SCHOOL OF GRADUATE STUDIES

CHEMOTHERAPY-RELATED ADVERSE DRUG REACTIONS AND ITS ASSOCIATED FACTORS AMONG ADULT CANCER PATIENTS WHO WERE ON TREATMENT AT Hon. DR. ARTIST ALI BIRA MEMORIAL CANCER TREATMENT CENTER, HIWOT FANA COMPERHENSIVE SPECIALIZED HOSPITAL, HARAR, EASTERN ETHIOPIA.

MSC THESIS

FEKADU MEGERSA (B.PHARM)

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HARAMAYA UNIVERSITY ETHIOPIA

CHEMOTHERAPY-RELATED ADVERSE DRUG REACTIONS AND ITS ASSOCIATED FACTORS AMONG ADULT CANCER PATIENTS WHO WERE ON TREATMENT AT Hon. DR. ARTIST ALI BIRA MEMORIAL CANCER TREATMENT CENTER HIWOT FANA COMPERHENSIVE SPECIALIZED HOSPITAL, HARAR, EASTERN ETHIOPIA

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In Partial Fulfillment of the Requirement for the Degree of

Masters in Clinical Pharmacy

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Haramaya University, Ethiopia

APPROVAL SHEET

HARAMAYA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

I am more than willing to perform the research on chemotherapy-related adverse drug reactions and its associated factors among adult cancer patients who are on treatment at Hon. Dr. Artist Ali Birra cancer treatment center Hiwot Fana Comprehensive Specialized Hospital, Harar, eastern Ethiopia and I, the undersigned declare that this research was my original work and that it had not been presented for the same or other purposes in any other institutions. I accepted the responsibility for the overall study project's scientific, ethical, and technical conduct.

1. Shambel Nigussie (MSc, Assistant Professor) _____ _____

Major advisors Signature Date

2. Bisrat Hagos (MSc, Assistant Professor) _____ _____

Co-advisors Signature Date

As a member of the Board of Examiners of the MSc thesis Open Defense Examination, I certify that I have read and evaluated the thesis prepared by Fekadu Megersa and examined the candidate. I recommend that the thesis be accepted as fulfilling the thesis requirement for the Master's Degree in Clinical Pharmacy.

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Final approval and acceptance of the thesis is contingent upon the submission of its final copy to the Council of Graduate Studies (CGS) through the candidate's department or School Graduate Committee (DGC or SGC).

STATEMENT OF THE AUTHOR

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Name: Fekadu Megersa

Date: _____/_____/_____

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School Pharmacy

BIOGRAPHICAL SKETCH

My name is Fekadu Megersa Obsie. I was born in 1986 G.C. in Asella, Oromia, Ethiopia. I completed my primary education at Gonde Primary and secondary School from 1996 to 2003. I completed Asella high school from1994 to 2008. I joined Haramaya University's College of Health and Medical Science in 2009 for tertiary education. After five years of pharmacy education, I graduated with a BSc Degree in Pharmacy in 2014. Then, I joined Haramaya University, College of Medicine and Health Science, School of Pharmacy in, 2015, and I had been working there for seven year and as a pharmacy laboratory assistant. After a year of work experience, I started my MSc study in clinical pharmacy at Haramaya University, College of Health and Medical Science, School of Pharmacy, in 2020.

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.

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ACRONYMS AND ABBREVIATIONS

ADR	Adverse Drug Reactions
AOR	Adjusted Odds Ratio
BSA	Body Surface Area
CI	Confidence Interval
COR	Crude Odd Ratio
HFCSH	Hiwot Fana Comprehensive Specialized Hospital
IHRERC	Institutional Health Research Ethics Review Committee
LMIC	Low and Middle Income Countries
MDDT	multi-disciplinary discussion team
MRN	Medical Record Number
NCD	Non-Communicable Disease
OR	Odds Ratio
PI	Principal Investigator
QOL	Quality Of Life
SPSS	Statistical Package for Social Science
SSA	Sub-Saharan African
UMC	Uppsala Monitoring Centre
WHO	World Health Organizations
YLD	Years Lived with Disability
YLL	Years of Life Lost

ABSTRACT

Background: Anticancer drugs account to high susceptibility towards adverse drug reactions due to their narrow therapeutic window and increased toxicity, which makes pharmacovigilance studies essential for prevention, diagnosis, reporting and management in current clinical practice.

Objective: To assess the chemotherapy-related adverse drug reactions and associated factors among adult cancer patients who are on treatment at Hon. Dr. Ali Birra cancer treatment center of Hiwot Fana Comprehensive Specialized Hospital, Eastern Ethiopia from July 10 to August 15, 2024.

Methods: A hospital-based cross-sectional study was conducted among 422 adult cancer patients who are on treatment at Hiwot Fana Comprehensive Specialized Hospital. All patients on chemotherapy treatment were included in the study. Data was collected by patient interview and medical record review. The collected data was cleaned, coded, and entered into using Kobo tool box and exported to Statistical Package for Social Science version 20.0 for analysis. With Factors significantly associated were identified using logistic regression model at P-value < 0.05 and 95%CI.

Results: From 422 study participants, 251 (59.5%) of them were females. Overall, 48.34% (95% CI: 43.6 – 53.6) of the included cancer patients developed chemotherapy related adverse drug reactions. Accordingly, for the Naranjo algorithm, of 2823 ADRs identified, probable account for 2122 (75.17%) followed by definite 508 (18.0%). Based on Hartwig severity assessment scale, majority ADRs were 2699 (95.87%) moderate. Cancer patients with weight of less than 50kg (AOR = 3.29, 95% CI: 1.82, 5.94), cancer patients with age range of 31- 40 years (AOR = 0.34% CI: 0.15, 0.74) were more likely associated with adverse drug reactions.

Conclusion: Overall, near to half of the included cancer patients developed ADRs. Having weight less 50 kg, and cancer patient with age range of 31- 40 years were associated with developing ADR. Therefore, special attention should be given for cancer patients with those condition so that adverse drug reactions can be minimized.

Keywords: Cancer, Chemotherapy, Adverse drug reactions, Harar, Eastern Ethiopia.

1. INTRODUCTION

1.1. Background

Cancer is a non-communicable disease (NCD) that reduces the quality of life and has become a global burden and one of the major causes of mortality in both developing and developed countries. The incidence of the disease is drastically escalating every year in the countries (Ephraim et al., 2022, Girum et al., 2020).

The major cancer treatment modalities include surgery, radiation therapy, chemotherapy and targeted remedy, which can further include gene expression modulators, immunotherapy, angiogenesis obstruction, hormone therapy, thus chemotherapy is administered in a wide variety of cancer therapies, both for curative and supportive care, and is used in the treatment of small children on up to elderly (Debela et al., 2021, Lau et al., 2004).

World Health Organization (WHO) defined as an adverse drug reaction (ADR) "a response to a medicine which is noxious and unintended, and which occurs at normal doses typically used or tested in man for prophylaxis, diagnosis, or curative treatment or for modifications of physiological function(Lau et al., 2004, Begum et al., 2022). ADRs associated with cancer chemotherapy guarantee analysis connected on their seriousness and avoidability(Wahlang et al., 2017a).

Population groups still, with satisfactory premedication, common ADRs like nausea and vomiting can be efficiently controlled and a recent study from a South Indian tertiary care tutoring sanitarium has reported antineoplastic agents as common an adverse drug event prevented by using premedication's(Lavan et al., 2019) ADEs causes serious problems to see in different aspects including hospitalizations so they affect the case's survival, overall treatment issues, morbidity, and mortality rate, and increase mainly the cost of care (Okoroiwu et al., 2020). Several factors have been supposed to contribute to the circumstance of chemotherapy- related adverse events in adult cancer cases including the type of chemotherapy involved, the number of chemotherapy, chemotherapy rules, chemotherapy cycle, frequency, and duration of administration, and pattern of administration practices is among the factors (Prieto-Callejero et al., 2020).

1.2. Statement of the problem

The aim of current study is to decrease the prevalence of adverse drug reactions in cancer patients. The high incidence of ADRs affect the treatment and prognosis of patients with cancer. A systematic

review that included many studies across the world showed that about 10% of hospital admissions worldwide are related to ADR (Angamo, 2018). According to a cross-sectional study conducted at Gondar Comprehensive University, Specialized Hospital and Felegehiwot referral hospital, in North-West Ethiopia, the result showed that 41.5 % of patients experienced ADRs ((Workalemahu et al., 2020a). ADRs increases with age, with doubly as numerous cases progressed and aged being rehabilitated because of ADR- related problems than their youngish counterparts (Lavan and Gallagher, 2016). Tamoxifen which is used for the treatment of breast cancer can cause endometrium cancer (Alomar, 2014). Africa has one of the highest rates of cancer deaths worldwide, but this may be significantly reduced with greater access to therapies for the major cancer killers on the continent breast, cervical, lung, and prostate cancers as well as Kaposi sarcoma that are now widely available in high-income nations. For instance, countries in the WHO African region had an estimated 811,200 new cancer cases (4.5% of the world population) and 534,000 cancer deaths (7.3% of the total world) in 2018 (Omotoso et al., 2023).

Multiple problem affect the capability of numerous cancer cases in sub-Saharan Africa (SSA) to pierce treatment and realize the benefits of advances in oncology medicine curatives(Getu et al., 2022). Adherence to cancer treatment is critical for achieving optimal health issues similar as a cure or an enhancement in quality of life(Alomar, 2014). Despite the vacuity of cancer treatment options, cases are vulnerable to adverse drug reaction for a variety of reasons, including poor medicine adherence and clinical conditions. As a result, poor chemotherapy adherence leads to medicine resistance, and poor quality of life in cases, negatively impacting the nation's health costs and eventually performing in mortality of chemotherapy. Cancer is a recently evolved noninfectious global complaint burden that accounts for a significant portion of global morbidity, mortality, and profitable loss (Samet et al., 2020). Cancer is the first or second leading cause of unreasonable death in 134 of the world's 183 countries(Wang et al., 2022). It ranks third or fourth in another 45 countries from age of 30–69 years (Sung et al., 2021). According to WHO protrusions, low and middle income countries(LMIC) will bear two- thirds of the cancer burden in 2040(Deo et al., 2022) In Ethiopia between 2010 and 2019, the absolute number of years lived with disability (YLD) and years of life lost (YLL) increased by 36% (95% UI 12–64%) and 19% (95% UI − 24.4%), respectively. However, the age standardized rate of YLD increased by 9% (95% UI − 4 to 24%), while the age standardized rate of YLL decreased by − 2% (95% UI 15–12%).

1.3. Significance of the Study

The chemotherapy-related ADRs and associated risk factors in adult oncology patients in Ethiopia, study setting is not well studied. So, the aim of this study is to assess adverse drug reactions associated with chemotherapy - related factors among adult cancer patients who were on treatment in HFCSH, Eastern Ethiopia. Adherence is explosively related to case- related factors, remedy-related factors, condition- related factors, healthcare system factors, and socioeconomic factors were not very well studied (Bekalu et al., 2023, Belachew et al., 2016). Studies showed that ADRs of chemotherapy in oncology- established settings in Nepal are scarce (Tamang et al., 2022). Likewise, the pharmacovigilance system of anticancer medicines is limited and under reported (Sewal et al., 2015).This may be due to a lack of support from medical center operation, lack of team spirit in the admission and reporting of ADRs by the healthcare professionals, and occasionally indeed the fear of legal counteraccusations from cases or the cases party (Danekhu et al., 2021).. The finding from this study might be used as planning for the hospital, and similar institutions serving the cancer patient treatment. The results of this study help health care providers of the hospital to give attention while prescribing and caring for adult patient with cancer, because it provides information about the current chemotherapy related ADRs and associated factors among adult patient with cancer. Additionally, it may also help in planning interventions like applying software application for Uppsala monitoring which helps to detect severity ADRs before administration of medications. Furthermore, the result of this study may be serve as a one re-sources for future researchers.

1.4. Objectives of the Study

1.4.1. General Objective

- To assess the prevalence of chemotherapy related ADRs and associated factors among adult cancer patients at Hon. Dr. Artist Ali Birra Cancer Treatment Center, HFCSH, Eastern Ethiopia from March 10 to August 15, 2024.

1.4.2. Specific Objectives

- To assess magnitude of chemotherapy related ADRs among adult cancer patients at the treatment center.
- Identify factors that contribute for chemotherapy related ADRs among adult cancer patients at the treatment center.

2. LITRATURE REVIEW

2.1. Magnitude of Chemotherapy related ADRs

Globally, literature shows that hospitalized adult patients across the globe reported an ADR prevalence of 11.5–24% (Yadesa et al., 2021). According to intensity, ADR can be divided into three catagories of mild (ADR that the subject tolerates well, causes minimum discomfort and doesn't intrude with diurnal conditioning), moderate(ADR that are bothersome enough to intrude with the normal prosecution of diurnal conditioning) and severe(ADR that don't allow diurnal conditioning(Monestime et al., 2021). Different studies revealed that the magnitude of ADR among patients treated with anticancer agents. A study conducted in Australia shows that 11% of ADRs in Australian Hospitals were associated with antineoplastic drugs and immunosuppressive drugs (Chopra et al., 2016b). A study revealed that in India 86.53% magnitude of chemotherapy related ADR (Sharma et al., 2015, Castelán-Martínez et al., 2016). Other study showed in Mexico also reported about 62.5% (Castelán-Martínez et al., 2016) chemotherapy related ADR. literature revealed that in South Africa showed 56.5%(Makiwane et al., 2019a) of chemotherapy related ADR. In Ethiopia, a cross sectional study conducted among 287 pediatric cancer patients at Gondar Comprehensive University hospital showed that ADR was reported among 41.5% of study participants(Workalemahu et al., 2020a). Another study conducted in Tikur Anbessa Specialized Hospital reported the prevalence of 45.5%(Workalemahu et al., 2020a)

2.2. Factors Associated with Chemotherapy related ADRs

2.2.1. Sociodemographic factors

Different factors including age, gender, weight, marital status, education level, occupations and residency factors were associated with chemotherapy related ADR. A cross-sectional study conducted among adult patients with cancer treated at Gondar University Referral Hospital, Ethiopia indicated that patients with age of > 65 years old (P = 0.001) were associated with chemotherapy related ARDs (Belachew et al., 2016). Age differences in treatment-related symptom burden are not well-documented in patients with colorectal cancer but studies shows common age is from 45 - 55 year or grown-ups over age 65 with cancer can have showed response to chemotherapy treatments (Sauder et al., 2021). This means that they may have worse side effect or take longer to recover after chemotherapy treatment ends with it's important to flash back that chemotherapy can be a treatment option for cases of any age (Rehman et al., 2021). Aged grown-ups have distinct requirements before, during, and after chemotherapy treatments and being

apprehensive of these requirements and planning for them can ameliorate how chemotherapy affects you therefore chemotherapy not only affects excrescence cells, but also human whole body.

2.2.2. Drug related factors

Different drug related factors including specific drug, number of chemotherapeutic agents, dose of chemotherapeutic agent, and drug related factors were associated with chemotherapy related ADRs.

According to hospital-based consecutive study conducted at two premiers (a government and a private) tertiary care centers in North-Western India a combination of 5-Fluorouracil, Cisplatin and Paclitaxel regimen was associated with the majority (91.42 %) of the adverse effects (AOR : 5.00; 95 % CI: 2.62 - 9.53, $p < 0.001$), combination regimen of 5-Fluorouracil, Cisplatin and Paclitaxel (AOR: 8.68; 95 % CI: 2.55 - 29.48, $p = 0.001$) (Sharma et al., 2023).

According to study conducted among hospitalized cancer patients in North-West Ethiopia, patients on etoposide (AOR: 1.99 (95% CI: 0.93– 4.27)), mercaptopurine (AOR: 3.91 (95% CI: 1.06– 14.46)) and doxorubicin (AOR: 2.32 (95% CI: 1.30– 4.15)) regimen were more likely associated with chemotherapy related ADRs (Workalemahu et al., 2020b).

A cross-sectional study conducted at Jimma University Medical Center showed that number of chemotherapy (AOR: 6.179, 95% CI: 1.894-20.165) was associated with chemotherapy related ADRs (Tola et al., 2023). Another study conducted among adult patients with cancer treated at Gondar university Referral Hospital, Ethiopia showed that patients with standard dose of thermotherapy ($P = 0.015$) and those with Polychemotherapy ($P = 0.031$) were associated chemotherapy related ADRs.

2.2.3. Comorbidity and cancer type related factors

Different disease related factors including type of cancer, presence of comorbidity, and other disease related factors were associated with chemotherapy related ADRs. A cross-sectional study done among adult patients with cancer treated at Jimma University Medical Center depicted that presence of comorbidity (AOR: 12.700, CI: 1.978–81.549) and cancer type (AOR: 13.332, CI 3.288–54.059) were associated with chemotherapy related ADRs (Tola et al., 2023).

According to prospective observational study conducted at Jimma University medical center the prevalence of ADRs were associated with Severe acute malnutrition(SAM) is the most common comorbidity present, 20 (27.40%) followed by pneumonia, 4(5.50%)(Alomar, 2014). Presence of

comorbidity (AOR: 12.700, CI 1.978–81.549), cancer type (AOR: 13.332, CI 3.288–54.059) (Tola et al., 2023). According to a retrospective cross-sectional study conducted at the Oncology Unit of the University of Gondar Comprehensive Specialized Hospital among a total of 203 drug-related problems were identified, breast cancer patients who had concurrent co-morbidities were almost three times (AOR: 3, p = 0.035) more likely to experience drug-related problems as compared to those patients without co-morbidity(Degu and Kebede, 2021).

2.3. Conceptual framework

Based on the review of different literatures, socio-demographic factors: age and sex of the patients; health related factors: comorbidity and drug related factors like polypharmacy were identified to be factors associated with chemotherapy related ADRs among adult patients (Figure 1)

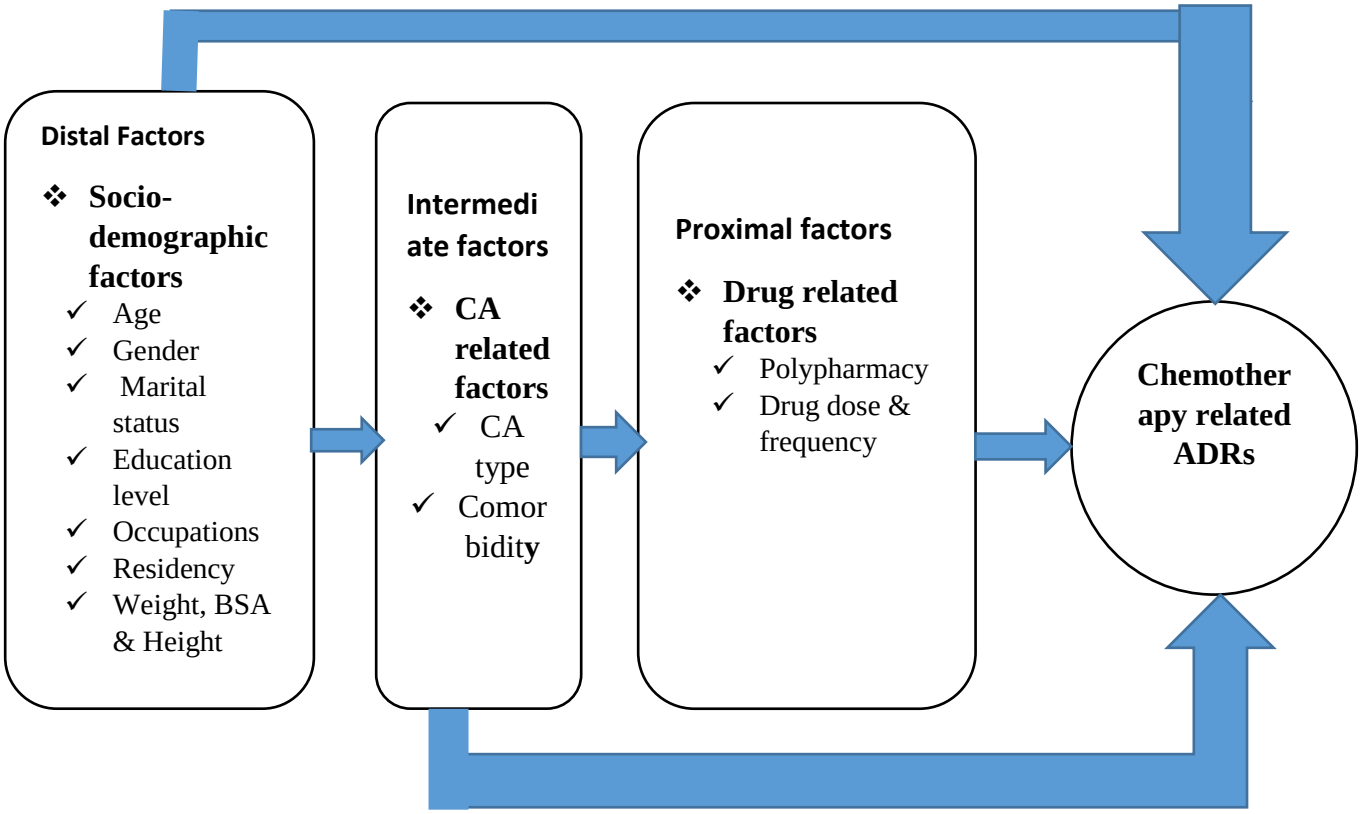

Figure 1: Conceptual Framework on chemotherapy related adverse drug reactions among adult patients and associated factors patients attending to Hon.Dr. Artist. Ali Birra memorial cancer treatment center Hiwot Fana Comprehensive Specialized Hospital (HFCSH), Harar, Eastern Ethiopia, 2024 Organized by the principal investigator.

3. MATERIALS AND METHODS

3.1. Study Area and Period

The study was conducted in HFCSH located in at Harari regional state. Harari regional state is one of the thirteen state in Ethiopia and it has a total population of 232,000 of those 116928 are males and the remaining are females. The estimated areas of Harari region is 333.94 square kilometers with estimated density of 595.9 people per square kilometer. The distance of Harari region from Addis Ababa is 526 kilometer to east. This region is bounded by east, west, north and south by Oromia regional state (CSA, 2007). There are 1 federal police, 2 public and 2 general hospitals, 8 health centers (4 urban and 4 rural), 27 health posts, 10 non-profit clinics in this region. One of the public hospital is HFCSH. HFCSH is a teaching hospital of Haramaya University and serves as a referral hospital for the entire Eastern part of Ethiopia including Eastern Oromia, Dire Dawa City Administration, Somali Regional State and Harari Regional State. There are different wards and clinics within HFCSH; those include internal medicine (medical) ward, surgery ward, pediatric ward, gynecology and obstetrics ward, antenatal clinic, dental clinics, tuberculosis clinic, anti-retroviral therapy clinic, oncology clinic, dermatology clinic and ophthalmologic clinic. The Hospital has 255 beds and it has 510 health professionals. Among those wards and clinics in HFCSH, Hon.Dr. Artist Ali Birra memorial cancer treatment center established in 2020 by one oncologist, four general physician, two oncology nurse (MSc). Ten nurse, three radiographer, two medical physics, three pharmacist and thirteen supportive staff is providing service to vast majority of cancer patient in east Ethiopia and across the country. The Center has 20 beds. The consecutive study design was conducted from July 10 to August 15, 2024.

3.2. Study Design

A facility based cross sectional study design was conducted.

3.3. Source population

All adult cancer patients on treatment at HFCSH.

3.4. Study population

All adult cancer patients on treatment at HFCSH from March 10 to August 15, 2024.

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3.5. Eligibility criteria

3.5.1. Inclusion criteria

All adult cancer patients who were on chemotherapy during the study period were included in the study.

3.5.2. Exclusion criteria

Adult patients who had incomplete medical records were excluded

3.6. Sample Size Determination

The sample size for first and second objective were calculated separately by adding 10% contingency on both specific objectives and the one with the larger number was considered.

For the first specific objective, sample size for the study was determined using single population proportion formula..

Specific objectives-1: $n = \frac{(Z\alpha_{/2})^2 \, P\,(1-P)}{d^2}$

When, n=the minimum sample size required, p= estimated proportion ADRs among adult oncology patients, z= the standard value of confidence level of alpha=95%, d=the margin of error between the sample and the population (0.05). For this study (p = 0.52864) which was the magnitude of ADRs (Belachew et al., 2016).

So, $n = \frac{(1.96)^2 \, 0.52864\,(0.47136)}{(0.05)^2} = \frac{(3.8416)(0.2491)}{0.0025} = 382.899 \approx 383$

After adding 10% of non-response rate, the final sample size was 422.

The second specific objective: factors associated with ADRs among adult oncology patients

The sample for the second specific objective was determined by considering the factors which were significantly associated with ADRs among adult cancer patients at (p=0.05), two sided confidence level of 95% and margin of error 5% and power=80% and ratio of exposed to unexposed 1:1 using the Epi Info version 7.

Table 1: Sample size determination for the factors associated with ADRs among patients with cancer.

Objective-2	Main factors	Specific factors		Proportion value			Final sample size (nf)
			% of exposed with outcome	% of unexposed with outcome	AOR	Reference	
Factors associated with chemotherapy related ADR	Sociodemographic	Sex	Female (58.6%)	Male (41.4%)	18.6	(Belachew et al., 2016)	286
	Drug related factors	Polychemotherapy	112(81.1)	26(18.8)	1.9	(Belachew et al., 2016)	24

Therefore, the total sample size will be considered from the sample size determination for the first specific objective which was 422.

3.7. Sampling Procedure/ Sampling Technique

The total numbers of adult cancer patients who were on the treatment of chemotherapy follow-up during the study period at the cancer treatment center were identified from the registration book and included until the required sample fulfilled by using consecutive sampling technique.

3.8. Data Collection Methods

3.8.1. Data collection tools

Data was collected from medical record cards of the patients using data collection format and semi-structured interview. The format was prepared by reviewing previous studies in consideration of the objective of the study by English and translated to Amharic and Afan Oromo. The data collection format has contain three subsections; the first section includes sociodemographic information, including age, sex, height, weight, BSA, past medical history and current diagnosis, comorbidities, complications, and ADR history of medications and related factors, the other was contain diagnosis (type of cancer, stage of cancer, comorbidities and laboratory investigation), and medications related information(type and number of chemotherapy, cycle of treatment, history of previous chemotherapy, concomitant medications and ADR). Naranjo's algorithm causality assessment tool was used to determine the causal relationship of a suspected chemotherapy related to ADR in question and causality is defined as “definite,” “probable,” and “possible,” . “Therefore: >9 = definite ADR; 5–8 = probable ADR; 1–4 = possible ADR; 0 = doubtful ADR. The modified Hartwig

and Siegel scale classifies severity of ADR as Mild = Levels 1 and 2; Moderate = Levels 3 and 4; Severe = Levels 5, 6 and 7.

3.8.2. Data collectors and supervisors

For data collection; two pharmacists and two nurses were assigned and supervised by one clinical pharmacists. Data was extracted from patients' medical record cards and structured interview was identified by WHO causality assessment scale were used to identify ADRs level.

3.8.3. Data collection procedures

Adult cancer patients' medical records in HFCSH were traced from the registration log book of the oncology ward of chemotherapy and participants' some-mutinously face to face interviews the data were collected. .

The structured questionnaire were uploaded to Kobo Toolbox and used in the data collection for this study. Two clinical pharmacists and two nurse to collect the data. The investigator was followed the data collection procedures explicitly. Data was also gathered through the review of patients' medical records. They strictly record the changes in medication experiences and abnormal laboratory values to identify the potential occurrence of ADRs. Each day of data collection, the patients' medical chart and documents such as medication orders, progress notes, laboratory results, and changes in medication experiences were assessed.

3.9. Variables of the Study

3.9.1. Dependent variable

- Chemotherapy related ADRs

3.9.2. Independent variables

- Sociodemographic Characteristic (age, gender, weight, body surface area, height, educational status, marital status, residency, etc.).
- Drug-related Variables (Drug name, frequency of administration, number of chemotherapy per cycle).
- Cancer-related Variables (comorbidity and cancer type).

3.10. Operational definition

Chemotherapy related adverse drug reactions: ADR related to chemotherapy is defined as if one of the following signs/reaction are noticed or diagnosed among patients who are on chemotherapy. Considering these ADRs we classified the chemotherapy related ADR using the ADR assessing tools.

Naranjo algorithm as defined having >9 score is defined as definite ADR, while 5–8 score is probable ADR, 1–4 score is possible ADR and 0 score doubtful ADR(Mohapatra et al., 2011) .

The modified Hart wig and Siegel scale classifies severity of ADR as Mild = Levels 1 and 2; Moderate = Levels 3 and 4; Severe = Levels 5, 6 and 7. With various levels, depending on a number of factors like the requirement for change in treatment, duration of hospital was assessed by patient interview(Begum et al., 2022).

3.11. Data Quality Control

Prior to data collection, data collectors were trained on data collection procedures and study objectives, and reviewed medical charts for respective patients. Before actual data collection, pre-test were done in Jigjiga karamara hospital with 5 % of randomly selected sample patients to assess the tool's quality. Finally, necessary changes were made before it were used to collect data.The principal investigator were monitor the whole data collection process and were check for the completeness of data. Intensive supervision were made by principal investigator. Data were checked and cleaned for any missed data through running of frequency before analysis.

3.12. Data Processing and Analysis

The completed data was coded and cleaned during collected by kobo tool box and analyzed with SPSS version 20. All covariate was considered for logistic bivariable analysis, and a covariate which has P-value less than 0.25 was analyzed in logistic multivariable analysis. Crude odd ratio (COR) and adjusted odd ratio (AOR) were calculated with the 95% confidence interval to measure the strength of the association between the outcome and independent variables and the variable with P-value less than 0.05 in multivariable analysis were considered as significantly associated with the outcome variable.

3.13. Ethical Considerations

Ethical clearance was obtained from Institutional Health Research Ethics Review Committee (IHRERC) of Haramaya University, College of health and medical sciences (CHMS), and given to concerned body of HFCSH in order to get permission to conduct the study. The purpose of the study and method of data collection was highlighted for the concerned body. Informed, volunteer, written and signed consent was obtained from participants and from the head of the hospital. After letter of permission obtained from respective body, the letter was given to card room managers. The information obtained for patient medical record cards was kept confidentially, and name of the patient and other information that specifically identify the patient was not recorded.

3.14. Dissemination of the results

Tthe result of the study will be presented to Haramaya University, CHMS school of Graduate Studies as a partial fulfillment of Masters in clinical Pharmacy. After approval, the result of the study will be sent to HFCSH in hard copy. The results of the research will be also presented on different seminars, meetings and workshops. Further attempt was made to publish the result for national and international scientific community.

4. RESULTS

4.1. Sociodemographic Characteristics of Study Participants

A total of 422 study were included in this study. Among the included participants, 251 (59.5%) were female. About 101 (23.9%) patients were with age range of 41 – 50 years. Around 175 (41.5%) study participants were attended secondary school. Four hundred (94.8%) participants were married. Of the total of the 422 participants, 277 (65.6%) patients were lived in the rural area (**Table 2**).

Table 2: Demographic Characteristics of study participants among adult cancer patients at HFCSH cancer center, Eastern Ethiopia (N=422), 2024

Variables		Frequency	Percent (%)
Age (in Years)	18-30	82	19.4
	31- 40	92	21.8
	41-50	101	23.9
	51- 60	89	21.1
	≥61	58	13.7
Sex	Female	251	59.5
	Male	171	40.5
Marital Status	Unmarried	21	5.0
	Married	400	94.8
	Divorced	1	.2
Place of Residency	Rural	277	65.6
	Urban	145	34.4
Educational Level	No formal	146	34.6
	Primary School	74	17.5
	Secondary School	175	41.5
	College	20	4.7
	University	7	1.7

4.2. Clinical and Treatment related characteristics of study participants

The majority of patients 259(61.4%) weight were >50 kg. Of 422 study participants, 266(63%) participants had body surface area of >1.5 m^2. The frequently diagnosed cancer was breast cancer 183 (43.4%) followed by gynecological malignance 127 (30.1%). Regarding the severity of the disease, majority of patients were with early stage of cancer (stage I and II) 403(95.5%). From a total of 422 study participants, 246 (58.3%) of them were treated with chemotherapy followed by chemotherapy and surgery 176(41.7%) treatment modalities. Regarding the chemotherapy treatment modalities, majority 397 (94.1%) of them were on mono-chemotherapy and 291(69%) of them were on 2nd cycles treatment stages (**Table 3**).

Table 3: Clinical and treatment related characteristics of study participants among adult cancer patients at HFCSH cancer center Eastern, Ethiopia, (N = 422), 2024.

Variables		Frequency	Percent (%)
Cancer Types	Gynecological malignance	127	30.1
	Breast Cancer	183	43.4
	Gastrointestinal malignance	56	13.3
	Lung Cancer	44	10.4
	(Esoph, Hcc,Nhl, Npc, Osteo)	12	2.8
Cancer Stage	Early (I and II)	403	95.5
	Late (III and IV)	19	4.5
Treatment Modalities	Chemotherapy and surgery	176	41.7
	Chemotherapy only	246	58.3
Number of CT Agents	Monochemotherapy	397	94.1
	Polychemotherapy	25	5.9
Number of CT Cycles	1st cycle	3	.7
	2nd cycle	291	69.0
	3rd cycle	67	15.9
	>3rd cycle	61	14.5

Esophageal cancer (Esoph), Hepatocellular carcinoma (HCC), Non-Hodgkin lymphoma (NHL), Naso-pharyngeal cancer (NPC), Osteosarcoma (Oesteo).

4.3. Commonly utilized drugs and specific observed ADRs among study participants

From a total of 422 included patients, 91(21.6%) of patients were on Cisplatin (CI) plus Paclitaxel (PA) followed by CI alone 79(18.1%), and Doxorubicin (DO) + Cyclophosphamide (CY) 48 (11.4%), respectively (**Figure 2**). Different chemotherapy relate ADRs were observed/reported among included patients. Accordingly, the most frequently observed chemotherapy relate ADRs were fatigue, tiredness and anorexia 420 (14.9%), followed by 375 (13.3%) nausea/vomiting, and diarrhea 366 (13.0%) (**Table 4**).

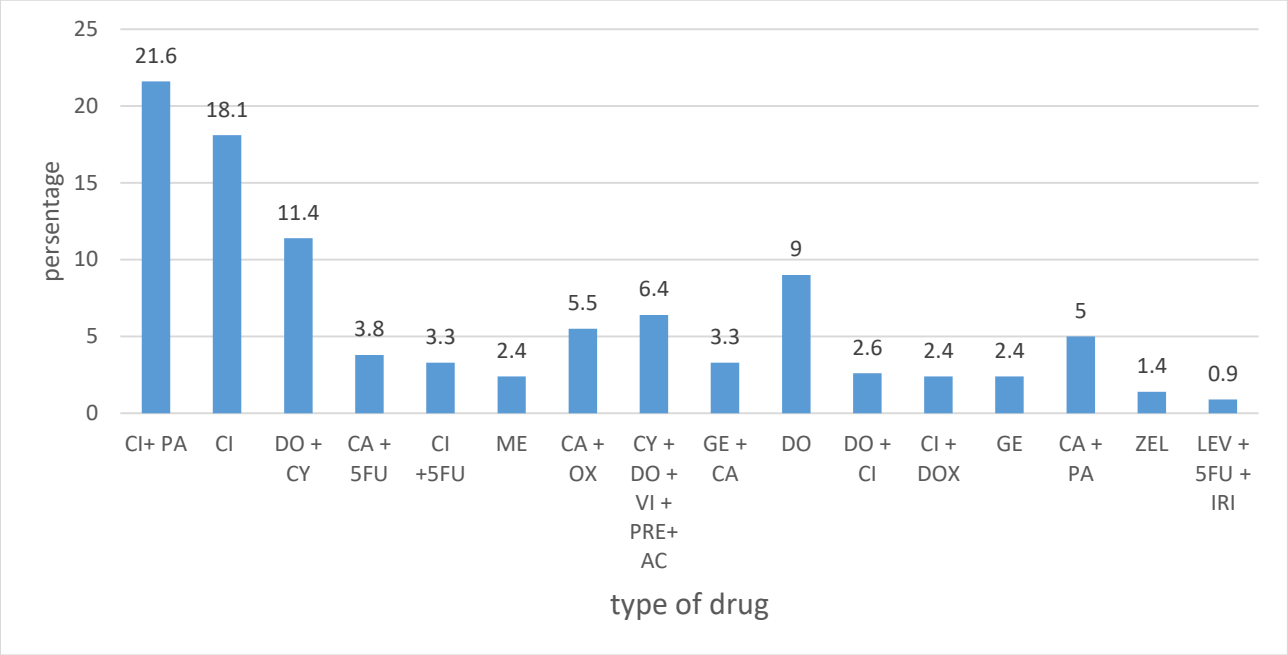

Figure 2: Commonly used chemotherapy among adult cancer patients at HFCSH cancer center Eastern Ethiopia (N = 422), 2024

Abbreviations: Cisplatin (CI), Paclitaxel (PA), Doxorubicin (DO), Cyclophosphamide (CY), Carboplatin (CA), Fluorouracil (5FU), Methotrexate (ME), Capecitabine(CA), Oxaliplatin (OX), Vincristine(VI), Prednisolone(PRE), Gemcitabine(GE), Docetaxel(DOX), Zoledronic Acid (ZEL), Leucovorin (LEV), Irinotecan(IRI),Actinomycin(AC).

Table 4: Specific observed ADRs among adult cancer patients at HFCSH from July 10 to August 15 (N = 422).

Variables	Frequency	Percent (%)
ADR		
Yes	204	48.3
No	218	51.7
Types of ADRs		
Diarrhea	366	13.0
Fatigue, tiredness and anorexia	420	14.9
Fever and chills	89	3.2
Nausea and vomiting	375	13.3
Malnutrition	262	9.3
Alopecia	332	11.8
Constipation	335	11.9
Anemia	159	5.6
Neutropenia	18	0.6
Thrombocytopenia	25	0.9
Infection	49	1.7
Electrolyte imbalance	9	0.3
Dehydration	360	12.8
Thrombosis/embolism	24	0.9

4.4. Causality Assessment of suspected ADR using Naranjo algorithm, and severity of ADR using Hartwig severity assessment

Accordingly, for the Naranjo algorithm a total of 2823 ADRs were identified for which probable ADRs account for 2122 (75.17%) followed by definite ADRs 508 (18.0%). Using Hartwig severity assessment scale, majority ADR were 2699 (95.87%) moderate ADRs (**Table 5**).

Table 5: Causality Assessment of chemotherapy related ADR using Naranjo algorithm and severity of chemotherapy related using Hartwig severity assessment among adult cancer patients at HFCSH from July 10 to August 15 (N = 422).

ADRs	Naranjo algorithm				Hartwig severity assessment			
	Possible	Probable	Definite	Total	Mild	Moderate	Severe	Total
Diarrhea	22	278	66	366	15	350	1	366
Fatigue tiredness,& anorexia	31	313	76	420	21	398	1	420
Fever and chills	4	71	14	89	2	86	1	89
Nausea and vomiting	27	280	68	375	14	360	1	375
Malnutrition	21	191	50	262	10	251	1	262
Alopecia	21	253	58	332	15	317	0	332
Constipation	25	251	59	335	13	321	1	335
Anemia	10	119	30	159	7	152	0	159
Neutropenia	0	16	2	18	1	17	0	18
Thrombocytopenia	2	18	5	25	0	25	0	25
Infection	3	40	6	49	1	48	0	49
Electrolyte imbalance	1	7	1	9	1	8	0	9
Dehydration	23	268	69	360	17	342	1	360
Thrombosis embolism	3	17	4	24	0	24	0	24
Total	193	2122	508	2823	117	2699	7	2823

4.5. Specific regimens associated with selected ADRs among study participants

From the total of 420 chemotherapy related Fatigue tiredness, & anorexia, majority were reported from CI plus PA (91). Similarly in the case of alopecia, nausea and vomiting, diarrhea and Dehydration the reported offending drug was CI plus PA (**Table 6**).

Table 6: Selected ADRs associated with specific regimens containing the most suspected agent among adult cancer patients at HFCSH from July 10 to August 15 (N = 422).

ADRs	Chemotherapy drugs											
	CI	CI+ PA	DO+ CY	CA+ FU	CI+ 5FU	CA+ OX	CY+DO+VI +PRE+AC	GE+ CA	DO	DO+ CI	CI+D OX	CA+PA
Diarrhea	69	80	40	17	13	19	24	14	35	17	18	20
Fatigue, tiredness & anorexia	76	91	48	20	16	22	27	20	38	21	20	21
Nausea, and vomiting	66	83	44	15	13	17	24	20	36	19	19	19
Malnutrition	44	52	22	12	13	16	20	7	33	10	15	18
Alopecia	73	87	25	16	14	16	17	16	24	6	18	20
constipation	68	68	39	19	17	20	18	13	27	15	15	14
Anemia	28	33	10	15	10	10	8	4	23	3	5	10
Dehydration	66	78	40	25	22	24	21	11	36	8	9	20

Abbreviations: Cisplatin (CI), Paclitaxel (PA), Doxorubicin (DO), Cyclophosphamide (CY), Carboplatin (CA), Fluorouracil (5FU), Methotrexate(ME), Capecitabine(CA), Oxaliplatin (OX), Vincristine(VI), Prednisolone(PRE), Gemcitabine(GE), Docetaxel(DOX), ZoledronicAcid(ZEL), Leucovorin (LEV), Irinotecan(IRI),Actinomycin(AC).

4.6. Factors with chemotherapy related ADRs among study participants

Outcome variable (ADR) was categorized into no chemotherapy related ADR and presence of chemotherapy related ADR (Yes). Accordingly, bivariable logistic regression was done to identify factors considered for multivariable analysis. Then, educational level, patient age, patient BSA, patient weight, patient place of residency and patient occupation were considered for multivariable regression with P value of less than 0.25.**(Table 7)**

Table 7: Bivariate Analysis of factors associated with chemotherapy related ADRs among adult cancer patients at HFCSH, Eastern Ethiopia (N = 422), 2024.

Variable	Categories	ADRs		COR(95%CI)	P-value
		No	Yes		
Weight	<=50	104	59	2.80(1.86,4.2050)	0.00
	>50	100	159	1	
Educational level	Illiterate	87	59	2.50(1.07,5.85)	0.03
	Primary school	40	34	1.05(0.58,3.57)	0.42
	Secondary school	102	73	1.25(0.52,2.81)	0.64
	College and above	10	17	1	
BSA	<=1.5	64	92	1.97(1.32,2.95)	0.001
	>1.5	154	112	1	
Age	18-30	39	43	1	
	31-40	57	35	0.51(0.25,1.02)	0.05
	41-50	57	44	0.55 (0.17,0.68)	0.02
	51-60	49	40	0.70(0.22,0.85)	0.01
	>=61	37	21	0.74(0.35,1.37)	0.29
Occupational status	House Wife	185	185	2.22(0.98,5.00)	0.54
	Student	10	13	1.70(0.54,5.34)	
	Business man	9	20	1	0.35

Key: *, variable had <0.25 p-value:

The result of multivariable regression analysis showed that cancer patients with those having weight less than 50 kg were 3.29 times more likely associated with ADR (AOR = 3.29, 95% CI: 1.82, 5.94). On the other hand, cancer patient with age categories between 31- 40 years 0.34 times (AOR = 0.34% CI: 0.15, 0.74), more likely associated with ADR respectively (**Table 8**).

Table 8: Multivariable analysis of factors associated with chemotherapy related ADRs among adult cancer patients at HFCSH, Eastern Ethiopia 2024, (N = 422).

Variable	**Category**	**ADRs**		**COR (95% CI)**	**AOR (95% CI)**	**P. value**
		No	Yes			

Educational level	Illiterate	87	59	2.50(1.07,5.85)	1.68(0.65, 4.37)	0.281
	Primary School	40	34	1.05(0.58,3.57)	1.22(0.47, 3.19)	
	Secondary School	102	73	1.25(0.52,2.81)	1.07(0.44, 2.58)	0.678
	College and above	10	17	1	1	
Weight	<=50	1 04	59	2.80(1.86,4.20)*	3.29(1.82, 5.94)	**0.001**
	>50	100	159	1		
Age	18 -30	39	43	1	1	
	31-40	57	35	0.51(0.25,1.02)	0.34(0.15, 0.74)	**0.007**
	41-50	57	44	0.55(0.17,0.68)	0.41(0.19, 0.85)	0.018
	51-60	49	40	0. 74 (0.22,0.85)	0.58(0.28, 1.18)	0.134
Occupational status	House Wife	185	185	2.22(0.98,5.00)	1.95(0.81, 4.68)	0.135
	Student	13	10	1		
	Business man	20	9	1.70(0.54,5.34)	1.36(0.37, 4.93)	0.632
Body surface area	<=1.5	92	64	1.97(1.32,2.95)	0.90(0.50, 1.62)	0.741
	>1.5	112	154	1		

Hosmer-Lemeshow .goodness of the fit test was fitted

P < 0.05. P < 0.001. CI: confidence interval, ADRs: Adverse drug reactions, COR: Crude Odd Ratio, AOR: Adjusted Odd Ratio.

5. DISCUSSION

This study included a total of 422 cancer patients. Of 422 study participants, 48.34% patients were developed chemotherapy relate ADR. Having weight less 50 kg, and patients with age range of 31-40 years were associated with developing ADR.

Most frequently observed ADRs include fatigue, tiredness, and anorexia followed by nausea and vomiting which in line with study conducted elsewhere(Keshri et al., 2017, Prasad et al., 2013), but different from a study conducted in India, mahatama Gandhi tertiary hospital that showed body pain was the most common ADR (Aghamohammadi et al., 2019). This difference might be due study design, included sample size and study setting differences. Accordingly, for the Naranjo algorithm a total of 2823 ADRs were identified for which probable account for 2122 (75.17%) followed by definite 508 (18.0%). Using Hartwig severity assessment scale, majority ADR were 2699 (95.87%) moderate. Unlikely in India that majority of the ADRs (77.4%) were mild followed by moderate (18.9%) and severe (3.8%)(Wahlang et al., 2017b) . In this study, a total of only 11.7% of patients experienced alopecia / hair loss and it is significantly less when compared with 51% and 58% that was stated in some other studies(Poddar et al., 2009, Surendiran et al., 2010).the reason is due to socio-demography locations, length of study and sample size of the participant.

In this study, around 21.6% participants were taken Cisplatin plus paclitaxel in India 2.2% therefore possible justifications due to sample size, lack of availability of alternative items, cancer type and stages of cancer can determine item of drug utilizations, life style modifications, continuous monitoring and geographical locations(Naresh and Rajshekar, Pentareddy et al., 2015) on the other hands 18.1% participants were taken Cisplatin which is similar with the study conducted in India cisplatin 18.5% (Bepari et al., 2019) Similar findings were seen in other related studies of Mary Rohini et al., 2015, Goyal et al., 2014 and Darshan et al., 2014(Pentareddy et al., 2015, Goyal et al., 2014).

The scrutiny of causal association using the Naranjo Scale of causality assessment showed that 75.17% ADR fell in the category of ‘Probable’ and 7% were ‘Possible’. These findings are s not consistent to other studies (Ramasubbu et al., 2021), with the use of this same scale, two other studies reported 100% and 61% of probable scores for causality (Singh et al., 2017). There is difference in result because of sample size, study period and geographical locations can play a grate

roll to cause ADRs. This study found that 48.34% cancer patients experienced an adverse drug reaction related to chemotherapy. More than three-fourth of the patients had moderate adverse drugs, according to the Hartwig and Siegel severity assessment scale. According to south Asian study 49% of ADRs were either probably or definitely preventable(Chopra et al., 2016a). This finding was in line with a study conducted in Tikur Anbessa Specialized Hospital, Ethiopia that reported the prevalence of 45.5 % ((Kifle et al., 2019). On the contrary, ADR was lower than studies reported from Eastern India 86.53%(Singh et al., 2018) Mexico City 62.5%(Castelán-Martínez et al., 2016) and south African 56.5% (Makiwane et al., 2019b). The difference is due to age variations, type of chemotherapy, cancer type, stage and comorbidity are of the factors that causes the difference in prevalence of ADRs. ADRs could have probably been prevented in patients who had symptoms of vomiting, general weakness and constipation where appropriate premedication was given and proper dietary counsel was ensured before the start of chemotherapy.

Patients those having weight less than 50 kg, were about three times to experience the adverse reaction. Other finding is similar to the research done in USA in underweight/low normal (BMI<23) and normal weight (BMI 23-25) categories, and found that any grade ≥3 adverse events, anemia, and neutropenia were more common in underweight/low normal weight individuals, indicating this subgroup's potential increased vulnerability to therapy-related toxicities(Lyman et al., 2003, Shayne et al., 2006). Another study in Ethiopia Nigist Elleni Mohamed memorial comprehensive specialized hospital study revealed that, association was found between low body weight and risk of ADR same dosed were being given and this exposed the patients to greater toxicity of the drugs which were most likely dose dependent(Menza, 2022). This could be due to the fact that low body weight patient more prone to adverse drug reactions.

In our study, ADRs mostly occurred in the age group of 31- 40 years which is similar to that reported by other studies in India (Kirthi et al., 2014, Poddar et al., 2009). In other study the common age group for ADR was between 50 and 70 years(Ramasubbu et al., 2020). Similarly in Ethiopia findings conducting Gondar University reviled that age groups greater than 61 years were prone to ADRs ((Belachew et al., 2016).Possible justifications for difference is life style modifications and participant awareness as the same time monitoring and follow up differences cause ADRs in early age.

6. STRENGTHS AND LIMITATIONS

6.1. Strengths and limitations

The study's strength was it covers a large samples and recent information. This study had some limitations, like the study was conducted at a single institution using a cross-sectional study design and adverse drug reactions were considered based on patients' responses and/or from medical records which is difficult to know a causal relationship. The result of the magnitude and associated factor of this study may not be generalized to all hospitals because the study was conducted in a single center.

7. CONCLUSION AND RECOMMENDATION

7.1. Conclusion

In Overall, near to half of the included cancer patients developed ADRs. Based on the Naranjo algorithm a total of 2823 ADRs were identified for which probable account for 2122 (75.17%) followed by definite 508 (18.0%). Using Hartwig severity assessment scale, majority ADR were 2699 (95.87%) moderate. Having weight less 50 kg, and cancer patient with age range of 31- 40 years were associated with developing ADR. Therefore, special attention should be given for cancer patients with those condition so that adverse drug reactions can be minimized.

7.2. Recommendations

I would like to recommend to the healthcare professional who work at the oncology ward of HFCSH to registered chemotherapy related ADR since their data management challenging to determine the appropriate prevalence.

Since the weight of the patient was one of the risk factor for developing ADR, the health care professional should assess the nutritional status of the patient to minimize this factor by intervening at the earliest phase.

To decrease the prevalence of ADRs of chemotherapy HFCSH.

- High percentage of prevalence should lead to a reinforcement of information about drug toxicities among patients and oncologists.
- To reduce the current prevalence of ADRs on chemotherapy, HFCSH oncology center should work on it.
- Health care professional should assess based on current result of this study to minimize this factor by intervening at the earliest phase.

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9. INFORMATION SHEET AND VOLUNTARY CONSENT FORM

9.1. Information sheet and informed consent for health facility medical director/CEO

My name is Fekadu Megersa. I am working as a principal investigator for the study being conducted in this health facility for studying masters' degree in clinical pharmacy at Haramaya University College of health and medical sciences. I kindly request you to lend me your attention; explain about the study and your health facility being selected as the study participant

The study title

Chemotherapy related adverse drug reactions among adult patients attending Hon.Dr. Artist Ali Birra memorial cancer treatment center of HFCSH, Harar, and Eastern Ethiopia.

Purpose of the study

The findings of this study can be of a paramount importance for the HFCSH to plan intervention programs to prevent chemotherapy related ADR. Moreover, the aim of this study is to write a thesis as a partial requirement for the fulfillment of a Master's Program in Clinical Pharmacy. For the principal investigator.

Data collection procedure and duration

Data collector was reviewing the medical records and interviewing the participant using a questionnaire to provide me with pertinent data that is helpful for the study. The interview was take about 20 minutes.

Risk and benefit of the study

The risk of being participating in this study is very minimal, but only taking few minutes from your time. There would not be any direct payment for participating in this study. But the findings from this research may reveal important information for the local health planners.

Confidentiality

The information collected in the way explained above will be confidential. There will be no information to be collected on particular study subject identification. Data collectors will be informed and trained to preserve patient confidentiality

Rights

Participation for this study is fully voluntary. Participants have the right to declare to participate or not to participate. Moreover participants have the right to withdraw from the study at any time. The hospital also has the right stop the study if any misconduct observed

Contact address

If there is any question or enquiries at any time about the study or procedure please contact the investigators;

Fekadu Megersa: mobile phone; +251-910-316-050.

Email address: fikeje@gmail.com

Haramaya university Institutional Health Research Review Ethics Committee Office Phone number; 0256661899.

Declaration of informed voluntary consent

I have read the participant information sheet. I have clearly understood the purpose, procedure of the research, confidentiality and risk and benefit issue of this study. I have been given the opportunity to ask questions for things that may have been unclear. I was informed that the participant have the right to decide a withdrawal from the study at any time. I am also informed that the Hospital has the right to stop this study from being conducted if any misdeeds and unethical procedures are observed during the data collection process in the Hospital's premises. Therefore, I declare my voluntary consent on behalf of the Hospital management to allow this study to be conducted in the Hospital with my initials (signature).

Name& signature of medical director /CEO---------- ---------- Date----------

Name& signature of principal investigator ---------- ----------Date----------

9.2. Participant information sheet and informed voluntary consent form

My name is _____. I am working as a data collector for the study being conducted in this health institution by Fekadu Megersa who is studying for his Master's degree in Clinical Pharmacy at Haramaya University, the College of Health and Medical Sciences. I kindly request you to lend me your attention to explain you about the study and being selected as the study participant.

The study/project title:

Chemotherapy related adverse drug reactions among adult patients with cancer attending Hon.Dr. Artist Ali Birra memorial cancer treatment center of HFCSH, Harar, and Eastern Ethiopia.

Purpose/aim of the study:

The aim of this study is to determine Chemotherapy related adverse drug reactions and associated factors among adult patients with cancer attending Hon.Dr. Artist Ali Birra memorial cancer treatment center of HFCSH. The finding of this study might be a paramount importance for patients. Therefore, the study will identify and investigate the gaps and will suggest the possible recommendations. Hence, it may benefit you in improving the medical care service for betterment of your treatment outcome. Moreover, the aim of this study is to write a thesis as a partial requirement for the fulfillment of a Master's program in Clinical Pharmacy for the principal investigator.

Procedure and duration:

Data collectors will interview you for 10 to 15 minute using questionnaire and also Data collectors collect data from your chart by using a questionnaire and check list. Moreover, Data collectors will also observing you prospectively until the date of your discharge from this institution.

Risks and Benefits:

The risk to you being a study participant is very minimal, but only taking few minutes from your time. There would not be any direct benefit for participating in this study. However, the findings from this research may reveal important information for Hospital/Organization and your health care providers and it may benefit them in improving the medical care service for betterment of patients' treatment outcome.

Confidentiality:

The information that data collectors will collect from this study will be kept confidential. There will be no information that identifies you in particular. The finding of the study will be general for the study community and no reference will be made in oral or written reports that could link the participants to the research.

Rights:

Participation for this study is fully voluntary. You have the right to declare to participate or not in this study. If you decide to participate, you have the right to withdraw from the study at any time and this will not label you for any loss of benefits which you otherwise are entitled. You do not have to answer any question that you do not want to answer.

Contact Address:

If there are any questions or enquire any time about the study or the procedures, please contact through the following addresses.

Principal investigator cell phone: +251-910-316-050, Email: fikeje@gmail.com. Contact address of the responsible Institutional Health Research Ethics Review Committee (IHRERC) at office phone: +254662011 or P.O. Box 235, Harar.

Declaration of informed voluntary consent:

I have read/ was read to me the participant information sheet. I have clearly understood the purpose of the research, the procedures, the risks and benefits, issues of confidentiality, the rights of participating and the contact address for any queries. I have been given the opportunity to ask questions for things that may have been unclear. I was informed that I have the right to withdraw from the study at any time or not to answer any question that I do not want. Therefore, I declare my voluntary consent to participate (be involved) in this study with my initials (signature).

Name and signature of Participant: _____ _____ Date: _____

Name and signature of Data Collector: _____ _____Date: _____

9.3. Participant information sheet and informed voluntary consent (Amharic Version)

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9.4. Participant information sheet and informed voluntary consent (A/ Oromo version)

Maqaan koo_____ Qorannoo dhaabbata fayyaa kana keessatti gaggeeffamaa jiruuf Daataa walitti qabaa ta'ee hojjechaan jira. Fiqaaduu Magarsaa Yunivarsiitii Haramayaatti, Kolleejjii Saayinsii Fayyaa fi Meedikaalaatti barnoota Faarmaasii Kilinikaatiin Digirii Lammaffaa barachaa jira. Waa'ee qorannichaa fi ati akka hirmaataa qorannichaa taataani filatamuu keessanif akkan siif ibsuuf xiyyeeffannoo keessan akka naaf liqeessitan kabajaan isin gaafadha.

Mata duree qo'annoo/pirojektichaa: keemooteraapii deebii badaa qorichaatiin walqabatee dhufu fi wantoota rakkoolee kanaan walqabatan dhukkubsattoota kaansarii Hospitaala Waliigalaa Ispeeshaalistii Hiwot Faanaa (HFCSH), seenan iratti, Baha Itoopiyaa.

Kaayyoo/kaayyoo qorannichaa: Kaayyoon qorannoo kanaa dhukkubsattoota ga'eessota kaansarii qaban kanneen wiirtuu wal'aansa kaansarii HFCSH yaalama jiran irraatti waa'ee keemooteraapii deebii badaa qorichaatiin walqabatee dhufufi waa'ee dhukkubsattoota kaansarii irraatti xiyyeefata. Argannoon qorannoo kanaa dhukkubsattootaaf barbaachisummaa olaanaa ta'uu danda'a. Kanaafuu, qorannichi qaawwa jiru adda baasee qoratee yaadota ta'uu danda'an kan dhiyeessu ta'a. Kanaaf, bu'aan wal'aansa keessanii akka fooyya'uuf tajaajila kunuunsa yaalaa fooyyessuudhaan isin fayyaduu danda'a. Kana malees, kaayyoon qorannoo kanaa qorataa muummichaaf sagantaa Maastarsii Faarmaasii Kilinikaalaa galmaan ga'uuf akka barbaachisummaa gartokkeetti barruu qorannoo (thesis) barreessuudha.

Adeemsaa fi yeroo: Qorannoo kanaaf daataa walitti qabaan Gaaffii caaseffama qabu fayyadamuun daqiiqaa 10 hanga 15tti si wallin gaaffii fi deebii nii godha akkasumas daataa walitti qabaan gaaffilee fi cheeklistti fayyadamuun chaartii(kaardii) keessanii irraa daataa walitti qaba.

Balaa fi Faayidaa: Hirmaataa qorannoo kanaa ta'uu keetiif balaan sirra gahuu hinjiru, garuu yeroo kee irraa daqiiqaa muraasa qofa naaf kennita. Qorannoo kana irratti hirmaachuudhaaf faayidaan kallattiin hin jiraatu. Haa ta'u malee, argannoon qorannoo kanarraa argamu odeeffannoo barbaachisaa ta'e hospitaalaaf/ dhaabataaf fi ogeeyyii fayyaa keessaniif kan mul'isu yoo ta'u, bu'aa wal'aansa keessanii fooyyessuuf tajaajila kunuunsa yaalaa fooyyessuu keessatti isin fayyaduu danda'a.

Iccitii: Odeeffannoon daataa walitti qabaan qorannoo kana irraa walitti qabu iccitii ta'ee ni eegama. Odeeffannoon addatti si adda baasu hin jiraatu. Argannoon qorannichaa hawaasa qorannichaaf waliigalaa

kan ta’u yoo ta’u, gabaasa afaaniin ykn barreeffamaan hirmaattoota qorannichaan walqabsiisuu danda’u keessatti eeruun hin kennamu.

Mirga: Qorannoo kanaaf hirmaannaan guutummaatti fedhii ofiitiin kan kennamudha. Qo’annoo kana irratti hirmaachuu fi dhiisuu kee labsuuf mirga qabda. Yoo hirmaachuuf murteessite yeroo barbaaddetti qorannicha keessaa ba’uuf mirga qabda kunis faayidaa kasaaraa karaa biraatiin siif malu kamiyyuu si hin madatu. Gaaffii deebii kennuu hin barbaanne kamiyyuu deebisuun si hin barbaachisu.

Teessoo Quunnamtii: Waa’ee qorannichaa ykn hojimaata yeroo kamiyyuu gaaffii yoo jiraate ykn gaaffii yoo qabaattan karaa teessoo armaan gadii qunnamaa.

Qorataa ijoo bilbila harkaa: 251-910-316-050, Imeelii: fikeje@gmail.com.

teessoo quunnamtii itti gaafatamummaa qabu koree gamaaggama naamusa qorannoo dhaabbilee fayyaa (IHRERC) bilbila waajjira: 254662011 ykn P.O. 235, Harar

Labsii hayyama tola beekumsa qabu: Waraqaa odeeffannoo hirmaataa dubbiseera/ naaf dubbifameera. Kaayyoo qorannichaa, hojimaata, balaa fi faayidaa, dhimmoota iccitii, mirga hirmaachuu fi teessoo quunnamtii gaaffii kamiifuu sirriitti hubadheera. Wantoota ifa hin taane ta’uu danda’aniif gaaffii akkan gaafadhu carraan naaf kennameera. Yeroo barbaadetti qorannoo keessaa ba`uu ykn gaaffii ani hin barbaanne kamiyyuu deebisuuf mirga akkan qabu naaf himameera. Kanaafuu, hayyama fedhii kootiin qorannoo kana irratti hirmaachuu koo mallattoo kootiinan ibsa.

Maqaa fi mallattoo Hirmaataa: _____ Guyyaa: _____
Maqaa fi mallattoo Walitti qabaa Odeeffannoo: _____Guyyaa: _____

H.B

•Kun bakka walitti qabaan odeeffannoo jirutti fuula fuulatti mallattaa'a.

•Maaloo waraabbii hayyama mallattaa’e kanaa hirmaataaf kenni

9.5. Questionnaire of Chemotherapy related ADR

Data collection date: _____/_____/_____. Card No: _____

Section-I: Sociodemographic characteristics

No	Question	Response	Remark
1	Age in years		
2	Sex	1-Male 2-Female	
3	Weight in kg		
4	Length in cent meter		
5	BSA		
6	Marital status	1-Unmarried 2-Married 3-Separated, divorced 4-Widowed 5-others specify_____	
7	Educational level	1-Illiterate 2-Primary school 3-Secondary school 4-College and 5-University	
8	Occupational status	1-Student 2-Manual laborer 3-Housewife 4-Government employee 5-Businessmen	
9	Place of Residency	1 Urban 2 Ruler	

Section-II: **Clinical characteristics of the patient**

Do you developed any ADR after starting chemotherapy? A. Yes B. No

No	Question	Response	Remark
10	Diarrhea?		
11	Fatigue /tiredness/anorexia?		
12	Fever and/or chills		
13	Nausea and vomiting		
14	Malnutrition (assessed by data collectors)		
15	Alopecia (assessed by data collectors)		
16	Do you have constipation?		
	Fill the following diagnosis from the patient card and/or investigation forms		
17	Anemia		
18	Neutropenia		
19	Thrombocytopenia		
20	Infection		
21	Electrolyte imbalance		
22	Dehydration		
23	Thrombosis/embolism		

Section-III Disease related factors

No	Question	Response	Remark
24	Do the patient have any family history of cancer?	1. Yes 2. No	
	Fill the following diagnosis from the patient card		
25	Cancer type	1- Breast cancer 2-Lung cancer 3- Hematologic malignancies 4-Gastrointestinal malignancies 5-Gynecologic malignancies 6-Others specify	
26	Cancer stages	1-Early (I and II))	

		2-Late (III and IV)	
27	Comorbidity	1. Yes 2. No	
	If yes specify		

Section-IV: Drug related information

No	Question	Response	Remark
28	Treatment Modalities	1. chemotherapy only 2. chemotherapy and surgery	
29	Number of Chemotherapeutic Agents	1- Monochemotherapy 2- Polychemotherapy	
30	Name of chemotherapy		
31	Number of Chemotherapeutic cycle	1st cycle 2nd cycle 3rd cycle 4 ≥ three cycle	
32	Dose of chemotherapeutic agents	1- Reduced 2- Standard	

Section V Lab Diagnosis

Lab Diagnosis		Result	Reference range
33)	HGB (g/dL		
34	WBC (×103 cells/µL)		
35	PLT (×103cells/µL)		
37	Organ function test	1.ALT_____ 2.AST _____ 3. Crcl_____ 4. T3 _____ 5. T4 _____	
	Others specify		

Section VI Hartwig severity assessment scale adverse drug reaction.

Level	**ADR: adverse drug reaction**.	Response	
		Yes	No
38	An ADR occurred but required no change in treatment with the suspected drug		
39	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS).		
40	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. AND/OR an Antidote or other treatment was required. No increase in length of stay (LOS).		
41	Any level 3 ADR which increases length of stay by at least 1 day or the ADR was the reason for the admission.		
42	Any level 4 ADR which requires intensive medical care.		
43	The adverse reaction caused permanent harm to the patient		
44	The adverse reaction either directly or indirectly led to the death of the patient.		

Mild = Levels 1 and 2; Moderate = Levels 3 and 4; and Severe = Levels 5, 6 and 7.

Section VII Naranjo ADR probability scale

Level	Description of ADR's characteristics	Response	
		Yes	No
45	Are there previous conclusive reports on this reaction?		
46	Did the adverse event appear after the suspected drug was administered?		
47	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?		
48	Did the adverse event reappear when the drug was re-administered?		
49	Are there alternative causes (other than the drug) that could on their own have caused the reaction?		
50	Did the reaction reappear when a placebo was given?		
51	Was the drug detected in blood (or other fluids) in concentrations known to be toxic?		
52	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?		
53	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?		
54	Was the adverse event confirmed by any objective evidence?		

For Naranjo algorithm: >9 = definite ADR; 5–8 = probable ADR; 1–4 = possible ADR; 0 = Doubtful.

Section VIII Schumock and Thornton preventability scale.

Level	**Definitely Preventable**	Response	
		Yes	No
55	Was the drug involved inappropriate for the patient's clinical condition?		
56	Was the dose, route or frequency of administration inappropriate for the patient's age, weight or disease state?		
57	Was a toxic serum drug concentration (or laboratory monitoring test) documented?		
58	Was there a known treatment for the Adverse Drug Reaction?		

	Probably Preventable		
59	Was required Therapeutic drug monitoring or other necessary laboratory tests not performed?		
60	Was a drug interaction involved in the ADR?		
61	Was poor compliance involved in the ADR?		
62	Were preventative measures not prescribed or administered to the patient?		
	Not preventable		
	If all above criteria not fulfilled		

9.6. Questionnaire

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6	ADR □□□□□□ □□ □□□ □□□ □□□□□		
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9.7. Questionnaire (Afaan Oromoo Version)

Guyyaa odeeffannoon walitti qabamu: ____/_____/_____. Lakk Kaardii: _____.

Kutaa-3.1: Amaloota hawaas-dimoogiraafii

lakkoofsa	Gaaffii	Deebii	Yaada
101	Umurii	_____	
102	Saalaa	Dhiira	
		Dhalaa	
103	Ulfaatina k.g	_____	
104	Dherinaa(M)		
105	BMI		
106	Haala gaa'elaa	1-Kan hin heerumne 2-Gaa'ela godhate 3-Adda gargar bahuu, wal hiikuu 4-Dubartoota abbaan manaa irraa du'e 5 kan birra yoo jirate ibsi	
107	Sadarkaa barnootaa	1- Hin baaranee 2-Mana barumsaa sadarkaa tokkoffaa 3-Mana barumsaa sadarkaa lammaffaa 4-Kolleejjii fi 5-Yuunivarsiitii	
108	Haala hojii	1-Barataa 2-Hojjetaa harkaa 3-Haadha manaa 4-Hojjetaa mootummaa 5-Daldaltoota	

109	Bakka Jireenyaa	1 Magaalaa 2 Badiyaa	

Kutaa-3.2: Amaloota kilinikaalaa dhukkubsataa

lakkoofsa	Gaaffii	Deebii	Yaada
201	Dhukkuba Garaachaa qabdaa?		
202	Dadhabbiin/dadhabbiin/anorexia sitti dhagahamaa?		
203	Ho'a qaamaa fi/ykn qorra qabdaa		
204	Garaa kaasaa fi garaa kaasaa qabdaa		
205	Hanqina nyaataa (kan madaalamu namoota odeeffannoo walitti qabuun).		
206	Alopecia (kan madaalamu namoota odeeffannoo walitti qabuun)		
207	Qufaa qabdaa?		
	Kaardii dhukkubsataa fi/ykn unka qorannoo irraa adda baasuu armaan gadii guuti		
208	Hir'ina dhiigaa		
209	Baay'ee muraasa, gosa seelii dhiiga adii		
210	Hirrinaa dhiigaa platileetii		
211	Hubama (infekshinii)		
212	Madaallii elektiroolayitii dhabuu		
213	Bishaan qaama keessaa hir'achuu		
214	Dhibee ujumoo dhiigaa.		

Kutaa-3.3: Odeeffannoo qoricha sammuu hadoochu waliin walqabatee

lakkoofsa	Gaaffii	Deebii	Yaada
301	Dhukkubsataan kun maatii isaa keessatti namni dhibee kaansarii qabu jiraa?		
Kaardii dhukkubsataa irraa adda baasuun kanneen armaan gadii guuti			
302	Kaansarii gosa	1- Kaansarii harmaa 2-Kaansarii sombaa 3- Dhukkuba hamaa dhiigaa (hematologic malignancies). 4-Dhukkuba hamaa garaachaa 5-Dhukkuba hamaa haadholii 6-Kanneen biroo	
303	Sadarkaa kaansarii	1-Jalqaba (I fi II). 2-Booda (III fi IV).	
304	Dhukkuba waliin dhufu	1. Eeyyee 2. Lakki	
305	eeyyee yoo ta'e, maqaa dhukkuba waliin dhufu tarreessi		

Kutaa-3.4: Odeeffannoo qorichaan walqabatu

Lakkoofsa	Gaaffii	Deebii	Yaada
401	Haala Wal'aansaa	1. kemooteraapii qofa 2. kemooteraapii fi baqaqsanii hodhuu	
402	Baay'ina Keemooteraapii	1-Monochemotherapy 2-Polikeemooteraapii	
403	Maqaa keemooteraapii tarreessi		
404	Baay'ina marsaa Keemooteraapii	1.Marsaa 1ffaa 2.Marsaa 2ffaa 3.Marsaa 3ffaa 4 .≥ marsaa sadii	
405	Doosii keemooteraapii	1- Hir'ate 2- Istaandardii	

Qorannoowwan laabraatoorii

Laabraatoorii	Daangaa wabii	Bu'aa
HGB (g/dL)		
HCT (%)		
WBC (×103 cells/µL)		
PLT (×103cells/µL)		

Iskeelii carraa Naranjo Deebiin qoricha hamaa—wantoota fi qabxii

Sadarkaa	Gaaffii Ibsa amala ADR's	Eeyyee	Lakki
1	ADRn uumame garuu qoricha shakkameen wal'aansa irratti jijjiirama hin barbaanne		
2	ADRn qoricha shakkame kanaan wal'aansi akka gaggeeffamu gaafate, addaan cite, ykn karaa biraatiin jijjiirame. Qorichi farra qoricha ykn wal'aansi biraa barbaachisu hin turre. Turtiin hospitaalaa dabaluu hin jiru.		
3	ADRn qoricha shakkame kanaan wal'aansi akka gaggeeffamu gaafate, .addaan cite, ykn karaa biraatiin jijjiirame FI/YKN farra qoricha ykn yaaliin biraa barbaachise. Turtiin hospitaalaa dabaluu hin jiru		
4	ADR Sadarkaa 3ffaa kamiyyuu kan yeroo turtii yoo xiqqaate guyyaa 1n dabalu		
5	ADR sadarkaa 4ffaa kamiyyuu kan kunuunsa fayyaa cimaa barbaadu		
6	ADR dhukkubsataa kana irratti miidhaa dhaabbataa geessiseera		
7	ADR kan du'a dhukkubsataa kanaaf sababa ta'e		

Qabxii algoritmiin Naranjo: >9 = Deebiin qoricha hamaa murtaa’aa; 5–8 = Deebiin qoricha hamaa ta’uu danda’u; 1–4 = Deebiin qoricha hamaa ta’uu danda’u; 0 = Deebiin qoricha hamaa shakkii qabufi Iskeelii Madaallii Cimina Hartwig. Deebiin qoricha hamaa: deebii qoricha hamaa.

Salphaa = Sadarkaa 1 fi 2; Giddugaleessa = Sadarkaa 3 fi 4; Hamaa = Sadarkaa 5, 6 fi 7.