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COLLEGE OF HEALTH SCIENCES

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DEPARTMENT OF NURSING POSTGRADUATE PROGRAM

INCIDENCE AND DETERMINANT FACTORS OF NEUTROPENIA AMONG CANCER PATIENTS RECEIVING CHEMOTHERAPY AT PUBLIC HOSPITALS, ADDIS ABABA, ETHIOPIA,2023.

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A THESIS SUBMITTED TO THE SCHOOL OF NURSING AND MIDWIFERY, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCES IN CLINICAL ONCOLOGY

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I, the undersigned, an oncology nursing student, declare that this thesis on the title "Incidence and determinant factors of Neutropenia among cancer patients receiving chemotherapy at Public Hospitals, Addis Ababa, Ethiopia, 2023." is my original work in partial fulfillment of the requirement for the degree of Master of Science in clinical oncology nursing.

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This thesis by incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy at Public Hospitals, in Addis Ababa, Ethiopia is accepted in its present form by the board of examiners as satisfying thesis requirement for the degree of masters in clinical oncology Nursing.

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Lists of abbreviations and Acronyms

ANC	**Absolute neutrophil count**
AEs	**Adverse effects**
ACR	**Adjusted crude ratio**
AOR	**Adjusted odds ratio**
BMI	**Body mass index**
BSA	**Body surface area**
CI	**Confidence interval**
CIN	**Chemotherapy-induced neutropenia**
ECOG-PS	**Eastern Cooperative Oncology Group performance status**
FN	**Febrile neutropenia**
G-CSFs	**Granulocyte colony-stimulating factors**
GLOBOCAN	**Global Cancer Observatory**
NHL	**Non-Hodgkin lymphoma**
SPHMMC	**Saint Paul's hospital millennium medical college**
SPSS	**Statistical Package for the Social Sciences)**
TASH	**Tikur Anbessa Specialized hospital**

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ABSTRACT

Background: Cancer is one of the most common causes of morbidity and mortality in the world. Around the globe, 19.3 million new cases of cancer were diagnosed in 2020, while about ten million people died from cancer. Patients receiving myelosuppressive chemotherapy for cancer face the risk of developing chemotherapy-induced neutropenia, which puts them at risk for serious consequences like febrile neutropenia.

Objectives: This study aimed to assess the incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy at public Hospitals, in Addis Ababa, Ethiopia.

Methods; This retrospective follow-up cohort study was carried out at Saint Paul Hospital Millennium Medical college and Tikur Anbessa Specialized Hospital. All eligible cancer patients' medical records from January 1st, 2020 to December 31st, 2022 were a source population. Computer generated simple random sampling technique was employed to select study participants. Data was collected by using Kobo toolbox software. SPSS version 26 was used for data analysis. Bi-variable logistic regression analysis was carried out to select variables with P-value <0.25. In multivariate analyses the significance of the association was interpreted using an Adjusted Odds Ratio (AOR) by considering a P-value <0.05 with 95% confidence interval. The results were summarized using text, tables and graphs.

Result; A response rate of 98.8% was achieved with 348 of the total 352 enrolled participants. The overall incidence of chemotherapy-induced neutropenia was 58.6% [53.6-63.9]. cervical cancer (AOR=0.31(95%CI: 0.096-0.997), normal baseline WBC (AOR =0.492 (95% CI: 0.279-0.867), and bone metastases (AOR= 2.536(95% CI:1.121-5.737) were significantly associated factors of chemotherapy-induced neutropenia.

Conclusion; the overall incidence of neutropenia was high. Baseline WBC, cervical cancer, and bone metastases were significantly associated determinant factors of neutropenia. Throughout the course of chemotherapy, it is critical to make every effort to limit the risk of neutropenia. Determinant factors of neutropenia are multifaceted, and healthcare providers should be familiar with these factors as much as possible.

Keywords; Incidence, chemotherapy-induced neutropenia, chemotherapy, cancer patients, Ethiopia.

1. INTRODUCTION

1.1. Background of the study

Non-communicable diseases (NCDs) are among the leading causes of death around the globe (1). There were an estimated 18.1 million new cases of cancer and 9.6 million deaths from cancer worldwide in 2018 (2). According to the Global Cancer Registry (GLOBOCAN), there were 19.3 million new cases of cancer detected in 2020, and nearly 10.0 million people died due to cancer, among those with an expected 2.3 million new cases, female breast cancer has surpassed lung cancer as the most frequently diagnosed cancer (3).

In 2040, GLOBOCAN predicts that there will be 28.4 million new cases of cancer (4). The GLOBOCAN report also emphasizes how cancer incidence rates for both men and women are currently three times higher in high-income countries (HIC) than they are in low- and middle-income countries (LMIC) (4). Based on cancer record results in 2018, approximately 8.6 million new cancer cases and greater than 4.1 million cancer deaths were recorded in women (1).

Estimates predict that in China and the USA, respectively, in 2022, there are expected to be 4.8 million and 2.3 million new cases of cancer and 3.2 million and 640,000 deaths due to cancer (5).

According to 2020 GLOBOCAN estimates, there were 520,158 cancer deaths and 801,392 new cancer cases in sub-Saharan Africa (3). Due to the varied distribution of cancer types, higher case fatality rates, and poor prognosis in these regions, Asia and Africa combined account for the majority of cancer deaths, accounting for 64.6% and 65.5% of all cancer deaths in 2018 and 2020, respectively (3, 4, 6). About half to two thirds of all white blood cells are neutrophils, which guard against bacterial infection (7). Chemotherapy-induced neutropenia (CIN) is a risk for cancer patients receiving myelosuppressive chemotherapy, and neutropenia increases the risk of potentially fatal side effects like febrile neutropenia (FN) (8).

According to a US study, chemotherapy-induced neutropenia/FN has a significant adverse effect on cancer patients' hospitalizations, mortality, and financial burden on healthcare systems (9, 10).

The inpatient case fatality rate of neutropenia was 10.6% overall and varied among cancer types in retrospective research carried out in the US (11). Patients who experience FN during chemotherapy treatment, a serious adverse event that frequently necessitates being hospitalized, have higher rates of morbidity and mortality and higher healthcare costs. They are also more likely to experience treatment delays, dose reductions, and treatment cessations, which may result in a worsening of their condition and a shorter life expectancy (11, 12). Therefore, identifying the incidence and determinant factors of neutropenia is essential to preventing its potentially fatal adverse consequences.

1.2.Statements of the problem

The second most common cause of morbidity and mortality worldwide is cancer (13). Its load is expected to double over the next 20 years, having a significant impact on global financial hardships, time expenditures, and human resources (14, 15). In the current world Multimodal treatments are available for cancer including chemotherapy (16). Chemotherapy, which is designed to destroy cancer cells, can also harm healthy cells, such as neutrophils, platelets, and red blood cells in the process, from which, Neutropenia is one of the causes of dose reduction during chemotherapy and the most common and dangerous adverse effects (AEs) of chemotherapy (17). Chemotherapy-induced neutropenia (CIN), a relationship between neutropenia and chemotherapy, has been linked to significant morbidity and mortality in cancer patients as well as high management costs (18-20).

According to a retrospective cohort study carried out in the USA, the mean hospital length of stay (LOS) was 8.4 days, and the inpatient mortality rate from febrile neutropenia was 8.1% (12). Real-world data from the USA show that the hospitalization rate for FN in patients with breast cancer was 13.9%, the mortality rate in these patients was estimated to be 2.0-2.6%, the mean length of stay ranged from 4.1 to 5.7 days, and the mean hospital costs ranged from $16,940 to USD 37,087 (21, 22). Based on a study done in Thailand, neutropenia in chemotherapy patients can cause treatment delays, dose reductions, and cessation of treatment (23). This reduced the effectiveness of chemotherapy for cancer patients (23).

The finding from a retrospective study conducted in Saudi Arabia, of the 211 patients who had febrile neutropenia reported, 21 (49%) of the 43 patients had FN during the first cycle of chemotherapy, which was highly prevalent (24).

One in three breast cancer patients who were receiving chemotherapy developed neutropenia throughout the course of a two-year prospective cross-sectional study in Nigeria with 113 female patients (25) as well as a one-year retrospective study conducted in Kenya found a 27.2% Incidence of neutropenia (26).

Empirically, administering antibiotics, using prophylactic colony-stimulating factors (CSFs), and initiating preventive antimicrobial therapy are crucial to lowering mortality, reducing hospital stays, and improving the quality of life for cancer patients with neutropenia (27-30). However, due to poor rates of screening for various malignancies brought on by a lack of organized healthcare facilities, a lack of antibiotic sensitivity tests, and incorrect antibiotic usage, such practices are not evident in developing countries, including Ethiopia. Filling in the therapeutic gap requires knowledge of the incidence and risk factors for neutropenia. Few studies have been conducted on the incidence and determinant factors of neutropenia among cancer patients in Ethiopia. But the study was not covered key laboratory indicators. Therefore, the purpose of this Hospital based retrospective follow-up cohort study was to give direction to how much is the incidence of CIN and which determinant factors are contributed to the occurrence of neutropenia among cancer patients receiving chemotherapy at public hospitals in Ethiopia.

1.3. Significance of the study

Currently, the number of cancer patients increased throughout the world and those patients are easily exposed to infections due to chemotherapy-induced neutropenia.

In Ethiopia few studies conducted on the incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy. After initiation of chemotherapy patient's absolute neutrophil count (ANC)level decreased from the normal level, and oncologists decide to reduce the dose, postponed the chemotherapy day, or complete the cessation of chemotherapy. Due to this reason, there is not enough evidence on which factors significantly contribute to developing neutropenia and how many patients develop neutropenia throughout chemotherapy cycles. This study will contribute to determining the incidence of neutropenia and identifying determinants among cancer patients receiving chemotherapy.

The study's findings and recommendations will assist decision-makers in revising the prevention and treatment guidelines for chemotherapy-induced neutropenia. The findings of this study will also be used by healthcare providers to provide screening and health education services. Researchers also may use it as a baseline for further investigations about incidence and factors contributing to the occurrence of neutropenia among cancer patients receiving chemotherapy.

2. LITERATURE REVIEW

2.1. Introduction

Cancer is the second leading cause of death worldwide. It has treatment options including chemotherapy, radiotherapy, immunotherapy, targeted therapy, and surgery. From which treatment options chemotherapy is highly prevalent. One of the most common adverse effects of chemotherapy is neutropenia, it is a life-threatening hematologic complication of cancer patients taking chemotherapy. It causes dose reduction, chemotherapy day postponed, complete cessation of chemotherapy administration, and admission. This literature review seeks to point out the impact of research findings on clinical practice, identify knowledge gaps in Ethiopia regarding the incidence of CIN and determinant factors, and summarize what is currently known about the incidence and determinant factors among cancer patients receiving chemotherapy globally. As a point to begin, studies regarding the incidence of CIN and patient-, disease-, and treatment-related factors among cancer patients has been reviewed and compiled (16).

2.2. Incidence of chemotherapy-induced neutropenia

chemotherapy inevitably induces neutropenia (31). In a retrospective study done in the US, 41% of the 520 patients experienced one or more episodes of CIN (32). In a Brazilian observational study, 63.3% of the participants developed neutropenia at some point throughout the course of their treatment (33).

In a retrospective study carried out in India, neutropenia developed in 59.7% out of 72 breast cancer patients (34). In a cross-sectional study conducted in Nepal out of 203 study participants, 80.2% suffered from neutropenia during chemotherapy (35). The finding in a retrospective study conducted in South Korea Among a total of 125 patients, 71.2% suffered from neutropenia (36).

A retrospective study was conducted in Japan(Osaka city university) out of 291 participants (50.5%) who developed neutropenia (37). In another retrospective study conducted in Japan of the 122 eligible respondents, 51% and 8% developed severe neutropenia and FN respectively (38).

In a time series study conducted in the Philippines, among 751 participants 3% developed neutropenia (39). From a total of 502 chemotherapy sessions, 113 patients underwent a prospective cross-sectional study in Nigeria, and 11.4% of the patients experienced neutropenia (40).

In a prospective study conducted in Tunisia, the mean time between the last treatment and fever onset was 10.67 days (41). The finding in a retrospective, observational study conducted in Kenya, among 173 participants 27.1% developed neutropenia (26). In a retrospective follow-up cohort study conducted in northwest Ethiopia from 416 study participants 62% developed neutropenia (42). In a longitudinal study conducted in SPHMMC (Addis Ababa) from 96 participants 70.5% experienced neutropenia (43).

2.3. Determinant factors of chemotherapy-induced neutropenia

Neutropenia is a series of complications of cancer patients receiving chemotherapy (44). Different factors contribute to the occurrence of chemotherapy-induced neutropenia, those factors can be classified as patient-specific, disease-specific, and treatment-specific factors (8, 44).

2.3.1. Patient-related factors

Age greater than 65 years is an independent risk factor for chemotherapy-induced neutropenia, according to numerous studies (32, 35, 36, 40, 45). In a case report study conducted in the United States hemoglobin <12 g/dl, and albumin ≤3.5 g/dl are independent risk factors of neutropenia during the first cycle (32). A study conducted in US, Japan, and northwest Ethiopia suggested that low baseline WBC count was associated CIN (12, 42, 46). A cohort study conducted in southern California The initial cycle of chemotherapy is more likely to result in neutropenia in NHL patients who also have anemia, HIV infection, AIDS, rheumatic illnesses, and thyroid issues (47). Diabetes mellitus was associated with chemotherapy-induced neutropenia in a retrospective study conducted in India (48). In a study conducted in Nepal and Kenya, female cancer patients had chemotherapy-induced neutropenia more frequently than male cancer patients (26, 35). In another study conducted in Kenya male gender was highly associated with chemotherapy-induced neutropenia (49).

A study conducted in Nepal smoking, and alcohol consumption had a risk to develop neutropenia (35). In a study conducted in Korea patients having BSA ≤ 1.45 m^2 are suggested as risk factors for CIN (36). A study conducted in Japan underweight individuals were likely at risk for CIN (45).

ECOG performance scores of greater than one in a prospective cross-sectional study conducted in Nigeria, were taken into consideration as a risk for CIN (40).

2.3.2. Disease-related factors

Based on a study done in Manchester, neutropenia was more frequent in patients with breast, gynecological, and lower gastrointestinal (GI) malignancies (50). Risk factors for severe neutropenia were identified in a multicenter prospective observational study on gastric cancer patients in Europe who had advanced disease (51). A study conducted in Japan chemotherapy-induced neutropenia was associated with disseminated disease (37). A study conducted in India tumor stage was significantly associated with chemotherapy induced neutropenia (48).

The study finding conducted on Nigeria the risk of developing CIN is increased by the presence of bone metastases. (40). In a study done in south Africa on HIV-infected breast cancer patients, CIN occurred at a faster rate (52). In a study conducted in Kenya, in 35.8% of stage III breast cancer patients, and hypertension was determinant in developing chemotherapy-induced neutropenia (49). A local study suggested that breast cancer patients were significantly associated with chemotherapy-induced neutropenia (42).

2.3.3. Treatment-related factors

In a study conducted in the **US** chemotherapy regimen and no prophylactic G-CSF use were associated with febrile neutropenia (16). In a prospective observational study conducted in Russia, among colorectal patients' irinotecan was a highly prevalent risk for developing neutropenia (53). In a study conducted in Japan, chemotherapy-induced neutropenia was associated with less than five previous chemotherapy cycles, disseminated disease, platinum-based regimens, taxon-containing regimens, alkylating agents, and the number of anticancer drugs in regimens (37, 45).

Regardless of age or the degree of their neutropenia, CIN still happened in breast cancer patients using filgrastim as the primary prophylaxis (54). In an Italian randomized trial research on advanced non-small-cell lung cancer (NSCLC), patients receiving the cisplatin plus gemcitabine combination had a 35.9% incidence of severe neutropenia (55). For many chemotherapy regimens, it appears that the first cycles have the highest risk of the initial neutropenic episode (56). In another study conducted in Kenya cyclophosphamide-based regimens taking patients developed neutropenia (49).

In a local prospective study conducted in 2020 among breast cancer patients receiving Anthracycline-Based Chemotherapy, 40.4% developed neutropenia (57).

In summary, very few number of studies have been done related to the incidence of neutropenia among cancer patients receiving chemotherapy in Africa, especially in sub-Saharan Africa compared to the developed countries. Even if, the studies were done in Africa some important factors were high determinants of CIN among cancer patients receiving chemotherapy in developing countries that were not addressed in sub-Saharan Africa including Ethiopia.

2.4. conceptual framework

The conceptual framework was adapted from multiple research papers to assess the incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy at public hospitals, in Addis Ababa, Ethiopia.

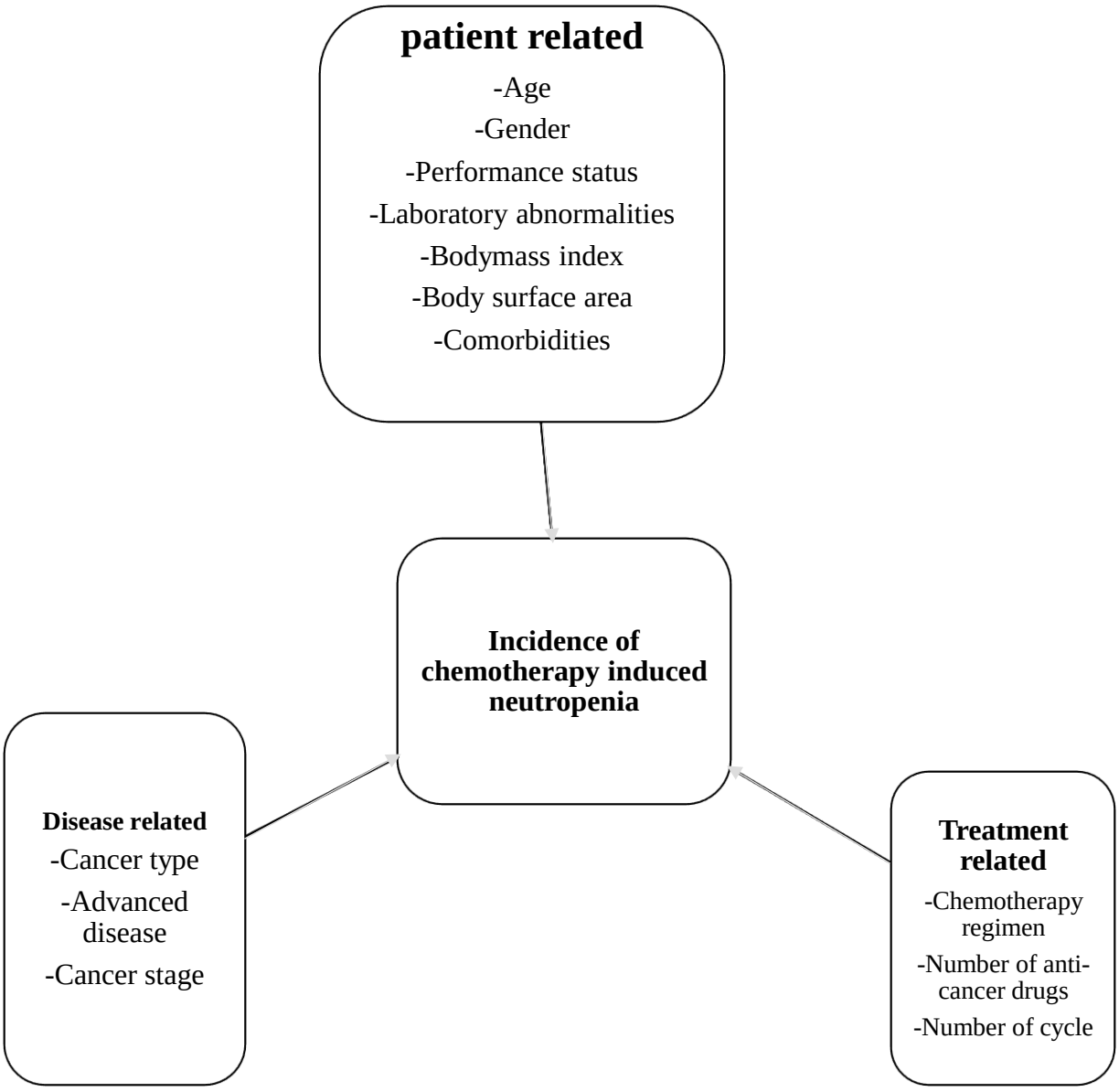


Figure 1; Conceptual framework of neutropenia and determinant factors among cancer patients receiving chemotherapy, adapted from different literature's(12, 26, 35, 47, 56, 58).

3. OBJECTIVES OF THE STUDY

3.1. General objective

To assess the incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy at Public Hospitals, in Addis Ababa, Ethiopia, 2023.

3.2. Specific objectives

I. To determine the incidence of neutropenia among cancer patients receiving chemotherapy at public hospitals.

II. To identify factors associated with CIN among cancer patients receiving chemotherapy at public Hospitals.

4. MATERIALS AND METHODS

4.1. Study setting

The study was done in public hospitals, Addis Ababa (TASH and SPHMMC).

Tikur Anbessa Specialized Hospital (TASH) is a referral teaching Hospital with a bed capacity of 800. It is located in Addis Ababa serving a population of over 4 million people. It is one of Ethiopia's few federal public hospitals, where patients can obtain advanced comprehensive treatments for cancer including chemotherapy, radiotherapy, and surgery. Under the haemato-oncology unit, there are over 90 staff members. It, therefore, has a high demand for services. Records indicate that there are approximately 25 new cancer patients every week, with 20 patients admitted into the haemato-oncology ward and about 110 patients attended at the outpatient clinic daily (59).

St. Paul's Hospital Millennium Medical College (SPHMMC) is a leading public Hospital and Medical college in Addis Ababa, Ethiopia with a bed capacity of 700. It is located in Addis Ababa serving a population of over 4 million people. It is one of Ethiopia's federal governmental hospitals where patients can obtain advanced comprehensive treatments for cancer including chemotherapy and surgery. Under haemato-oncology unit there are over 50 staff members. It, therefore, has a high demand for service. Records indicate that there are approximately 15 new cancer patients every week, and with 9 patients admitted into the haemato-oncology ward, and on average, about 100 patients attended the outpatient clinic daily.

4.2. study design and period

An Institution based retrospective follow-up cohort study was conducted among cancer patients who received chemotherapy from 1st, January 2020 to 31st December 2022.

4.3. Population

4.3.1. Source population

All medical records of cancer patients at public Hospitals, in Addis Ababa.

4.3.2. Study population

All medical records of cancer patients in TASH and SPHMMC who were receiving chemotherapy from January 1st, 2020 to December 31st, 2022 who fulfill eligibility criteria.

4.3.3. Inclusion and exclusion criteria

4.3.3.1. Inclusion criteria

- Availability of participant's records.
- Participants aged 18 and above.
- Participants that have confirmed diagnosis of a malignant by histopathology (solid tumors plus Hodgkin and Non- Hodgkin lymphoma)
- Participants who are in their first cancer treatment regimen.
- Participants who have ≥ 1500 cells/mm^3 ANC before starting their chemotherapy.

4.3.3.2. Exclusion criteria

- Incomplete medical and laboratory records.
- Participants who have been diagnosed with leukemia.

4.4. Sample size determination

The sample size was calculated by using a single population proportion formula with considering a 95% confidence interval, a 5% margin of error, and a previous study from Ethiopia with a 70.5% incidence rate that was used in the thesis sample size calculation (43). It was used to determine the sample size with considering:

n= (Z a/2)2 *p (1-p/ (d) 2

Where: n= minimum sample size required

Zα/2= standard normal variable with 95% CI (1.96)

d= margin of error =0.05, p= 70.5% = 0.705

n= (1.96)2*0.705(0.295)/0.0025=320

By adding a 10% non-response rate, the sample size was 320+32=352

4.5. Sampling procedure and sampling technique

The two federal public hospitals were selected purposively. Based on their respective populations, the sample size was proportionally distributed to both hospitals. Finally, a sample of 352 records was selected by using a computer-generated simple random sampling technique. Total number of patients who received chemotherapy starting from 2020 January 1st to December 31st 2022, were 4520 and 1608 records existed on TASH and SPHMMC, respectively.

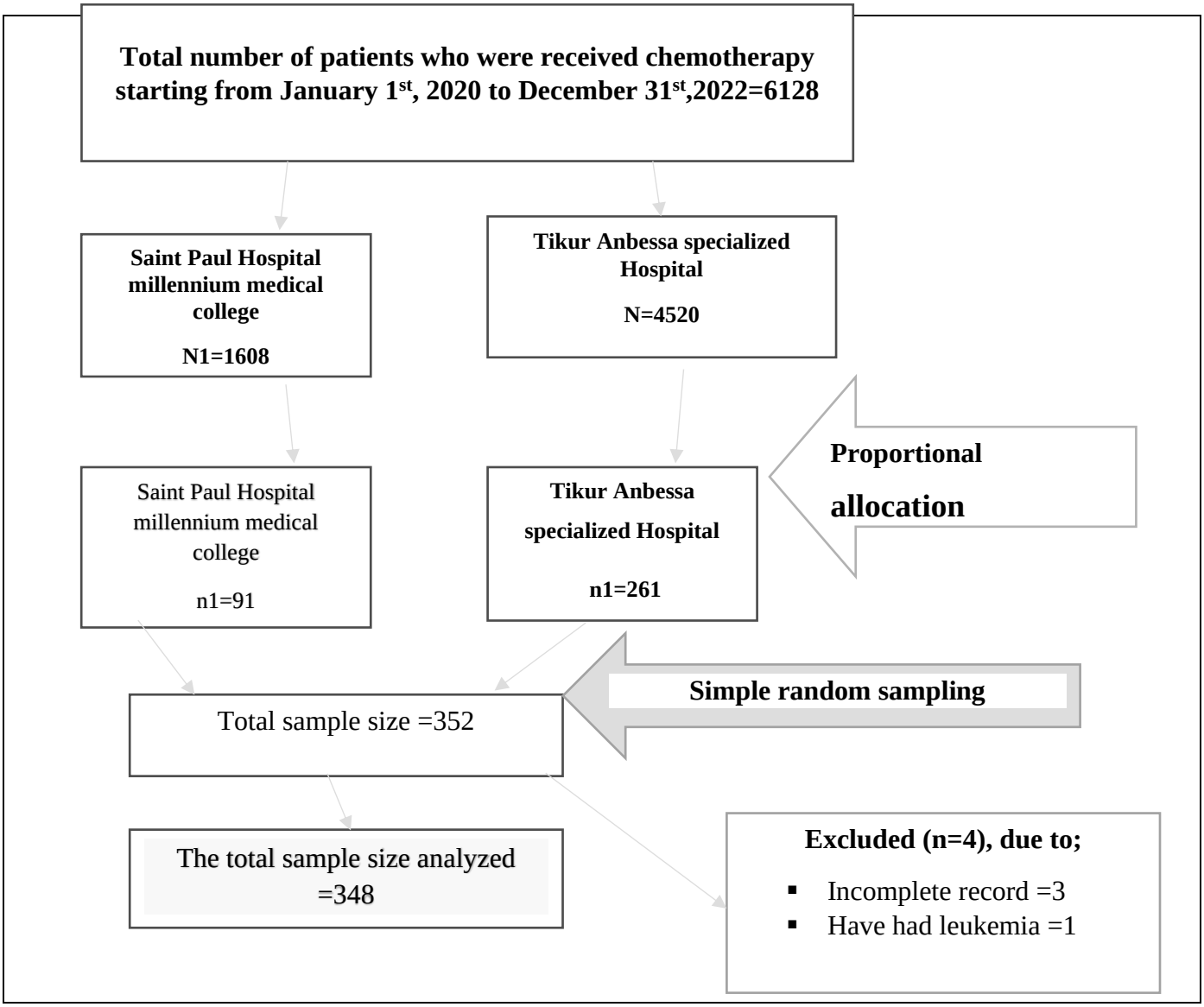


Figure 2; Diagrams illustrating the procedure for sampling employed for selecting study participants from cancer patients receiving chemotherapy at public hospitals, Addis Ababa from January 1st, 2020 to December 31st ,2022.

4.5. Variables of the study

4.5.1. Dependent variables

Incidence of chemotherapy-induced neutropenia.

4.5.2. Independent variables

 Patient-related factors- (Age, Gender, Marital status, occupational status, comorbidities, ECOG PS, BMI, BSA, and laboratory abnormalities).

 Disease-related factors - (type of cancer, stage of cancer, and advanced disease)

 Treatment-related factors – (regimens type, number of anti-cancer drugs, number of cycles).

4.6. Operational definitions

Absolute neutrophil count (ANC) /mm3: measures the number of neutrophils in the blood with the total white blood cell count multiplied by (Neutrophil % +%band)]/100 (35).

Chemotherapy-induced neutropenia (CIN): A reduction of ANC lowers than 1500 cells /mm3 after exposure to chemotherapeutics. Mild, moderate, and severe neutropenia, is defined as when ANC is 1000-1500 cells/mm3, 500-1000/mm3, and lower than 500 cells/mm3, respectively (16).

Febrile neutropenia (FN); is defined as a single temperature measurement by the oral of ≥38.3 °C (101 °F) or a temperature of >38.0 °C (100.4 °F) for greater than 1 hour with <500/mm^3 ANC (60, 61).

Treatment delay; is defined as if a patient experienced a delay of 7 or more days in the administration of at least 1 myelosuppressive agent in any chemotherapy cycle relative to the standard day of administration (58, 62, 63).

Dose reduction: is defined as a decrease in chemotherapy dose of 15% or more for at least one myelosuppressive drug throughout any chemotherapy cycle as compared to the recommended dose (58, 62, 63).

Baseline ANC: the value of ANC prior to starting the first cycle of chemotherapy (64).

Neutropenia recovery: ANC>1500 cell/mm3 (36, 63).

Performance Status: Eastern Cooperative Oncology Group (ECOG ≥2) has a poor performance and a good performance status of (0-1) (37).

Incomplete records; A record does not include essential information on a patient's treatment plan; like: treatment cycle, and post-cycle laboratory results (WBC, ANC, HGB, and PLT).

4.7. Data collection tool and procedure

The data extraction checklist was Adapted from the different guidelines and pieces of literature (12, 16, 19, 26, 35, 37, 44, 45, 56, 63, 65, 66). The checklist was included detailed information on three parts patient-related, disease-related, and treatment-related questions, with a total of 40 questions. The data was collected by four trained clinical oncology Nurses with one supervisor by using the kobo toolbox version 2022.3.6. Each patient chart was given a code when the data extraction process from their charts was finished in order to prevent duplication.

4.8. Data quality assurance

Before one-week period of actual data collection, in TASH performed a pretest on 20 medical records to test the consistency of the abstraction tool; however, those records were not used in the final analysis. The validity of the extracted checklist was evaluated by clinical oncologist experts. To ensure consistency and minimize differences between data collectors, and the supervisor was given training on how to properly use data collection tools, maintain the confidentiality of the data collected, and how to extract information from medical records through the process. This training took place one day prior to the study period. The data collectors, supervisor, and finally the principal investigator daily reviewed the filled-out forms to ensure their accuracy. Throughout the data collection process, daily communications were held between the principal investigator and the data collectors.

4.9. Data processing and Analyses

Kobo toolbox version 2022.3.6 was used by the data collectors to fill out the questionnaires, which were then exported to SPSS version 26 for analysis. The chi-square test was used to analyses proportional expressions of categorical variables. The Hosmer-Lemeshow goodness of fit test (0.154) was used to assess the model fit test, and the standard error was used to evaluate multicollinearity.

To identify associated variables, bivariate and multivariate logistic regression analysis was also carried out. Candidates for multivariate analysis included variables significant at the p-value < 0.25 level in the bivariate analysis.

Using the Adjusted Odds Ratio (AOR) with a 95% Confidence Interval (CI), the strength of the association was calculated. In multivariable analyses P-value less than 0.05 with 95% CI was considered as statistically significant with CIN. Finally, the results were reported by using texts, tables, and graphs.

4.10. Ethical consideration

Ethical approval was received from the Addis Ababa University College of Health Sciences School of Nursing and Midwifery Ethical Review Committee. A formal letter of cooperation was written to Addis Ababa Public Hospitals to get cooperation. Data was kept confidential by using coding to maintain anonymity, avoiding information sharing, and locking the questionnaire.

4.11. Dissemination plan

The finding of this study will be submitted and presented to Addis Ababa University, College of Health Sciences School of Nursing and Midwifery. The result will also be disseminated to TASH, SPHMMC, and other stakeholders. The manuscript will also be submitted for presentation at different workshops and seminars. A final attempt will be made to publish in a medical journal.

5. RESULT

5.1 Socio-Demographic characteristics of the study participants

A total of 348 patient Records were included in this study, which yielded a 98.8% response rate. The mean age of the patients was 44.15 ±14.6(SD)years; of those, 133(38.2%) were between 45 and 64 years old. More than half of the patients were female (189 (54.3%)); of those participants 116(33.3%) were housewives. Regarding their residence ,205 (58.9%) of participants were from urban areas. More than three-fourths of patients were married (275(79%)) (Table 1).

Table 1: Socio-Demographic characteristics of cancer patients at Addis Ababa public Hospitals from January 2020 to December 31st, 2022 (n=348).

Variables	Category	Frequency, n	%
Age	18-34	87	25.1
	35-44	92	26.4
	45-64	133	38.2
	>65	36	10.3
Gender	Male	159	45.7
	Female	189	54.3
Residence	Urban	205	58.9
	Rural	143	41.1
Occupation	Employed	94	27.0
	unemployed	27	7.8
	merchant	37	10.6
	housewife	116	33.3
	farmer	40	11.5
	student	34	9.8

Marital status	Single	54	15.5
	married	275	79.0
	divorced	8	2.3
	widowed	9	2.6
	separated	2	.6

5.2. Patient-related characteristics of the study participants

The mean weight and height of the patient record were 57.87±12.3 Kg and 161.98±8.167 cm respectively. Above the average of study participants (217 (62.4%)) have normal range of BMI (18.5 – 24.9 Kg/m2). (287(82.5%)) of the patients had more than 1.5m^2 of BSA. From the respondents, 38 (10.9%), 30 (8.6%), and 28 (8%), respectively, had a habit of consuming alcohol, smoking cigarettes, and chewing khat. About (251 (72.1%)), of the patients had good performance status. More than one-fourth (100, 28.7%) of the patients had comorbidity conditions, of which 37 (29.8%) and 30 (24.2%) were related to hypertension and RVI, respectively. Twenty (5.7%) of the study participants had two or more comorbidities (Table 2).

In the present study ,110(31.6%) patients had <3.5 cells/mm^3 WBC count, and its mean value was 6.7±2.9 cells/mm^3. Based on the finding 292(83.9%) had greater than 2000 cells per microliter of ANC. More than three quarter (272(78.2%) of patients had ≥ 12g/dl baseline hemoglobin level. More than half (179(51.4%)) of patients had normal creatinine level (0.7-1.3 mg/dl). About 328(94.3%) patients had <40 u/l of AST level (Table 2).

Table 2; Distributions of patients who received chemotherapy for cancer by body composition (BSA, BMI), performance status, substance abuse, comorbidity condition and baseline laboratory results at Addis Ababa public Hospitals from January 1st ,2020 to December 31st, 2022 (n=348).

Variables	Category	Frequency (n)	%
Weight (kg)	<58	58	16.7
	≥58	290	83.3
Height (cm)	<162	200	57.5
	≥162	148	42.5
BSA(m^2)	≤1.5	61	17.5
	>1.5	287	82.5
BMI (kg/m^2)	<18.5	40	11.5
	18.5-24.9	217	62.4
	25-29.9	74	21.3
	≥30	17	4.8
ECOG-PS	0-1 good	251	72.1
	≥2 poor	97	27.9
Smoking	No	318	91.4
	Yes	30	8.6
Khat	No	320	92.0
	Yes	28	8.0
Alcohol	No	310	89.1
	Yes	38	10.9
Comorbidity	No	248	71.3
	Yes	100	28.7
Number of comorbidities	Zero	248	71.3
	one	80	23.0
	two	16	4.6
	three	4	1.1

Types of comorbidities	Hypertension	37	29.8
	RVI	30	24.2
	asthma	5	4.0
	diabetes mellites	18	14.6
	deep vein thrombosis	15	12.2
	tuberculosis	4	3.2
	renal problems	7	5.6
	cardiac problems	5	4.0
	osteo arthritis	3	2.4

Mean ± SD of baseline laboratory results with references

WBC (103cells/mm3)	6.74±2.99	3.5-10
ANC	4.12± 2.36	2-7.8
LYMPHOCYTE (%)	28.3± 11.38	20-40%
HGB(g/dl)	13.14± 1.9	12-16
PLT (103cells/mm3)	318.9±151.2	145-450
CREATENINE (mg/dl)	0.73±0.41	0.6-1.3
BUN (mg/dl)	21.2±16.31	15-40
LDH (u/l)	391.2±285.73	225-480
AST(SGOT) (U/L)	23.39±15	≤40
ALT(SGPT) (U/L)	21.2±14.4	≤40
ALP (U/L)	115±68.8	≤147

BSA: body surface area; BMI: body mass index; ECOG-PS: Eastern Cooperative Oncology Group performance status; RVI: Retroviral infection; BUN: blood urea nitrogen; LDH: lactate dehydrogenase; PLT: platelet count; WBC: white blood cell; Hgb, hemoglobin; ALT: alanine transferase; AST: Aspartate transferase; ALP: Alkaline phosphatase ANC: absolute neutrophil count.

5.3. Disease -related characteristics of study participants

The study includes twenty cancers in the hospital (18 solid cancers and two lymphoma). The five common cancers in this study were breast cancer, colorectal cancer, lung cancer, nasopharyngeal cancer, and rectal cancer, with breast cancer being the most common (70(20.1%)), from those 8(11.4%)) was male. Over three quarters of the patients (271, 77.9%)) had cancer that had reached at an advanced stage (stages III and IV). Almost half, 169(48.6%) patients had distance metastases to the liver, lung, bone, chest and other sites of metastases. From those patients (61(29.8%) had liver metastases, and (56(27.3%)) had metastases to the lung (Table 3).

Table 3; Distributions of patients who received chemotherapy for cancer by stage of cancer, tumor metastases, cycle of neutropenia occurrences, degree of neutropenia, and interventions taken to treat neutropenia at public Hospitals, Addis Ababa from January 1st 2020, to December 31st ,2022 (n=348).

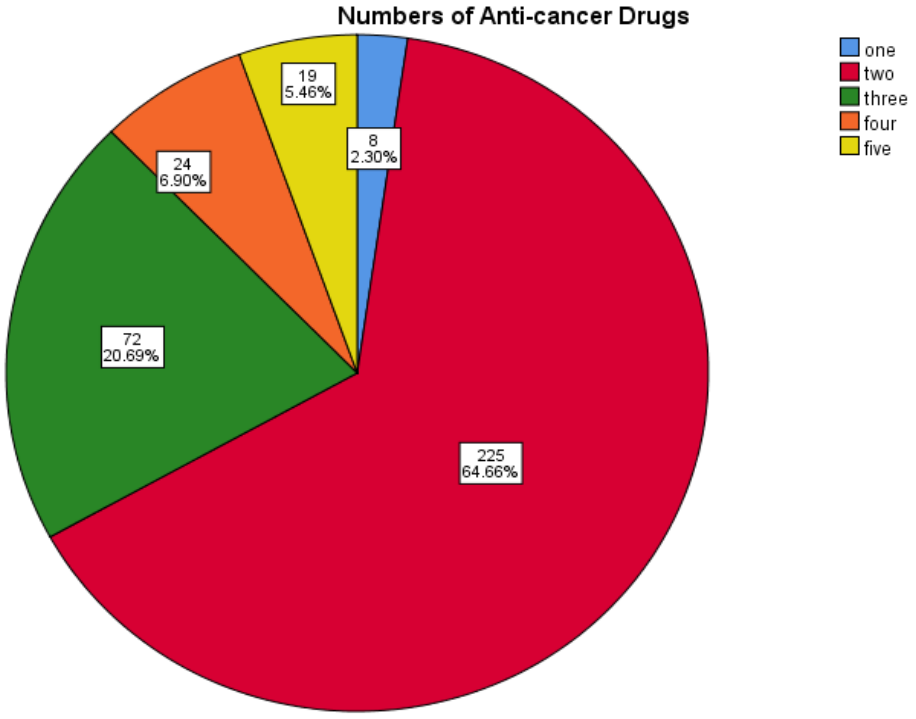
Variable	category	frequency	%
Stage of cancer	I	7	2.0
	II	70	20.1
	III	114	32.8
	IV	157	45.1
Tumor metastases	No	179	51.4
	Yes	169	48.6
Site of distal metastases	Liver	61	29.8
	Lung	56	27.3
	Bone	35	17.1
	Chest	16	7.7
	Abdomen	12	5.9
	Brain	9	4.3
	Bladder	5	2.4
	Kidney	4	2.0
	Peritoneum	4	2.0
	ovary	2	1.0
	rectum	1	0.5

	No	144	41.4
Neutropenia	Yes	204	58.6
Neutropenic fever	No	296	85.1
	Yes	52	14.9
Cycle of neutropenia occurrence	One	31	15.2
	two	54	26.5
	three	56	27.5
	four	24	11.8
	five	17	8.3
	six	21	10.2
	eight	1	.5
Degree of neutropenia	Mild	86	42.2
	Moderate	85	41.7
	Severe	33	16.1
Interventions taken to neutropenia	postponed	153	55.0
	change regimen	45	16.3
	complete cessation	2	0.7
	dose adjustment	4	1.4
	GCSFs administration	74	26.6
Interventions taken to neutropenic fever	Antibiotics	49	46.7
	antipyretics	27	25.7
	antivirals	10	9.5
	antifungals	2	1.9
	admission	17	16.2
Length of neutropenia resolution time	1-7	94	46.1%
	>7	110	53.9%
Mean duration of neutropenia	9.57±4.13 days		

5.4. Treatment related characteristics of the study participants

Throughout their course of treatment, 348 patients received a total of 348 course of chemotherapy, 20 different types of chemotherapy regimens, and 1968 chemotherapy cycles. The treatment course's mean cycle was 5.66±1.106. Based on the finding the most prevalent chemotherapy regimens were FOLFOX (60(17.2%)) and Adriamycin plus cyclophosphamide (62(17.8%)). In this particular study, 225 patients (64.7%) were receiving two anti-cancer drugs while 307 patients (88.2%) received six cycles.

Figure 3; Number of anti-cancer drugs which patients received at Addis Ababa public hospitals from January 1st,2020 to December 31st ,2022 (n=348)



5.5. Incidence of chemotherapy induced neutropenia

From the total number of study participants, 204 patients 58.6% [95% CI: 53.6- 63.9] developed neutropenia, and of these, 52 (14.9%) experienced neutropenic fever. 86 (42.2%) out of 204 neutropenic patients experienced mild neutropenia. Third-cycle chemotherapy was the time that neutropenia was more frequently encountered (56(27.5%)).

Neutropenia postponed the initiation of chemotherapy for more than half of the patients (153(55%)), and 46(46.7%) of the patients having neutropenic fever received antibiotics. More than half 110(53.9%) of patients had >7 days of neutropenia resolution time and its mean duration was 9.57±4.13 days (Table 3).

5.5.1. Type of cancer and neutropenia

From a large number of neutropenia patients (41(11.8%)) were breast cancer, of which (7(2.0%)) happened on male patients. The second most common cancer type to experience neutropenia was colorectal cancer (26(7.5%)) (Table 4).

Table 4; Distribution of chemotherapy induced neutropenia among cancer patients based on cancer type at public Hospitals from January 1st,2020 to December 31st ,2022 (n=348)

Type of cancer	Frequency	Neutropenia, n (%)
Breast cancer	70(20.1) ,8(2.29%) M	41(11.8%), 7(2.0%)
Lung ca	36(10.3)	21(6.0%)
Cervical ca	20(5.7)	6(1.7%)
Colorectal ca	37(10.6)	26(7.5%)
Nasopharyngeal ca	30(8.6)	19(5.5%)
Esophageal ca	20(5.7)	13(3.7%)
Non-Hodgkin lymphoma	20(5.7)	11(3.2%)
Hodgkin lymphoma	13(3.7)	6(1.7%)
Rectal ca	22(6.3)	16(4.6%)
Anorectal ca	11(3.2)	8(2.3%)
Gastric ca	18(5.2)	12(3.4%)

Endometrial ca	2(.6)	2(0.6%)
Rhabdomyosarcoma	7(2.0)	6(1.7%)
Soft tissue sarcoma	5(1.4)	2(0.6%)
Tongue ca.	6(1.7)	1(0.3%)
Oropharyngeal ca	11(3.2)	5(1.4%)
Osteosarcoma	6(1.7)	3(0.9%)
Ewing sarcoma	4(1.1)	1(0.3%)
Prostate ca.	4(1.10	0(0.0%)
Bladder ca.	6(1.7)	5(1.4%)

Ca.: cancer; M: Male

5.5.2. Chemotherapy regimen and neutropenia

From those neutropenic patients (42(12.1%)) accounts FOLFOX prescribed chemotherapy regimens followed by AC regimen (37(10.6%) (Table 5).

Table 5; Regimen of chemotherapy administered among cancer patients from January 1st, 2020 to December 31st, 2022 at public Hospitals, Addis Ababa, Ethiopia (n=348)

Regimen	Total number of patients	Total number of cycles	Neutropenia, n (%)	Neutropenic fever, n (%)
VAC/IE	11(3.2%)	61	6(1.7%)	2(0.6%)
VAC	5(1.4%)	30	4(1.1%)	2(0.6%)
IE	2(0.6%)	12	1(0.3%)	0(0.0%)
AC	62(17.8%)	363	37(10.6%)	10(2.9%)
FOLFOX	60(17.2%)	338	42(12.1%)	19(5.5%)
ACP	9(2.6%)	54	5(1.4%)	0(0.0%)
Cisplatin	5(1.4%)	30	1(0.3%)	0(0.0%)
Cisplatin, Gemcitabine	33(9.5%)	195	23(6.6%)	2(0.6%)
Cisplatin, paclitaxel	56(16.1%)	289	30(8.6%)	5(1.4%)
Cisplatin, 5FU	22(6.3%)	111	9(2.6%)	3(0.9%)

Paclitaxel	3(0.9%)	17	0(0.0%)	0(0.0%)
paclitaxel, carboplatin	24(6.9%)	136	11(3.2%)	4(1.1%)
R CHOP	7(2%)	42	2(0.6%)	0(0.0%)
CHOP	10(2.9%)	60	6(1.7%)	2(0.6%)
Oxaliplatin, capecitabine	15(4.3%)	79	12(3.4%)	1(0.3%)
FOLFIRI	1(0.3%)	5	1(0.3%)	1(0.3%)
ABVD	14(4%)	90	7(2%)	1(0.3%)
Cisplatin, capecitabine	6(1.7%)	36	5(1.4%)	0(0.0%)
Cisplatin, Docetaxel	2(0.6)	12	1(0.3%)	0(0.0%)
Cyclophosphamide, 5Fu	1(0.3%)	6	1(0.3%)	0(0.0%)
Total	**348(100%)**	**1968**	**204(58.6%)**	**52(14.9%)**

VAC/IE; vincristine, Adriamycin, and cyclophosphamide, followed by ifosfamide and etoposide; VAC; vincristine, Adriamycin, and cyclophosphamide Adriamycin–cyclophosphamide; ACP: Adriamycin–cyclophosphamide, and paclitaxel; IE: Ifosfamide-etoposide;

R-CHOP: rituximab, cyclophosphamide, Adriamycin, vincristine, and prednisone; CHOP: cyclophosphamide, Adriamycin, vincristine, and prednisone; ABVD: Adriamycin, bleomycin, vinblastine, and dacarbazine; FOLFIRI: folic acid–fluorouracil–irinotecan; FOLFOX: folic acid–fluorouracil–oxaliplatin;5FU:5-fluorouracil.

Neutropenia and number of cycles

Of 204 neutropenic patients (33(16.1%)) had severe neutropenia. The incidence of neutropenia was more frequently encountered in the third cycle of chemotherapy (56(27.5%)). But the incidence of neutropenic fever was more frequently encountered in the second cycle of chemotherapy (17(32.7%)).

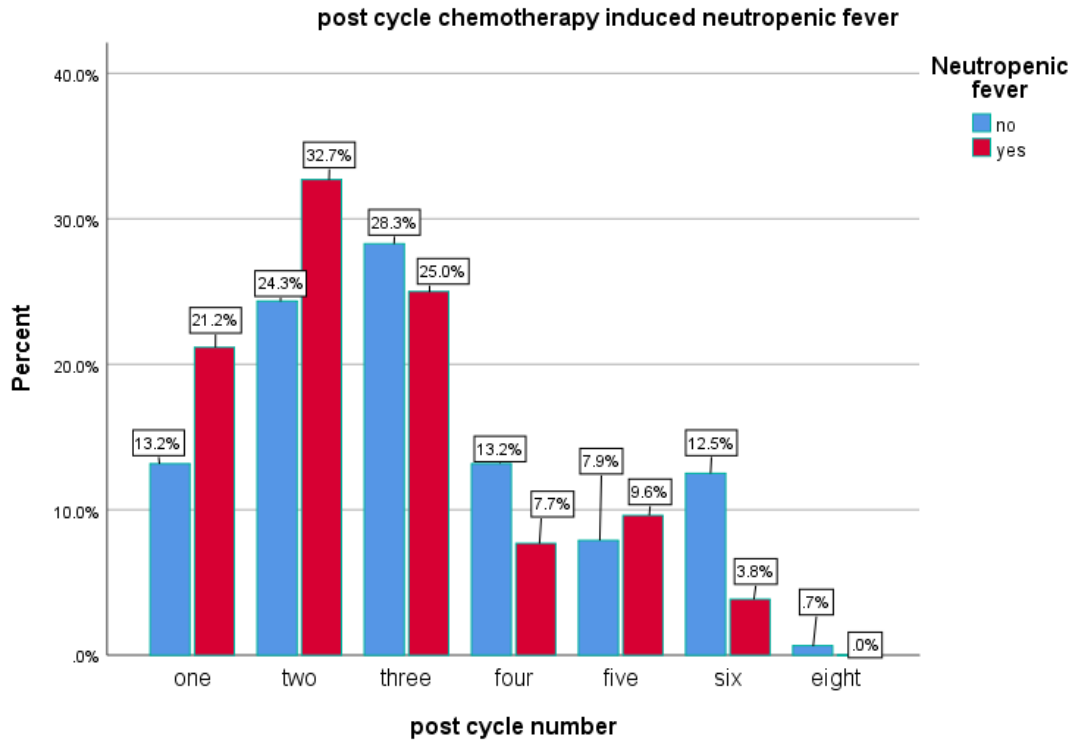


Figure 4; Incidence of neutropenia among cancer patients based on post cycle of chemotherapy at public hospitals, Addis Ababa from January 1st, 2020 to December 31st, 2022 (n=348).

5.6. Factors associated with chemotherapy-induced neutropenia

To know the associations of predictor variables with neutropenia both bivariate and multivariable logistic regression were done. Bivariate logistic regression analysis was performed to identify variables associated with neutropenia and variables with a p-value less than 0.25 were entered into multivariable logistic regression.

In bivariate logistic regression occupational status, baseline WBC count, type of cancer, number of anti-cancer drugs, and tumor metastases were variables associated with neutropenia.

In the multivariate analysis cervical cancer, bone metastases, and baseline white blood cell count were significantly associated with neutropenia at p-value less than 0.05. Among the study participants who had cervical cancer were 69% less likely to develop neutropenia than who had Breast cancer (AOR=0.31; 95% CI: 0.096-0.997). Patients with normal baseline WBC had 50.8% less likely to develop Neutropenia compared to those patients with low base line WBC count: AOR =0.492 :95% CI: 0.279-0.867). patients with bone metastases had a risk to develop neutropenia by odds of 2.5 than patients without metastases to the bone: (AOR =2.536: 95% CI :1.121-5.737).

Table 6; Multivariate logistic regression for incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy in Addis Ababa public hospitals from January 1st, 2020, to December 31st, 2022 (n=348)

Variable	Category	Neutropenia %		COR (95% CI)	AOR (95%CI)	P-value
		yes	No			
WBC	<3.5	76(21.8)	34(9.8)	1	1	
	3.5-10	99(28.4)	86(24.7)	0.515(0.313-0.847)	0.492(0.279-0.867)	.014*
	>10	29(8.3)	24(6.9)	0.541(0.275-1.062)	0.525(.252-1.095)	.086
Types of cancer	Breast ca	41(11.8)	29(8.3)	1	1	
	Cervical ca	6(1.7)	14(4)	0.303(0.104-0.882)	0.310(0.096-0.997)	.049*
Bone metastases	No	189(54.3)	124(35.6)	1	1	
	Yes	15(4.3)	20(5.7)	2.03(1.002-4.2)	2.5(1.12-5.73)	.025*

Note :1 indicate for reference group, *significant association at P-value <0.05; COR: crude odds ratio; AOR; adjusted odds ratio

6. DISCUSSION

The study was conducted among 348 cancer patients, to assess incidence and determinant factors of neutropenia who received chemotherapy.

6.1. Incidence of CIN

In this study, the incidence of neutropenia was 58.6% [95%CI: 53.6- 63.9], which means, more than half of the study participants develop chemotherapy induced neutropenia throughout their treatment cycle. The present finding was consistent with those of studies done in India (59.7%), Brazil (63.3%), and north west Ethiopia (62%) (33, 34, 42). However, the finding was higher than earlier studies done in Japan (51%), Philippines (3%), Nigeria (31.9%), and Kenya (27.1%) (26, 37, 39, 67).

This discrepancy might be due to lack of regular chemotherapy risk assessment and primary administration of GCSFs. For example; a study done in Philippines had regular chemotherapy risk assessment for breast cancer patients on every follow-up period. Another reason could be that most patients in this study presented with advanced stages, it might have contribution to the occurrence of neutropenia (68). In addition, this discrepancy might be attributed to driven on by genetic variation because black populations' neutrophil counts were lower than those of white populations (35). However, it also exceeded the results of studies conducted in Kenya (27.1%) and Nigeria (31.9%) (26, 67). This difference may be the result of first-time chemotherapy exposure, as these cases are more vulnerable to the adverse consequences of chemotherapy than cases that recur (40). Also, the data source, sample size, study period, and setting could all contribute to the reason for the disparity.

However, the finding of this study (58.6%) was lower than compared to those of studies carried out in Nepal (80.2%), South Korea (71.2%), and (SPHMMC) in Addis Ababa (70.7%) (35, 36, 43). This possible variation may result from different combinations of treatment modalities, such as high-risk chemotherapy regimens and radiation (69, 70). The study done in Nepal participants were taken chemotherapy and radiation treatment, due to this reason high incidence of neutropenia was expected. The other possible discrepancy was small sample size. The study done in SPHMMC had only 96 participants.

6.2. Determinant factors of CIN

The present study has shown that patients with breast cancer had a greater incidence of CIN than those with other cancers.

Participants in the study who had metastatic bone cancer were more likely to suffer from CIN than those who did not have metastatic bone cancer (AOR: 2.536:95% CI: 1.121-5.737). The study conducted in Nigeria supported this finding (40). The possible justification might be related to decrease in normal productions of white blood cell. The normal production of blood cells becomes eventually drowned out and suppressed as a result of the proliferation of cancer cells in the bone marrow (71).

Participants in the study who had a normal baseline WBC count had a lower risk of chemotherapy-induced neutropenia than those who had a low baseline WBC count (AOR; 0.492: 95 % CI: 0.279-0.867). This finding was supported by study done in US, Japan, and north west Ethiopia (12, 42, 46). The possible justification might be related to the body's immune system uses white blood cells to fight against infections and other disorders, However, a patient's chance of developing chemotherapy-induced neutropenia increases if their baseline WBC count is low. At the same time, chemotherapy by itself lowers neutrophil counts over the course of treatment. The other possible justification might be in the present study 271(77.9%) of patients had stage III/IV cancer prior to start chemotherapy. The lower WBC and the higher the stage implies, the smaller the life expectancy is (72). The lower baseline WBC count could be a result of the direct effect of cancer (71).

Among the patients who were diagnosed cervical cancer were less likely had risk of developing CIN than patients who had breast cancer (AOR: 0.310 :95% CI ;0.096-0.997). This finding was supported by the previous studies done in Saudi Arabia, Nigeria and North west Ethiopia (40, 42, 73). The possible justification might be, in the present study most of the patients had advanced stage of cancer prior to start chemotherapy, and metastases to bone, liver, lung and other parts of the body. In the present study, bone metastasis was also associated with a greater risk of developing neutropenia. More than 60% of patients with metastatic breast cancer at initial presentation have bone involvement, making the bone a common location for breast cancer metastases (74).

The osteolytic and osteoblastic effects of bone metastases can cause the bone marrow to atrophies and produce fewer healthy blood cells, which raises the risk of CIN (75).

Notably; in the present study 8(2.29%) male patients had breast cancer, of these ,7(87.5%) experienced chemotherapy induced neutropenia. It indicates the rate at which chemotherapy-induced neutropenia develops in male breast cancer and the periodic increments of cancer in males.

Adriamycin with cyclophosphamide (AC) was the most recommended chemotherapy regimen in this study (17.8%). However, according to another study done in Japan, Taxol + Carboplatin (TC) therapy was the most popular chemotherapy regimen used in those patients. Only 24 (6.9%) of the participants in the current study had this combination given to them. The reason for this could be that various regimens are employed for various cancer types (37).

6.3. Limitations of the study

Based on the design of this study some variables, such as, quality of life, nutritional status, educational status, and income status which were not addressed that might have impact on incidence of neutropenia. Despite limitations, the present study is the first multicenter study to be carried out in Ethiopia that focuses on determining the incidence and contributing factors of neutropenia among cancer patients who received chemotherapy.

7. Conclusion and recommendation

7.1. conclusion

One out of six cancer patients develop chemotherapy induced neutropenia throughout chemotherapy cycle. More than half (55%) of neutropenic patients postponed their treatment administration date, it reduces the drug efficacy and cause for mortality and morbidity. CIN occurs most frequently during the third cycle of chemotherapy than other cycles with a mean duration of 9.57±4.13 days. Baseline WBC count, cervical cancer, and bone metastases were significantly associated factors of chemotherapy induced neutropenia.

7.2. Recommendation

Determinant factors of CIN are multidimensional and needs multidisciplinary workforce.

- **To Health professionals**
  - Prior to administering chemotherapy, healthcare providers should be aware of the patient's baseline test results, type of cancer, type of chemotherapy regimen, and clinical conditions in order to reduce the incidence of CIN.
- **To Hospital administrators**
  - For the management of patients with CIN, hospital administrators ought to set up separate inpatient rooms.
- **To Ministry of Health**
  - The Ministry of Health should develop local guidelines that clarify how to manage chemotherapy-induced neutropenia.
  - The ministry of health also should give special attention about screening, and early detection of male breast cancer as female.
- **To Researchers**
  - Researchers should investigate further about determinant factors of chemotherapy induced neutropenia by using a superior design, is advisable to assess the overall condition.
  - Other studies are recommended to explore why currently the number of male breast cancer is increased.

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ANNEXES

Annex I: Information sheet

Title of the research project: Incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy at Public Hospitals, in Addis Ababa, Ethiopia;2023

Name of principal investigator: Degayehu Mebrie

Name of the organization: Addis Ababa university college of health sciences, school of Nursing and Midwifery

Name of sponsoring organization: St. Paul hospital millennium medical college

Introduction: The information sheet is prepared for Addis Ababa public hospital administration offices. The form aims to make the above–concerning office clear about the purpose of the research, and data collection procedures, and get permission to conduct the research.

The objective of the research project: is to assess the incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy at public hospitals, Addis Ababa, Ethiopia.

Procedure: To achieve the above objective, this information will be necessary. The patient's medical record number will be taken from the oncology unit registry BOOK. Then by using MRN, the patient record will be selected by computer generated simple random sampling technique.

Risk and/or discomfort: Since the study will be conducted by taking appropriate information from a medical record, it did not inflict any harm on the patients. The name or any other identifying information was not recorded on the questionnaire and all information will be kept confidential. The information will be used only for the study purpose.

Benefit: there is no direct benefit for them, but the result of the study will be highly important for the individual and the community.

Confidentiality: To reassure confidentiality, the data will be collected without the names of the patients, and the information which is collected from this research project will keep confidential. In addition, it will not be revealed to anyone except the investigator.

Annex II; Data collection checklist

To assess the incidence and determinant factors of neutropenia among cancer patients receiving chemotherapy at public hospitals, Addis Ababa, Ethiopia;2023.

Date of data collection _____Name of hospital_____ MRN_____

Code number_____. Name of data collector_____

Part I patient-related factors

Serial number	Variables	Labels
101	Age in years	____
102	Gender	1. male 2. female
103.	Weight in kg	_____
104.	Height in cm	_____
105.	BMI in kg/m^2	_____
106.	BSA in M2	1.<1.45/m^2 2.>1.45/m^2
107.	ECOG-PS	1.zero 2.one 3.two 4.three 4.four
108.	Residence	1. urban 2. rural

109.	Marital status	1. single 2. married 3. divorced 4. widowed 5. separated
110.	Occupation	1. Employed 2. Merchant 3. Housewife 4. Student 5. Farmer
111.	Do the participants smoke	1. yes 2. no
112.	Do the participant chewing khat?	1. YES 2. NO
113.	Do the participants take alcohol	1. yes 2. no
114.	Do the participants have comorbidity?	1. yes 2.no
115.	If yes, Which types of comorbidities?	1. Diabetes mellites 2. Hypertension 3. Renal failure 4. HIV/AIDS

		5. Tuberculosis 6. COPD 7. CHF 8. Asthma 9. others
116	Number of comorbidities	1. One 2. Two 3. Three
117. Baseline laboratory values		
WBC		
ANC		
Lymphocyte		
HGB		
PLT		
Creatinine		
BUN		
LDH		
AST(SGOT)		
ALT(SGPT)		
ALP		
Part II Disease-related factors		

201.	Type of cancer diagnosed	1. Breast cancer 2. Cervical cancer 3. non-Hodgkin lymphoma 4. Hodgkin lymphoma 5. Lung cancer 6. Epigastric cancer 7. Prostate cancer 8. Uterine cancer 9. Colon cancer 10. gastric cancer 11. others
202.	Stage of cancer	1. Stage I 2. Stage II 3. Stage III 4. Stage IV
203.	Has the tumor metastasized?	1. yes 2. no
204.	If yes, the site of metastasis	1. Bone 2. Lung 3. Liver 4. Brain 5. Abdomen

		6. kidney 7. others
Part III Treatment-related factors		
301.	Chemotherapy regimen	1. VAC/IE 2. Ifosfamide + etoposide 3. Adriamycin + Cyclophosphamide 4. Adriamycin + Cyclophosphamide + Paclitaxel 5. Adriamycin + Cyclophosphamide + docetaxel 6. Cyclophosphamide + 5-fluorouracil 7. Cyclophosphamide + 5-fluorouracil + methotrexate 8. Cyclophosphamide + 5-fluorouracil + Adriamycin 9. Cisplatin + oxaliplatin + epirubcin + capecitabine 10. Cisplatin + Gemcitabine 11. Cisplatin + Paclitaxel 12. Cisplatin + Capecitabine 13. Cisplatin + docetaxel 14. Cisplatin alone 15. Oxaliplatin + 5-fluorouracil 16. Oxaliplatin + gemcitabine 17. Oxaliplatin + Capecitabine 18. Paclitaxel + Carboplatin 19. Paclitaxel only.

		20. L-asparaginase + vincristine 21. R-CHOP 22. CHOP 23. ABVD 24. B-R 25. Others
302.	Number of anti-cancer drugs	1. Five 2. Four 3. Three 4. Two 5. One

303. Do the participants develop neutropenia?

a. yes

b. no

304. if yes Q 303 specifies the degree of neutropenia

a. Mild

b. moderate

c. severe

305.if yes Q 303, In which cycle the neutropenia was occured?

a. cycle one

b. cycle two

c. cycle three

d. cycle four

e. cycle five

f. cycle six

g. cycle seven

h. cycle eight

306. does the patient develop a neutropenic fever?

a. yes

b. no

307. If yes Q 306 interventions taken against neutropenic fever

a. antipyretics

b. antibiotics

c. antifungals

d. antivirals

e. admission

308.Interventions taken against neutropenia	
1.	complete cessation of chemotherapy
2.	postponed administration date
3.	adjustments of dosages
4.	Change of chemotherapy regimen
5.	administration of a granulocyte colony-stimulating factor
6	no intervention

309. Duration of Neutropenia; ----------days

THANK YOU!