advanced oncological care, and the diversity of cancer cases they manage. This multi-center approach was essential to enhance the external validity and generalizability of the findings, ensuring that the study captured a wide spectrum of clinical practices and patient demographics across the Iraqi oncology landscape (Lone et al., 2024; Salako et al., 2021).

Study Population and Eligibility Criteria

The target population comprised adult patients (aged 18 years and older) with a confirmed diagnosis of cancer who developed neutropenia following chemotherapy. Neutropenia was defined in accordance with standard hematological criteria based on absolute neutrophil count. In order to be included in the study, patients had to have clear documentation of chemotherapy administration and a corresponding neutropenia event. Exclusion criteria were applied to patients whose medical records lacked essential information or who did not provide consent for their data to be used for research purposes. The establishment of these criteria was driven by the necessity to maintain methodological rigor and to ensure that only reliable and complete data were analyzed.

Data Collection

The data were subsequently extracted from the patients' medical records using a standardized data collection form that was developed by the research team. The form was subjected to a pilot test to assess its consistency and comprehensiveness. The extracted data included demographic characteristics (age, gender, and ethnicity), clinical parameters such as the number of chemotherapy cycles completed at the time neutropenia developed, the severity of neutropenia (categorized as mild, moderate, or severe), and whether chemotherapy was continued or discontinued after neutropenia onset. Furthermore, detailed information regarding the specific chemotherapy regimens received was documented, including multi-drug combinations utilized for various malignancies such as Hodgkin lymphoma, acute lymphoblastic leukemia (ALL), and non-Hodgkin lymphoma (NHL). This level of detail enabled a thorough examination of the risk of regimen-specific neutropenia.

Data Analysis

The statistical analysis was conducted using IBM SPSS Statistics version 26. Descriptive statistics, incorporating frequencies and percentages, were calculated to summarize demographic and clinical characteristics of the study population. Categorical variables, including neutropenia severity and chemotherapy regimens, were subjected to a chi-square test to assess associations with statistically significant differences. A p-value of less than 0.05 was considered to be indicative of statistical significance. This analytical approach enabled the researchers to identify meaningful patterns and potential risk factors associated with neutropenia severity in relation to specific chemotherapy regimens.

Results

The study's participants included 98 neutropenic cancer patients. An analysis of the demographic characteristics revealed that the majority of the subjects were female (68.4%, n = 67), over the age of 50 (75.5%, n = 74), and of Arab ethnicity (74.4%, n = 73). Hematological malignancies were predominant among the cohort, accounting for 81% (n=79) of cases, while solid tumors constituted 19% (n=19).

The prevalence of neutropenia across chemotherapy cycles (**Table 1**) demonstrated that neutropenia occurred most frequently during the second cycle (47%, n=47), followed by the first cycle (19%, n=19) and the third cycle or more (32%, n=32).

The severity of neutropenia indicated that moderate neutropenia was the most common presentation, observed in 68.4% (n=44) of patients. The prevalence of mild neutropenia was found to be 31.6% (n=35) among the cases, while severe neutropenia accounted for 19.4% (n=19).

With respect to the administration status of chemotherapy (**Table 2**), the majority of patients (70.5%, n = 69) continued their chemotherapy regimen despite developing neutropenia, while 29.5% (n = 29) had their treatment interrupted.

The chemotherapy regimens received by neutropenic patients (**Table 3**) exhibited significant variation. The most frequently administered regimen consisted of doxorubicin, bleomycin, vinblastine, and

dacarbazine for Hodgkin lymphoma (HL), accounting for 14.3% (n = 14) of patients. This regimen showed a statistically significant association with neutropenia (p = 0.012)

Table 1. Chemotherapy Cycles and Neutropenia Prevalence and Severity (n=98)

Chemotherapy Cycle	Number of Patients	Percentage
1st Cycle	19	52.9
2nd Cycle	47	33.3
3rd Cycle or more	32	13.7
Total	**98**	**100**

Table 2. Chemotherapy Administration Status (n=98)

Status	Number	Percentage
Stopped	29	29.5
Continued	69	70.5
Total	**98**	**100**

Table 3. Chemotherapy Regimens Received by Neutropenic Patients (n=98)

Chemotherapy regimen	Number of Patients	Percentage	*P* value
Decitabine (AML).	6	6.1	0.058
Cladribine + Cytarabine + G-CSF + Mitoxantrone (AML)	5	5.1	0.196
Cyclophosphamide+ Vincristine Sulfate+ Doxorubicin Hydrochloride + Dexamethasone (ALL)	11	11.2	**0.031***
Cyclophosphamide + Vincristine Sulfate + Doxorubicin Hydrochloride + Dexamethasone + Imatinib (ALL/ Ph +ve)	5	5.1	0.303
Cyclophosphamide + Vincristine Sulfate + Doxorubicin Hydrochloride + Dexamethasone (NHL)	11	9.1	**0.044***
Rituximab + Cyclophosphamide + Doxorubicin Hydrochloride + Vincristine Sulfate + Prednisone (NHL).	7	9.1	0.087
Taxol (Breast)	4	4.1	0.223
Xeloda + Navelbine (Breast)	6	6.1	0.071
Doxorubicin, Bleomycin, Vinblastine, and Dacarbazine (HL)	14	14.3	**0.012***
Adriamycin, Bleomycin, Vinblastine and Cyclophosphamide, Vincrestine, Prednisone, and Procarbazine (HL)	8	8.1	0.051
Carboplatin + Pemetrexed (NSCLC)	5	5.1	0.066
Carboplatin + Paclitaxel (NSCLC)	2	2.1	0.113
Etoposide + Carboplatin (SCLC)	1	1	0.653
Cisplatin + 5-Fluorouracil (Naso)	6	6.1	0.055
Paclitaxel + Cisplatin + 5-Fluorouracil (Naso)	3	3.1	0.080
Paclitaxel + Carboplatin (Ovarian cancer)	4	4.1	0.291
Total	**98**	**100**	

*p < 0.05, Chi-Square test/ Ph +ve= Philadelphia chromosome

Other regimens with significant associations included Cyclophosphamide + Vincristine Sulfate + Doxorubicin Hydrochloride + Dexamethasone for Acute Lymphoblastic Leukemia (ALL) (11.2%, n=11; p = 0.031), and Cyclophosphamide + Vincristine Sulfate + Doxorubicin Hydrochloride + Dexamethasone for Non-Hodgkin Lymphoma (NHL) (9.1%, n=11; p = 0.044).

The following regimens and their respective associations were also examined: Dacogen (AML) (6.1%, n = 6; p = 0.058), cladribine + cytarabine + G-CSF + mitoxantrone (AML) (5.1%, n = 5; p = 0.196), cyclophosphamide + vincristine sulfate + doxorubicin hydrochloride + dexamethasone + imatinib (ALL/Ph +ve) (Ph +ve = Philadelphia chromosome) (5.1%, n = 5; p = 0.303), rituximab + cyclophosphamide + doxorubicin hydrochloride + vincristine sulfate + prednisone (NHL) (9.1%, n = 7; p = 0.087), and taxol (breast) (4.1%, n = 4; p =The following medications were studied: Xeloda and Navelbine (breast) (6.1%, n = 6; p = 0.071); Adriamycin, bleomycin, vinblastine, and cyclophosphamide, vincristine, prednisone, and procarbazine (HL) (8.1%, n = 8; p = 0.051); cisplatin, carboplatin, pemetrexed, paclitaxel, docetaxel, gemcitabine, and vinorelbine (NSCLC) (7.1%, n = 7; p = 0.066); and etoposide and carboplatin (SCLC) (1%, n = 1; p = 0.653). The last medication was studied in the nasal cavity (6.1%, n = 6; p =The following results were obtained: A 3.1% response rate (n = 3; p = 0.080) was observed for the combination of paclitaxel, 5-fluorouracil, and cisplatin in patients with nasopharyngeal cancer. Similarly, a 4.1% response rate (n = 4; p = 0.291) was observed for the combination of carboplatin and paclitaxel in patients with ovarian cancer.

Discussion

The present study offers critical insights into the demographic and clinical characteristics of neutropenic cancer patients, along with a detailed analysis of chemotherapy patterns and neutropenia severity across three oncology centers. The predominance of female patients (68.4%) and those over 50 years of age (75.5%) among those who developed neutropenia aligns with findings in existing literature, suggesting that age and gender may serve as important demographic risk factors for chemotherapy-induced neutropenia (Ceken et al., 2020; Kirolos et al., 2023). The high incidence of neutropenia among patients with hematological malignancies (81%) is consistent with the extant literature, as these cancers often necessitate more intensive and myelosuppressive chemotherapy regimens (Gargiulo et al., 2021; Min & Byeon, 2025).

The findings regarding neutropenia severity indicated that moderate neutropenia was the most common presentation (68.4%), followed by mild (31.6%) and severe (19.4%) cases. This distribution indicates that while chemotherapy regimens are intensive, their effects on neutrophil counts are frequently within a manageable range, consistent with the use of combination therapies designed to balance efficacy with tolerability (Al-Shammary & Mohammed, 2020; Dessalegn et al., 2023; Dinakaran et al., 2023). A noteworthy finding was that a considerable proportion of patients (70.5%) persisted in chemotherapy despite the development of neutropenia. This high rate underscores the clinical imperative to maintain treatment intensity, especially for aggressive hematological diseases, where reductions in dosage or delays in treatment could compromise therapeutic outcomes (Abdul Rasool Hassan et al., 2011; Morecroft et al., 2024). However, this practice simultaneously underscores the critical need for robust monitoring strategies and proactive prophylactic measures, including the judicious use of granulocyte-colony stimulating factors (G-CSF) and prophylactic antibiotics, to prevent progression to febrile neutropenia and other serious infectious complications (Ba et al., 2020; Blayney & Schwartzberg, 2022).

Significantly, this study identified substantial associations between particular chemotherapy regimens and the development of neutropenia. The chemotherapy regimen consisting of doxorubicin, bleomycin, vinblastine, and dacarbazine, which is commonly used for Hodgkin lymphoma, was not only the most frequently administered (14.3%) but also demonstrated a statistically significant association with neutropenia ($p=0.012$). This finding is of particular importance in light of the known myelosuppressive properties of these agents, both individually and in combination (Sureda et al., 2019). Doxorubicin, an anthracycline, is recognized for its potential to induce bone marrow toxicity, while vinblastine, a vinca alkaloid, has been observed to exhibit the capacity to suppress leukocyte production (Straus et al., 2011). In a similar vein, treatment regimens for Acute Lymphoblastic Leukemia (ALL) — including Cyclophosphamide + Vincristine Sulfate + Doxorubicin Hydrochloride + Dexamethasone ($p = 0.031$) — and non-Hodgkin lymphoma (NHL) regimens — such as Cyclophosphamide + Vincristine Sulfate + Doxorubicin Hydrochloride + Dexamethasone ($p = 0.044$) — have been shown to have a significant association with neutropenia (Sebastian et al., 2021). These cyclophosphamide-based combinations, frequently incorporating multiple myelosuppressive agents, inherently carry a heightened risk of bone marrow suppression. These specific associations underscore the significance of comprehending regimen-specific myelotoxicity profiles for effective risk stratification (Sebastian et al., 2021).

The observed associations highlight the importance of personalized risk assessment and customized supportive care for individuals with neutropenia. For patients receiving these identified high-risk regimens (Hodgkin lymphoma, acute lymphoblastic leukemia [ALL], and non-Hodgkin lymphoma [NHL] regimens), proactive strategies are paramount. This includes a lower threshold for initiating prophylactic G-CSF, more intensive and frequent monitoring of complete blood counts, and comprehensive patient education regarding the signs and symptoms of neutropenia and febrile neutropenia. The implementation of regimen-specific guidelines, embedded within institutional protocols, has been demonstrated to contribute to the mitigation of neutropenic complications, the reduction of hospitalizations, and the enhancement of patient safety and treatment continuity (Blayney & Schwartzberg, 2022). The insights derived from this study can also inform the development of local or regional clinical guidelines for neutropenia prevention and management, especially in LMICs like Iraq, where access to granulocyte-colony stimulating factors (G-CSF) and supportive resources may be limited. Risk-adapted strategies informed by regimen-specific neutropenia patterns can help prioritize limited resources and reduce preventable treatment interruptions.

This study provides significant contributions to the existing body of knowledge by offering insights into local chemotherapy practices and their associated risks of neutropenia. Future research should build upon these findings by exploring predictive biomarkers for neutropenia susceptibility, developing real-time risk modeling tools, and evaluating the effectiveness of targeted prophylactic interventions based on regimen-specific risk stratification in prospective studies. A more profound comprehension of the pharmacologic burden and myelosuppressive potential of each

chemotherapy regimen, in conjunction with individual patient characteristics, is imperative for refining preventive strategies and enhancing overall patient outcomes in oncology.

Conclusion

This study offers critical insights into the clinical characteristics, chemotherapy practices, and neutropenia severity among cancer patients. The findings emphasize the necessity for customized management strategies, continuous patient monitoring, and supportive interventions to mitigate risks associated with neutropenia and enhance patient outcomes. These findings support the integration of neutropenia risk assessments into pre-chemotherapy planning, particularly for high-risk regimens, to guide early intervention and optimize treatment continuity.

Declarations

Ethics approval and consent to participate

The study protocol received ethical clearance from the Iraqi Ministry of Health (Approval number: 19000). All procedures involving human participants were conducted in accordance with the ethical standards outlined in the Declaration of Helsinki. Prior to data collection, written informed consent was obtained from each participant or their legal representatives. The maintenance of confidentiality and anonymity was strictly enforced through the de-identification of personal information and the implementation of password-protected systems for all data. The ethical safeguards in place aimed to ensure the rights and privacy of patients were respected throughout the research process.

Consent for Publication

Not applicable.

Availability of Data and Material

The data that supports the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest / Competing Interests

The authors declare that there are no conflicts of interest.

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Author Contributions

E.A.J: Conceptualization, Methodology, Writing of original draft.

A.F.A: Conceptualization, Methodology, Writing of original draft.

R.H.A: Conceptualization, Methodology, Writing of original draft.

M.K.AQ: Investigation, Resources.

M.K.A: Investigation, Resources.

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Use of Generative AI and AI-Assisted Technologies

The authors declare that no generative AI or AI-assisted technologies were used in the preparation of this work.

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