MAGNITUDE AND PREDICTORS OF DRUG THERAPY PROBLEMS AMONG PATIENTS WITH LEUKEMIA AT KENYATTA NATIONAL HOSPITAL

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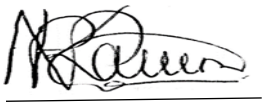
1. Signature  Date: 27/11/2023

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DEDICATION

I wish to dedicate this work to my Late Mother Emmy Imali who passed away on the 31st of March 2023 3 weeks after approval of this study. May your soul be at peace Mama. I Love You.

To my father Ephraim Savwa Ajohn,proud to be your Son.

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To God for the far I have come

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ABBREVIATIONS AND ACRONYMS

ALL	Acute lymphoblastic leukemia
ADR	Adverse Drug Reaction
AML	Acute myeloid leukemia
BMA	Bone Marrow Aspirate
B.D	Twice daily
CML	Chronic myeloid leukemia
CLL	Chronic lymphoblastic leukemia
DTP	Drug Therapy Problems
ENT	Ear Nose and Throat
ERC	Ethics and Review Committee
G-CSF	Granulocyte Colony Stimulating Factor
H	High
IT	Intrathecal
IM	Intramuscular
IV	Intravenous
Kg	Kilograms
KNH	Kenyatta National Hospital
L	Low
M^2	Meters squared
Mg	Milligrams
MTX	Methotrexate
N	Normal

No.	Number
PO	Per oral
RVD	Retroviral disease
UoN	University of Nairobi
USA	United States of America
USD	United States Dollar

OPERATIONAL DEFINITION OF TERMS

Adjunct therapy - Type of treatment that compliments and intended to enhance the primary treatment.

Adherence -The extent by which a patient retains individual treatment according to the dose and interval of drug prescribed by a health practitioner. Used interchangeably with compliance.

Chemotherapy -The use of aggressive chemical agents to treat a disease, especially the rapid growing abnormal cells in cancer

Comorbidity - An underlying chronic or long-term illness that occur alongside a primary disease.

Extravasation -The accidental leakage of vesicant chemotherapeutic agents into the subcutaneous and perivascular spaces during intravenous administration.

Medication errors -Avoidable events due to inappropriate use of medication and may occur at any point along a treatment pathway from a prescriber to a patient.

Palliative therapy -A treatment approach that aims to relieve or manage symptoms of a serious illness to help optimise quality of life and mitigate patient suffering.

Polypharmacy - The use of multiple medications by an individual patient, usually more than 5 drugs simultaneously.

Prognosis - The predictable likely outcome or course of a disease or illness over a duration of time.

ABSTRACT

Background

Drug therapy problems (DTP) are undesirable effects and experiences that occur to a patient during drug treatment and tend to alter the desired therapeutic outcomes. Patients with leukemia are susceptible to DTPs due to the use of multiple cytotoxic drugs. There is limited data on drug therapy problems among these patients in sub-Saharan Africa.

Objectives

To assess the magnitude and predictors of drug therapy problems among patients with leukemia at Kenyatta National Hospital.

Methodology

A cross-sectional study to assess the magnitude and predictors of drug therapy problems among a random sample of 89 patients with leukemia at inpatient oncology units at Kenyatta National Hospital. Approval to conduct the study was sought from Kenyatta National Hospital-University of Nairobi Ethics and Review Committee and permission from the management of the hospital prior to data collection. A structured questionnaire was the main data collecting tool. Patient's sociodemographic features, leukemia type, disease state, comorbidity present, length of hospital stay, phase of treatment, treatment regimen and patients experience with medication were collected from interviews and medical records. Data was collected over a period of four months between March to August 2023 and coded, entered into an excel sheet and cleaned. The coded data was exported and analysed using a statistical software STATA version 13. A bivariate and multivariate logistic stepwise forward regression analysis was done to determine the significant predictors of drug therapy problems.

Results

The study had a total of 89 participants with the majority as females (53.9%).Most of study participants were aged between 1-12 years (53.9%) with a mean age of 22(±20)years. Of the participants,78.6% had normal body mass index,78.6% were unemployed while majority (88.8%) had an active health insurance cover. Acute lymphoblastic leukemia was the most common leukemia at 53.9% with 79.8% of patients still in the disease state as initially diagnosed. Fifty five percent of study participants were in the induction phase of treatment. Majority (88.8%) of study participants had no comorbidity. Majority (57.3%) of the study participants reported to have stayed in the hospital for a period of twenty days and less.

Prevalence of drug therapy problems was 91% with total a of 204 DTPs identified (average of 2.5 per patient). Adverse drug reaction (88.8%),non-compliance (58.4%) and need for additional therapy (37.1%) were the majority types of therapy problems identified. Factors significantly associated with drug therapy problems were age, employment status, phase of treatment and chemotherapy regimens used.

Conclusion

The prevalence of drug therapy problems among patients with leukemia at Kenyatta National Hospital was high. Age, employment status, phase of treatment and chemotherapy regimens used were the significant predictors of drug therapy problems.

Recommendation

To increase identification and earlier resolution of drug therapy problems ,pharmacists should advance patient centred pharmaceutical care services in the oncology units. Standardised drug therapy problem assesment tools should be incorporated as part of care for leukemia patients with factors shown to significantly predict occurrence added as baseline guide.

CHAPTER ONE: INTRODUCTION

1.1 Background to the Study

Leukemia is an aggregation of haematological malignancies due to pathological variation of the white blood cells in the bone marrow, the vascular system and lymphatic system. It is classified based the predominant cell type and disease progression (1). According to recent data by the International Agency for Research on cancer, leukemia ranked 13th most common amongst cancer types based on annual incidence. There were an estimated 474,519 new cases in the year 2020 in both sexes and all age categories (2).There has been an accelerated increase in the prevalence and incidence of leukemia cases globally with Asia accounting for the larger percentage of incidence at about 48.6% of the total number of new cases (3). Incidence in Africa accounted for 6.8% of the new cases in 2020 with Eastern Africa having a majority at 33.4% of this total (3).

Drug therapy problems (DTP) are undesirable effects and experiences by the patients during drug therapy and tend to alter expected treatment outcomes (4). They can occur during different stages of treatment process majorly at prescribing, dispensing and the use of medication by the patient (5). According to Cipolle and Strand (2008) classification method, DTPs have seven distinct classes. They include; unnecessary drug therapy, ineffective drug therapy, dosage too high, need for additional therapy, non-compliance, dosage too low and adverse drug reaction (6). According to World Health Organisation (WHO) estimates, an average of more than half of all medications have at least one therapy problem in the prescription or administration (7).

There is significant magnitude of drug therapy problems common in inpatient setting especially in cancer related admissions (8). A study of cancer pain patients in a teaching hospital in China reported a DTP prevalence of 78%, with an average of 1.4 per patient requiring intervention (7). A similar cross sectional study conducted in Ethiopia showed a prevalence of 74.7% (9). A prospective observational study conducted at the same hospital among paediatric hematology patients yielded a prevalence of 68.6% (8). There are a number of studies on drug therapy problems done at Kenyatta National Hospital that show a significant burden of DTPs. A study conducted in medical outpatient clinic showed presence of at least one therapy problem in 95.7% of study participants (10).

Compliance is also a key factor in long term oral medication use. A study in chronic myeloid leukemia(CML) patients carried out in multi-haematological centers ,in Lodz,Torun,Gdansk and Warsaw in Poland to assess adherence, showed about 50% of patients were non-compliant to prolonged treatment course (11).

The findings also indicated that patients aged above 65 years of age with presence of at least one comorbidity had better overall compliance. Younger subjects have reduced rate of adherence to oral medications compared to older subjects with a median age of about 53years (11).

During chemotherapy of leukemia, there is high potential for drug therapy problems due to prolonged treatment periods with multiple chemotherapeutic agents that are highly toxic (8). In a prospective study to assess treatment outcomes in patients aged 15-39 years with newly diagnosed acute lymphoblastic leukemia(ALL) at Kamuzu Central Hospital, Malawi, grade 3 or 4 neutropenia occurred in 60% of the participants. This was common especially during induction. Grade 3 or 4 anemia occurred in 33% while 40% experienced grade 3 or 4 thrombocytopenia (12).

Extended hospital stays by some of these patients predisposes them to nosocomial infections that may require additional therapy, further increasing risk of DTPs. Patient related factors such as extreme age and comorbidities are widely mentioned as risk factors for drug therapy problems (6). Advanced age and polypharmacy were identified as the biggest risk factor for ADRs in most patients (13). Most drug therapy problems that are not identified or resolved may manifest as drug-related morbidity and ineffective therapeutic outcomes (5).

A well declared DTP should include characterization of patient problem, drug therapy in use, distinct drug-disease interactions and drug-drug interactions (6). Assessment of DTPs has to factor in their effect and severity to the patient which guides on the timelines within which they should be resolved. This study intends to evaluate the DTP in both pediatrics and adult patients with leukemia at KNH.

1.2 Problem statement

Treatment of leukemia incorporates use of multiple drug therapies, with some as active treatment and others as adjunct therapies (8). Some of these patients have other underlying comorbidities and hospital acquired infections that may require use of other drugs. This exposes the patient to multiple agents at almost the same time posing a greater risk of developing drug therapy problem.

The burden of DTP has contributed immensely to challenges in the healthcare practice both in clinical outcomes, cost and rational use of available resources. They all tend to affect the quality of life of patients and sustainability of an efficient health care system due to high costs involved. Law suit cost, lost income, expenses on disability and hospital bills go up to an annual estimate of US$29 billion each year for some countries (6). In a meta-analysis of prospective studies across United States of America hospitals, the overall incidence of serious ADRs was 6.7% and of fatal ADRs was 0.32% of hospitalized patients (14).DTPs have far reaching consequences on both the patient and healthcare system.

Effect on the patient include poor treatment outcomes, frequent or prolonged hospital stay, increased cost of treatment, a bearing on their socioeconomic life and ultimately poor health-related quality of life. The burden on healthcare system is as a result of high cost of treatment and hospital stay which depletes the resources available to deal with other health related problems (6).

1.3 Justification

There are limited studies on drug therapy problems among patient with leukemia in most developing countries, Kenya included. A review of paediatric treatment protocols of cancer at Kenyatta National Hospital from the previously used Kasili's protocol altered the treatment regimens. Paediatric patients with ALL are currently initiated on standardised aggressive therapy regardless of the risk group. This is likely to bring about an increase in drug toxicities among the low risk patient groups. Introduction of other agents raises the need for patient monitoring to identify any significant outcome. The use of oral medications common in CML, a prevalent leukemia type in adults also raises the need to identify adherence problems especially with preexisting comorbidities.

The study aim was to identify and help address the gaps during chemotherapy to promote desirable therapeutic outcomes. The findings will help emphasize on the key roles of clinical pharmacists in patient care and pinpoint the areas of focus in optimizing therapeutic outcomes.

1.4 Objectives

1.4.1 General objectives

To evaluate the magnitude and predictors of drug therapy problems among patients with leukemia at Kenyatta National Hospital.

1.4.2 Specific Objectives

1. To describe the types and prevalence of drug therapy problems among patients with leukemia at KNH
2. To analyze the effect of Sociodemographic factors on DTPs among patients with Leukemia at KNH.
3. To examine the influence of Clinical factors on DTPs among patients with leukemia at KNH

1.5 Research questions

The study seeks to answer the following questions**:**

1. What are the types and prevalence of DTP among patients with Leukemia at KNH?
2. What are the effects of patient factors on DTPs among patients with leukemia at KNH?
3. What is the influence of prescribing patterns on DTPs among patients with leukemia at KNH?

1.6 Significance and anticipated output of the study

The study is expected to give health care providers both in private and public practice, an insight into the types and scale of drug therapy problems in leukemia. The study findings will highly benefit the pharmaceutical care practitioners, specifically the clinical pharmacist in offering educational pharmacy services based on the common types of DTPs in leukemia and the onset. This will guide on drug information services and development of appropriate tailored DTP assesment tool for prompt monitoring. The outcomes of this paper are likely to impact on the strategies by decision makers on pharmacovigilance resource allocations and trainings.

The risk factors for DTPs highlighted will guide healthcare policy makers on the strategy and policy development to improve healthcare delivery. The findings will give a proper reference point on the need to increase resource allocation and funding of pharmacovigilance in cancer units countrywide. It will also offer a basis to increase the training and uptake of more clinical pharmacists in the oncology field, to address healthcare staff shortage. The additional knowledge will also contribute to the literature on drug therapy problems.

1.7 Delimitations

The study was carried out at inpatient oncology units in both adult and pediatric haematological wards at Kenyatta National hospital. The participants were patients undergoing treatment for leukemia who met stipulated inclusion criteria of this study

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CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

This chapter contains comprehensive review of current literature on burden of leukemia, drug regimen used in the management of leukemia, types and magnitude of drug therapy problems during management of leukemia and their predictors. It also gives a summary of the review which identifies gaps in the literature and a conceptual framework illustrating interrelation between the study variables.

2.2. The Burden of Leukemia

Leukemia is a group of malignant disorders that affects the blood, blood forming tissues in the bone marrow and lymphatic system characterised by accumulation of abnormal white blood cells (15,16). Leukemia is classified based on cell of origin and on the progression of the untreated disease. Lymphoid and myeloid are the two main cells of origin. Based on clinical course, acute leukemia is more aggressive and characterized by undifferentiated immature cells. The chronic form on the other hand is characterised by the presence of differentiated and relatively mature abnormal white blood cells (17). There are four major types of leukemia: acute lymphoblastic leukemia(ALL),acute myeloblastic leukemia(AML), chronic lymphoblastic leukemia(CLL) and chronic myeloblastic leukemia(CML) (18).

Leukemia is relatively more prevalent in children and adolescents below 20 years of age which represents 25.1% of cancer cases in this group. It also represents about 4.6% of all types of cancers in adolescents and young adults aged between 15-39 years, which makes it the tenth most frequent cancer across all races and ethnicities (19). The incidence of childhood leukemia peaks at 4years with AML with ALL as the most common type while ALL peaks between 2-3 years of age (18).

In Kenya, leukemia was ranked the seventh most common cancer with about 1579 new cases in the year 2020, representing 3.7% of all cancers (2). According to a study done on prevalence and incidence of childhood cancers at KNH between 2009 to 2019, leukemia had the highest prevalence. ALL and AML were the most prevalent at 19.5% and 6.6%, respectively. Amongst the 650 cases of leukemia found, chronic lymphoblastic leukemia had a prevalence of 1.4% while chronic myeloid leukemia was at 1.2% (20). A local prospective study conducted between the year 2001 to 2010, reported that majority of patients diagnosed with ALL were below 5 years of age (21). Chronic lymphocytic leukemia is a relatively more common leukemia in adults, accounting for up to two thirds of cases in the age above 55 years. It is rare in age below 30 years and more prevalent in males than females (15). AML has a predominant onset age of above 60 years in adults and may result from treatment of childhood ALL.

2.3 Treatment of Leukemia

The most effective primary treatment for leukemia is drug therapy. The therapies might be recommended as curative, adjuvant therapy, neoadjuvant and palliative therapy (22). The desired goals may be interpreted clinically as cure of the disease, slowed progress of the disease, prevention and relief of symptoms(22).The primary utilisation of drug therapy in leukemia is to arrest replication of the malignant cells and to treat systemic disease through cure and palliative care (15).

There are standard protocols established to guide in treatment of each specific type leukemia. However some symptoms in the same patient require use of other supportive medications that may not be based on standard protocols (23). Most drugs used to manage leukemia are administered parenterally and a few others via the oral route (14)**.** In the year 2022, new treatment protocols were introduced at KNH which had a slightly different approach to management of ALL in paediatric patients. The number of treatment phases were increased with more aggressive drug regimens and prolonged duration of treatment (24).

2.3.1 Phases of Treatment

Treatment of leukemia is implemented in three main phases namely;induction,consolidation and maintenance (24). The initial phase of treatment is induction that aims to eradicate leukemic cells in peripheral blood, in the organs and bone marrow tissues. The attainment of a complete remission is an essential requirement for patients' long term clinical stability (18). Consolidation phase is aimed at destroying any remaining malignant cells after remission. In case of a relapse especially with children, reinduction and reconsolidation phases are added after the initial consolidation phase (15). Maintenance phase has a prolonged duration with less intense chemotherapeutic agents intended to retain remission. The dosage of drug regimen in this phase are relatively low compared to the induction and consolidation phase. Other medications required for supportive care in these phases include antibiotics, granulocyte colony-stimulating factor and post-treatment medications to reduce chemotherapy side effects (15).

2.3.2 Acute Lymphoblastic leukemia

Treatment of ALL is based on risk stratification of these patients due to varied outcomes in response to chemotherapy. In the risk classification systems, the lower risk group are subjected to less toxic therapy while the high risk group are treated with more aggressive drug therapies (18). ALL in older adults has definite genomic features which by wide margin define the poor prognosis in such patients. About one third of older adults with ALL have a unique Philadelphia chromosome(Ph) which yields two categories of patients; Ph-negative and Ph-positive ALL that indicates a favorable prognosis (25).

Table 1:Treatment protocol for paediatric acute lymphoblastic leukemia at KNH (24,26)

Chemotherapy	Dose
Induction Phase (1month)	
Prednisolone	PO 40mg/m² per day.
Vincristine	IV 1.5 mg/m² Day 1,8,15 & 22
Daunorubicin	IV 25 mg/m² Day 1,8,15 & 22.
L-asparaginase	IM 600 I.U/ m² Day 2,4,6,9,11,13,16,18,20
Cytarabine Intrathecal	1-1.99 years 30mg,2-2.99years 50mg,>3years 70mg
Methotrexate Intrathecal	1-1.99 years 8 mg, 2.99years 10mg ,3-9 years 12 mg, >9years 15 mg) Day 15 &29.
Consolidation Phase (1.5 Months)	
Cyclophosphamide	IV 1g/ m² Day 1 & 29
Cytarabine	IV/SC 75mg m² Days 1-4, 8-11, 29- 32 & 36-39
6 mercaptopurine	PO 60mg/ m² Days 1-14, & 29 – 42
Methotrexate IT	Age dose (1-1.99 years 8 mg, 2.99years 10mg ,3-9 years 12 mg, >9years 15mg) Days1,8,15 & 22
Interim maintenance (2 months)	
Vincristine	IV 1.5mg/ m² Day 1 & 29
Prednisolone	PO 40mg/ m² Days 1-5 & 29-33
6 mercaptopurine	PO 75mg/ m² Days 1-28
Methotrexate	PO 20mg/ m² Days1,8,15,22,29,36,43 & 50
Methotrexate IT	1-1.99years 8 mg, 2-2.99 Years 10mg, 3- 9years 12mg,>9years 15mg) Day 1,8,15 22
Delayed intensification- re-induction (1month)	
Dexamethasone	PO 10mg/ m² Days 1-21
Vincristine	IV 1.5mg/ m² Day 1, 8, 15 Max 2 mg

Daunorubicin L-asparaginase IT methotrexate	IV 25mg/ m² Day 1, 8,15 Infused over 30 – 60 mins IM 6000 i.u/ m² Day 2,4,6, 9,11 & 13 (total 6 doses) 1-1.99years 8 mg, 2-2.99years 10 mg, 3- 9years 12 mg, >9years 15 mg)
Delayed intensification re-consolidation -(1month) Cyclophosphamide Cytarabine 6 mercaptopurine I.T methotrexate	 IV 1g/ m² Day 29 SC 75mg/m² Days 29-32 & 36- 39. PO 60mg m² Days 29-43 Age based dose (1-1.99year 8 mg, 2-2.99years 10 mg, 3- 9years 12 mg, >9years 15 mg) Day 29& 36
Maintenance – 84 days Vincristine Prednisolone 6 mercaptopurine Methotrexate	 IV 1.5mg/ m² Day 1, 29 & 57 PO 40mg/m² 1-5, 29-33, 57-62 (Don't taper) PO 75mg/ m² Days 1-84 PO 20mg/ m² Weekly. Administer on the same day each week. Day 29

At the end of the induction phase, bone marrow examination (BMA) is done to assess for remission. Consolidation phase is started when remission is achieved normally 10-14 days after induction. Interim maintenance is started within 14 days of end of consolidation phase and re-induction phase is started within 7-10 days after interim maintenance. The maintenance cycle is repeated 8 times for female patients for a total of 2 years and 12 times for male patients for a total of 3-years.

Treatment for older adults group poses huge challenges due to the comorbidities that hinder effectiveness of curative drug regimens. An example of protocol utilised in adults is the United Kingdom acute lymphoblastic leukemia (UKALL) XIV (**Table *2***).

Table 2: **UKALL XIV protocol for treatment of ALL in adults(27)**.

Chemotherapy	**Dose**
Induction phase 1	
Vincristine	1.4mg/m² IV Day 1,8,15 and 22
Asparaginase	10,000iu IM Day 17,19,21,23,25 and 27
Daunorubicin	30mg/m² IV Day 1,8,15 and 22
Dexamethasone	10mg/m² PO Day 1-4,8-11,15-18
Methotrexate	12.5mg Intrathecal Day 14
Induction phase 2	
Methotrexate	12.5mg IT Day 1,8,15 and 22
Cytarabine	75mg/m² IV Day 2-5,9-12,16-19 and 23-26
Mercaptopurine	60mg/m² PO Day 1-28
Cyclophosphamide	1000mg/m IV Day 1 and 15.
Intensification	
Folinic acid	15mg/m² IV Day 2-5 and 16-18
Asparaginase	10,000iu IM Day 2,9 and 23
Methotrexate	3g/m² IV Day 1 and 15.
Consolidation phase	
Asparaginase	10,000iu IM Day 6-8,10-12-14-16 (6doses)
Etoposide	100mg/m² IV Day 1-5
Methotrexate	12.5mg IT Day 1
Cytarabine	75mg/m² IV Day 1-5

In Philadelphia chromosome positive category, Tyrosine kinase inhibitors is started. The consolidation phase is initiated if a patient is not qualified for a transplant.

2.3.3 Acute Myeloid Leukemia

Over the years there has been development of high dose drug therapy for AML due to its relative resistance to treatment. Cytarabine and anthracyclines combination are the foundation of drug therapy. The treatment protocol for paediatric AML at KNH is shown in **Table *3***.

Table 3: Treatment protocol for pediatric acute myeloid leukemia at KNH.

Chemotherapy	**Dosage**
Induction course 1 Daunorubicin Cytarabine	 25mg/m² infusion day 1,3 & 5 100mg/m² infusion days 1-7
Induction course 2 Cytarabine	 1000mg/m² BD Day 1,3 & 5
Consolidation phase Cytarabine Triple IT (Hydrocortisone, cytarabine and methotrexate)	 1g/m² BD Day 1,3 &5

Treatment of AML for adult patients involves a combination chemotherapy with a two-phase approach; induction & consolidation referred to as 3 and 7. Three days of IV infusions with idarubicin or daunorubicin followed by infusions of cytarabine over 24 hours every day for 7 days. High dose cytarabine is used in the consolidation phase

2.3.4 Chronic Myeloid Leukemia

Chemotherapy in CML is individualized based on case presentation with any of the following drug regimens as an option (28)

1. Hydroxyurea PO 1gm/ m² or 40mg/kg/day PO daily – used in elevated WBC count to normalize the levels.

   Divided doses of Hydroxyurea have proved more effective compared with single dose.

2. Busulphan PO 0.1mg/kg/day intermittently.

   High doses of up to 6mg per day can still be given to 6-8-year-old patient.

3. 6-mercaptopurine 80mg/ m² PO when used in combination with Busulphan, it is the first to be stopped
4. Cytosine infusion 500mg/ m² in saline run over 24 hours

Allopurinol is a schedule accompaniment until WBC count fall to levels below 15 X10^9 /l. If WBC count rise above 20 X10^9 /l during patient follow up, Hydroxyurea or Busulphan therapy is re-instituted (28).

2.3.5 Chronic lymphoblastic leukemia

There are several combination regimen options that are utilized in management of CLL as shown in **Table *4***.

Table 4 :Treatment regimens for chronic lymphoblastic leukemia for adults.

Regimen	**Dose**
BR- every 28 days for 6 cycles Bendamustine Rituximab	 70-90mg/m² IV day 1-2 375mg/m² IV day1 for cycle 1 and 500mg/m cycles 2-6
RC Rituximab Chlorambucil	 375mg/m² IV day1 for cycle 1 and 500mg/m cycles 2-6 10mg/m² day 1-7 every 28days for 6 cycles.
FCR- every 28days for 6 cycles Fludarabine Cyclophosphamide Rituximab	 25mg/m² IV day 1-3 250mg/m² IV day 1-3 375mg/m² IV day1 for cycle 1 and 500mg/m cycles 2-6
FC – oral alternative Fludarabine Cyclophosphamide	 24mg/m² PO day 1-5 (5 doses) 150mg/m² PO day 1-5 (5 doses)

2.4 Drug Therapy Problems

According to Cipolle-Strand-Morley 2012 criteria (29),a DTP is any undesirable event experienced by a patient that involves, or is suspected to involve drug therapy, and that interferes with achieving the desired goals of therapy and requires pharmaceutical intervention to resolve. This method placed DTPs into seven main categories as illustrated in **Table *5***

Table 5: **DTP categories and their description** (30)

DTP Categories	Description
Non-compliance	Failure to take the drug as indicated intentional or unintentional
Dosage too low	Dose of drug given is too low to exert the needed therapeutic effect
Ineffective drug	The drug therapy provided is not effective at attaining the desired response
Need for additional therapy	Addition of drug therapy for treatment or prevention of a condition i is required.
Adverse drug reactions	Unintended and harmful effects that are not dose related
Dosage too high	The dosage of the drug given is too high and unsafe
Unnecessary drug therapy	There is no indication for the drug therapy given to a patient

Drug therapy problems are a result of unmet drug-related patient needs. The four main patient needs related to drug therapy are indication,effectiveness,safety and adherence (30). Indication is associated with need for additional therapy and unnecessary therapy. Effectiveness is related to too low doses and ineffective drug therapy. Safety is associated with adverse drug reactions (ADR) and dosage too high while non-adherence DTP is associated with patient compliance to drug therapy.

Unnecessary drug therapy may occur in leukemia as a result of duplication of therapy, use of multiple drugs when a single drug is appropriate or use of drug therapy when no drug is required at that specific time. A study done at KNH on prevalence of DTPs in outpatient medical clinic ranked unnecessary drug therapy problems as the least occurring DTP (10).

Need for additional therapy in leukemia patient aims to offer preventive therapy as well as target the untreated condition. Leukemia may be associated with other additional systemic conditions due to high susceptibility to nosocomial infections (17)

Dosage too high may be as a result of shorter dose frequency, longer duration of treatment than the recommended standard or due to rapid administration of medication. Dosage too low leads to very low levels of systemic drug unable to produce the desired therapeutic effect. The causes include infrequent dosing interval, shorter than standard period of therapy and drug interactions. An ADR is an unintended harmful drug effect that occurs at normal human dose during diagnosis or treatment of a disease (31,32). The causes of ADRs are drug interactions, incorrect or rapid administration, allergic reaction, dosing too fast and use of highly toxic drugs (14). Many ADRs are inevitable and are commonly acceptable in drug therapy.

Non-adherence is the failure to take prescribed drug and may be due to refusal by a patient due to physical and social challenges, high cost of the drug and unclear instructions. Most medications used in leukemia treatment are administered intravenously, so adherence is majorly focused on palliative care and supportive medications. In leukemia chemotherapy, adherence monitoring is mainly for patients on allopurinol, oral corticosteroids and oral chemotherapy agents (33).

DTPs have many harmful consequences which include long term hospital admissions, frequent hospital visits, drug related morbidity & mortality and undesirable therapeutic outcome(8). There is also huge direct and indirect cost implication on patients and the healthcare system as a whole. Studies done in the United States of America estimated the total cost of DTPs at 122 billion USD annually. Adverse drug reaction had the highest cost per patient, followed by non-compliance (34).

2.5 Magnitude of DTPs during treatment of Leukemia

DTPs are a very common occurrence in cancer patients. A study in hospitalised cancer pain patients in China showed 78.6% had drug therapy problems and were in need of pharmaceutical care intervention (7). In Los Angeles,USA,a retrospective study of cancer pain clinic patients by Semerjian *et al.* resulted in a 98.7% prevalence of DTPS (7). A study done in children with cancer in Ethiopia showed that frequently occurring drug therapy problems in this category of patient were inappropriate dosing, need for additional therapy and non-adherence to drug therapy (8).

Locally, a study by Gaceri et al on DTPs in head and neck cancer patients at Kenyatta National Hospital had 92.2 % of participants with at least one DTP. Adverse drug reaction was the most prevalent in this patient category (35). A closely related study by Degu et al at the same institution among patients with cervical cancers reported a drug therapy problem prevalence of 93.8% with adverse drug reaction as the majority

(69.1%) (36). A recent publication by Degu et al on drug related problems reported a high prevalence among patients with esophageal (51.9%), gastric (59.2%) and colorectal (62.5%) cancer at a referral hospital in Kenya (37).

2.6 Predictors of Drug Therapy Problems

2.6.1 Sociodemographic Factors

Limited studies have been done on sociodemographic factors as predictors factor for DTPs. A prospective multicenter study done between 2006 to 2009 showed that 53% of older adults experience at least a severe to life threatening drug toxicity (38)**.** Advanced age,≥ 60 years, was a consistent significant risk factor for use of 3 to 5 medications (39). There is decreased renal function in elderly patients which alters the pharmacokinetics of drugs. Elderly patients are at higher risk of myelosuppression by the chemotherapy drugs due to reduced bone marrow reserve associated with advanced age (38). Children are relatively more prone to DTPs due to notable difference in their body weight, body surface area and crucial organ development. This tends to alter the ability to effectively metabolize and eliminate drugs (8).

A review of several studies showed a significant association between education level and compliance to treatment. Patients with higher education tend to have high compliance due to better knowledge and understanding of the disease and its equivalent therapy(40)

There are several factors outlined under patient clinical characteristic which include the type of leukemia, co-morbidity, and length of hospital stay. Presence of comorbidities is closely associated number of medications and duration of stay in the hospital. These risk factors may lead to drug toxicity great impact on drug toxicity through interactions (38). In a study by Mwangi et al on DTPs in cervical cancer, hypertension was noted to be the most prevalent comorbidity associated with therapy problems (41). This by extension signifies the likely comorbidities in older adult patients and the multiple number of medications such patients use.

2.6.2 Clinical Factors

According to meta-analysis of prospective studies in the United states ,up to 76.2% incidence of ADRs in hospitalised patients was as a result of use of highly toxic drugs (31). Findings from a previous study carried out in hospitalised patients in Singapore showed that concurrent use of more than five drugs pose a risk of occurrence of an adverse drug reaction.(13).Similarly, a study in Norway indicated that increase in number of medicines by a unit resulted in 8.6% increase in the number of DTP(38).

Most cancer therapies have complicated pharmacological profiles that include narrow therapeutic index, variation within and between patients and high toxicity nature. There are major primary mechanisms through which drug interactions (DIs) occur; pharmacological interaction, pharmacokinetic interactions and pharmaceutical interactions (42). Detection and screening for DIs poses a big challenge thus there is need to establish methods of classification of patients based on risk (23,39).

Pre-treatment checks for potential drug interactions and therapeutic drug monitoring(TDM) are crucial approaches in detection and control of the interactions (23). Polypharmacy is known to increase the probability of drug interactions which is a risk factor for adverse reaction

An earlier study done in Ethiopia on hospitalised cancer patients showed about 76.1% of patients who were on a deviated treatment protocol had DTPs.Regimen deviation from the local protocols was listed as common practice in their healthcare system and a risk factor of drug therapy problems in this group of patients (38). Another factor that is mentioned under clinical factors is the length of hospital stay. In a study in a specialized hospital in Ethiopia among cancer patients, length of hospital stay was reported as a risk factor in the occurrence of drug related problems. The average days for these patients was set at twenty days (9).

Presence of comorbidity was also a significant predictor of drug therapy problems among these patients. A study on determinants of drug therapy problems in diabetes mellitus type two patients in Ethiopia reported presence of comorbidities as significantly associated with drug therapy problems (43).This study also indicated a significant association between low family income and drug therapy problems (43). Among local studies done, comorbidity and advanced stage of disease were reported to be associated with drug therapy problems among patients with esophageal, gastric and colorectal cancer (37).

2.7 Summary of the Review

Leukemia is a group of malignant disorders with characteristic accumulation of abnormal white blood cells in blood, in the bone marrow tissues, in spleen and the lymphatic system. There are four major categories of leukemia; acute lymphoblastic leukemia, acute myelogenous leukemia, chronic lymphoblastic leukemia and chronic myelogenous leukemia. Leukemia is the most prevalent childhood cancer, predominantly AML and ALL, although it has relatively low incidence in adults. The treatment of leukemia is based on standard protocols with an approach guided by the primary classification. ALL has the most aggressive therapy approach with high number of medications used and slight regimen modifications between adults.

Drug therapy problem (DTP) is an occurrence in patients during treatment which is associated with drug in use and is known to hinder desired therapeutic outcomes. that hinders desired therapeutic outcomes and requires professional clinical expertise to identify and resolve. Based on cipolle criteria, there are seven classes of DTP: unnecessary drug therapy, need for additional therapy, ineffective drug therapy, dosage too low, dosage too high, adverse drug reaction and non-adherence to drug therapy.

The various factors that contribute to DTPs in leukemia can be majorly categorized into sociodemographic factors and clinical factors. The sociodemographic factors include age, education level, employment status and health insurance cover. The clinical factors include type of leukemia, disease status since diagnosis, chemotherapy regimen ,phase of treatment and length of hospital stay.

After review of the available literature on DTP in leukemia both globally and in local settings some gaps were identified. Locally there is no published studies on assesment of DTPs in leukemia as whole both in paediatric and adult patients. Since the introduction of new paediatric treatment protocols at KNH, no single study has been done to assess the impact of new regimen on the patients. This indicates that the study will have a huge contribution to the existing literature and practice.

2.8 Conceptual Framework

This section outlines the relationship between the dependent and independent variables. The 7 main categories of drug therapy problems are the dependent variables while the independent variables are classified as sociodemographic factors and clinical factors.

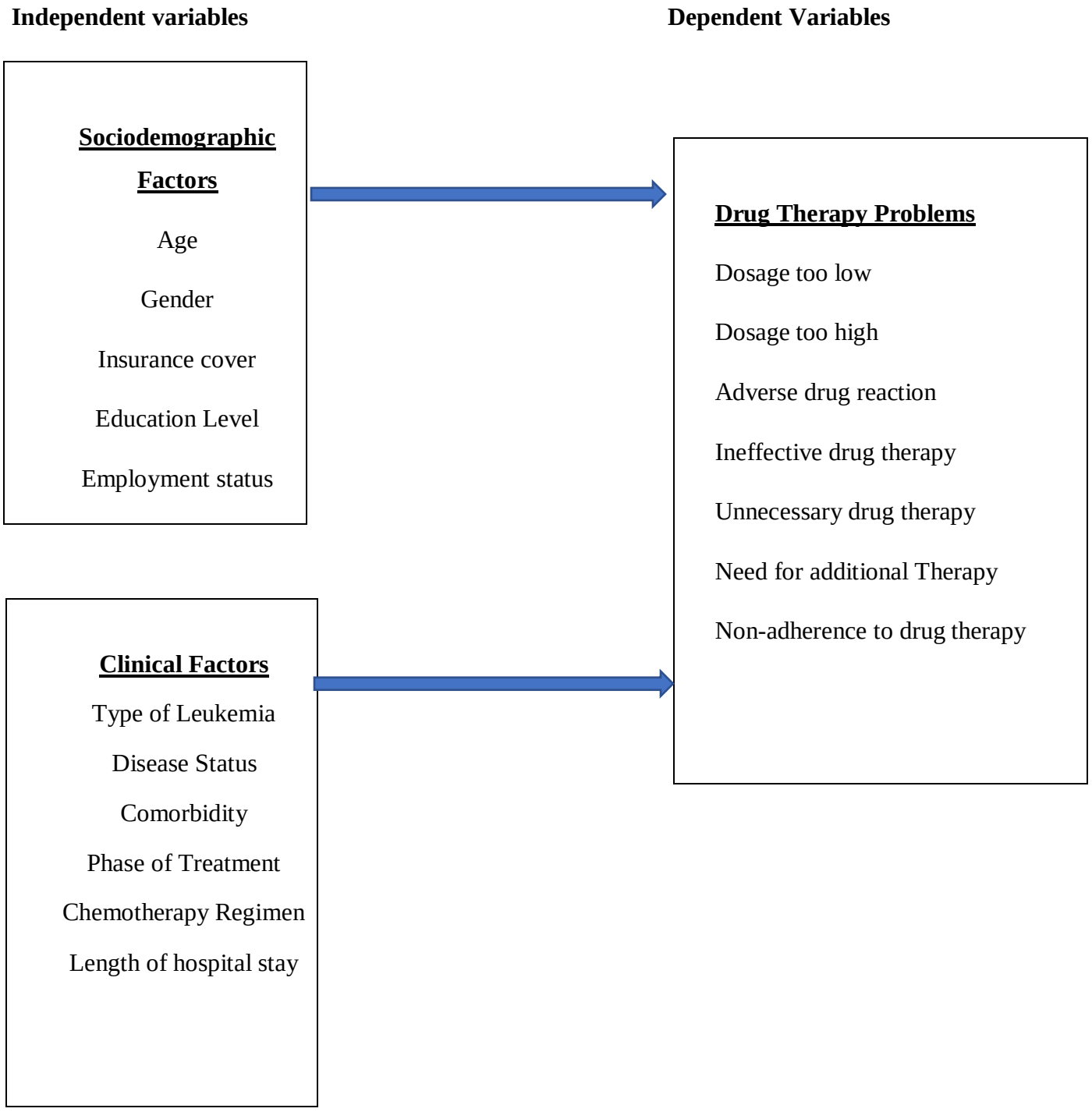

Figure 1: Conceptual Framework **(Author: Savwa, 2022)**

Sociodemographic characteristics of patients may influence drug therapy problems occurrence among patients with leukemia. Under sociodemographic factors for instance, age is a risk factor for non-adherence oral therapy which leads to outcome variable of non-compliance. Adolescent patients have rebellious tendencies which affect compliance to therapy (40). Older adult patients have certain physiological changes including cardiovascular impairment and metabolic problems that lead to high drug doses with a risk for toxicity (38).This directly affects the magnitude of adverse drug reaction. Level of income is a significant predictor factor of compliance especially for the drugs to be procured by a patient (34) .

Clinical characteristics of patients can directly influence drug therapy problems. Drug regimens differ based on type of leukemia which poses a risk to the patient depending on dose intensity and level of drug toxicity (38). Patients with Co-morbidities and longer duration of hospital stay tend to have a relatively high number of medications which may increase the probability of drug interactions, a risk factor for adverse drug reaction and unexpected high dosage (18). Length of hospital stay has been reported to influence occurrence of adverse drug reaction, unnecessary drug therapy and need for additional therapy (8). A prolonged duration of treatment, which is a case in majority of these leukemias increase patient's exposure to chemotherapeutic agents with a greater risk of adverse reactions (22).

CHAPTER THREE: METHODOLOGY

3:1 Introduction

This chapter outlines the instruments and methodological approach to achieve study objectives. It includes research design, location of the study, target population, inclusion and exclusion criteria, sampling method, data collection and data analysis tools and ethical consideration.

3:2 Research Design

This was a cross-sectional study to measure the magnitude and predictors of drug therapy problems among patients with leukemia at Kenyatta National Hospital. The exposure and outcome variables were determined at the same time, which enabled assessment of different variables that may help in generation of hypothesis for future studies. The dependent variables were the seven drug therapy problems including unnecessary drug therapy, need for additional therapy, ineffective drug therapy, dosage too low, dosage too high, adverse drug reaction and non-adherence to drug therapy. The independent variables were the possible predictors of DTP occurrence including age, gender, employment status, health insurance cover, and level of education. Clinical factors included the type of leukemia, status of disease since diagnosis, presence of comorbidity, phase of chemotherapy, chemotherapy regimen and the length of hospital stay.

3:3 Location of Study

The study was conducted within the inpatient oncology units, at Kenyatta National Hospital. KNH is the oldest public hospital in Kenya established in the year 1901 at Upper Hill area, Nairobi Kenya. Originally, it was known as Native Civil hospital and later King George VI hospital with a total bed capacity of forty. In 1963 after independence, it was renamed to Kenyatta National Hospital and promulgated as a National teaching and referral hospital. Currently, it is the largest referral hospital in East and Central Africa. It has 50 wards, a bed capacity of 1800,22 specialized clinics,24 operating theatres and an Accident and Emergency unit with an average of 6000 staff members.

At KNH, leukemia patients are admitted at wards; 3D and 1E for the paediatric patient and GFD for the adult patients. The main paediatric ward,3D,has two cubicles mainly for hematological cancers and admits patients from newborn to five years while 1E has patients aged 6 years to 12 years old who may require less parent or guardian presence. The average bed capacity in leukemia cubicles is 15 beds and with about 20 leukemia patients in a month.1E has an average bed capacity of 28 with around 21 leukemia patients in a month.GFD has a 40-bed capacity, with patients aged above 13 years and about twenty-five leukemia admissions each month.

The study site was suitable due to its capacity as a major national referral centre with patients from all counties across the country. It also boasts of high capacity for cancer care.

3.4 Target Population and Study Population

3.4.1 Target population

All patients who had been diagnosed with Leukemia and undergoing treatment.

3.4.2 Study population

Included all patients diagnosed with leukemia and undergoing treatment at KNH inpatient oncology units and met the inclusion criteria of the study. Patients were included as participants based on the eligibility criteria.

3.5 Inclusion and Exclusion Criteria

3.5.1 Inclusion criteria

1. Paediatric and adult in-patients who had a definitive diagnosis of leukemia
2. Patients who had completed at least one cycle of chemotherapy treatment. This was a key criterion to identify any DTP associated with chemotherapy.
3. Patients who consented or gave assent to participate the study.

3.5.2 Exclusion criteria

1. Patients whose data on therapeutic management was missing. For example: the treatment sheet.
2. Patients with conditions that limited their participation, for example psychiatric disorders.

3.6 Sampling

3.6.1 Sampling size determination

There are no previous studies on DTPs in leukemia in Kenya. A closely- related study done in Ethiopia in 2013 on DTPS in cancer patients ,reported a prevalence of 74.7%(9).Therefore in sample size calculation ,estimated prevalence was 74.7%**.** Calculation was done using the Cochrane formula (44):

$$n_o = \frac{Z^2 \times P \times q}{e^2}$$

n_o = Sample size

z is the standard normal deviate at 95% confidence interval set at 1.96

p is the estimated prevalence of DTPs set at 0.747.

q = 1-p

e = 0.05 Margin of error set at 5%

$$n_{\circ} = \frac{1.96^2 \text{ x } 0.747 \text{ x } (1-0.747)}{0.05^2} = 290.42 \sim 290$$

$n_{\circ} =$ 290 patients.

Since the study population was less than 10,000, a correction formula was used to calculate estimated sample size. A finite population correction factor was applied (44). The total number of leukemia cases at KNH in the year 2021 was 612 according to the data obtained from the KNH Health Information System department. These was three months data, similar period through which the study data was collected. The 3-month average number of leukemia cases based on annual data from the 3-year period was 132.

$$n = \frac{n_{\circ}}{1+(n_{\circ}-1)/N}$$

n = adjusted sample size

$n_{\circ}$ = Calculated sample size =290 subjects

N = Average number of Leukemia cases at KNH for three months in the year 2021 equated to be the same number of months of data collection for this study.

$$n = \frac{290}{1+(290-1)/132} = 90.9$$

n = 91 patients

The sample size was adjusted for non-response at an additional 10% which was added to the final adjusted sample size.

91 + (10/100 x 90) = 100 patients.

Data for this study was collected from a total of 89 participants.

3.6.2 Sampling Technique

During recruitment of study participants, a simple random sampling was applied. Patient list was obtained from drug inpatient admission book at the nursing station of the three oncology wards. Patient were randomly selected from the list and screened for eligibility to participate in the study.

3.7 Research Instruments

A screening eligibility form guided on selection of eligible patients for the study based on inclusion criteria (**Appendix 1**). Adult consent form (**Appendix 2**),parental consent form for minors (**Appendix 3**) and assent form (**Appendix 4**) to seek permission from patients. Data collection tool that combined a structured questionnaire and data extraction form was used (**Appendix 5**). The questionnaire included sections on patient's biodata, clinical and medicines use history, adherence to medication prescribed and any drug side effect experienced by the patient.

The reference materials utilized for drug information source included KNH paediatric oncology treatment protocols (24), Kasili's protocol (28), Kenya National cancer treatment protocols (26) and android Medscape application.

3.8 Pre-test

A pretest study was carried out on 10 percent of the study population within the oncology wards to assess the clarity and convenience of collecting data. Patients with leukemia were randomly selected by the principal investigator from the three wards and subjected to screening to check for eligibility. Participants who met the inclusion criteria were included and the questionnaire administered to each participant after explaining contents of the study and obtaining voluntary consent.

3.9 Validity

The internal validity of the study was maintained by ensuring the questionnaire was relevant and aligned with objectives of the study. The questions asked were simple, clear and in an acceptable language for all the participants.KNH is the largest referral hospital in the country which gave a good representation of the general population from the patients who are referred from facilities across the country. This study outlined clear association between predictor variables and outcome variables

3.10 Reliability

The data collection instruments were pretested as outlined in the pretest study to ensure reproducibility and consistency.

3.11 Data Collection Technique

Every inpatient ward had a nursing desk where admission records that identifies patients with their specific diagnosis are kept. Perusal of these records gave patients name and file number to locate active patients file at the same station. A consent form was presented to identified patients for voluntary signing. Most clinical data were obtained from the patients' files including treatment regimen. The data extraction form was used at this point. Biodata, patient clinical history, adherence to medication and any side effects were obtained from the patient through administration of the structured questionnaire. The interview was conducted at the patient's bedside at a close distance to ensure privacy. This took approximately 10 minutes to complete.

3.12Data management

3.12.1 Data Processing

The data collected was coded and entered into Microsoft Excel 2019 and a database generated. A unique patient identifier code was created from patient category, patient gender and serialised number assigned from 001 to 089. For instance, a 10-year-old female patient appearing at serial number 57 was coded as P/F/057. The electronic database was password protected and access limited to only the principal investigator. The hard copies of data collection tool were kept in a lockable cabinet with access limited only to the principal investigator

3.12.2 Data Analysis

Analysis of data was done using STATA software version 13. The study variables were summarised using descriptive statistics. The independent variables assessed include age of patients, education level, employment status ,comorbidities, type of leukemia disease status, chemotherapy regimen and length of hospital stay. against the outcomes, drug therapy problems. The categorical data in the study were summarised using frequency tables while the continuous data was expressed as mean and standard deviation. The relationship between the variables was determined by Chi-squared test and Fischer's exact test. The predictor variables for DTPs were determined using the bivariate and multivariate logistic stepwise regression analysis. The analysis was conducted at 95% confidence limit.

3:13 Logistical and Ethical Considerations

3.13.1 Study Approvals

Ethical approval and permission to conduct the research was obtained from KNH/UON Ethics and Review Committee, approval number P861/11/2022 ref:KNH-ERC/A/2020,on 10 March 2023. Institutional approval was granted by KNH on 2 May 2023.Additional approval, ref:KNH-ERC/PAEDS-HOD/48 Vol.11 was granted by the paediatrics department on 12 May 2023.

3.13.2 Informed consent

Permission for patient participation was obtained voluntarily by signing of the informed consent forms for the adult patients (**Appendix 2**). Parental consent form (**Appendix 3**) was used to seek approval from the parents, guardians or caregivers of the participants who are legal minors, children below 18 years of age. The assent form (**Appendix 4**) was used to seek for permission and approval from paediatric participants.

3.13.3 Confidentiality and Privacy.

There were unique patient identifier codes that were generated as explained in the data processing section to hide patient details. Hard copies of the questionnaire are stored under lockable cabinet accessible to the principal investigator only. The data collected was stored electronically under password protected database.

Patient interview was conducted at the patient's bedside while ensuring adequate distance from the next patient for utmost privacy.

3.13.4 Benefits of the study

The study findings will help promote better patient care through improved pharmacovigilance strategies

3.13.5 Risks from the study

There was no harm endured by the participants during the study. No medication or any other form of intervention was administered.

CHAPTER FOUR: RESULTS

4.1 Introduction

This chapter contains results of data collected in the study and analysed based on study objectives. It includes patient's socio-demographics, clinical factors ,drug therapy problems and their specific causes. Descriptive analysis was done to organize the data into frequencies and proportions. Logistic regression was done to show the association between predictor variables versus the outcome variables, measured as the drug therapy problems. The outcome variables were dichotomous data.

4.2 Sociodemographic Characteristics

A total of 89 participants were included in the study of which a slight majority (48,53.9%) were females as shown in **Table *6*** .

Table 6: Sociodemographic characteristics of study population (n=89).

Variable	Frequency (n)	Percentage (%)
Gender		
Male	41	46.1
Female	48	53.9
Age Category (years)		
0-1	2	2.3
>1-12	43	48.3
13-19	13	14.6
20- 60	23	25.8
>60	8	9.0
BMI Category		
Underweight	8	9.0
Normal Weight	70	78.6
Overweight	8	9.0
Obese	3	3.4
Education Level		
None	14	15.7
Primary	48	54.0
Secondary	21	23.6
College	6	6.7
Employment Status		
Employed	19	21.4
Non-employed	70	78.6
Health Insurance Cover status		
Yes	79	88.8
No	10	11.2

Key: BMI – Body Mass Index.

The mean age of the participants was 22(±20.5) years and ranged from 0.67 to 71 years. Participants with age above one year to 12 years were the majority (43,48.3%). Seventy (78.6%) participants had normal BMI.Those with primary level of education and lower were the majority (62, 69.7%). Seventy respondents (78.6%) had no formal source of income and seventy-nine (88.8%) had an active health insurance cover (**Table *6***).

4.2 Clinical Characteristics

The most common type of leukemia was ALL (48,53.9%). Majority of study participants(71, 79.8%) had their disease status still as initially diagnosed . Ten (11.2%) participants had co-morbidities with RVD (4, 4.5%) and Hypertension (4, 4.5%)identified as the most prevalent**.** Some participants had more than one comorbidity. More than half of the patients (51,57.3%) had stayed in the hospital for up to 20 days or less (**Table *7***).

Table 7: Clinical Profile of study participants (n=89).

Variable	Frequency (n)	Percentage (%)
Type of Leukemia		
ALL	48	53.9
AML	39	43.8
CML	2	2.3
Disease Status		
At Initial diagnosis	71	79.8
Relapse	15	16.8
Refractory	3	3.4
Presence of Comorbidity		
Yes	10	11.2
No	79	88.8
Comorbidities Present		
RVD	4	4.5
Hypertension	4	4.5
Diabetes type 1 & 2	2	2.3
DVT	1	1.1
Asthma	1	1.1
Down syndrome	1	1.1
Compressive Myelopathy	1	1.1
Length of Hospital stay (Days)		
≤20 days	51	57.3
> 20 days	38	42.7

Key: ALL-Acute lymphoblastic Leukemia, AML- Acute myelogenous leukemia, CML- Chronic myeloid leukemia,DVT- Deep venous thrombosis, RVD- Retroviral Disease.

4.3 Treatment Profile

4.3.1 Phases of Treatment

A slight majority of study participants (49,55.1%) were in the induction phase of treatment with chemotherapy as shown in **Figure *2***.

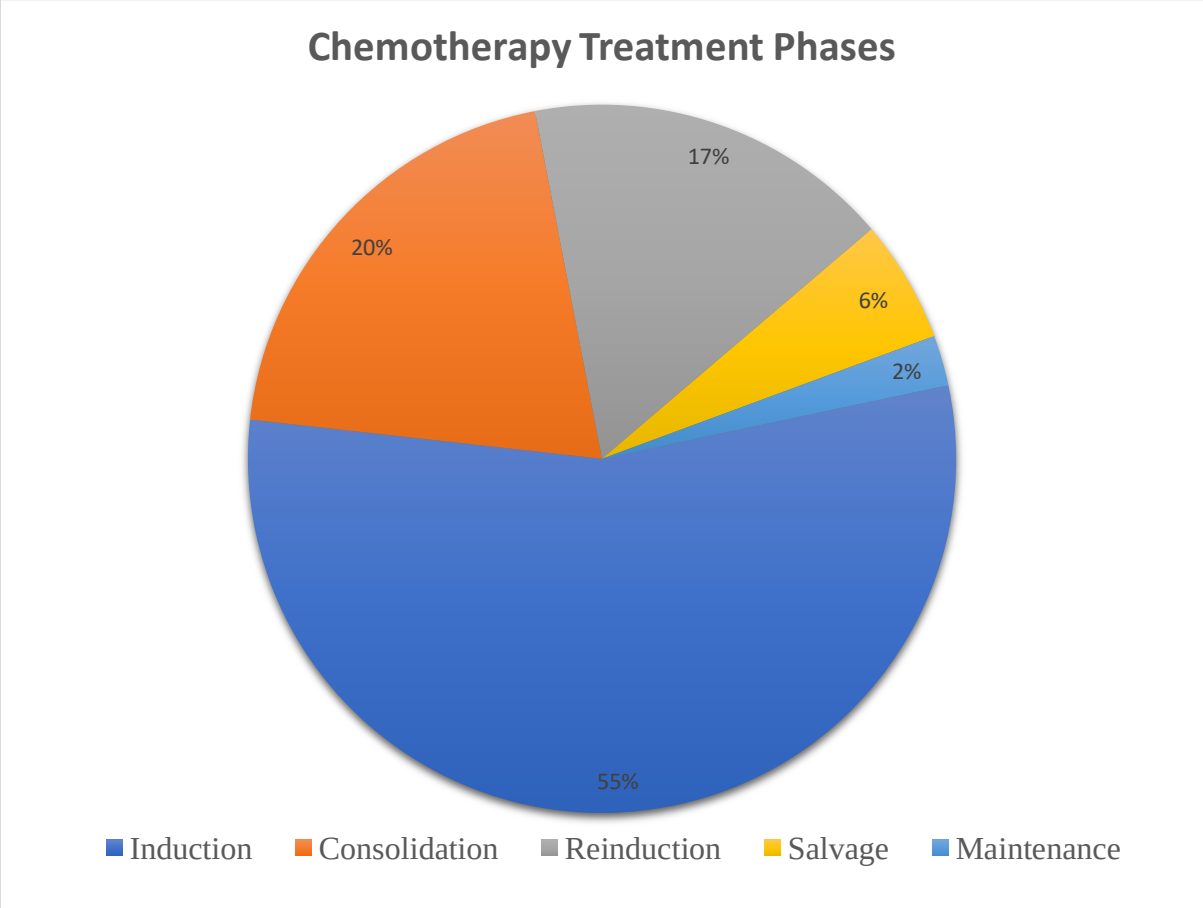

Figure 2:Chemotherapy Treatment Phases of study participants

4.3.2:Chemotherapy Regimens

Various chemotherapy regimens were used to manage the patients and were selected based on type of Leukemia and phase of treatment. Azacitidine was the most commonly used (22, 24.7%) regime (**Table *8***.

Table 8: Chemotherapy Regimens used in the management of Leukemia (n=89)

Regimen number	Regimen	Number of patients (n)	Percentage (%)
R1	Azacitidine	22	24.7
R2	Vincristine/Daunorubicin/Prednisolone/L-asparaginase / IT Cytarabine /IT MTX.	13	14.6
R3	Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/ IT MTX	13	14.6
R4	High Dose Cytarabine(HIDAC)	11	12.4
R5	Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/ /IT MTX	9	10.1
R6	Daunorubicin/Cytarabine	7	7.9
R7	Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose Cytarabine /Folinic acid	5	5.6
R8	Daunorubicin/IV Cytarabine/Etoposide	4	4.5
R9	Hyper CVAD	3	3.4
R10	Vincristine/Prednisolone/6-mercaptopurine/PO Methotrexate/IT MTX	2	2.3
R11	Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	2	2.3
R12	Vincristine/Prednisolone/L-Asparaginase/IT MTX	2	2.3
R13	Fludarabine /Cytarabine/G-CSF	1	1.1

Key;IV-Intravenous,IT-Intrathecal,PO-Per-oral,SC-Subcutaneous,CVAD-Cyclophosphamide, Vincristine, Doxorubicin & dexamethasone,G-CSF-Granulocyte colony stimulating factor,

MTX -Methotrexate

4.4 Classes of chemotherapy agents for the management of Leukemia

The most frequently used class of chemotherapeutic agents in treatment of leukemia were antifolate metabolites (52, 58.5%), and pyrimidine antimetabolites (50,56.2%). Daunorubicin was the most utilised (33, 37.1%) anthracycline while Prednisolone(19,21.4%) was the most used corticosteroid in leukemia treatment (**Table *9***)

Table 9: Chemotherapy agents used in the Study Participants(n=89)

Drugs	**Frequency(n)**	**Percentage(%)**
Folate Antimetabolites		
IT Methotrexate	43	48.3
High Dose Methotrexate	7	7.9
PO Methotrexate	2	2.3
Pyrimidine antimetabolites		
Cytarabine	39	43.8
High Dose Cytarabine	11	12.4
Anthracyclines		
Daunorubicin	33	37.1
Doxorubicin	5	5.6
Vinca alkaloids		
Vincristine	31	34.8
L-asparaginase	31	34.8
Corticosteroids		
Prednisolone	19	21.4
Dexamethasone	14	15.7
Azacitidine	22	24.7
Alkylating agents		
Cyclophosphamide	16	17.9
Purine antimetabolites		
6-Mercaptopurine	15	16.8
Hydroxyurea	4	4.5
Fludarabine	1	1.1
Topoisomerase II Inhibitors		
Etoposide	9	10.1

4.4 Drug Therapy Problems

Prevalence of drug therapy problems among the study participants are shown in **Figure *3***.Out of 89 patients assessed, 81 (91%) had at least one drug therapy problem reported. A total of 204 DTPs were identified. Adverse drug reaction was the most common occurring (79,88.8%) therapy problem.

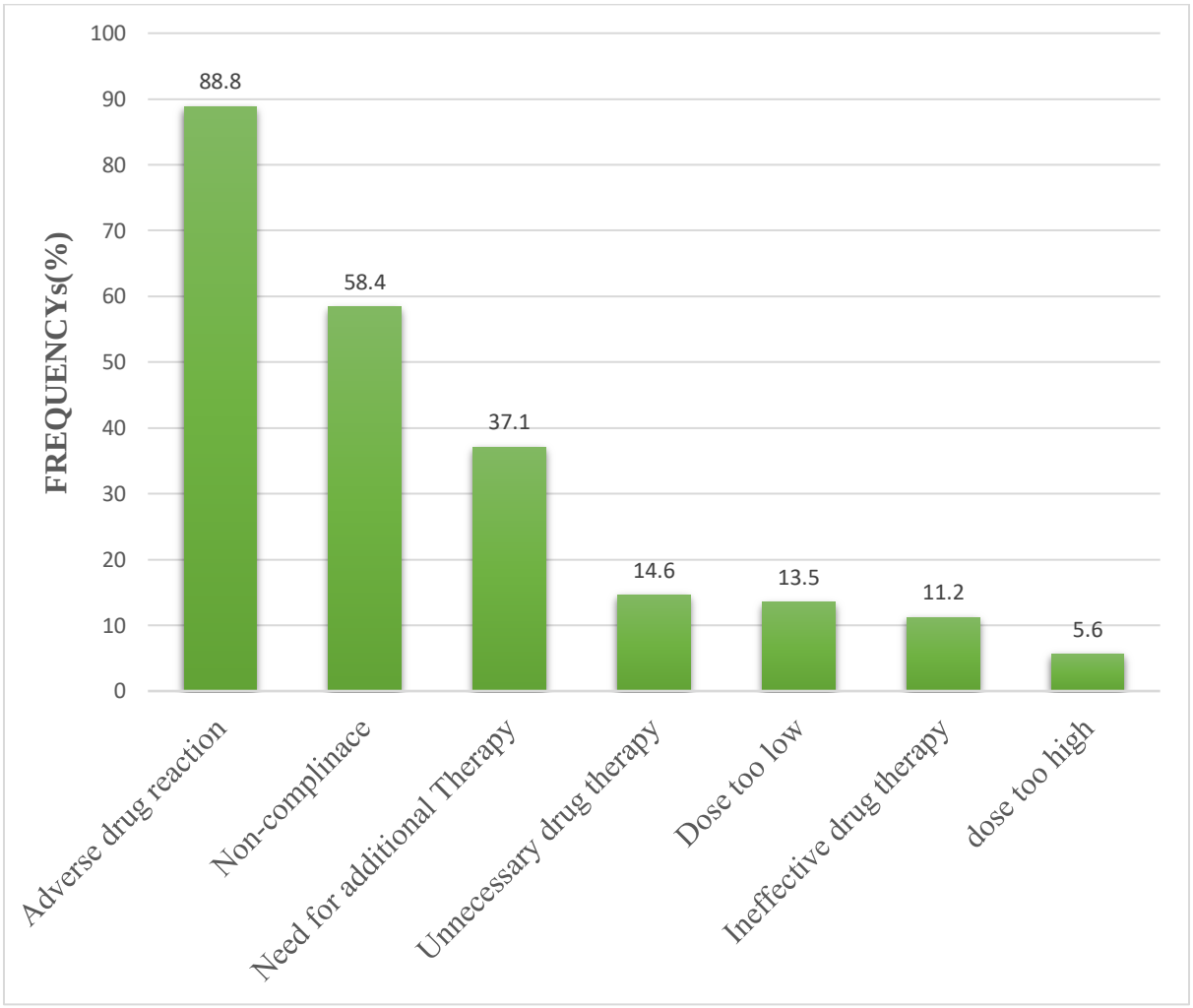

Figure 3:Prevalence of drug therapy problems (n=89).

4.5 Causes of Drug therapy problems

Toxicity effects of drugs (77,37.7 %) and postponement of chemotherapy (36,17.6%) were the major causes of overall drug therapy problems (**Table *10***).

Table 10 Causes of drug therapy problems among leukemia patients (n=89)

DTP Causes	Frequency (n)	Percentage(%)
Adverse Drug Reaction		
Drug Toxicity	77	97.5
Infusion reaction	2	2.5
Non-compliance		
Postponed due to neutropenia	36	69.2
Unable to afford drug	10	19.2
Cannot swallow drug	5	9.6
Failure to understand instructions	1	2
Need for Additional Therapy		
Untreated Condition	14	42.4
Preventive therapy required	12	36.4
Synergistic therapy required	7	21.2
Unnecessary Drug Therapy		
Duplicate Therapy	7	53.8
No medical indication	6	46.2
Dose too Low		
Reduced Frequency	12	100
In-effective Drug Therapy		
Drug not effective	8	80
Inappropriate dosage form	2	20
Dose too High		
High drug dose	5	100

4.5 Factors Associated with Drug Therapy Problems

Associations were done using the chi-squared test and Fisher's exact test because both variables were categorical. The level of significance was set at p=0.05.

4.5.1 Association between independent variables and Adverse drug reaction

The relationship between sociodemographic factors; age and Employment status with adverse drug reaction was statistically significant. The clinical factors that had statistically significant association with adverse drug reaction were type of leukemia, length of hospital stay and phase of chemotherapy treatment(**Table *11***).

Table 11: Association between sociodemographic and clinical factors with ADR (n=89)

Variable	Category	Adverse Drug Reaction		P-Value
		No	Yes	
Gender	Male	4	37	
	Female	6	42	0.748
Age	≤12 Years	1	44	
	>12 years	9	35	0.007
BMI	≤24.9	7	70	0.130
	>24.9	3	9	
Education Level	≤Primary	6	56	0.484
	>Secondary	4	23	
Employment status	No	4	66	**0.005**
	Yes	6	13	
Health Insurance cover	No	1	9	1.000
	Yes	9	70	
Type of Leukemia	ALL	1	47	
	AML	9	30	
	CML	0	2	**0.011**
Disease Status	Initial diagnosis	9	62	
	Refractory	0	3	
	Relapse	1	14	1.000
Comorbidity	Absent	10	69	0.595
	Present	0	10	
Length of Hospital stay	≤20 Days	9	42	**0.039**
	>20 Days	1	37	
Phase of Treatment	Induction	9	40	
	Re-induction	0	15	0.039
	Consolidation	0	18	
	Maintenance	1	1	
	Salvage	0	5	

Key: ADR – Adverse drug reaction, ALL-Acute lymphoblastic Leukemia, AML-Acute myelogenous leukemia, CML-Chronic myeloid leukemia

There was a statistically significant association between the use of Azacitidine regimen and occurrence of adverse drug reaction(**Table *12***).

Table 12: Association between chemotherapy regimens with adverse drug reaction (n=89)

Regimen	**Category**	**Adverse Drug Reaction**		**P-Value**
		No	**yes**	
Hydroxyurea	No	9	76	
	Yes	1	3	0.385
Azacitidine	No	1	66	
	Yes	9	13	**0.001**
High Dose Cytarabine(HIDAC)	No	10	68	
	Yes	0	11	0.352
Fludarabine /Cytarabine/G-CSF	No	10	78	
	Yes	0	1	1.000
Daunorubicin/Cytarabine	No	10	72	
	Yes	0	7	1.000
Vincristine/Daunorubicin/Prednisolone/ L-Asparaginase/IT Cytarabine /IT MTX	No	10	66	
	Yes	0	13	0.347
Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/IT Methotrexate	No	10	66	
	Yes	0	13	0.347
Vincristine/Prednisolone/6-Mercaptopurine/PO MTX /IT MTX	No	9	78	
	Yes	1	1	0.213
Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/IT MTX	No	10	70	
	Yes	0	9	0.590
Vincristine/Prednisolone/L-Asparaginase/IT MTX	No	10	77	
	Yes	0	2	1.000
Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	No	10	77	
	Yes	0	2	1.000
Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose Cytarabine /Folinic acid	No	10	74	
	Yes	0	5	1.000
Daunorubicin/IV Cytarabine/Etoposide	No	10	75	1.000
	Yes	0	4	
Hyper CVAD	No	10	76	1.000
	Yes	0	3	

Key: IV- Intravenous, IT-Intrathecal, PO-Per oral, SC-Subcutaneous,CVAD-Cyclophosphamide, Vincristine, Doxorubicin & dexamethasone,G-CSF-Granulocyte colony stimulating factor,HIDAC-high dose cytarabine,MTX-Methotrexate.

4.5.2 Association between independent variables and Non-compliance.

There was statistically significant association between education level, employment status, type of leukemia and phase of treatment with non-compliance to therapy problem (**Table *13***).

Table 13: Sociodemographic and clinical factors association with non-compliance (n=89)

Variable	Category	Non-compliance		P-Value
		No	Yes	
Gender	Male	18	23	
	Female	19	29	0.680
Age	≤12 Years	16	29	0.244
	>12 years	21	23	
BMI	≤24.9	30	47	
	>24.9	7	5	0.205
Education Level	≤Primary	21	41	
	>Secondary	16	11	**0.025**
Employment status	No	23	47	
	Yes	14	5	***0.001**
Health Insurance cover	No	4	6	
	Yes	33	46	1.000
Type of Leukemia	ALL	15	33	
	AML	20	19	**0.031**
	CML	2	0	
Disease status	Initial diagnosis	34	37	
	Refractory	20	3	0.047
	Relapse	3	12	
Comorbidity	Absent	34	45	0.513
	Present	3	7	
Length of Hospital stay	≤20 Days	21	30	0.930
	>20 Days	16	22	
Phase of Treatment	Induction	32	17	
	Re-induction	3	12	**0.001**
	Consolidation	1	17	
	Maintenance	1	1	
	Salvage	0	5	

Key: BMI –Body Mass Index, ALL-Acute lymphoblastic Leukemia, AML-Acute myelogenous leukemia, CML-Chronic myeloid leukemia.

There was statistically significant association between R3,R4 and R6 regimen (**Table *8***) with non-compliance to treatment among the study participants (***Table 14).***

Table 14: Chemotherapy regimens association with non-compliance (n=89)

Regimen	**Category**	**Non-compliance**		**P-Value**
		NO	**YES**	
Hydroxyurea	No	34	51	
	Yes	3	1	0.303
Azacitidine	No	26	41	
	Yes	11	11	0.355
High Dose Cytarabine(HIDAC)	No	35	43	
	Yes	2	9	0.113
Fludarabine /Cytarabine/G-CSF	No	37	51	
	Yes	0	1	1.000
Daunorubicin/Cytarabine	No	30	52	
	Yes	7	0	**0.001**
Vincristine/Daunorubicin/Prednisolone/ L-Asparaginase/IT Cytarabine /IT MTX	No	28	48	
	Yes	9	4	**0.036**
Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/IT Methotrexate	No	37	39	
	Yes	0	13	**0.001**
Vincristine/Prednisolone/6-Mercaptopurine/PO Methotrexate/IT MTX	No	36	51	
	Yes	1	1	1.000
Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/ /IT Methotrexate/	No	35	45	
	Yes	2	7	0.295
Vincristine/Prednisolone/L-Asparaginase/IT Methotrexate	No	35	52	
	Yes	2	0	0.170
Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	No	37	50	
	Yes	0	2	0.509
Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose cytarabine/ Folinic acid	No	37	47	
	Yes	0	5	0.073
Daunorubicin/IV Cytarabine/Etoposide	No	36	49	0.638
	Yes	1	3	
Hyper CVAD	No	36	50	1.000
	Yes	1	2	

Key: IV- Intravenous, IT-Intrathecal, PO-Per oral, SC-Subcutaneous,CVAD-Cyclophosphamide/ Vincristine/Doxorubicin/ dexamethasone,G-CSF-Granulocyte colony stimulating factor,HIDAC-high dose cytarabine,MTX-Methotrexate

4.5.3 Association between independent variables and Need for additional Therapy

There was a statistically significant association between gender, type of leukemia and phase of treatment with need for additional therapy (**Table *15***).

Table 15: Sociodemographic and clinical factors association with Need for additional therapy

Variable	Category	Need for additional Therapy		P-Value
		NO	YES	
Gender	Male	21	20	**0.035**
	Female	35	13	
Age	≤12 Years	24	21	0.058
	>12 years	32	12	
BMI	≤24.9	46	31	0.198
	>24.9	10	2	
Education Level	≤Primary	40	22	0.637
	>Secondary	16	11	
Employment status	No	41	15	0.117
	Yes	29	4	
Health Insurance cover	No	6	50	1.000
	Yes	4	29	
Type of Leukemia	ALL	24	24	**0.015**
	AML	30	9	
	CML	2	0	
Disease Status	Initial Diagnosis	48	23	0.120
	Refractory	2	1	
	Relapse	6	9	
Comorbidity	Absent	49	30	0.739
	Present	7	3	
Length of Hospital stay	≤20 Days	35	16	0.268
	>20 Days	21	17	
Phase of Treatment	Induction	38	11	**0.011**
	Re-induction	7	8	
	Consolidation	9	9	
	Maintenance	1	1	
	Salvage	1	4	

Key: BMI-Body Mass index, ALL-Acute lymphoblastic Leukemia, AML-Acute myelogenous leukemia, CML-Chronic myeloid leukemia

Use of Azacitidine regimen and High dose Cytarabine had a statistically significant association with need for additional therapy(**Table *16***).

Table 16: Chemotherapy regimen association with Need for additional therapy (n=89)

Regimen	**Category**	**Need For additional Therapy**		**P-Value**
		No	**Yes**	
Hydroxyurea	No	52	33	
	Yes	4	0	0.292
Azacitidine	No	36	31	
	Yes	20	2	**0.002**
High Dose Cytarabine(HIDAC)	No	54	24	
	Yes	2	9	**0.002**
Fludarabine /Cytarabine/G-CSF	No	55	33	
	Yes	1	0	1.000
Daunorubicin/Cytarabine	No	51	31	
	Yes	5	2	1.000
Vincristine/Daunorubicin/Prednisolone/ L-Asparaginase/IT Cytarabine /IT MTX	No	47	29	
	Yes	9	4	0.760
Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/IT Methotrexate	No	49	27	
	Yes	7	6	0.464
Vincristine/Prednisolone/6-MP/PO Methotrexate/IT methotrexate	No	55	32	
	Yes	1	1	1.000
Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/ /IT Methotrexate/	No	53	27	
	Yes	3	6	0.072
Vincristine/Prednisolone/L-Asparaginase/IT Methotrexate	No	54	33	
	Yes	2	0	0.528
Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	No	55	32	
	Yes	1	1	1.000
Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose Cytarabine/Folinic acid	No	55	29	
	Yes	1	4	0.061
Daunorubicin/IV Cytarabine/Etoposide	No	52	33	0.292
	Yes	4	0	
Hyper CVAD	No	56	30	0.048
	Yes	0	3	

Key: IV- Intravenous, IT-Intrathecal, PO-Per oral, SC-Subcutaneous,CVAD-Cyclophosphamide/ Vincristine/Doxorubicin/ dexamethasone,G-CSF-Granulocyte colony stimulating factor,HIDAC-high dose cytarabine,MTX-Methotrexate

4.5.4. Association between independent variables and unnecessary drug therapy

There was no significant association between sociodemographic and clinical factors with unnecessary drug therapy problem(**Table *17***).

Table 17:Sociodemographic and clinical factors association with unnecessary drug therapy (n=89)

Variable	Category	Unnecessary Drug Therapy		P-Value
		NO	YES	
Gender	Male	33	8	
	Female	43	5	0.226
Age	≤12 Years	35	10	
	>12 years	41	3	0.069
BMI	≤24.9	66	11	1.000
	>24.9	10	2	
Education Level	≤Primary	52	10	0.747
	>Secondary	24	3	
Employment status	No	59	11	0.727
	Yes	17	2	
Health Insurance cover	No	8	2	0.636
	Yes	68	11	
Type of Leukemia	ALL	40	8	
	AML	34	5	
	CML	2	0	0.819
Disease Status	Initial Diagnosis	60	11	
	Refractory	2	1	
	Relapse	14	1	0.419
Comorbidity	Absent	67	12	1.000
	Present	9	1	
Length of Hospital stay	≤20 Days	47	4	0.066
	>20 Days	29	9	
Phase of Treatment	Induction	43	6	
	Re-induction	12	3	
	Consolidation	14	4	0.694
	Maintenance	2	0	
	Salvage	5	0	

Key: BMI-Body Mass index, ALL-Acute lymphoblastic Leukemia, AML-Acute myelogenous leukemia, CML-Chronic myeloid leukemia

Use of daunorubicin/cytarabine/etoposide regimen had a statistically significant association with unnecessary drug therapy problem (**Table *18***).

Table 18: Association between Chemotherapy regimens and unnecessary drug therapy (n=89)

Regimen	**Category**	**Unnecessary Drug Therapy**		**P-Value**
		No	**Yes**	
Hydroxyurea	No	73	12	
	Yes	3	1	0.475
Azacitidine	No	56	11	
	Yes	20	2	0.506
High Dose Cytarabine	No	65	13	
	Yes	11	0	0.356
Fludarabine /Cytarabine/G-CSF	No	75	13	
	Yes	1	0	1.000
Daunorubicin/Cytarabine	No	69	13	
	Yes	7	0	0.588
Vincristine/Daunorubicin/Prednisolone/ L-Asparaginase/IT Cytarabine /IT MTX	No	66	10	
	Yes	10	3	0.395
Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/IT Methotrexate	No	67	9	
	Yes	9	4	0.093
Vincristine/Prednisolone/6-Mercaptopurine/PO Methotrexate/IT MX	No	74	13	
	Yes	2	0	1.000
Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/ /IT Methotrexate/	No	68	12	
	Yes	8	1	1.000
Vincristine/Prednisolone/L-Asparaginase/IT Methotrexate	No	74	13	
	Yes	2	0	1.000
Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	No	74	13	
	Yes	2	0	1.000
Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose Cytarabine/Folinic acid	No	71	13	
	Yes	5	0	1.000
Daunorubicin/IV Cytarabine/Etoposide	No	75	10	
	Yes	1	3	**0.009**
Hyper CVAD	No	73	13	
	Yes	3	0	1.000

Key: IV- Intravenous, IT-Intrathecal, PO-Per oral, SC-Subcutaneous,CVAD-Cyclophosphamide/ Vincristine/Doxorubicin/ dexamethasone,G-CSF-Granulocyte colony stimulating factor,HIDAC-high dose cytarabine,MTX-Methotrexate

4.5.5 Association between independent variables and ineffective Drug therapy problem

None of the sociodemographic and clinical factors had statistically significant association with ineffective drug therapy problem (**Table *19***)

Table 19: Sociodemographic and clinical factors association with ineffective drug therapy (n=89)

VARIABLE	CATEGORY	Ineffective Drug Therapy		P-Value
		NO	YES	
Gender	Male	37	4	
	Female	42	6	0.748
Age	≤12 Years	38	7	
	>12 years	41	3	0.315
BMI	≤24.9	68	9	
	>24.9	11	1	1.000
Education Level	≤Primary	54	8	
	>Secondary	25	2	0.717
Employment status	No	60	10	
	Yes	19	0	0.111
Health Insurance cover	No	9	1	1.000
	Yes	70	9	
Type of Leukemia	ALL	41	7	
	AML	36	3	0.608
	CML	2	0	
Disease Status	Initial Diagnosis	65	6	
	Refractory	2	1	0.130
	Relapse	12	3	
Comorbidity	Absent	70	9	1.000
	Present	9	1	
Length of Hospital stay	≤20 Days	47	4	0.315
	>20 Days	32	6	
Phase of Treatment	Induction	43	6	
	Re-induction	13	2	0.732
	Consolidation	17	1	
	Maintenance	2	0	
	Salvage	4	1	

Key: BMI-Body Mass Index, ALL-Acute lymphoblastic Leukemia, AML-Acute myelogenous leukemia, CML-Chronic myeloid leukemia

There was statistically significant association between high dose cytarabine and hyper CVAD regimen with ineffective drug therapy problem (**Table *20***).

Table 20: Association between Chemotherapy regimen and Ineffective drug therapy (n=89).

Regimen	**Category**	**Ineffective Drug Therapy**		**P-Value**
		No	**Yes**	
Hydroxyurea	No	75	10	
	Yes	4	0	1.000
Azacitidine	No	57	10	
	Yes	22	0	0.062
High Dose Cytarabine(HIDAC)	No	72	6	
	Yes	7	4	**0.019**
Fludarabine /Cytarabine/G-CSF	No	78	10	
	Yes	1	0	1.000
Daunorubicin/Cytarabine	No	73	9	
	Yes	6	1	0.579
Vincristine/Daunorubicin/Prednisolone/ L-Asparaginase/IT Cytarabine /IT MTX	No	68	8	
	Yes	11	2	0.636
Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/IT Methotrexate	No	66	10	
	Yes	13	0	0.347
Vincristine/Prednisolone/6-Mercaptopurine/PO Methotrexate/IT MTX	No	77	10	
	Yes	2	0	1.000
Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/ /IT Methotrexate/	No	71	9	
	Yes	8	1	1.000
Vincristine/Prednisolone/L-Asparaginase/IT Methotrexate	No	74	9	
	Yes	1	1	0.213
Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	No	77	10	
	Yes	2	0	1.000
Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose Cytarabine/Folinic acid	No	75	9	
	Yes	4	1	0.457
Daunorubicin/IV Cytarabine/Etoposide	No	76	9	
	Yes	3	1	0.385
Hyper CVAD	No	78	8	
	Yes	1	2	**0.032**

Key: IV- Intravenous, IT-Intrathecal, PO-Per oral, SC-Subcutaneous,CVAD-Cyclophosphamide/ Vincristine/Doxorubicin/ dexamethasone,G-CSF-Granulocyte colony stimulating factor,HIDAC-high dose cytarabine,MTX-Methotrexate.

4.5.6 Association between independent variables and Dose Too low Therapy

There was no statistically significant association between sociodemographic characteristics and patient clinical factors with dose too low (**Table *21***).

Table 21: Sociodemographic and clinical factors association with dose too low (n=89).

Variable	Category	Dose Too Low		P-Value
		NO	YES	
Gender	Male	34	7	
	Female	43	5	0.535
Age	≤12 Years	36	9	0.118
	>12 years	41	3	
BMI	≤24.9	67	10	0.662
	>24.9	10	2	
Education Level	≤Primary	53	9	1.000
	>Secondary	24	3	
Employment status	No	58	12	0.063
	Yes	19	0	
Health Insurance cover	No	8	2	0.619
	Yes	69	10	
Type of Leukemia	ALL	38	10	0.084
	AML	37	2	
	CML	2	0	
Disease Status	Initial Diagnosis	62	9	
	Refractory	3	0	0.634
	Relapse	12	3	
Comorbidity	Absent	68	11	1.000
	Present	9	1	
Length of Hospital stay	≤20 Days	45	6	0.755
	>20 Days	32	6	
Phase of Treatment	Induction	45	4	
	Re-induction	11	4	
	Consolidation	14	4	0.234
	Maintenance	2	0	
	Salvage	5	0	

Key: BMI-Body Mass Index, ALL-Acute lymphoblastic Leukemia, AML-Acute myelogenous leukemia, CML-Chronic myeloid leukemia

Among the regimens used only Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate had statistically significant association with dose too low therapy problem(**Table *22***).

Table 22: Association between Chemotherapy regimen given and dose too low (n=89).

Regimen	**Category**	**Dose Too Low**		
		No	**Yes**	**P-Value**
Hydroxyurea	No	73	12	
	Yes	4	0	1.000
Azacitidine	No	56	11	
	Yes	21	1	0.280
High Dose Cytarabine(HIDAC)	No	66	12	
	Yes	11	0	0.348
Fludarabine /Cytarabine/G-CSF	No	76	12	
	Yes	1	0	1.000
Daunorubicin/Cytarabine	No	70	12	
	Yes	7	0	0.587
Vincristine/Daunorubicin/Prednisolone/ L-Asparaginase/IT Cytarabine /IT MTX	No	66	10	
	Yes	11	2	1.000
Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/IT Methotrexate	No	66	10	
	Yes	9	4	0.070
Vincristine/Prednisolone/6-MP/PO Methotrexate/IT MTX	No	75	12	
	Yes	2	0	1.000
Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/ /IT Methotrexate/	No	69	11	
	Yes	8	1	1.000
Vincristine/Prednisolone/L-Asparaginase/IT Methotrexate	No	76	11	
	Yes	1	1	0.253
Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	No	77	10	
	Yes	0	2	**0.017**
Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose/Cytarabine /Folinic acid	No	72	12	
	Yes	5	0	1.000
Daunorubicin/IV Cytarabine/Etoposide	No	74	11	0.446
	Yes	3	1	
Hyper CVAD	No	74	12	0.644
	Yes	3	0	

Key: IV- Intravenous, IT-Intrathecal, PO-Per oral, SC-Subcutaneous,CVAD-Cyclophosphamide/ Vincristine/Doxorubicin/ dexamethasone,G-CSF-Granulocyte colony stimulating factor,HIDAC-high dose cytarabine,MTX-Methotrexate

4.5.7 Association between independent variables and Dose Too High

There was no statistically significant association between sociodemographic factor and clinical factors with dose too high (**Table *23***).

Table 23: Sociodemographic and clinical characteristic association with Dose too high (n=89)

Variable	Category	Dose Too High		P-Value
		No	Yes	
Gender	Male	37	4	
	Female	47	1	0.176
Age	≤12 Years	40	5	0.056
	>12 years	44	0	
BMI	≤24.9	72	5	1.000
	>24.9	12	0	
Education Level	≤Primary	57	5	0.317
	>Secondary	27	0	
Employment status	No	65	5	0.580
	Yes	19	0	
Health Insurance cover	No	9	1	0.457
	Yes	75	4	
Type of Leukemia	ALL	43	5	
	AML	39	0	
	CML	2	0	0.165
Disease Status	Initial Diagnosis	68	3	
	Refractory	3	0	
	Relapse	13	2	0.335
Comorbidity	Absent	74	5	1.000
	Present	10	0	
Length of Hospital stay	≤20 Days	49	2	0.647
	>20 Days	35	3	
Phase of Treatment	Induction	48	1	
	Re-induction	14	1	
	Consolidation	16	2	
	Maintenance	2	0	
	Salvage	4	1	0.171

Key: BMI-Body Mass Index, ALL-Acute lymphoblastic Leukemia, AML-Acute myelogenous leukemia, CML-Chronic myeloid leukemia

There was no statistically significant relationship between chemotherapy regimen with dose too high therapy problem (**Table *24***).

Table 24: Chemotherapy Regimens association with Dose Too High Therapy (n=89).

Regimen	**Category**	**Dose Too High**		**P-Value**
		No	**Yes**	
Hydroxyurea	No	80	5	
	Yes	4	0	1.000
Azacitidine	No	62	5	
	Yes	22	0	0.327
High Dose Cytarabine(HIDAC)	No	74	4	
	Yes	10	1	0.491
Fludarabine /Cytarabine/G-CSF	No	83	5	
	Yes	1	0	1.000
Daunorubicin/Cytarabine	No	77	5	
	Yes	7	0	1.000
Vincristine/Daunorubicin/Prednisolone/ L-Asparaginase/IT Cytarabine /IT MTX	No	72	4	
	Yes	12	1	0.555
Cyclophosphamide/IV or SC Cytarabine/6-mercaptopurine/IT Methotrexate	No	73	3	
	Yes	11	2	0.153
Vincristine/Prednisolone/6-MP/PO Methotrexate/IT MTX	No	82	5	
	Yes	2	0	1.000
Vincristine/Daunorubicin/PO Dexamethasone /L-Asparaginase/ /IT Methotrexate/	No	76	4	
	Yes	8	1	0.421
Vincristine/Prednisolone/L-Asparaginase/IT Methotrexate	No	82	5	
	Yes	2	0	1.000
Vincristine/prednisolone/Doxorubicin/L-asparaginase/IT Methotrexate	No	82	5	
	Yes	2	0	1.000
Etoposide/L-asparaginase/IV High dose Methotrexate/IV High dose Cytarabine/Folinic acid	No	80	4	
	Yes	4	1	0.256
Daunorubicin/IV Cytarabine/Etoposide	No	80	5	1.000
	Yes	4	0	
Hyper CVAD	No	81	5	1.000
	Yes	3	0	

Key: IV- Intravenous, IT-Intrathecal, PO-Per oral, SC-Subcutaneous,CVAD-Cyclophosphamide/ Vincristine/Doxorubicin/ dexamethasone,G-CSF-Granulocyte colony stimulating factor,HIDAC-high dose cytarabine,MTX-Methotrexate

4.6 Logistic Regression Analysis for Identification of Predictor factors of DTPs.

A bivariate analysis was run using a forward stepwise model building approach. Independent variables picked for regression included all those with p value of less than 0.25. Each category of DTP was regressed against each covariate and in multivariate analysis regressed against all covariates. Data was summarised as crude Odds ratio (cOR),adjusted Odds ratio (aOR),Confidence interval at 95% (95% CI) and the P-value.

4.6.1 Independent Predictors of Adverse Drug Reaction

In binary analysis, four predictor variables had a statistically significant association with adverse drug reaction namely, age, employment status, type of leukemia and azacitidine Regimen (**Table *25***).

Cumulatively ,only age of a patient was an independent predictor for occurrence of adverse drug reaction. Patients older than 12years old had 1.59 times odds of having adverse drug reaction compared to those aged 12 years and below (***Table 25***).

Table 25: Logistic Regression results for Adverse drug reaction

Category of DTP	Variable	Bivariate Analysis		Multivariate Analysis	
		COR (95% CI)	**P-Value**	**aOR(95% CI)**	**P-Value**
ADR	Age (≤12 years, >12years)	0.88 (0.01-0.73)	**0.024**	1.59(1.20-2.1)	**0.001**
	BMI (≤24.9, >24.9)	0.3 (0.07-1.37)	0.121	0.90(0.13-6.34)	0.916
	Employment status	0.13 (0.03-0.53)	**0.004**	0.46(0.73-2.86)	0.402
	Type of Leukemia	0.20 (0.05-0.77)	**0.019**	-	-
	Length of Stay ≤ 20 days > 20 days	7.93 (0.96-65.58)	0.055	2.52(0.16-38.39)	0.507
	Phase of Treatment	2.14 (0.81-5.66)	0.125	1.03(0.35-3.05)	0.961
	R1 regimen	0.02 (0.003-0.188)	**0.001**	-	-
	R5 regimen	0.12 (0.01-2.007)	0.138	-	-

Key: BMI-Body Mass Index, ADR-Adverse drug reaction

4.6.2 Independent Predictors of Non-Compliance

In bivariate regression, the factors that had a statistically significant association with non-compliance were employment status, type of leukemia, status of disease, phase of treatment level of education and R2 regimen. (***Table 26***)

Cumulatively, age, employment status and phase of treatment were independent predictors of non-compliance to treatment. Patients over the age of 12 years old had 11.62 times odds of being non-compliant compared to those aged 12 years and below. Patients employed with income had 0.13 times odds of being non-compliant to treatment, which means unemployment increased predisposition to non-compliance. Patients in the consolidation phase of treatment had 3.58 times odds of being non-compliant to treatment compared to patients in the induction phase (***Table 26***).

Table 26: Logistic Regression results for Non-compliance

Category of DTP	Variable	Bivariate Analysis		Multivariate Analysis	
		cOR (95% CI)	P-Value	aOR(95% CI)	P-Value
Non-Compliance	Age (≤12 years, >12years)	0.60 (0.26-1.41)	0.245	11.62(1.83-73.93)	**0.009**
	BMI (≤24.9, >24.9)	0.46 (0.13-1.57)	0.213	0.52(0.08-3.32)	0.320
	Employment status	0.18 (0.06-0.55)	**0.003**	0.13(0.03-0.67)	**0.014**
	Type of Leukemia	0.37 (0.17-0.84)	**0.018**	0.41(0.11-1.55)	0.190
	Disease Status(initial diagnosis, Relapse)	2.091 (1.04-4.19)	**0.038**	1.26(0.49-3.26)	0.628
	Phase of Treatment (Induction, Consolidation)	4.086 (1.99-8.35)	**0.001**	3.58(1.39-9.23)	**0.008**
	R2 Regimen(No, Yes)	0.259 (0.07-0.92)	**0.037**	0.51(0.07-3.53)	0.497
	Education level (below primary, above primary)	0.352 (0.139-0.89)	**0.028**	0.22(0.04-1.14)	0.072

Key: BMI -Body Mass Index, Regimen numbering refer to **Table *8***

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4.6.3 Independent Predictors of Need for Additional therapy

In bivariate analysis, the regimen R9 was not included as it perfectly predicts success (**cOR=1**).

Statistically significant predictor variables were gender, type of leukemia and phase of treatment. Among regimens, high dose cytarabine and azacitidine had statistically significant association.

Cumulatively, use of high dose cytarabine regimen was an independent predictor for the need for additional therapy.Patiens on this regimen had 17.26 times odds of having the need for additional therapy compared to other regimens (**Table *27***).

Table 27: Logistic Regression results for Need for Additional Therapy

Dependent Variable =DTP	**Predictor Variables**	**Bivariate Analysis**		**Multivariate Analysis**	
		cOR (95% CI)	**P-Value**	**aOR (95% CI)**	**P-Value**
Need for Additional Therapy	Age (≤12 years, >12years)	0.43 (0.18-1.04)	0.061	0.69 (0.051-9.46)	0.787
	Gender	0.39 (0.16-0.94)	**0.037**	0.98(0.20-4.71	0.981
	BMI (≤24.9, >24.9)	0.29 (0.06-1.45)	0.133	0.19(0.02-2.00)	0.170
	Employment status	0.38 (0.11-1.25)	0.111	2.09(0.29-14.9)	0.460
	Type of Leukemia	0.28 (0.12-0.70)	**0.006**	0.38(0.09-1.45)	0.155
	Disease Status	1.74 (0.98-3.05)	0.055	1.17(0.51-2.67)	0.712
	Phase of Treatment	1.85 (1.23-2.79)	**0.003**	1.22(0.67-2.27)	0.511
	R4 regimen	10.13 (2.03-50.44)	**0.005**	17.26 (2.0-148.31)	**0.009**
	R1 regimen	0.16 (0.03-0.54)	**0.006**	0.61(0.05-7.64)	0.698
	R10 regimen	3.93 (0.91-16.93)	0.067	3.88(0.75-19.98)	0.105
	R7 regimen	7.59 (0.81-71.05)	0.076	0.57(0.02-19.85)	0.758
	R9 regimen	1			

Key: BMI-Body Mass Index, regimen numbering based on **Table *8***

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4.6.4 Independent Predictors of Unnecessary drug therapy and Ineffective drug therapy

In bivariate analysis, use of daunorubicin/cytarabine/etoposide regimen for acute myeloid leukemia had a statistically significant association with unnecessary drug therapy problem. Cumulatively patients on this regimen had 22.93 times odds of having unnecessary drug therapy (***Table 28***).

In bivariate analysis, use of high dose cytarabine and Hyper CVAD regimens had a statistically significant association with ineffective drug therapy problem. In multivariate analysis, there was no significant predictor factor of ineffective drug therapy (***Table 28***).

Table 28: Logistic Regression Results for Unnecessary and Ineffective drug therapy

Category of DTP	**Variable**	**Bivariate Analysis**		**Multivariate Analysis**	
		cOR (95% CI)	**P-Value**	**aOR(95% CI)**	**P-Value**
Unnecessary Drug Therapy	Age (≤12 ,>12years)	0.26(0.07-1.00)	0.051	0.65(0.13-3.22)	0.601
	Gender(Male, Female)	0.48 (0.14-1.60)	0.232	0.62(0.15-2.51)	0.503
	Length of hospital stay (	0.26(0.07-1.00)	0.051	.87(0.42-8.36)	0.409
	R3 Regimen(No, Yes)	3.31 (0.84-12.99)	0.086	3.18(0.67-15.11)	0.146
	R8 Regimen(No, Yes)	22.5 (2.13-237.67)	**0.010**	22.93(1.76-298.43)	**0.017**
Ineffective Drug Therapy	Disease status	1.69(0.82-3.54)	0.156	1.64(0.67-4.00)	0.276
	Regimen 4 (No, Yes)	6.86(1.55-30.25)	**0.011**	3.81(0.62-23.39)	0.148
	R11 regimen(No,Yes)	8.67(0.49-150.79)	0.138	18.92 (0.97-368.22)	0.052
	R9 regimen (No, Yes)	19.5(1.58-239.54)	**0.020**	14.34 (0.85-240.72)	0.064
	R1 regimen(No, Yes)	1	-		
	Employment status	1	-		

Key: Regimen numbering refer to ***Table 8***.

4.6.6 Independent Predictors of Dose Too Low and Dose too High

In bivariate analysis, the type of leukemia had a statistically significant association with dose too low (**Table *29***). The significance was however lost in multivariate regression.

For the dose too high, none of the independent variables had significant association (***Table 29***).

Table 29: Logistic regression results for Dose too low and Dose too high

Category of DTP	**Predictor Variables**	**Bivariate Analysis**		**Multivariate Analysis**	
		cOR (95% CI)	**P-Value**	**aOR(95% CI)**	**P-Value**
Dose Too Low	Age (≤12 years, >12years)	0.29 (0.07-.16)	0.081	0.41 (0.09-1.87)	0.254
	Type of leukemia	0.20 (0.04-0.96)	**0.044**	0.28 (0.05-1.54)	0.143
	Phase of treatment	01.11 (0.67-1.84)	0.664	0.67 (0.30-1.49)	0.330
	R3 Regimen	3.78 (0.94-15.12)	0.060	3.11(0.49-19.81)	0.230
Dose Too High	Gender(male,female)	0.19 (0.02-1.84)	0.154	0.23(0.02-2.27)	0.210
	Phase of treatment (induction, consolidation)	1.77 (0.93-3.37)	0.081	1.68 (0.79-3.56)	0.179
	R3 Regimen	4.42 (0.66-29.52)	0.125	2.30 (0.97-368.22)	0.410

Key: Regimen numbering refer to **Table *8***.

CHAPTER FIVE: DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter contains discussion of the results from analysis of the collected data. All the categories of study participants characteristics are described and compared to other similar studies. A conclusion of the study findings and recommendations are also given in this section**.**

5.2 Discussion

The age distribution in the study population showed that most patients were aged between 1 to 12 years. There were more female patients than male patients. According to lymphoma and leukemia society data published in 2018, leukemia is more common in males than females (19).The difference can be attributed to the better health seeking behavior among females demonstrated across related studies (10,45).It may also be due to inclusion of more females in the source population in this study. A huge proportion of patients had normal body mass index. Nutritionist being part of the multidisciplinary team at the wards ensure appropriate interventions that enable patients to stay within normal weight ranges. Majority of the participants had education level of primary and below. This is because most of the participants were children of school going age group which is below 12 years and at appropriate level of education according to age. Majority of patients in the oncology units had an active health insurance which caters for the cost of most health services.

The most common type of leukemia was acute lymphoblastic leukemia, followed by acute myeloid leukemia while chronic myeloid leukemia was the least prevalent. According to published data by the blood cancer society in the USA , acute lymphoblastic leukemia is the most occurring leukemia (19). Globocan 2020 also share the same findings that cut across the world (2,3). According to American cancer society data in 2023,ALL and AML are more common among children and adolescents ,ages 0 to 19 years (46). This age category formed the majority of study participants in this study. Chronic lymphocytic leukemia was not observed among study participants. This can be related to statistics showing a very low prevalence and a lifetime risk of diagnosis of 0.6% (19). Majority of patients stayed at the hospital for less than 20 days while those staying longer days did not necessarily define their state of illness. Some stayed longer due to the distance of their geographical residence which affected their treatment. A study in Brazil among hospitalized cancer patients noted some reasons for overstay in hospital was due to pathological illnesses that require close monitoring (47).Majority of the patient who stayed longer than 20 days had persistent neutropenia that led to postponement of chemotherapy administration. Neutropenia has been shown as the most common toxicity effects of chemotherapy in a closely related study (12).

All the seven categories of drug therapy problems were noted and comprehensively assessed in the study population. Majority (91%) of the participants had experienced at least one drug therapy problem during the course of chemotherapy. A total of 204 DTPs were reported which gives a frequency of 2.5 therapy problem per patient. This magnitude is closely related to a study by Amsalu et al on drug therapy problems among cervical cancer patients that had a prevalence of 93.8% (31). The three major drug therapy problem categories reported were adverse drug reaction,non-compliance and need for additional therapy while the dose too high was the least occurring problem.

Majority of the participants had experienced adverse drug reactions during chemotherapy. A higher proportion of this was due to undesirable effects of chemotherapeutic agents. Patients reported adverse effects as mostly toxicities related to specific chemotherapy agents. The events occurred either immediately after chemotherapy administration or few days later. Most hematological toxicities were picked from laboratory reports and some as signs and symptomatic manifestations. The findings were closely related to study done by Mwangi et al among colorectal cancer patients which had ADRs at as the majority of drug therapy problems (41).Similar findings were observed in a study by Reji et al to assess drug related admission among cancer patients at a tertiary institution in India, that reported high adverse drug reaction (48).High percentage of adverse drug reaction in cancer patient is due to the high toxicities and narrow therapeutic window of the chemotherapeutic drugs (8). Another reason is that majority of patients in this study were at the induction phase of treatment which utilizes more aggressive chemotherapy agents.

Non-compliance to treatment protocols and medical instructions on therapy was the second most common DTP. The unaffordability of azacitidine regimen contributed highly to this. Low socioeconomic status of the majority of the patients based on the high percentage of the unemployed, illustrates that the relatively high price was beyond their reach. The other factor for non-compliance focused on the oral chemotherapy that were mostly self-administered. Five patients reported to have been unable to swallow the medication mostly due to prevailing physiological status. There are very few studies on non-compliance with chemotherapy regimens. A study on non-compliance for self-administered chemotherapy done in the USA shows high prevalence of 84% compared to intravenously administered regimens especially in hematological cancers (49). The determinants for this included income, protocol complexity, social support, physical functioning and symptoms. Another study on the challenges of adherence to antineoplastic oral agents reported high percentage due to purposely missed doses, late dosing and concerns on side effects of the regimens (33).

About a third of participants had a need for additional therapy mostly as supportive treatment. The DTP occurred due to untreated condition, need for preventive therapy and need for synergistic therapy. A study by Yismaw et al in childhood cancers in Ethiopia reported that need for preventive therapy was the major cause of need for additional therapy (8). This was too high compared to this study that had untreated condition as the major cause. This difference could be attributed to multidisciplinary care involved in haemato-oncology units at KNH. A study of drug therapy problems in Head and neck cancer at KNH attributed the need for additional therapy to the inadequacy of managing chemotherapy side effects (32).

Unnecessary drug therapy was mostly due to either duplicate therapy of the supportive treatments or use of a drug with no definitive medical indication. It was observed that some patients continued with supportive treatment even after resolution of the same symptoms. In findings of six studies evaluating overuse of antiemetics in cancer patients, the estimated rate of overuse was high (50).Dose too low, ineffective drug therapy and dose too high were the other drug therapy problems observed. Dose too low was caused mainly by reduced dose frequency of the supportive treatment drugs. This is because some prescribers tend to be cautious when prescribing certain medications or do not use the updated treatment protocols for the supportive therapy. The element of a clinical pharmacist being involved in such intervention is key optimization of therapy (51). A similar study by Yismaw et al in childhood cancers had dose too low and dose too high as the most prevalent therapy problem (8). This was mainly a dosing problem and in comparison, means a clinical pharmacist greater involvement in clinical care in the oncology units at KNH may help curb dosing problems.

The main predictors of DTPs were age, employment status, phase of treatment and certain chemotherapy regimens. Multiple regression resulted in age as the key predictive factor for occurrence of adverse drug reaction. A study done by Lazarou et al to evaluate incidence of adverse drug reactions in hospitalised patients showed age as a great influencing factor for occurrence of adverse drug reaction (14). In another study done to assess patterns of chemotherapy related adverse effect in a tertiary hospital in Ethiopia, there was a positive association between age and adverse drug events. Older patients have slowed physiological metabolism which decreased metabolic elimination of many agents from the body thus an increase in toxicity (45).

Age was also a significant predictor of non-compliance among leukemia patients. This can be attributed to the post-chemotherapy neutropenia, which was the major reported adverse drug reaction that led to chemotherapy postponement to allow for bone marrow recovery. A systematic review of several studies showed close association between age and compliance. In the elderly the general view was that most of their non-compliance in chronic treatment is non-intentional. For adolescent however, it may be due to rebellious tendencies especially for long term and oral medication (40).

Employment status which is related to income was also predictor of non-compliance in leukemia patients. Some chemotherapy drugs that were out of stock within the hospital required patients to purchase out of pocket. Most patients on azacitidine were unable to afford the drug, which led to missing therapy on the days it was due. This clearly supported the results on employment status in which most participants had no stable income. From the systematic review done for several studies on relating cost of therapy with income, there was significant relation with non-compliance to long term treatment (40).

Need for additional therapy was associated with gender, type of leukemia, phase of treatment, high dose cytarabine regimen and azacitidine based regimens but use of high dose cytarabine was the significant predictor. Most patients had unmet therapy needs especially supportive treatment for prophylaxis against the adverse effects of this regimen. This regimen is known to cause ophthalmic keratitis which is usually prevented by routine use of corticosteroid containing ophthalmic medication (52). Most study participants were not on this prophylaxis either due to stock outs or failure to be issued with one.

The use of daunorubicin/cytarabine/etoposide in patients with relapsed AML was associated with unnecessary drug therapy. This is mostly the case for the supportive treatment incorporated in this course of treatment. This means that patients on this regimen would get supportive care and some post chemotherapy medication that were not necessary. Some study participants on this regimen had prophylaxis for ophthalmic keratitis which occurs only with high dose cytarabine(53).

5.3 Study strengths, weaknesses and Limitations

This was a cross sectional study with a small sample size that made it relatively quick and inexpensive to conduct. Data all on variables was collected at the same time point thus multiple outcomes and exposures were studied. The findings of the study also gave a good start for generating future hypothesis for in-depth research.

Some of the study limitations were the period in which the study was conducted, which was around the end of a fiscal year. This meant that a lot of health insurance covers were almost exhausted that tend to decrease patient turnover and reduced patient discharges. This limited attainment of the initially calculated sample size of 100 patients.

5.3 Conclusions

1. There was high prevalence (91%)of DTPs among leukemia patients at Kenyatta National Hospital.
2. Adverse drug reaction (88.8%), non-compliance (58.4%) and need for additional therapy (37.1%) were the majority types of DTPs identified among the leukemia patients
3. Age and employment status were the significant sociodemographic predictors of drug therapy problems among leukemia patients.
4. The phase of treatment and chemotherapy regimens given were the significant clinical predictors of drug therapy problems among leukemia patients

5.4 Recommendations for Policy and Practice

To increase identification and earlier resolution of drug therapy problems ,pharmacists should advance patient centred pharmaceutical care services in the oncology units. Standardised drug therapy problem assesment tools should be established and incorporated as part of care for leukemia patients with factors shown to significantly predict occurrence added as baseline guide.

5.5 Recommendation for further research

Further prospective research should be done with a larger sample focusing on the adverse drug reactions in among leukemia during chemotherapy. ADRs occurred in more than two thirds of study participants which highly contributed to the overall drug therapy problems prevalence .This would enable identify the major chemotherapy toxicities and the potential intervention.

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APPENDICES

Appendix 1: **Eligibility Screening Form**

All identified participants will be screened based on inclusion and exclusion criteria outline in chapter 3.

Study Details

Title	Magnitude and predictors of drug therapy problems among patients with leukemia at Kenyatta National Hospital
Principal investigator	Dr. Savwa Brian Odondi
KNH/UoN ERC No.	

Participant Details

Study unique No: _____

Inpatient No: _____

Age: _____ Gender: Male ☐ Female ☐

Inclusion Criteria

Criteria	**YES**	**NO**
Patients with definitive diagnosis of Leukemia		
Patients on chemotherapy treatment with at least first cycle completed.		
Patients who will consent or assent to take part in the study		

Exclusion Criteria

Criteria	**YES**	**NO**
Patients with missing therapy management records		
Patients with condition that limit their participation		

Eligibility Declaration

The participant is: Eligible ☐

Not Eligible: ☐ Reason _____

Signature:	Date:

Appendix 2: **Informed Consent**

A consent form for leukemia patients at the haemato-oncology ward invited to participate willingly in the study on drug therapy problems.

Part 1. Participant Information Form

Title of the Study: Drug therapy problems among patients with leukemia at Kenyatta National hospital**.**

Principal Investigator. Savwa Brian Odondi-Masters of Pharmacy in Clinical Pharmacy.3rd year student, University of Nairobi. P.O Box 36838-00200 Nairobi.

Supervisors: Dr. P. N Karimi PhD, UoN; Dr. Nyamu D. Gitonga PhD, UoN.

Introduction

I am Savwa Brian Odondi, a 3rd year postgraduate student at the school of pharmacy, University of Nairobi. As part of the curriculum program I am conducting a study to determine drug therapy problems and amongst inpatients with leukemia at Kenyatta National hospital. My focus will be on both paediatric and adult patients admitted and undergoing treatment at the 3 main oncology wards at KNH.

Purpose of the study

The primary treatment for leukemia is drug therapy. The study seeks to determine the extent of DTPs during chemotherapy which might be a huge hindrance in achieving desired therapeutic goals. The study will also focus on the predictors of such problems in patients and this may impact positively in minimizing such occurrences to improve patient's quality of life. The main purpose is therefore to determine if your drug related needs are being met.

Procedures involved

If you agree to participate in this study, a structured questionnaire will be availed to you to enable a short interview by a trained interviewer at your convenience. The questions will include your biodata, medical history, review of systems, medication history and your experience with drug treatment. The interview will last approximately 20 minutes. The investigator will also extract more information from our medical records. Your privacy during data collection will be ensured.

The rights of a participant

Voluntary participation

Right to withdraw from the study at will

Right to ask any questions before consenting to participate in the study

No information provided will be traced back to you

Participant information will be utilized sorely for this study.

Risks, harms and cost of participation

There will be no direct risks to the patients since there will be no drug or intervention administered to the patients. Study will involve extraction of information from medical records and patient interviews.

Benefits of participation

The study findings will help improve treatment monitoring and address the key drug therapy problems to maximize desired therapeutic outcomes Findings from this study will help improve pharmacovigilance in all other patients including participants.

Reimbursements for participation

There will be no fiscal payments, incentives or tokens for participating in this study.

Confidentiality

Note that all information collected will be regarded as confidential. The questionnaires and any other data will be stored under lock and key and password protected for the electronic data. Only the investigator will have access to the information.

Contacts

In case you have any questions regarding the study before, during or after participation, you can contact the following anytime.

1. **Dr. Savwa Brian Odondi.**
   Department of Pharmacology, Clinical pharmacy and Pharmacy practice,
   School of Pharmacy, University of Nairobi.
   Mobile; 0710 961 653.
   Email: savwabrian7@gmail.com
2. **Dr. P.N Karimi PhD -Supervisor**
   Department of Pharmacology, Clinical Pharmacy and Pharmacy practice,
   School of Pharmacy, University of Nairobi.
   Mobile: 0722 436 019

Email: ndirang15@gmail.com

3. **Dr. D.G Nyamu PhD – Supervisor**

Department of Pharmacology, Clinical Pharmacy and Pharmacy practice,

School of Pharmacy, University of Nairobi.

Mobile: 0722 403 671

Email: dgnyamu@gmail.com

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee **Telephone No. 2726300 Ext. 44102. Email uonknh_erc@uonbi.ac.ke.** The study staff will pay you back for your charges to these numbers if the call is for study-related communication

Part 2: Certificate of consent.

I have read the above information or had the information read to me. I have had the study sufficiently explained to me by Dr. Savwa Brian Odondi and/his assistant. Any questions I asked were answered in a clear language and to my satisfaction. I voluntarily give my written and informed consent to participate in the study through answering a questionnaire and allow review of my medical records. I understand that my rights will be respected throughout the study period

Print Name of Participant_____

Signature of Participant _____

Date _____/_____/_____

Day/month/year

Statement by the investigator

I have adequately and accurately explained the contents of this study and information sheet to the participant named above. I addressed any questions and concerns raised by the participant to the best of my knowledge and they were satisfied. I confirm that the participant has voluntarily given his/her consent without any coercion.

A copy of this informed consent form has been provided to the participant.

Name of the Investigator_____

Signature of Participant _____

Date _____/_____/_____

Day/ month/ year

APPENDIX 2B: KISWAHILI VERSION-MAELEZO KUHUSU KUSHIRIKI KATIKA UTAFITI

MADA YA UTAFITI: Kutathmini shida za matibabu zinazoweza kutokea miongoni mwa wagonjwa wa lukemia ambao wanapata matibabu katika hospitali ya rufaa ya Kenyatta.

MCHUNGUZI MKUU

Mchunguzi mkuu katika utafiti huu ni Dkt. Savwa Brian Odondi ambaye ni mwanafunzi wa somo la Famasia, mwaka wa tatu wa masomo ya upeoni, katika chuo kikuu cha Nairobi.

WASIMAMIZI / WACHUNGUZI WA USHIRIKIANO NA USHIRIKA WA KITAASISI

1) Dkt. P.N Karimi

   Idara ya Pharmacology, Clinical Pharmacy na Pharmacy Practice

   Shule ya Famasia, Chuo Kikuu cha Nairobi

2) Dkt. D.G Nyamu

   Idara ya Pharmacology, Clinical Pharmacy na Pharmacy Practice

   Shule ya Famasia, Chuo Kikuu cha Nairobi

UTANGULIZI

Jina langu ni Dkt. Savwa Brian Odondi, mwanafunzi wa shahada ya uzamifu katika kitengo cha "Clinical Pharmacy" katika chuo kikuu cha Nairobi.

Nina nia ya kufanya utafiti katika eneo la "KUTATHMINI SHIDA ZA MATIBABU ZINAZOWEZA KUTOKEA KWA WAGONJWA WA LUKEMIA AMBAO WANAPATA MATIBABU KATIKA HOSPITALI YA RUFAA YA KENYATTA" na ninaomba fursa ya kukuongelesha kuhusu utafiti huu na ikiwezekana unipe fursa ya kukujumulisha kwa utafiti huu.

Kuwa huru kuniuliza swali lolote ambalo unaeza kuwa nalo kuhusu utafiti huu wakati wowote ukisoma hii nakala ama nikiwa katika hali ya kukuelezezea kuhusu huu utafiti ama hata baada ya ukisoma. Baada ya ukisoma nakala hii ama hata baada ya kukuelezea ana kwa ana kuhusu utafiti huu, ukiridhika nakusihi ujisajili kuwa mmoja wa watakaoshiriki katika huu utafiti. Kuna nakala baada ya hii ambayo utajaza kuonyesha kwamba umeelezewa kuhusu utafiti huu na umekubali kuwa mhusika katika hii utafiti

Kabla tundelee, yafaa ujue kwamba kuhusika katika utafiti wowote ni kwa hiari na hakuna mtu atakulazimisha nyume na hiari yako. Pili, hata baada ya kujisajili kuwa mhusika katika utafiti wowote, uko na haki ya kujiuzulu kutoka kwa utafiti wakati wowote bila kujieleza. Tatu, hata ukitataa kuwa mhusika katita utafiti huu, hakuna haki zako ambazo utanyimwa na utapata matibabu yako kama tu wengine bile ubaguzi.

Je, tuendelee? **YES / NO**

Utafiti huu umeidhinishwa na Kamati ya Kitaifa ya Hospitali ya Maadili na Utafiti ya Kenya ya Kenyatta na Chuo Kikuu cha Nairobi kupitia itifaki nambari. _____

JE UTAFITI HUU NI KUHUSU NINI?

Wagonjwa wengi wa lukemia hutibiwa na madawa. Baadhi ya wagonjwa hutumia Zaidi ya dawa moja kwa muda mrefu kwa minajili ya kutibu hali zao. Matatizo ambayo hutokea wakati wagonjwa hawa wanatumia hizi madawa yanaweza changia hali kuwa mbaya Zaidi, kudhoofika kwa afya na mara kwa mara inachangia wagonjwa kutopata afueni.

Utafiti huu una nia ya kuchunguza baadhi ya shida za matumizi ya dawa ambazo wagonjwa wa lukemia hupata mara kwa mara wanapotumia dawa kutibu shida hii. Kwa kupitia rekodi zako za hospitali na kuongea na wewe ana kwa ana nina nia ya kutambua haya matatizo. Matokeo ya utafiti huu yatasaidia pakubwa kupambana na haya matatizo na kusaidia washiriki kutambua mbinu za kuzuia hayo matatizo kutokea tena kwako na kwa wengine.

NI NINI KITATOKEA IKIWA UTAAMUA KUWA KATIKA UTAFITI HUU?

Ikiwa utakubali kuwa sehemu ya utafiti huu, mhojiwa atapata habari kutoka kwa faili yako ya matibabu inayohusiana na historia yako ya kijamii, matibabu, na dawa. Kando na hayo, ntakuuliza maswali kuhusu matumizi yako ya dawa na taarifa yoyote ambayo itasaidia katika utafiti huu

HAKI ZA MSHIRIKI

Uhuru wa kushiriki kwa hiari yako.

Uhuru wa kuuliza swali lolote kabla ya kushiriki kwenye utafiti

Ujumbe wowote utakao toa hautashikiana nawe kibinafsi

Ujumbe utakotoa hautatumika kwingine mbali na hii utafiti

NI NINI KITATOKEA IKIWA UTAAMUA KUWA KATIKA UTAFITI HUU?

Ikiwa utakubali kuwa sehemu ya utafiti huu, mhojiwa atapata habari kutoka kwa faili yako ya matibabu inayohusiana na historia yako ya kijamii, matibabu, na dawa. Kando na hayo, ntakuuliza maswali kuhusu matumizi yako ya dawa na taarifa yoyote ambayo itasaidia katika utafiti huu

USHIRIKI WA KUJITOLEA

Kushiriki katika utafiti huu ni kwa hiari yako na kujitolea kwako. Sio lazima ushiriki katika utafiti huu. Ikiwa utaamua kwamba hutaki kushiriki, hakutakuwa na ubaguzi wowote katika matibabu yako. Utahudumiwa tu kama kawaida na utatibiwa sawa na wengine bila ubaguzi. Ikiwa utakubali kuwa mhusika katika utafiti huu na ifike mahali uamue kujitoa kwa utafiti, una huru wa kufanya hivyo.

JE! KUNA HATARI YOYOTE AU HUDHURU USUMBUFU UNAOHUSISHWA NA UTAFITI HUU?

Kutoka kwa utafiti huu, unaeza kupoteza faragha. Walakini, habari yote itayokusanywa kutoka kwa faili yako itahifadhiwa kwa siri. Katika utafiti huu, nambari ya kisiri itatumiwa kukurejelea kwenye hifadhidata ya kompyuta ambayo inalindwa na nenosiri, na rekodi zote za karatasi zitahifadhiwa kwenye baraza la mawaziri lenye usalama. Tafadhali kumbuka kuwa bado inaweza kuwa mtu anaweza kupata rekodi za utafiti na kugundua kuwa wewe ni mmoja wa washiriki kwani hakuna mfumo wa kuhifadhi data ambao unaweza kuwa salama kabisa. Utafiti huu hahutahitaji mshirika kutumia madawa za ziada na operesheni za kudhuru mwili wa mshirika hazitatumika.

JE! KUNA FAIDA YOYOTE KUWA KATIKA UTAFITI HUU?

Unaweza kufaidika kwa kuwa sehemu ya utafiti huu. Ikiwa shida yoyote itagunduliwa, daktari atajulishwa na hii itakuwa ya faida kwako. Pia, matokeo ya utafiti huu yatakuwa muhimu kwa kuboresha ubora wa huduma unayoipokea wewe na wagonjwa wa baadaye.

JE! KUWA KATIKA UTAFITI HUU KUTAGHARIMU CHOCHOTE?

kushiriki katika utafiti huu hakutakugharimu pesa yoyote.

JE! UTAPATA MAREJESHO YA PESA YOYOTE ILIYOTUMIWA KAMA SEHEMU YA UTAFITI HUU?

Kwa kuwa hakuna matumizi ya kuonekana kwa kushiriki katika utafiti huu, hakutakuwa na Fidia inayotokana na kuwa mshiriki katika utafiti huu.

JE! IKIWA UNA MASWALI KATIKA SIKU ZIJAZO?

Ikiwa una wasiwasi zaidi kuhusu kuwa sehemu ya utafiti huu, tafadhali tuma ujumbe mfupi, au piga simu kwa mchunguzi kwa nambari ifuatayo:

Dkt. Savwa Brian Odondi

Number ya simu: 0710 961 653

Barua ya pepe: savwabrian7@gmail.com

Ikiwa unahitaji habari zaidi kuhusu haki yako kama mshiriki wa utafiti, tafadhali wasiliana na Katibu / Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Kamati ya Maadili na Utafiti ya Chuo Kikuu cha Nairobi kupitia:

Nambari ya simu 2726300 Ext. 44102 au

Anwani ya barua pepe: uonknh_erc@uonbi.ac.ke

Utafiti huu una idhini ya kimaadili kutoka kwa chombo hiki.

Baada ya kupitia fomu hii ya idhini, kama umeridhika na unataka kushiriki katika utafiti huu, tafadhali idhinisha Fomu ya Ridhaa (SEHEMU YA PILI) inayofuata

SEHEMU YA PILI: FOMU YA RIDHAA (KUKUBALI KUSHIRIKI)

Taarifa ya Mshiriki

Hii ni kudhibitisha kuwa nimesoma habari hii ya idhini au nimesomewa. Nimejadiliana na mshauri wa utafiti kwa undani kuhusu utafiti huu, na maswali yangu yameshughulikiwa kwa lugha ambayo ninaelewa.

Ninajua faida au/na hatari za kuwa mmoja wa washiriki. Ni wazi kwangu kwamba ushiriki wangu ni wa hiari, na wakati wowote katika somo hili, niko huru kujiondoa. Kwa hivyo, nimekubali kushiriki katika utafiti huu kwa uhuru.

Ninaelewa kuwa mtafiti atafanya juhudi zote iwezekanavyo kudumisha usiri wa rekodi zangu za kibinafsi na kitambulisho. Ninaelewa kuwa kwa kukubali utafiti huu, sijatangulia haki zangu za kisheria, ambazo ninastahiki kama mshiriki wa utafiti**.**

Mshiriki: …… Tarehe: ……...

Shahidi: …… Tarehe: …….

Taarifa ya Mtafiti

Baada ya kuelezea mshiriki kila kitu kuhusu utafiti huu, hii ni kudhibitisha kuwa mshiriki anajua haki zake, anaelewa utafiti ni kuhusu nini na nimejibu maswali yote aliyouliza na amesema ameelewa kila kitu na ametoa ruhusa ya hiari kuwa mhusika katika huu

Jina la Mtafiti: …… ……

Tarehe: …… Sahihi: ……

Appendix 3: Parental consent form

Title of Study: Magnitude and Predictors of Drug Therapy Problems among patients with leukemia at Kenyatta National Hospital.

Principal Investigator \ and institutional affiliation: Brian Odondi Savwa / University of Nairobi.

Co-Investigators and institutional affiliation: Dr. P. N Karimi/ University of Nairobi.

Introduction:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not your child should participate in the study. Feel free to ask any questions about the purpose of the research, what happens if your child participates in the study, the possible risks and benefits, the rights of your child as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide if you want your child to be in the study or not. This process is called 'informed consent'. Once you understand and agree for your child to be in the study, I will request you to sign your name on this form. You should understand the general principles which apply to all participants in a medical research: i) Your child decision to participate is entirely voluntary ii) You child may withdraw from the study at any time without necessarily giving a reason for his/her withdrawal iii) Refusal to participate in the research will not affect the services your child is entitled to in this health facility or other facilities.

May I continue? YES / NO

For children below 18 years of age we give information about the study to parents or guardians. We will go over this information with you and you need to give permission in order for your child to participate in this study. We will give you a copy of this form for your records.

WHAT IS THE PURPOSE OF THE STUDY?

We are interviewing children who are hospitalised for Leukemia treatment. The purpose of the interview is to find out the magnitude and predictors of drug therapy problems among these children during treatment. Participants in this research study will be asked questions about their experience with medication specifically the chemotherapy drugs and any other medication they receive in the wards during treatment of leukemia and adherence to the same. There will be approximately 100 participants in this study randomly chosen. We are asking for your consent to consider your child to participate in this study.

The information will help us learn the level at which our guidelines are followed so as to improve in the future.

WHAT WILL HAPPEN IF YOU DECIDE YOU WANT YOUR CHILD TO BE IN THIS RESEARCH STUDY?

If you agree for your child to participate in this study, the following things will happen:

Data will be taken from the patient file onto a form. If there are any clarifications required about the patient, you will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately 10 minutes. The interview will cover topics such as the type of leukemia diagnosis, time it was diagnosed, chemotherapy medication that your child has received and adherence to it, their weight, allergy status and any side effect as a result of any of the medication administered. After the interview, your child will be examined physically to check for manifestation as a result of chemotherapy use.

ARE THERE ANY RISKS, HARMS, DISCOMFORTS ASSOCIATED WITH THIS STUDY?

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify your child in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting confidentiality can be absolutely secure so it is still possible that someone could find out your child was in this study and could find out information about your child.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

Furthermore, all study staff and interviewers are professionals with special training in these interviews

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

Your child may benefit by having more efficient monitoring of medication use. Overall information that will be obtained will allow us to learn more about any drug therapy problems in overall leukemia patients and enable for proper and timely interventions in current or future treatment of such patients.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

Your child participating in this study will not cost anything.

IS THERE REIMBURSEMENT FOR PARTICIPATING IN THIS STUDY?

There are no financial benefits for participation in this study.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about your child participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your child's rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke. The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to have your child participate in this research is voluntary. You are free to decline or withdraw participation of your child in the study at any time without injustice or loss of benefits. Just inform the study staff and the participation of your child in the study will be stopped. You do not have to give reasons for withdrawing your child if you do not wish to do so. Withdrawal of your child from the study will not affect the services your child is otherwise entitled to in this health facility or other health facilities. For more information, contact:

1. **Dr. Savwa Brian Odondi.**
   Mobile; 0710 961 653.
   Email: savwabrian7@gmail.com
2. **Dr. P.N Karimi PhD -Supervisor**
   Mobile: 0722 436 019
   Email: ndirang15@gmail.com

From 9:00 a.m. to 4:30 p.m.

CONSENT FORM (STATEMENT OF CONSENT)

The person being considered for this study is unable to consent for him/herself because he or she is a minor (a person less than 18 years of age). You are being asked to give your permission to include your child in this study.

Parent/guardian statement

I have read this consent form or had the information read to me. I have had the chance to discuss this research study with a study counselor. I have had my questions answered by him or her in a language that I understand. The risks and benefits have been explained to me. I understand that I will be given a copy of this consent form after signing it. I understand that my participation and that of my child in this study is voluntary and that I may choose to withdraw it any time. I understand that all efforts will be made to keep information regarding me and my child's personal identity confidential. By signing this consent form, I have not given up my child's legal rights as a participant in this research study.

I voluntarily agree to my child's participation in this research study:

Yes [ ]No [ ]

Parent/Guardian signature /Thumb stamp: _____ Date _____

Parent/Guardian printed name: _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given his/her consent.

Printed Name: _____Date: _____

Signature: _____

Role in the study: _____

Witness Printed Name (If witness is necessary) _____

Signature: _____Date; _____

Appendix 3B: Kiswahili translation- fomu ya kuridhia

MAADA YA UTAFITI: Kutathmini shida za matibabu zinazoweza kutokea miongoni mwa wagonjwa wa lukemia ambao wanapata matibabu katika hospitali ya rufaa ya Kenyatta.

Mtafiti Mkuu: Brian Odondi Savwa/Chuo kikuu cha Nairobi

Wachunguzi-wenza na uhusiano wa kitaasisi: Dkt. P.N Karimi, Chuo Kikuu Cha Nairobi.

Ningependa kukuambia kuhusu utafiti unaofanywa na watafiti walioorodheshwa hapo juu. Kusudi katika fomu hii ya idhini ni kukupa taarifa utakayohitaji ili kukusaidia kuamua kama mtoto wako anapaswa kushiriki katika utafiti. Jisikie huru kuuliza maswali yoyote kuhusu madhumuni ya utafiti, nini kitatokea ikiwa mtoto wako atashiriki katika utafiti, hatari na faida zinazowezekana, na haki za mtoto wako kama mtu wa kujitolea, na kitu kingine chochote kuhusu utafiti au fomu hii ambacho hakiko wazi. Wakati tumejibu maswali yako yote kwa kuridhika kwako, unaweza kuamua ikiwa unataka mtoto wako awe katika utafiti huu.

Utaratibu huu unaitwa 'ridhaa iliyoarifiwa'. Mara tu unapoelewa na kukubali mtoto wako kuwa ndani ya utafiti, nitakuomba utie sahihi jina lako kwenye fomu hii. Unapaswa kuelewa kanuni za jumla ambazo zinatumika kwa washiriki wote katika utafiti wa matibabu: i) Uamuzi wa mtoto wako kushiriki ni kwa hiari ii) Mtoto wako anaweza kujiondoa kwenye utafiti wakati wowote bila ya kutoa sababu ya kujiondoa iii) Kukataa kushiriki katika utafiti hakutaathiri huduma ambazo mtoto ana haki nazo katika kituo hiki cha afya au vituo vingine.

Naweza kuendelea? NDIO LA

Kwa watoto walio chini ya umri wa miaka 18 tunatoa taarifa kuhusu utafiti kwa wazazi au walezi. Tutayatapitia maelezo haya na wewe na unahitaji kutoa ruhusa ili mtoto wako afanye kushiriki katika utafiti huu. Tutakupa nakala ya fomu hii kwa rekodi zako.

NINI KUSUDI LA UTAFITI HUU?

Tunawahoji wagonjwa walio na lukemia na wanapata tiba kwenye hospitali. Madhumuni ya mahojiano ni kujua kutathmini shida za matibabu zinazoweza kutokea miongoni mwa wagonjwa wa lukemia ambao wanapata matibabu katika hospitali ya rufaa ya Kenyatta.

Washiriki katika utafiti huu wataulizwa maswali kuhusu aina ya lukemia, muda wa kuugua, madawa aliyopewa kwa ajili ya matibabu na utumizi kulingana na masharti, kilo zao, na shida yoyote iliyoletwa na utumizi wa madawa.

Kutakuwa na takriban washiriki mia moja katika utafiti huu waliochaguliwa bila mpangilio.

Tunauliza kwa idhini yako ya kuzingatia mtoto wako kushiriki katika utafiti huu. Taarifa zitatusaidia kujifunza kiwango ambacho miongozo yetu inafuatwa ili kuboresha utumizi wa madawa kwa wanaogua lukemia.

NINI KITAENDELEA UKIAMUA UNATAKA MTOTO WAKO AWE KATIKA

UTAFITI HUU?

Ukikubali mtoto wako kushiriki katika utafiti huu, mambo yafuatayo yatafanyika: Data itachukuliwa kutoka kwa faili ya mgonjwa hadi kwenye fomu. Ikiwa kuna ufafanuzi wowote unaohitajika kuhusu mgonjwa, utahojiwa na mhoji aliyefunzwa katika eneo la faragha ambapo unahisi huru kujibu maswali. Mahojiano yatachukua takriban dakika kumi.

Baada ya mahojiano, mtoto wako ataangaliwa kwa ujumla kama kuna tataizo lolote kwenye wmili lililosababishwa na utumizi wa madawa ya lukemia.

JE, KUNA MADHARA YANAYOHUSIANA NA UTAFITI HUU?

Utafiti wa kimatibabu una uwezo wa kuanzisha madhara za kisaikolojia, kijamii, kihisia na kimwili. Jitihada zinapaswa kuwekwa kila wakati ili kupunguza hatari. Hatari moja inayoweza kutokea ya kuwa katika utafiti ni kupoteza faragha. Tutaweka kila kitu unachotuambia siri iwezekanavyo. Tutatumia nambari ya msimbo ili kumtambua mtoto wako katika hifadhidata ya kompyuta iliyolindwa na nenosiri na tutahifadhi rekodi zetu zakaratasi kwenye kabati ya faili iliyofungwa. Hata hivyo, hakuna mfumo wa kulinda usiri unaweza kuwa salama kabisa kwa hivyo, bado kuna uwezekano kwamba mtu anaweza kujua mtoto wako alikuwa katika utafiti huu na unaweza kupata habari kuhusu mtoto wako. Pia, kujibu maswali katika mahojiano kunaweza kuwa na wasiwasi kwako. Ikiwa kuna maswali yoyote hutaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano yoyote au maswali yaliyoulizwa wakati wa mahojiano. Zaidi ya hayo, wafanyakazi wote wa utafiti na wahojaji ni wataalamu walio na mafunzo maalum katika mahojiano haya.

JE, KUNA FAIDA YOYOTE KUWA KATIKA UTAFITI HUU?

Mtoto wako anaweza kufaidika kwa kuwa na ufuatiliaji bora zaidi wa matumizi ya dawa. Taarifa za jumla zitakazopatikana zitaturuhusu kujifunza zaidi kuhusu ubora wa kuagiza, kwa hiyo itawezesha uboreshaji kwa siku za usoni.

JE, KUWA KWENYE SOMO HILI LITAKUGHARIMU LOLOTE?

Mtoto wako akishiriki katika utafiti huu hakutagharimu chochote.

JE, KUNA MALIPO KWA KUSHIRIKI KATIKA SOMO HILI?

Hakuna manufaa ya kifedha kwa kushiriki katika utafiti huu

VIPI IKIWA UNA MASWALI BAADAYE?

Ikiwa una maswali zaidi au wasiwasi kuhusu mtoto wako kushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe mfupi wa maandishi kwa wafanyikazi wa utafiti kwa nambari iliyotolewa chini ya ukurasa huu. Kwa maelezo zaidi kuhusu haki za mtoto wako kama mshiriki wa utafiti unaweza kuwasiliana na:

Katibu/Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Maadili na Utafiti cha Nairobi Nambari ya Simu ya Kamati: 2726300 Ext. 44102 na barua pepe uonknh_erc@uonbi.ac.ke.

Wafanyikazi wa utafiti watakulipa malipo ya simu kwa nambari hizi ikiwa mawasiliano inayohusiana na masomo

UAMUZI WAKO MWINGINE NI UPI?

Uamuzi wako wa kumfanya mtoto wako ashiriki katika utafiti huu ni wa hiari. Uko huru kukataa au kuondoa ushiriki wa mtoto wako katika utafiti wakati wowote bila dhuluma au hasara ya manufaa. Wajulishe tu wafanyakazi wa utafiti na ushiriki wa mtoto wako katika utafiti utasitishwa. Sio lazima utoe sababu za kumwondoa mtoto wako ikiwa hutaki kufanya hivyo. Uondoaji wa mtoto wako kutokana na utafiti hautaathiri huduma ambazo mtoto wako anastahiki kupata katika kituo hiki cha afya au vituo vingine vya afya.

Kwa habari zaidi, wasiliana na;

1. **Dr. Savwa Brian Odondi.**
   Nambari ya simu; 0710 961 653.
   Barua pepe: savwabrian7@gmail.com
2. **Dr. P.N Karimi PhD -Msimamizi Mkuu**
   Nambari ya simu: 0722 436 019
   Barua pepe: ndirang15@gmail.com

Kuanzia muda wa 9:00 Asubuhi hadi 4:30 Jioni.

FOMU YA RIDHAA (TAARIFA YA RIDHAA)

Mtu anayezingatiwa kwa ajili ya utafiti huu hawezi kujikubali kwa sababu ni mtoto mdogo (mtu chini ya miaka 18). Unaombwa kutoa idhini yako ya kujumuisha mtoto wako katika utafiti huu.

Taarifa ya mzazi/mlezi

Nimesoma fomu hii ya idhini au nimesomewa maelezo. Nimepata nafasi ya kujadili utafiti huu na mshauri wa utafiti. Nimejibiwa maswali yangu na yeye katika lugha ninayoielewa. Hatari na faida zimeelezewa kwangu. Ninaelewa kuwa mimi nitapewa nakala ya fomu hii ya idhini baada ya kusaini. Ninaelewa kwamba ushiriki wangu na wa mtoto wangu katika utafiti huu ni wa hiari na kwamba ninaweza kuchagua kuiondoa wakati wowote. Ninaelewa kuwa juhudi zote zitafanywa ili kuweka maelezo kunihusu mimi na mtoto wangu za kibinafsi siri.

Kwa kutia sahihi kwenye fomu hii ya idhini, sijaachana na haki za kisheria za mtoto wangu kama mshiriki katika huu utafiti.

Ninakubali kwa hiari ushiriki wa mtoto wangu katika utafiti huu:

Ndio la

Sahihi ya Mzazi/Mlezi /Muhuri wa kidole gumba: _____

Tarehe _____

Jina lililochapishwa la Mzazi/Mlezi: _____

Kauli ya mtafiti

Mimi, niliyetia sahihi hapa chini, nimeeleza kikamilifu maelezo muhimu ya utafiti huu kwa mshiriki zilizotajwa hapo juu na kuamini kuwa mshiriki ameelewa na ametoa idhini lake kwa kujua ridhaa.

Jina Lililochapishwa: _____ Tarehe: _____

Sahihi: _____

Jukumu katika utafiti: _____

Jina Lililochapishwa na Shahidi (Ikiwa shahidi ni muhimu) _____

Sahihi: _____Tarehe; _____

Appendix 4: Assent Form

Title of the Study: MAGNITUDE AND PREDICTORS OF DRUG THERAPY PROBLEMS AMONGPATIENTS WITH LEUKEMIA AT KENYATTA NATIONAL HOSPITAL

Principal Investigator \ and institutional affiliation: Brian Odondi Savwa /University of Nairobi

Co-Investigators and institutional affiliation: Dr. P.N Karimi, University of Nairobi,

Introduction:

I would like to tell you about a study being done. The information on this form will help you decide if you want to take part or not. Feel free to ask any questions that you may have. When we have answered all your questions, you may decide if you want to be in the study or not. This process is called 'informed consent'. When you understand and agree to be in the study, I will request you to write your name on this form. You should understand the general rules of the research:

i) It is up to you if you want to participate or not. No one should force you

ii) You may decide that you don't want to be part of the study at any point and without saying why.

iii) If you don't participate in the research you will still be cared for like all other patients

May I continue? YES / NO

We will go over this information with you and you need to give permission to participate in this study. We will give you a copy of this form for your records.

WHY ARE WE DOING THE STUDY?

We are talking to children who are on treatment for leukemia in the wards at KNH. We would like to find about the magnitude and predictors of drug therapy problems among patients with leukemia. Participants in this research study will be asked questions about their experience with medication specifically the chemotherapy drugs and any other medication they receive in the wards during treatment of leukemia and adherence to the same. There will be approximately 100 participants in this study randomly chosen. We are asking for your consent to consider your child to participate in this study. The information will help us learn the level at which our guidelines are followed so as to improve in the future.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

Data will be taken from the patient file onto a form. If there are any clarifications required about you, you will be interviewed by a trained interviewer in a private area where you feel comfortable answering questions. The interview will last approximately 10 minutes. The interview will cover topics such as the type of leukemia diagnosis, time it was diagnosed, chemotherapy medication that your child has received and adherence to it, their weight, allergy status and any side effect as a result of any of the medication administered. After the interview, you will be examined physically to check for manifestation as a result of chemotherapy use.

ARE THERE ANY RISKS, HARMS, DISCOMFORTS WITH THIS STUDY?

We will always try our best to reduce any risks to do with the study. One possible risk of being in the study is that your information will be shared with other people. We will keep everything you tell us so that information will not be traced back to you. We will use a code number instead of your name, the file in a computer will have a password and our paper records will be locked. Even then, someone could find out you were in this study.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer; you can skip them. You have the right to refuse the interview or any questions asked during the interview. Know that all study staff are professionals with special training in these interviews.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

You may benefit by having better checking of your medication use. The information that we will collect will allow us to learn more about how well antibiotics are prescribed, which will help us to improve.

WILL BEING IN THIS STUDY COST YOU ANYTHING?

You participating in this study will not cost anything.

IS THERE PAYMENT FOR PARTICIPATING IN THIS STUDY?

There is no pay for being in this study.

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions about being in this study, please call or send a text message to the study staff. The numbers are at the bottom of this page.

For more information about your child's rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee **Telephone No. 2726300 Ext. 44102 email uonknh_erc@uonbi.ac.ke.** The study staff will pay you back for your charges to these numbers if the call is for study-related communication.

The study staff will pay you back for your charges to these numbers if the call is for study related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to be part of this research is voluntary, no one should force you. You are free to say you don't want to be part of the study at any time. Just tell the study staff and your participation in the study

will be stopped. You do not have to give reasons for stopping the study if you do not wish to do so. You will not be treated differently after that and will be cared for in the same way.

For more information, contact:

1. **Dr. Savwa Brian Odondi.**
   Mobile; 0710 961 653.
   Email: savwabrian7@gmail.com
2. **Dr. P.N Karimi PhD -Supervisor**
   Mobile: 0722 436 019
   Email: ndirang15@gmail.com

ASSENT FORM (STATEMENT OF ASSENT)

I have read this consent form or the information was read to me. I have had the chance to talk with the interviewer. I have had my questions answered by him or her in a language that I understand. The risks and benefits have been explained to me. I understand that I will be given a copy of this form after signing it. I understand that my participation in this study is not forced and that I may choose to stop at any time. I understand that all efforts will be made to keep information about who I am secret.

By signing this assent form, I have not given up my legal rights as a participant in this research study.

I voluntarily agree to my participation in this research study:

Yes **No**

Participant signature /Thumb stamp: _____ Date _____

Participant name: _____

Researcher's statement

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given his/her assent.

Printed Name: _____ Date: _____

Signature: _____

Role in the study: _____

Witness Printed Name (If witness is necessary) _____

Signature: _____Date: _____

Appendix 4B: Kiswahili Translation: Fomu Ya Kuridhia

MAADA YA UTAFITI: Kutathmini shida za matibabu zinazoweza kutokea miongoni mwa wagonjwa wa lukemia ambao wanapata matibabu katika hospitali ya rufaa ya Kenyatta.

Mtafiti Mkuu: Brian Odondi Savwa/Chuo kikuu cha Nairobi

Wachunguzi-wenza na uhusiano wa kitaasisi: Dkt. P.N Karimi, Chuo Kikuu Cha Nairobi

Utangulizi:

Ningependa kukuambia kuhusu utafiti tunaofanywa. Kusudi ya fomu hii ni kukusaidia kuamua kama ungependa kushiriki. Jisikie huru kuuliza maswali yoyote kuhusu utafiti huu. Wakati tumejibu maswali yako yote, unaweza kuamua kama ungependa kuwa katika utafiti au la.

Utaratibu huu unaitwa 'ridhaailiyoarifiwa'. Baada ya kuelewa na kukubali kuwa katika utafiti, nitakuomba utie sahihi jina lako kwenye fomu hii. Unapaswa kuelewa sheria za jumla pia i) Uamuzi wako wa kushiriki si wa kulazimishwa ii) Unaweza kujiondoa kwenye utafiti wakati wowote bila ya kutoa sababu ya kujitoa iii) Kukataa kushiriki katika utafiti hakuabadilisha huduma utakayopata katika kituo hiki cha afya.

Naweza kuendelea? NDIO LA

Tutapitia habari hii na wewe na unahitaji kutoa ruhusa ili kushiriki katika utafiti huu. Tutakupa fomu hii kwa rekodi zako.

NINI SABABU YA MASOMO HAYA?

Tunawahoji wagonjwa walio na lukemia na wanapata tiba kwenye hospitali. Madhumuni ya mahojiano ni kujua kutathmini shida za matibabu zinazoweza kutokea miongoni mwa wagonjwa wa lukemia ambao wanapata matibabu katika hospitali ya rufaa ya Kenyatta.

Washiriki katika utafiti huu wataulizwa maswali kuhusu aina ya lukemia, muda wa kuugua, madawa aliyopewa kwa ajili ya matibabu na utumizi kulingana na masharti, kilo zao, na shida yoyote iliyoletwa na utumizi wa madawa.

Kutakuwa na takriban washiriki mia moja katika utafiti huu waliochaguliwa bila mpangilio.

Tunauliza kwa idhini yako ya kushiriki katika utafiti huu. Taarifa zitatusaidia kujifunza kiwango ambacho miongozo yetu inafuatwa ili kuboresha utumizi wa madawa kwa wanaogua lukemia.

NINI KITAENDELEA UKIAMUA KUTAKA KUWA KATIKA UTAFITI HUU?

Ukikubali kukua katika utafiti huu, mambo yafuatayo yatafanyika: Data itachukuliwa kutoka kwa faili yako hadi kwenye fomu. Ikiwa kuna maelezo zaidi yanaohitajika, utaulizwa maswali na mhoji. Mahojiano yatachukua kama dakika kumi.

Baada ya mahojiano, mtoto wako ataangaliwa kwa ujumla kama kuna tataizo lolote kwenye wmili lililosababishwa na utumizi wa madawa ya lukemia

JE, KUNA MADHARA ZINAZOHUSIANA NA UTAFITI HUU?

Daima tutajaribu zaidi ili kupunguza madhara kwako. Dhara moja inayoweza kutokea ya kuwa katika utafiti ni kuwa mambo kukuhusu hayatakua siri, lakini tutajaribu vyovyote iwezekanavyo ili watu wasijue kwamba uko katika utafiti huu.

Tutatumia nambari badala ya jina ili kukutambua katika kompyuta iliyolindwa na nenosiri na tutaweka rekodi zetu zote za karatasi kwenye kabati iliyofungwa. Hata hivyo, bado kuna uwezekano kwamba mtu anaweza kujua ulikuwa katika utafiti huu.

Pia, kujibu maswali katika mahojiano kunaweza kuwa na wasiwasi kwako. Ikiwa kuna maswali yoyote hutaki kujibu, unaweza kuyaruka. Una haki ya kukataa mahojiano au maswali yoyote yaliyoulizwa wakati wa mahojiano. Zaidi ya hayo, wafanyakazi wote wa utafiti na wahojaji ni wataalamu walio na mafunzo maalum katika mahojiano haya.

JE, KUNA FAIDA YOYOTE KUWA KATIKA UTAFITI HUU?

Unaweza kufaidika kwa kuwa na ufuatiliaji zaidi wa matumizi ya dawa. Taarifa itakayopatikana itaturuhusu kujifunza zaidi kuhusu ubora wa maagizo, kwa hivyo itawezesha uboreshaji siku zijazo.

JE, KUWA KWENYE SOMO HILI LITAKUGHARIMU LOLOTE?

Ukiwa kwa utafiti huu hautaambiwa ulipe kitu chochote.

JE, KUNA MALIPO KWA KUSHIRIKI KATIKA SOMO HILI?

Hautalipwa pesa kwa kushiriki katika utafiti huu

VIPI IKIWA UNA MASWALI BAADAYE?

Ikiwa una maswali zaidi au wasiwasi kuhusu kushiriki katika utafiti huu, tafadhali piga simu au tuma ujumbe mfupi wa maandishi kwa wafanyikazi wa utafiti kwa nambari iliyotolewa chini ya ukurasa huu.

Kwa maelezo zaidi kuhusu haki zako kama mshiriki wa utafiti unaweza kuwasiliana na

Katibu/Mwenyekiti, Hospitali ya Kitaifa ya Kenyatta-Chuo Kikuu cha Maadili na

Utafiti cha Nairobi nambari ya simu ya kamati 2726300 Ext. 44102 barua pepe

uonknh_erc@uonbi.ac.ke.

Wafanyikazi wa utafiti watakulipa malipo ya simu ikiwa mawasiliano inahusiana na utafiti.

UCHAGUZI WAKO MWINGINE NI UPI?

Uamuzi wako wa kushiriki katika utafiti huu ni wa hiari. Uko huru kukataa au kuondoka katika utafiti wakati wowote bila hasara ya faida. Wajulishe tu wafanyakazi wa utafiti. Sio lazima utoe sababu za kujiondoa ikiwa hutaki kufanya hivyo. Kujitoa kwenye utafiti hakutaathiri huduma unazostahili kupata.

Kwa habari zaidi, wasiliana na;

1. **Dr. Savwa Brian Odondi.**
   Nambari ya simu; 0710 961 653.
   Barua pepe: savwabrian7@gmail.com
2. **Dr. P.N Karimi PhD -Msimamizi Mkuu**
   Nambari ya simu: 0722 436 019
   Barua pepe: ndirang15@gmail.com

Kuanzia muda wa 9:00 Asubuhi hadi 4:30 Jioni.

FOMU YA KURIDHIA (TAARIFA YA RIDHAA)

Nimesoma fomu hii au nimesomewa maelezo. Nimepata nafasi ya kuzungumza na mtafiti. Nimejibiwa maswali yangu katika lugha ninayoielewa. Hatari na faida zimeelezewa kwangu. Ninaelewa kuwa mimi nitapewa fomu hii ya idhini baada ya kusaini.

Ninaelewa kuwa sijalazimishwa kushiriki na kwamba ninaweza kuchagua kuondoka wakati wowote. Ninaelewa kuwa juhudi zote zitafanywa ili kuweka utambulisho wangu wa kibinafsi siri. Kwa kusaini fomu hii, sijaacha haki zangu za kisheria kama mshiriki katika utafiti huu.

Ninakubali kwa hiari ushiriki wangu katika utafiti huu: Ndio la

Sahihi la mshiriki /Muhuri wa kidole gumba: _____

Tarehe _____

Jina lililochapishwa la mshiriki: _____

Kauli ya mtafiti

Mimi, niliyetia sahihi hapa chini, nimeeleza kikamilifu maelezo muhimu ya utafiti huu kwa Mshiriki zilizotajwa hapo juu na kuamini kuwa mshiriki ameelewa na ametoa idhini lake kwa kujua ridhaa.

Jina Lililochapishwa: _____Tarehe: _____

Sahihi: _____

Jukumu katika utafiti: _____

Jina Lililochapishwa na Shahidi (Ikiwa shahidi ni muhimu) _____

Sahihi: _____ Tarehe: _____

Appendix 5: **Questionnaire**

Research Topic: Drug therapy problems among patients with leukemia at Kenyatta National Hospital.

Questionnaire code:

Date:

Kindly answer the following questions as truthfully as possible. Your information will be highly confidential

A. Patients Socio-demographic Data

1. Age: _____ Years
2. Sex: Male **[ ]** Female **[ ]**
3. Weight: ____ Kgs. Height: ____ Meters (m)
4. Body Surface Area (BSA): _____ M^2
5. Marital Status: . Married [ ] .single [ ] Non-applicable[ ]
6. Education Level:

- None [ ]
- Primary [ ]
- Secondary [ ]
- College [ ]

7. Occupation:

- Salaried **[ ]**
- Self Employed **[ ]**
- Unemployed **[ ]**
- Student **[ ]**
- Not-applicable **[ ]**

8. Do you have Health Insurance: Yes [ ] No. [ ]

B. Clinical Profile

9. Definitive Diagnosis?

- ALL [ ]
- AML [ ]
- CML [ ]
- CLL [ ]

10. At what age were you first diagnosed with this condition? _____ Years Old

11. How long has been your current hospital stay?_____ Days

12. Do you have any other underlying medical condition(comorbidities)? Yes [ ] No [ ]

13. If yes, which illness _____

14. Which medication are you currently using for the underlying illness

Medication	Condition

C. Leukemia treatment information

15. Date initiated:_____/____/__

Day/Month/Year

16. Current phase of treatment :

- Induction [ ]
- Consolidation [ ]
- Maintenance [ ]

17. Chemotherapy agent given:

Drug	(Tick if given)
Prednisolone	
Vincristine	
Daunorubicin	
L-asparaginase	
Cytarabine	

Methotrexate	
Dexamethasone	
Mercaptopurine	
Folinic acid	
Cyclophosphamide	
Etoposide	
Hydroxyurea	
Busulphan	
Cytosine	
Bendamustine	
Chlorambucil	
Rituximab	

18. Supportive treatment given (Tick where appropriate)

- Antiemetic: [ ]
- Platelets [ ]
- GCSF [ ]
- Whole blood [ ]
- Anti-infective [ ]
- Allopurinol [ ]
- Antibiotic [ ]
- Antiparasitic [ ]
- Analgesic/anti-inflammatory [ ]
- Dermatological [ ]

D. Medication Experience

19. Have you ever had an adverse drug reaction in the past 6 months due to chemotherapy drugs?

Yes **[ ]** No **[ ]**

20. If yes, can you recall which drug(s) caused the reaction? _____

21. What kind of reaction was it?

- Rash [ ]
- Nausea or vomiting [ ]
- Diarrhoea [ ]
- Constipation [ ]
- Epigastric Pain [ ]

- Cushingoid/moonface [ ]
- Neutropenia [ ]
- Hyperkalemia [ ]
- Nephrotoxicity [ ]
- Neutropenia [ ]
- Anemia [ ]
- Hepatotoxicity [ ]
- Others [ ]

E. Patients medication taking behavior (MMAS-4)

22. Please tick one box on each line

Question	**Yes**	**No**
1. Do you ever forget to take your medicine?		
2. Do you ever have problems remembering to take your 3. medication		
4. Do you sometimes stop taking your medicine when you feel 5. better?		
6. If you feel worse after taking your medicine, do you stop 7. taking		
Total **Yes** score		

23. The total "Yes" score for patient's adherence is;

- [0]- High
- [1-2] -Moderate
- [3-4]- Poor

24. Have you ever missed to take medicine due to failure to understand instructions given?

Yes **[ ]** No **[ ]**

F. Patient Physical assesment

Carry out a comprehensive physical assesment of the patient to check for any abnormal changes or appearance due to a drug related problem. Note any significance sign or symptom.

Vitals: BP_____ mm/Hg Heart rate _____ bpm Respiratory rate ___ Bpm Temp ____

General Examination

Review of Systems

Skin

ENT

Cardiovascular

Pulmonary

Gastrointestinal

Nutrition

- Normal weight [ ]
- Underweight [ ]
- Obese [ ]

Summary of Laboratory Results

Electrolytes

Potassium Level: …….mmol/L :Normal [ ] High[ ] Low [ ]

Sodium Levels: …….mmol/L : Normal [ ] High [ ] Low [ ]

Renal function

- Urea: N [ ] L[ ] H [ ]
- Creatinine: N [ ] L[ ] H [ ]

Full Blood count

- Neutrophils: N [ ] L [ ] H [ ]
- Red blood cells: N [ ] L [ ] H [ ]
- Haemoglobin: N [ ] L [ ] H [ ]
- Platelets: N [ ] L [ ] H [ ]

25.Did the patient have any DTP? Yes [ ] No [ ]

26 If yes, indicate on the next table the type of DTP and its associated cause by ticking where appropriate

H. Summary of DTPs in the patient

An evaluation from the section E, F, G to summarise the next table (**Tick appropriately)**

DTP	**Cause**	**Present**	**Absent**
Unnecessary drug therapy	Duplicate therapy		
	No medical indication		
	Non- drug therapy more appropriate		
	Treating avoidable ADR		
Need for additional	Untreated condition		
	Preventive therapy required		
	Additional therapy required for synergism		
Ineffective Drug	Drug not effective for condition		
	Inappropriate dosage form		
Dosage too low	Ineffective dose		
	Inappropriate frequency		
	Inappropriate duration		
	Drug interaction		
Adverse drug reaction	Undesirable effect		
	Unsafe drug for patient		
	Allergic reaction		
	Administration		
	Frequency too short		
	Drug interaction		
Non -adherence	Patient forgot to drug		
	Instructions not understood		
	Patient cannot afford drug		
	Unable to swallow or administer drug		
	Medication not available		

Appendix 6: KNH/UON Ethics and Review Committee approval

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

10 MAR 2023

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/103

10th March, 2023

Brian Odondi Savwa
Reg.No.U56/38266/2020
Dept. of pharmacy
Faculty of Health Science
University of Nairobi

Dear Brian,

RESEARCH PROPOSAL: MAGNITUDE AND PREDICTORS OF DRUG THERAPY PROBLEMS AMONG PATIENTS WITH LEUKEMIA AT KENYATTA NATIONAL HOSPITAL (P861/11/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P861/11/2022.** The approval period is 10th March 2023 – 9th March 2024.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Appendix 7:Kenyatta National Hospital approval

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   BRIAN ODONDI SAYWA
2. Email address: Sayvabrian7@gmail.com Tel No. 0710961653
3. Contact person (if different from PI).....
4. Email address: ..... Tel No. .....
5. Study Title
   Magnitude and Predictors of Drug Therapy Problems among Patients with Leukemia at Kenyatta National Hospital
6. Department where the study will be conducted Oncology
   (Please attach copy of Abstract)
7. Endorsed by Research Cordinator of Department where study will be conducted.

   Name: ..... Signature ..... Date .....
8. Endorsed by KNH Head of Department where study will be conducted.

   Name: Dr A. NBIRU Signature ..... Date 02/05/2023
9. KNH UoN Ethics Research Committee approved study number P861/11/2022.
   (Please attach copy of ERC approval)
10. I Brian Sayvwa Odondi commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Medical Research.

    Signature ..... Date 2/5/2023.
11. Study Registration number (Dept/Number/Year) CIC /163/ 2023
    (To be completed by Medical Research Department)
12. Research and Program Stamp 04 MAY 2023

~~All studies~~ conducted at Kenyatta National Hospital **must** be registered with the Department of Medical Research and Investigators **must commit** to share results with the hospital.

Version 2: August, 2014

Appendix 8: Paediatric Department Approval

KENYATTA NATIONAL HOSPITAL
P.O. BOX 20723, 00202 Nairobi

Tel.: 2726300/2726450/2726550
Fax: 2725272
Email: knhadmin@knh.or.ke

Ref: KNH/PAEDS-HOD/48 Vol.II

Date: 12th May 2023

Brian Odondi Savwa
Reg.No.U56/38266/2020
Dept. of Pharmacy
Faculty of Health Sciences
University of Nairobi

Dear Brian

RE: AUTHORITY TO COLLECT DATA IN PAEDIATRICS DEPARTMENT

Following approval of your Research proposal by the KNH/UON-Ethics & Research Committee and subsequent filing of the Study Registration Certificate, this is to inform you that authority has been granted to collect data in ***Paediatrics Department***, on your study titled ***"Magnitude and predictors of drug therapy problems among patients with leukemia at Kenyatta National Hospital"***. Kindly liaise with the Principal Nursing Officer, Paediatric General wards.

You will also be required to submit a report of your study findings to the office of the HOD, Paediatrics - KNH after completion of your study.

Dr. Anne-Marie Macharia
Ag. HOD Paediatrics

cc. Principal Nursing Officer, Paediatric General wards

Similarity Index

DRUG THERAPY PROBLEMS AMONG PATIENTS WITH LEUKEMIA AT KENYATTA NATIONAL HOSPITAL

ORIGINALITY REPORT

Dr. E.M. Gwantai
Chair DDPCPPP
Endorsed 28/11/2023

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