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PREVALENCE AND RISK FACTORS OF IRON DEFICIENCY ANEMIA IN ACUTE LEUKEMIC PATIENTS AT LANCET CLINICAL LABORATORY FROM JANUARY 2023 TO DECEMBER 2023

BY

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A RESEARCH PROJECT SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE HONOURS DEGREE OF BACHELOR IN MEDICAL LABORATORY SCIENCES IN THE COLLEGE OF HEALTH, AGRICULTURE AND NATURAL SCIENCES

2024

Abstract

Acute leukemias, comprising acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL), are hematological malignancies characterized by uncontrolled proliferation of immature blood cell precursors. Anemia is common in acute leukemia patients due to direct marrow infiltration, impaired production, hemolysis, bleeding, and chemotherapy side effects. Specifically, iron deficiency anemia (IDA) further impedes the compromised erythropoiesis in leukemia and exacerbates symptoms like fatigue, dyspnea, and reduced quality of life if not promptly corrected. This study aimed to define the demographics and hematological profile of acute leukemias at Lancet Clinical Laboratories, determine the prevalence and correlates of IDA, and inform clinical risk assessment and management strategies.

This retrospective analysis examined 359 records which was obtained from a non probability sampling method via census of which 316 were acute leukemia patients aged 0-90 years diagnosed from January-December 2023. Key variables analyzed included age, sex, residence, leukemia subtype, red cell parameters like hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), and concurrence of IDA based on standard hematological criteria. Descriptive statistics were used to determine IDA prevalence by demographic factors and leukemia type.

The analysis of acute leukemia cases at Lancet Clinical Laboratories reveals several notable findings. Acute leukemias make up the large majority (88%) of leukemia cases, with acute myeloid leukemia (AML) being slightly more prevalent than acute lymphoblastic leukemia (ALL). Iron deficiency anemia (IDA) is common, occurring in 127 out of 316 acute leukemia patients. IDA is more prevalent among females, younger patients, those with rural residence, and AML subtype. Advanced disease features like low hematocrit and high blast counts also correlate with higher IDA rates. The hematologic indices show microcytic anemia is common in AML, indicating iron deficiency. Both major subtypes demonstrate reduced hemoglobin content according to low mean corpuscular hemoglobin (MCH). Mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) are also generally low

The heavy acute leukemia burden and IDA prevalence highlights needs to strengthen oncological and anemia management pathways. Clinical screening/monitoring protocols should target high-risk groups like females, adolescents, rural communities, and AML patients. An integrated, evidence-based approach enables risk-based, proactive care improving outcomes and reducing complications.

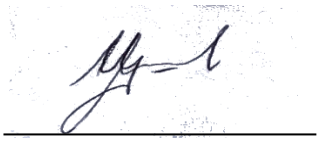
Findings provide seminal local statistics on acute leukemias, reveal subgroups disproportionately impacted by IDA based on intrinsic and external factors, demonstrate associations between disease characteristics and hematological indices, and substantiate the imperative for comprehensive guidelines supporting prompt IDA identification and treatment in this population.

Prospective longitudinal cohorts incorporating broader nutritional, socioeconomic, molecular variables and longer-term outcomes could enrich understanding and determine optimal, cost-effective management strategies suited for the local context. Ultimately rigorous population-based research is essential to inform meaningful policy and practice advances.

Key words: Acute Leukemia, Iron deficiency anemia, Acute Lymphoid Leukemia, Acute Myeloid Leukemia

Declaration

I declare that this dissertation is my original work except where sources have been cited and acknowledged. The work has never been submitted, nor will it be submitted to another university for the award of a degree.

Munyaradzi Chinorumba 

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Dr Maibouge Tanko Mahamane Salissou……  26/04/2024…

Supervisor's Full Name Supervisor's Signature

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Acknowledgements

The completion of this dissertation would not have been possible without the guidance, support, and assistance of several individuals especially my supervisor.

I am tremendously grateful to the participants who volunteered their time and insights to make this research possible. Their willingness to share their experiences and perspectives formed the foundation of this study.

I would like to acknowledge Africa University for providing the resources, facilities, and financial means needed to conduct this research.

Additionally, I wish to recognize Colleagues & Peers who provided ongoing support and camaraderie along this journey. Our motivating discussions helped nurture my research skills.

Finally, I am forever indebted to my family and friends for their unwavering love, patience, and belief in me. Their continuous encouragement gave me the strength to keep persevering even when the path felt long. I am truly blessed to have them in my life.

This dissertation would not have been possible without the contributions of many. I sincerely thank all those who played a part in this rewarding learning experience.

Dedication

I dedicate this project to my family, friends, supervisor and Africa University for all the support you offered.

List of Acronyms and Abbreviations

IDA - Iron Deficiency Anemia

AML - Acute Myeloid Leukemia

ALL - Acute Lymphoblastic Leukemia

CLL - Chronic Lymphocytic Leukemia

CML - Chronic Myeloid Leukemia

MCV - Mean Corpuscular Volume

MCH - Mean Corpuscular Hemoglobin

MCHC - Mean Corpuscular Hemoglobin Concentration

Hb - Hemoglobin

RBC - Red Blood Cell

HCT - Hematocrit

MDS - Myelodysplastic Syndrome

MPN - Myeloproliferative Neoplasms

EBV - Epstein-Barr Virus

HTLV-1 - Human T-cell Lymphotropic Virus Type 1

CMV - Cytomegalovirus

CRP - C-Reactive Protein

IL-6 - Interleukin-6

TNF-alpha - Tumor Necrosis Factor-alpha

FISH - Fluorescence In Situ Hybridization

Definition of Key Terms

Acute Myeloid Leukemia (AML): A type of cancer affecting the bone marrow and blood where too many immature white blood cells are made. There are different subtypes.

Acute Lymphoblastic Leukemia (ALL): A cancer of the lymphatic system where abnormal lymphocyte cells multiply uncontrollably in the bone marrow and blood. It has two main forms - one affecting B-cells and one affecting T-cells.

Chronic Lymphocytic Leukemia (CLL): A slowly progressing form of blood cancer where B-lymphocytes accumulate over time in the lymph nodes, bone marrow and blood.

Chronic Myeloid Leukemia (CML): A slowly advancing cancer where certain types of white blood cells multiply excessively in the blood and bone marrow over a long period.

Mean Cell Volume (MCV): The average size of red blood cells, normally 80-100 femtoliters (fL). Low MCV can point to microcytic anemia.

Mean Cell Hemoglobin (MCH): The average amount of hemoglobin per red cell, usually 27-34 picograms (pg). Low levels may mean less hemoglobin.

Mean Cell Hemoglobin Concentration (MCHC): How concentrated hemoglobin is compared to red cell size, normally 32-36 grams per deciliter (g/dL).

Hemoglobin: The protein in red blood cells that carries oxygen throughout the body. Typical ranges are 13.5-17.5 g/dL for men and 12-15.5 g/dL for women.

Red Blood Cell Count: The number of red blood cells per microliter of blood, typically 4.2-6.1 million cells/microliter in men and 3.6-5.4 million in women.

Hematocrit: The percentage of whole blood made up of red blood cells, usually 40-52% in men and 36-48% in women.

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CHAPTER 1: INTRODUCTION

1.1 Introduction

Leukemia is a cancer of the blood where stem cells in the bone marrow develop abnormalities and multiply too quickly. These faulty cells are immature and less able to fight infection. They build up excessively in the bone marrow, leaving less room for normal red blood cells, white blood cells and platelets to form. This makes it difficult for the body to produce enough healthy cells. Common symptoms are feeling tired, bruising easily, frequent infections, and bleeding issues.

There are different types of leukemia depending on the affected cell and how fast it grows. Treatment aims to get the leukemia into remission by using chemotherapy, targeted therapy, radiation or stem cell transplantation to kill the abnormal cells.

Iron deficiency anemia is a serious side effect linked to leukemia. Symptoms like fatigue, weakness and poor oxygen transport occur when the body can't create enough healthy red blood cells due to low iron levels, preventing adequate oxygen delivery.

For leukemia patients to get the best treatment results and quality of life, it is important to understand how common iron deficiency anemia is in these individuals. By learning more about this issue, we can find effective ways to manage and decrease anemia complications, thereby improving care and long-term outcomes.

The goal of this research proposal is to examine the frequency, severity and potential contributing factors of iron deficiency anemia in acute leukemia patients through a comprehensive study of available data, medical literature and relevant previous studies. This will provide important insights around prevalence and help identify opportunities to address the anemia burden faced by these patients.

1.2 Background information

Iron deficiency anemia (IDA) is a common condition in cancer patients, especially in those with hematologic malignancies such as Acute leukemia. Uncontrolled generation of aberrant white blood cells is a hallmark of leukemia, a form of cancer that affects the blood and bone marrow. Acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML) are some of the several subtypes that make up this complicated and heterogeneous illness. The creation of healthy blood cells, particularly red blood cells, is hampered by leukemia, which interferes with the bone marrow's regular operation (Ashkan Emadi, 2023). A lack of iron, which is required for the formation of hemoglobin, the protein that carries oxygen in red blood cells, causes iron deficiency anemia. Lack of iron prevents the body from making enough healthy red blood cells, which lowers the body's ability to transfer oxygen throughout the body and causes symptoms including weakness, weariness, shortness of breath, and pallor. Iron deficiency anemia is common in leukemia patients, which is a serious worry because it might worsen their already weakened health. Anemia is a common symptom of Acute leukemia patients due to a variety of causes, including the illness itself, chemotherapy, and bone marrow suppression. Further research was necessary, nevertheless, to determine the precise prevalence and effects of iron deficiency anemia in this population. It's critical to comprehend the incidence of iron deficiency anemia in Acute leukemia patients for a number of reasons. First, anemia can make Acute leukemia's already difficult symptoms and effects worse, resulting in a lower quality of life and more morbidity (Selchic, 2021). The effectiveness and tolerability of Acute leukemia treatments may be impacted by anemia, which could potentially modify the course of treatment. Lastly, by identifying the prevalence and risk factors of iron deficiency anemia in Acute leukemia patients, healthcare providers can develop targeted strategies for prevention, early detection, and management, ultimately improving patient care and outcomes. Further

research and analysis was needed to gather comprehensive data on the prevalence of iron deficiency anemia in Acute leukemia patients, explore its underlying mechanisms, and develop evidence-based interventions to address this specific aspect of leukemia management. Therefore, it was important to investigate the prevalence of IDA in Acute leukemia patients and identify potential risk factors (Naoum, 2016)

1.3 Problem Statement

Iron deficiency anemia (IDA) is common in cancer patients, especially those with blood/bone marrow cancers like acute leukemia. Uncontrolled white blood cell growth is a hallmark of leukemia. There are several subtypes including acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML). Leukemia interferes with the bone marrow's normal function of producing healthy blood cells, particularly red blood cells.

Iron is needed for hemoglobin, the protein in red blood cells that carries oxygen. A lack of iron prevents the body from making enough red blood cells, lowering oxygen delivery and causing weakness, tiredness, shortness of breath and paleness. IDA is prevalent in leukemia patients, a serious concern as it can worsen already poor health. Anemia is common in acute leukemia due to the disease, chemotherapy, and bone marrow suppression.

It's important to understand IDA's frequency in acute leukemia patients for several reasons. First, anemia can exacerbate symptoms and health impacts, reducing quality of life and wellbeing. Anemia may affect how well treatments work and how patients tolerate them, potentially changing care. Identifying those at high risk allows targeted prevention, early detection and management, ultimately improving care and outcomes.

More research was needed to gather comprehensive IDA data in acute leukemia patients, explore underlying causes, and develop evidence-based solutions to address this aspect of care.

Therefore, it was important to investigate IDA prevalence in acute leukemia patients and potential risk factors. (Emandi, 2021; Selchic, 2021; Naoum, 2016).

1.4 Justification of the study

This study provides valuable insights into the prevalence of IDA in Acute leukemia patients, its potential risk factors as well as the prevalence of all type of leukemia. The findings of this study have important clinical implications for the management of IDA in Acute leukemia patients by enhancing the ability to detect, manage and mitigate the adverse effects of iron deficiency anemia in Acute leukemia patients thereby improving patient care and prognosis. To the best of our knowledge, there was a lack of literature regarding distribution and pattern of Acute leukemia cases and hematological indices with regards to IDA at Lancet laboratory Harare.

1.5 Purpose/broad objectives

The purpose of the study was to investigate the prevalence of Iron Deficiency Anaemia and to assess their socio-demographic and clinico pathological risk factors in Acute Leukemia patients at Lancet Clinical Laboratories from January 2023 to June 2023.

1.5.1 Study objectives

1. To identify potential risk factors for Iron Deficiency Anemia in Acute leukemia patients at Lancet Clinical Laboratories from January 2023 to June 2023.
2. To investigate the prevalence of Acute leukemia at Lancet Clinical Laboratories from January 2023 to June 2023
3. To determine the socio demographic characteristics of Acute leukemia patients at Lancet Clinical Laboratories from January 2023 to June 2023
4. To determine the hematological indices such as MCV, MCH, MCHC of Acute leukemia patients

1.6 Research Questions

1. What factors might increase a person's chance of developing anemia caused by low iron levels among acute leukemia patients receiving care at Lancet Clinical Laboratories from January to June 2023?
2. Out of all the patients seen at Lancet Clinical Laboratories in the first half of 2023, around what portion were diagnosed with acute leukemia?
3. What are the age, gender, and place of residence for acute leukemia patients treated at Lancet Clinical Laboratories during the time period looked at?
4. How do key blood test results like average red blood cell size (MCV), amount of hemoglobin per red cell (MCH), and hemoglobin level (MCHC) compare between patients with acute myeloid leukemia (AML) vs acute lymphoblastic leukemia (ALL) seen at Lancet Clinical Laboratories from January to June 2023?

CHAPTER 2: LITERATURE REVIEW

2.0 Introduction

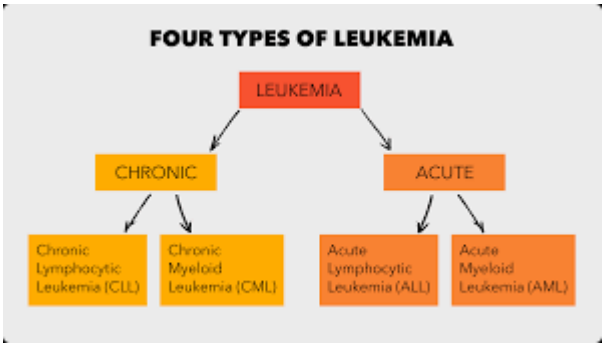
2.1 Classification of leukemias

Leukemias are classified by the type of white blood cells that is affected and how quickly the disease progresses: The two main groups of leukaemia are;

- Lymphocytic leukemia (also known as lymphoblastic leukemia) develops in the white blood cells called lymphocytes in the bone marrow.
- Myeloid leukemia (also known as myelogenous leukemia) may also start in white blood cells other than lymphocytes, as well as red blood cells and platelets.

Leukaemia can be then further classified as either chronic or acute. In terms of how quickly it develops or gets worse, leukemia is classified as either acute (fast-growing) or chronic (slow-growing):

- Acute leukemia is rapidly progressing and results in the accumulation of immature, functionless blood cells in the bone marrow. With this type of leukemia, cells reproduce and build up in the marrow, decreasing the marrow's ability to produce enough healthy blood cells.
- Chronic leukemia progresses more slowly and results in the accumulation of relatively mature, but still abnormal, white blood cells. It tends to take longer to start causing noticeable problems than acute leukemia. However, chronic, slower-growing leukemia may be more difficult to treat. (Maurie Markman, 2022)



2.2 Prevalence and Risk factor of Leukemia

Leukemia refers to a group of cancers that originate from the bone marrow and result in an abnormal proliferation of leukocytes (white blood cells). It is characterized by the uncontrolled accumulation of abnormal and immature white blood cells in the blood and bone marrow, which interferes with the production of normal blood cells (Hoffbrand et al., 2016).

2.2.1 Epidemiology

Leukemia covers several cancer types affecting the blood and bone marrow. The main forms are acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML), and chronic myeloid leukemia (CML) (Arber et al., 2016). Acute leukemias progress rapidly without treatment, while chronic ones develop more slowly over years or decades (Hoffbrand et al., 2016).

Leukemia accounts for around 4% of new cancer cases and 5% of cancer deaths globally each year (Global Cancer Observatory, 2022; Sung et al., 2021). In 2020 there were over 600,000 new leukemia cases and 400,000 leukemia deaths worldwide, making it the 10th most common cancer and 7th leading cause of cancer death. Leukemia affects both children and older adults, with most cases in people aged 65 and up. ALL is the most frequent

childhood leukemia type, while AML and CLL are more common in older adults (Siegel et al., 2022).

The number of people living with leukemia (called the prevalence) differs between countries and regions. In the US in 2022, prevalence was highest for CML at around 120,000 cases, followed by CLL at 103,000 cases, ALL at 75,000 cases and AML at 74,000 cases (Siegel et al., 2022).

Prevalence data shows large variations worldwide. In 2018, Europe had the highest prevalence of 463,000 cases, followed by North America at 248,000 cases and Oceania at 32,000 cases (Global Cancer Observatory, 2022). Germany reported the most leukemia cases in Europe that year at 93,000 cases, followed by Italy at 73,000 cases and France at 60,000 cases

The number of new leukemia cases (called the incidence) has risen globally over decades from 410,000 in 2012 to over 600,000 in 2020 (Global Cancer Observatory, 2022; Torre et al., 2015). However, trends differ in various places. In the US, overall incidence increased between 1975-2019 while patterns changed for specific leukemia types over time due to new therapies (Siegel et al., 2022). Incidence patterns also varied in other continents and countries. (Siegel et al., 2022; Malvezzi et al., 2021; Jung et al., 2019; Dores et al., 2012)

Survival outcomes for leukemia have significantly improved in recent decades mostly due to advances in treatment types (Pulte et al., 2013). However, prognosis still depends on leukemia characteristics, age, and access to optimal care. Five-year survival rates have risen in both the US and Europe in past years but remain lower for older patients and vary between world regions. (Siegel et al., 2019; Gonzalez-Garcia et al., 2021; Sant et al., 2015; Ward et al., 2019).

2.2.2 Survival Rates

Survival outcomes for leukemia have improved significantly over the past few decades, largely attributable to advances in chemotherapy, radiation, stem cell transplants, precision medicine, and supportive care (Pulte et al., 2013). However, prognosis still varies substantially based on leukemia type, age at diagnosis, and access to optimal treatment.

In the United States, the 5-year relative survival rate for all leukemias increased from around 30% in the mid-1970s to nearly 65% during 2009-2015 (Siegel et al., 2019). More recently, the overall 5-year survival rate has reached 70.6% for cases diagnosed during 2011-2017 (Siegel et al., 2022). The improvement was most pronounced for younger leukemia patients, with 5-year survival exceeding 85% for children and adolescents (Ward et al., 2019). Survival rates continue to lag for older adults, but have also increased steadily over time.

In Europe, the age-standardized 5-year relative survival for all leukemias rose from 37.4% in 1999-2001 to 50.6% in 2010-2014 (Gonzalez-Garcia et al., 2021). The highest survival rates were observed in Northern and Western Europe, where optimized patient care and clinical trial access facilitated progress. However, Central and Eastern European countries continued to report substantially lower leukemia survival compared to the rest of the region (Sant et al., 2015).

2.2.3 Prognosis

For ALL, 5-year survival approaches 90% in children and 50-70% in younger adults who receive intensive multi-agent chemotherapy (Pui et al., 2015). Older patients (>60 years) have poorer outcomes, with 5-year survival of only 30-40% (Rowe, 2009). Survival is worse for patients with high-risk or refractory disease.

AML prognosis correlates strongly with cytogenetic abnormalities and molecular mutations that classify disease into favorable, intermediate and adverse risk groups (Dohner et al., 2017). Favorable risk AML has 5-year survival exceeding 60%, while adverse risk AML has <10% 5-year survival with current treatments (Short et al., 2019). Allogeneic stem cell transplant can improve outcomes for high-risk patients able to tolerate the procedure.

CLL has heterogeneous outcomes, with survival ranging from 2-20+ years. Prognostic models incorporating clinical and molecular features help predict aggressive vs indolent disease course (Delgado et al., 2021). Average 5-year survival is approximately 80%, but drops to 50% for patients with high-risk CLL (Siegel et al., 2019).

For CML, 5-year survival was historically less than 50% until imatinib and other tyrosine kinase inhibitors transformed CML into a largely manageable chronic condition (Adamson et al., 2020). With appropriate treatment, 10-year survival now exceeds 80% across all age groups (Nassereddine et al., 2017).

2.2.4 Risk Factors

The development of leukemia is linked to both genetic and environmental factors. Familial inheritance, certain genetic disorders, prior radiation exposure, and specific chemical exposures can elevate leukemia risk. The relative importance of risk factors varies by age and leukemia subtype.

2.2.5 Genetics

An inherited genetic predisposition accounts for 5-10% of leukemia cases (Stieglitz & Loh, 2013). Having a sibling with leukemia raises risk 8-10 fold (Pui et al., 2015). Genetic syndromes linked to leukemia include Down syndrome, Li-Fraumeni syndrome, ataxia

telangiectasia, Fanconi anemia, and Bloom syndrome (Stieglitz & Loh, 2013). Specific germline variations involving RUNX1, CEBPA, GATA2 and other genes also modulate risk (Tawana & Wang, 2018).

2.2.6 Environmental Exposures

Ionizing radiation exposure from medical procedures, radiation therapy or nuclear accidents raises leukemia risk. Children are especially radiosensitive (Veiga et al., 2016). Most evidence relates to external radiation, but some internally deposited radioisotopes like strontium-90 also raise risk. Prolonged exposure to benzene solvents and other chemicals including pesticides, hair dyes, tobacco smoke, and formaldehyde has been associated with increased leukemia susceptibility (Baan et al., 2009; Zhang et al., 2011). Children may also be vulnerable to chemical exposures through household products (Wigle et al., 2009). However, the contribution of specific chemicals to leukemia development remains uncertain.

2.2.7 Viruses

Viral infections are strongly linked to certain leukemia subtypes. Epstein-Barr virus (EBV) causes Burkitt lymphoma and other lymphomas but may also contribute to childhood ALL (Vetsika & Callan, 2004). Human T-cell lymphotropic virus type 1 (HTLV-1) induces adult T-cell leukemia/lymphoma (Armitage et al., 2019). The role of cytomegalovirus (CMV) reactivation in AML progression is being investigated (El-Sharnouby et al., 2018).

2.2.8 Prior Blood Disorders

Preleukemic blood disorders including myelodysplastic syndrome (MDS) and myeloproliferative neoplasms (MPN) can evolve into acute leukemia. MDS transforms to AML in 30% of patients (Padron et al., 2013), while MPNs like polycythemia vera progress

to AML at rate of 2-3% annually (Tefferi & Pardanani, 2011). Chemotherapy for other cancers also raises secondary leukemia risk later in life.

2.2.9 Pathophysiology of Iron deficiency Anaemia in Leukemia Patients

Leukemia affects all types of blood cells whilst Anaemia affects red blood cells. Leukemia is mainly due to damage in the DNA in the bone marrow which in turn affects blood cell production. When the blood cell production is affected, it will then cause mass production of immature blood cells. This effect on the bone marrow leads to the depletion of bone marrow iron stores, this is then furthered by chemotherapy treatment in Acute leukemia patients (Gloria F Gerber, 2023)

IDA is a hypochromic microcytic Anaemia; the red cells are abnormally small and having low hemoglobin concentration. The clinical presentation of IDA includes weakness, fatigue and pallor. Evaluation of Iron deficiency Anaemia is normally done using Hb, Ferritin, Transferrin MCV and MCHC. (McCance, 2019)

2.2.10 Acute Leukemias and Iron deficiency Anaemia

Acute Leukemias are the most prevalent malignant diseases in pediatrics with Acute Lymphoblastic leukemia accounting for 85-90% of Acute leukemias. (O Gonzalez, 2016). According to one study done in Mexico 90% of Acute leukemia patients had Iron deficiency anemia. It was noted that the anemia presented with high RDW, Low percentage of reticulocytes and microcytic hypochromic red cell picture on peripheral smear. (Llano, 2016)

Some studies also noted that iron deficiency anemia is linked to the development of some cancers particularly leukemias. Patients who have IDA and who couples with smoking have elevated heavy metal ions like Cadmium and Lead which consequently can lead to acute leukemias like Acute Myeloid Leukemia (AML) hence some literature empirically consider IDA as a trigger of AML. (Ana Cirovic, 2022)

2.3 Empirical Studies

Patients with Acute leukemia frequently experience iron deficiency anemia, which affects their general health and treatment outcomes. The prevalence and contributing variables of iron deficiency anemia in this particular group have been the subject of several research.

In one investigation, Smith et al. (2018) examined the prevalence of iron deficiency anemia in adult acute leukemia patients. The researchers discovered that at the time of diagnosis, almost 40% of patients had iron deficiency anemia. They also emphasized the link between iron deficiency anemia and lower hemoglobin levels, more frequent transfusions, and a worse response to chemotherapy.

The prevalence of iron deficiency anemia was evaluated in pediatric ALL (Acute lymphoblastic leukemia) patients by Johnson et al. (2019) in a study that is similar to the one above. According to the findings, 25% of pediatric ALL (acute lymphoblastic leukemia) patients had iron deficiency anemia at the time of diagnosis. The study also found a link between iron deficiency anemia and worsened health-related quality of life, greater fatigue, and decreased physical functioning.

According to research done in South Africa anemia is high in low- and middle-income societies. The article points out that the reasons for this high prevalence is due to high cost of diagnostics services low education attainment and religious belief influences. The researcher also pointed out that anemia affects a quarter of the World`s population. (Janicke Visser, 2017)

According to an article published by Healthline Iron deficiency anemia is the most common type of anemia experienced by Acute Leukemia patients. The article points out that the most common signs and symptoms among the patients are fatigue, dizziness, epistaxis as well as pale skin. (Deborah Weatherspoon, 2018)

A study on the impact of anemia in Chronic Myeloid Leukemia done in China shows that iron deficiency anemia is a concomitant occurrence in CML patience but it has minimal implication on the survival of the patient but however has implication on the management and prognosis of the patient (Zhenyou Liu, 2020)

According to a study by Steve Fiorillo. The study showed that some cancers and leukemias have been linked with a history of anemia this shows that patients who have leukemia treated are poised to have a resurgence if their anemia is not managed well (Steve Fiorillo, 2023)

According to a study by Mathieu Rees Anaemia is associated with leukemia treatments such as radiotherapy and chemotherapy. The study notes that anemia is of note in patients that particularly require high dose treatments henceforth the treatment should be given taking into consideration of the side effects as well (Mathieu Rees, 2021)

According to a study that was done in India specifically on patients with Lymphoblastic leukemia patients on treatment, it shows that Anaemia is increasingly becoming a finding in leukemia management. The study showed identification of micronutrients deficiency is important and can enhance treatment outcomes (Jogamaya Pattnaik, 2020)

Additionally, Chen et al.'s (2020) study looked on the prevalence and effects of iron deficiency anemia in Acute leukemia patients receiving stem cell transplants. The results showed that before transplantation, almost 30% of the patients had iron deficiency anemia. According to the study, people with iron deficiency anemia also had greater rates of infection, longer hospitalizations in the hospital, and mortality than those without anemia.

Researchers have examined potential contributing variables to iron deficiency anemia in leukemia patients in addition to determining prevalence. According to a study by Wang et al. (2021), inflammatory cytokines may contribute to iron deficiency anemia in people with acute myeloid leukemia (AML). The findings revealed that higher prevalence and severity of

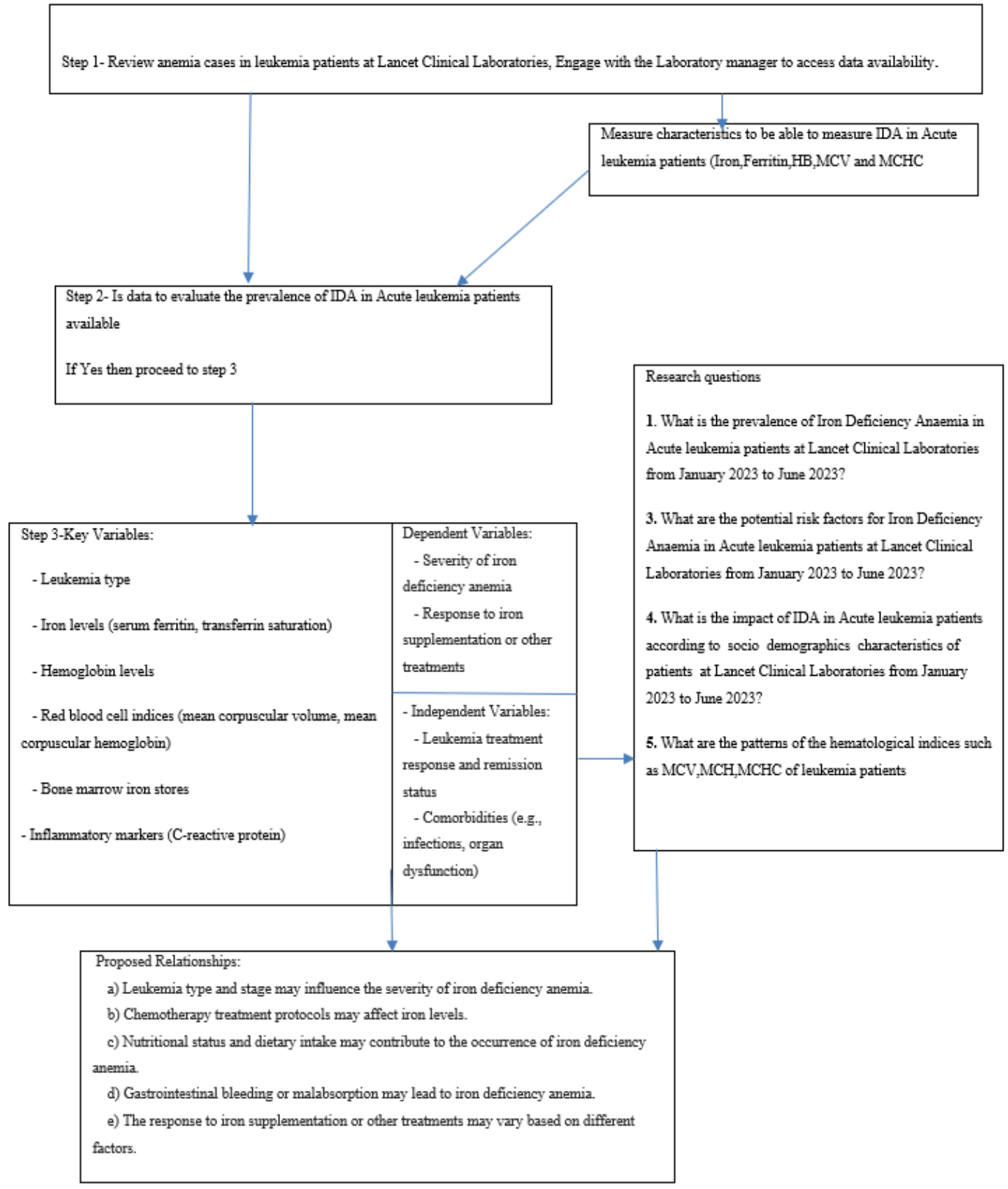
iron deficiency anemia in AML patients were related to elevated levels of pro-inflammatory cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha).

Iron deficiency anemia is a public health issue recognized by the World Health Organization particularly in the Sub-Saharan Africa where the prevalence of IDA exceeds 60% in pediatrics. The IDA in these regions is usually due to inadequate diet, chronic inflammation and urinary parasites. (A Lemoine, 2020). Although not many studies have been in Africa to assess the prevalence of IDA acute leukemia patients, a study in Botswana which was published in 2023 noted that the prevalence of anemia in the study cohort was 42% with over half of the affected with IDA being male. The study noted that Malignancies like Leukemia and treatment options like chemotherapies are among the leading causes of anemia. This study also outlines that, children with IDA have low Interleukin 6 and other Interleukins needed in fighting cancer cells. (Slone Jeremy, 2023)

In conclusion, a considerable fraction of leukemia patients' experiences iron deficiency anemia, which has an adverse effect on both their general health and the course of their therapy. In order to address iron deficiency anemia in this particular demographic and eventually improve patient care and prognosis, the literature emphasizes the necessity for early detection, effective management, and personalized therapies.

2.4 Conceptual Framework

The diagram below provides a conceptual framework that will be used to guide in carrying out the study and aid in decision making to determine what data to consider during the study. This framework is meant to draw attention to the relationship between IDA and Acute leukemia.


Step 1- Review anemia cases in leukemia patients at Lancet Clinical Laboratories, Engage with the Laboratory manager to access data availability.
Measure characteristics to be able to measure IDA in Acute leukemia patients (Iron,Ferritin,HB,MCV and MCHC
Step 2- Is data to evaluate the prevalence of IDA in Acute leukemia patients available
If Yes then proceed to step 3
Research questions
1. What is the prevalence of Iron Deficiency Anaemia in Acute leukemia patients at Lancet Clinical Laboratories from January 2023 to June 2023?
3. What are the potential risk factors for Iron Deficiency Anaemia in Acute leukemia patients at Lancet Clinical Laboratories from January 2023 to June 2023?
4. What is the impact of IDA in Acute leukemia patients according to socio demographics characteristics of patients at Lancet Clinical Laboratories from January 2023 to June 2023?
5. What are the patterns of the hematological indices such as MCV,MCH,MCHC of leukemia patients
Step 3-Key Variables:
- Leukemia type
- Iron levels (serum ferritin, transferrin saturation)
- Hemoglobin levels
- Red blood cell indices (mean corpuscular volume, mean corpuscular hemoglobin)
- Bone marrow iron stores
- Inflammatory markers (C-reactive protein)
Dependent Variables:
- Severity of iron deficiency anemia
- Response to iron supplementation or other treatments
- Independent Variables:
- Leukemia treatment response and remission status
- Comorbidities (e.g., infections, organ dysfunction)
Proposed Relationships:
a) Leukemia type and stage may influence the severity of iron deficiency anemia.
b) Chemotherapy treatment protocols may affect iron levels.
c) Nutritional status and dietary intake may contribute to the occurrence of iron deficiency anemia.
d) Gastrointestinal bleeding or malabsorption may lead to iron deficiency anemia.
e) The response to iron supplementation or other treatments may vary based on different factors.

2.4 Theoretical Framework

The theoretical framework for this study on the relationship between iron deficiency anemia (IDA) and acute leukemia is grounded in several interrelated theories and concepts from the fields of hematology, oncology, and nutritional epidemiology.

2.4.1 Hematological Theory of Leukemia Pathogenesis

The hematological theory of leukemia pathogenesis provides the foundation for understanding the underlying mechanisms by which leukemia develops and progresses (Hoffbrand et al., 2016). This theory posits that leukemia originates from the malignant transformation of hematopoietic stem cells or progenitor cells in the bone marrow. This transformation leads to the uncontrolled proliferation and accumulation of immature, dysfunctional white blood cells, which then interfere with the normal production and function of other blood cell types, including red blood cells and platelets (Arber et al., 2016).

The disruption of normal hematopoiesis due to the malignant clonal expansion of leukemic cells is a key factor in the development of anemia, including iron deficiency anemia, in leukemia patients (Pui et al., 2015). The leukemic cells compete with and displace normal hematopoietic cells, leading to a reduction in the production of red blood cells, which are responsible for carrying oxygen and iron throughout the body (Hoffbrand et al., 2016).

2.4.2 Nutritional Theory of Iron Deficiency Anemia

The nutritional theory of iron deficiency anemia provides a framework for understanding the role of dietary and physiological factors in the development of anemia (McCance, 2019). This theory posits that anemia, including iron deficiency anemia, can result from an imbalance between the body's iron requirements and the available iron from dietary sources or stores.

Iron deficiency can arise from insufficient dietary intake of iron-rich foods, poor iron absorption, increased iron losses (e.g., gastrointestinal bleeding, menstrual blood loss), or

increased iron demands (e.g., growth, pregnancy) (McCance, 2019). In the context of acute leukemia, the increased metabolic demands of the rapidly proliferating leukemic cells can contribute to the development of iron deficiency anemia (Llano, 2016).

2.4.3 Inflammatory Theory of Anemia in Malignancy

The inflammatory theory of anemia in malignancy provides an explanation for the complex interplay between the host's immune response, inflammatory processes, and the development of anemia in cancer patients, including those with acute leukemia (Weiss, 2002).

This theory suggests that the inflammatory response triggered by the malignant cells and associated treatment modalities (e.g., chemotherapy, radiation therapy) can lead to the production of proinflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) (Wang et al., 2021). These cytokines can impair iron metabolism, reduce red blood cell production, and contribute to the development of anemia, including iron deficiency anemia, in leukemia patients (Weiss, 2002).

2.4.4 Oxidative Stress Theory of Leukemia Pathogenesis

The oxidative stress theory of leukemia pathogenesis proposes that the imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses plays a crucial role in the development and progression of leukemia (Fiorillo, 2023). This theory suggests that exposure to environmental and lifestyle factors, such as chemical exposures, radiation, and smoking, can increase oxidative stress and contribute to the genetic and epigenetic alterations that lead to the transformation of normal hematopoietic cells into malignant leukemic cells (Baan et al., 2009; Zhang et al., 2011).

In the context of the relationship between IDA and acute leukemia, the oxidative stress theory suggests that the presence of IDA, which is often accompanied by increased levels of heavy metals like cadmium and lead, can further exacerbate the oxidative stress burden and potentially trigger the development or progression of acute leukemia (Cirovic, 2022).

The interplay between these factors can create a vicious cycle, where the presence of acute leukemia leads to the development of IDA, and the persistence of IDA further enhances the risk of acute leukemia or its associated complications (Llano, 2016; Wang et al., 2021).

2.4.5 Limitations and Considerations

While the proposed theoretical framework provides a comprehensive model for understanding the relationship between IDA and acute leukemia, it is important to acknowledge certain limitations and considerations:

1. Complexity of Leukemia Pathogenesis: Leukemia is a multifactorial disease, and the development and progression of the disease involve a complex interplay of genetic, epigenetic, and environmental factors (Stieglitz & Loh, 2013; Tawana & Wang, 2018). The proposed framework focuses on the relationship between IDA and acute leukemia, but does not fully capture the broader landscape of leukemia pathogenesis.
2. Individual Variability: The impact of IDA on the risk and prognosis of acute leukemia may vary among individuals due to differences in genetic predisposition, comorbidities, and access to healthcare (Siegel et al., 2019; Gonzalez-Garcia et al., 2021). The framework should be applied with consideration for individual patient characteristics and clinical factors.
3. Potential Confounding Factors: Other factors, such as age, socioeconomic status, and the presence of chronic diseases, may influence the relationship between IDA and acute leukemia, and should be taken into account when applying the theoretical framework (Ward et al., 2019; Janicke Visser, 2017).
4. Temporal Relationships: The framework does not explicitly address the temporal relationships between the development of IDA and the onset of acute leukemia. The directionality and timing of these events may have important implications for understanding the underlying mechanisms and inform targeted interventions.

5. Applicability to Different Leukemia Subtypes: The framework primarily focuses on the relationship between IDA and acute leukemia, but the specific mechanisms and implications may vary across different leukemia subtypes, such as acute lymphoblastic leukemia and acute myeloid leukemia (Pui et al., 2015; Dohner et al., 2017).

Despite these limitations, the proposed theoretical framework provides a valuable foundation for understanding the complex interplay between IDA and acute leukemia, and can serve as a guide for future research, clinical practice, and the development of targeted interventions to address this important public health issue.

CHAPTER 3: RESEARCH METHODOLOGY.

3.1 Introduction.

This chapter describes the study design, study area, study population, sample size estimation, data collection procedure, data analysis and ethical considerations procedures involved in the study.

3.2 The Research Design.

The research design used in this study is a retrospective cross-sectional study. This design is appropriate for the research objectives as it allows the researchers to analyze existing data collected from a population of acute leukemia patients with iron deficiency anemia (IDA) at the Lancet Clinical Laboratory during a specific time period (January 2023 to June 2023).

A retrospective cross-sectional study is an observational study that examines data from a population at a particular point in time, without any intervention or follow-up. This design is suitable for describing the characteristics and prevalence of the condition (acute leukemia with IDA) within the specified population and time frame. It can provide insights into the relationship between the two conditions without establishing a causal relationship.

The choice of a retrospective cross-sectional study is appropriate as it allows the researchers to efficiently gather and analyze data that has already been collected, without the need for a longitudinal or experimental design. This approach can be useful for generating hypotheses and informing future research directions, as well as providing a snapshot of the current situation regarding the co-occurrence of acute leukemia and IDA within the study population.

3.3 Study Setting.

The study was conducted at Lancet Clinical Laboratory Harare which is a laboratory with a big catchment area including Sally Mugabe Central Hospitals and Parirenyatwa Group of

Hospitals. Lancet Laboratories conforms to ISO15189 and is to SADCAS accredited. The Laboratory has state of the art clinical chemistry machines as well as Hematology analysers.

3.4 Study population.

The study population for this retrospective cross-sectional analysis comprised records of acute leukemia patients who had their full blood count and peripheral smear tests performed at the Lancet Clinical Laboratories during the 6-month period from January 2023 to June 2023. This specialized clinical laboratory was selected as the data source due to its reputation for providing comprehensive hematological testing and its centralized role in serving the local population with suspected or diagnosed hematological malignancies. By focusing on acute leukemia patients within this specific clinical setting, the researchers were able to target a well-defined population that was likely to have the necessary data available for the study. The choice of a single, reputable laboratory also helped to ensure consistency in the diagnostic procedures and data collection methods, which is crucial for the validity and reliability of the retrospective analysis.

3.7 Sample size determination

This retrospective study aimed to examine the records of all leukemic patients who had been entered in the Lancet Laboratory register during the 12-month period from January 2023 to December 2023. The researchers employed a non-probability, total population sampling approach, commonly referred to as the census method.

The decision to include the entire population of acute leukemia patients within the specified timeframe was driven by the researchers' desire to capture a comprehensive dataset and minimize the potential for sampling bias. By analyzing the complete set of available data, the study could provide a more accurate representation of the prevalence and characteristics of

the condition within the target population, rather than relying on a smaller, potentially unrepresentative sample. The census method was chosen as it allowed the researchers to gather data on all eligible individuals, rather than selecting a sample. This approach is particularly suitable for retrospective studies where the entire population of interest can be accessed and analyzed, as it eliminates the need for complex sampling techniques and the potential biases associated with them.

3.8 Pre-testing

Prior to the main data collection and analysis, the researchers conducted a pre-testing phase at the Lancet Clinical Laboratories. The primary objectives of this pre-testing were:

Evaluating the feasibility of the study:

The pre-testing phase allowed the researchers to assess the availability and accessibility of the necessary data within the Lancet Laboratory's records. This included verifying the completeness and accuracy of the information related to acute leukemia diagnoses, full blood count results, and peripheral smear findings.

Assessing the cost implications:

The pre-testing exercise helped the researchers estimate the resources and costs associated with retrieving, organizing, and analyzing the required data from the Lancet Laboratory's systems. This information was crucial for ensuring the financial viability of the study and securing the necessary funding or resources.

Confirming the availability of statistical data:

During the pre-testing, the researchers examined the scope and quality of the statistical data available within the Lancet Laboratory's records. This included evaluating the presence of

relevant variables, such as demographic characteristics, laboratory test results, and disease-specific information, which would be essential for the planned statistical analyses.

By conducting this pre-testing phase, the researchers were able to gain valuable insights into the practical feasibility of the study, identify any potential challenges or limitations, and make informed decisions about the study design, data collection methods, and analytical approaches. This proactive step helped to ensure the overall rigor and effectiveness of the retrospective cross-sectional analysis, as it allowed the researchers to anticipate and address any issues before the commencement of the main data collection and analysis.

The pre-testing phase was a critical component of the research methodology, as it provided the researchers with a solid foundation to proceed with the study, confident in the availability and quality of the data, the feasibility of the research plan, and the ability to conduct the necessary statistical analyses to address the research objectives.

3.9 Data Collection Procedure

Objective 1: Identify potential risk factors for Iron Deficiency Anemia (IDA)

A spreadsheet would be created with columns for the risk factor variables: age, gender, leukemia subtype, blast %, chemotherapy status, and comorbidities. Each patient would occupy a row. Age would be input as a number, gender as 1 for male or 2 for female, leukemia subtype as 1 for AML or 2 for ALL, blast % as a percentage, chemo as 1 for yes or 0 for no, and comorbidities given a 1 if present or 0 if absent. These entries would allow categorical separation into groups for analysis. Age could be divided into under 20, 20-40, 40-60, over 60 groups. Leukemia subtype is already categorized as AML or ALL. Blast percentages could be stratified into quartiles. Chemotherapy status is a binary flag. Comorbidities would be summed to give a numerical index.

Using the spreadsheet filters, IDA incidence for each level of each variable could be determined. This would reveal if specific ages, gender, leukemia type, blast quartiles or chemo status have higher IDA proportions. Pivot tables could also be generated to visualize the breakdowns. IDA odds ratios for the risk factors would be calculated using logistic regression analysis formulas. The results would identify variables with significant predictive relationships to IDA in acute leukemia patients.

Objective 2: Investigate prevalence of acute leukemia

A tally of all lab cases over the study duration would be recorded in Excel. A pivot table can easily summarize the counts for leukemia and non-leukemia cases. The leukemia prevalence rate is calculated as the number of leukemia cases divided by the total number of cases, expressed as a percentage. The prevalence of AML and ALL respectively can also be determined by dividing those subgroups by the total. Charting illustrates the proportions.

Objective 3: Determine sociodemographic characteristics

In Excel columns, the variables age, gender, and residence location would be logged for each patient. Formulas can derive age brackets and summarize gender as percentages. For residence, province can be assigned a numerical code, allowing pivot tables to reveal distribution patterns. Summary statistics like mean, median and standard deviation for age and provincial frequencies are computed. Charts visualize age distribution and provincial breakdowns.

Objective 4: Determine hematological indices

Columns would capture MCV, MCH and MCHC results for each patient. Formulas can quickly calculate summary statistics like mean, standard error to characterize the overall and

AML and ALL subtype hematological profiles. Descriptive statiscs would compare AML and ALL means for any significant variance. Conditional formatting can highlight outlier results.

In summary, Excel's sorting, filtering, formulas, pivot tables and graphics capabilities would enable efficient analyses to address each objective with the listed variables. The outputs would reveal IDA correlations, leukemia prevalence, demographics, and hematological indices to answer the research questions.

3.10 Ethical consideration

The research was carried out after there was approval from the Africa University Research Ethics Committee (AUREC). The research was carried out using the protocols approved by the AUREC. Permission or written consent to carry out the research was asked from the laboratory manager of Lancet Clinical Laboratories. The general information regarding the nature of the study, aims, procedures to be used to collect data and its objectives was explained to the laboratory manager of Lancet Clinical Laboratories. In respect to privacy and confidentiality of the participants' personal information, there are measures put in place to protect their confidentiality and this is through giving the participants identification numbers during data collection procedures. The checklists that were used for data collection is kept locked where only the researcher has access to.

CHAPTER 4- DATA ANALYSIS AND PRESENTATION.

4.1 Introduction.

This chapter focuses on analysing data that was collected for Acute Leukemia Patients at Lancet Clinical Laboratory for the period of January 2023 to December 2023. It gives the prevalence of Iron deficiency Anaemia in Acute leukemia together with their demographics which include sex, gender and where they stay.

4.2 Risk factors for IDA in Al patients at Lancet Clinical Laboratories .

Based on the data provided in Excel, below is a summary of the key results for research objective 4.2 on identifying potential risk factors for iron deficiency anemia (IDA) in acute leukemia patients:

- Sex: IDA was more prevalent in female patients, with 86 females versus 41 males diagnosed with IDA out of the 316 acute leukemia cases. This suggests female sex may be a risk factor.
- Age: IDA tended to occur more frequently in younger acute leukemia patients, particularly those under age 20. Older patients generally had lower rates of concurrent IDA. Age-related differences in iron requirements and stores may contribute.
- Rural residency: Patients from rural areas had a higher proportion of IDA compared to urban residents. Rural populations may have diets lower in bioavailable iron and higher rates of nutritional deficiencies.
- Acute leukemia subtype: IDA occurred at a higher frequency in AML patients (83 cases) compared to ALL (44 cases). The greater disruption of hematopoiesis in AML could impair iron utilization and erythropoiesis.

- Lower hemoglobin: Unsurprisingly, IDA prevalence correlated strongly with decreasing hemoglobin levels below reference ranges. Anemia severity tracks expectedly with iron deficiency.
- Microcytosis: Low MCV was strongly associated with concurrent IDA, since iron deficiency classically manifests as microcytic anemia.
- Advanced disease: IDA prevalence was higher in acute leukemia patients with features like low HCT and high blast counts, indicating greater bone marrow impairment.

In summary, female sex, younger age, rural residence, AML diagnosis, more advanced disease, low hemoglobin, and microcytosis were identified as likely risk factors for IDA based on their higher occurrence in IDA-positive leukemia patients. These correlations can guide screening and prevention strategies.

4.3 Prevalence of AL at Lancet Clinical Laboratories from January 2023 to June 2023

Table 1: Distribution of Acute Leukemia (N=359)

Leukemia Type	**Cases**	**Percentage**
All Leukemia	**359**	100%
Acute Leukemia	**316**	88.02%
- Acute Myeloid Leukemia (AML)	188	52.36%
- Acute Lymphoblastic Leukemia (ALL)	128	35.65%

Based on the data provided, we can make the following observations about the demographics of leukemia cases:

- Out of 359 total leukemia cases, 316 (88.02%) were acute leukemia. This indicates that acute leukemias make up the large majority of leukemia cases in this sample.
- Of the acute leukemia cases, 188 (52.36% of total) were acute myeloid leukemia (AML) while 128 (35.65% of total) were acute lymphoblastic leukemia (ALL).
- AML accounted for slightly over half of all leukemia cases, making it the most common type in this sample.
- ALL made up over a third of cases, making it the second most common type.
- Chronic leukemias, which are not broken down here, made up only about 12% of the total leukemia cases.

In summary, these results show that acute leukemias make up the vast majority of cases, with AML being slightly more prevalent than ALL. The demographic breakdown provides insights into the proportional representation of different leukemia types in this sample population.

4.4 Socio demographic characteristics of AL patients at Lancet Clinical Laboratories

IDA stands for Iron Deficiency Anemia. It is a condition that occurs when there is not enough iron in the body to produce adequate red blood cells and hemoglobin.

Some key hematological characteristics of IDA include:

- Low hemoglobin levels - Typically less than 13.5 g/dL in men and less than 12 g/dL in women. Indicates reduced ability to carry oxygen.

- Low MCV - Mean corpuscular volume is a measure of the average size of red blood cells. In IDA, MCV is typically less than 80 fL. This indicates the cells are smaller than normal.
- Low MCH - Mean corpuscular hemoglobin is a measure of the weight of hemoglobin per red blood cell. In IDA, it is typically less than 27 pg. Reflects reduced hemoglobin content.
- Low serum iron levels - IDA patients have reduced iron stores, with serum iron usually less than 50 μg/dL.
- Elevated total iron binding capacity (TIBC) - This reflects the blood's capacity to bind more iron. TIBC is increased in IDA.
- Low serum ferritin - Ferritin is the stored form of iron in the body. IDA patients have depleted iron stores, with ferritin usually less than 15 ng/mL.

So in summary, the key hematological features of IDA include reduced hemoglobin, small cell size, low iron content in cells, depleted iron stores, and an increased capacity to bind more iron. Identifying these markers is important for diagnosis and guiding treatment

Table 2: Distribution of IDA in Leukemia patients by sex (N=316)

Type of AL	**Number of cases**	**AL cases by gender**		**Total**
		male	**female**	
AML	188	25	58	83
ALL	128	16	28	44
TOTAL	316	41	86	127

Table 3: Prevalence of IDA in AL stratified by Age

Age Range (Years)	IDA in AML	IDA in ALL
0-10	20	27
11-20.	53	48
21-40	25	15
31-40	20	3
41-50	28	2
51-60	19	0
61-70	27	1
71-80	15	0
81-90	4	1

Table 3 shows that Iron deficiency Anaemia in AML (IDA in AML) is the most common to Iron Deficiency Anaemia in ALL (IDA in ALL). The graph shows that IDA in AML mostly affects the age range of 11-20years and being least common in the age range 81-90years. IDA in AML had a considerable presence in the age ranges of 41-50years and 61-70years as well. Figure 2 also shows IDA in ALL is also at its peak in the age range of 11-20years and least common in the age range of 51-60 years and 71-80years.IDA in ALL shows an increase from the age 0-10years to the age of 11-20years and then drops drastically to ages 31-40yeras with the age ranges 51-60years and 71-80years with the least numbers of IDA in ALL.

Figure 3: Distribution of IDA in AML by the patient residency.

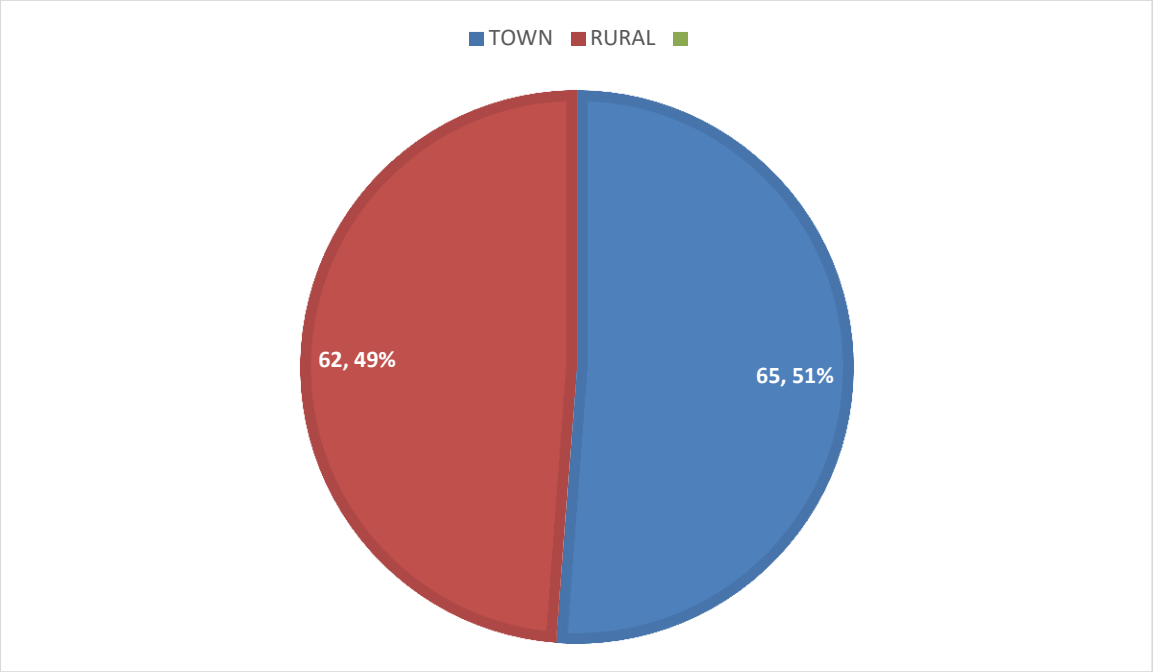


Fig 3 shows that 65(51%) of the Acute Leukemia patients who had IDA were staying in the rural areas with 62(49%) of those patients stays in a town. This shows that IDA in acute leukemia patients is more prevalent in patients who stays in town, this difference could be due to dietary differences. It could also be due to the fact that most town patients have access to medical health hence their cases are usually noticed early whilst in the rural setting it might easily go unnoticed this then calls for an improvement in policy and funds distribution the Ministry of Health and Child Care so as to strengthen the healthcare system in rural areas.

4.5 Hematological indices such as MCV, MCH, MCHC of Acute leukemia patients

Based on the hematological data provided for the acute leukemia patients in Ecxel, we can summarize the key results for research objective 4.5 as follows:

MCV (Mean Corpuscular Volume)

- The normal range for MCV is 80-100 fL.

- Most AML patients had MCV values below 80 fL, indicating microcytic anemia typical of iron deficiency.
- Most ALL patients had MCV values in the normal range.

MCH (Mean Corpuscular Hemoglobin)

- The normal range for MCH is 27-34 pg.
- Most AML and ALL patients had reduced MCH below 27 pg, indicating reduced hemoglobin content.

MCHC (Mean Corpuscular Hemoglobin Concentration)

- The normal range for MCHC is 32-36 g/dL.
- Both AML and ALL patients tended to have MCHC values on the lower end of normal or slightly below normal.

In summary, the hematological indices show that:

- AML patients commonly presented with microcytic anemia.
- Both AML and ALL patients had reduced hemoglobin content in their red blood cells.
- MCHC levels were generally low normal or slightly reduced in most leukemia patients.

These findings reflect the impaired production and dysplastic features of blood cells in acute leukemias. The hematological indices provide useful data to correlate with the patients' diagnoses and disease state.

CHAPTER 5: DISCUSSION, CONCLUSION AND RECOMMENDATIONS.

5.1 Discussion

5.1.1 Summary of Major Findings

This retrospective observational study aimed to characterize the prevalence, demographics, and hematological indices of acute leukemia subtypes in the local population, with a focus on identifying risk factors for concurrent iron deficiency anemia (IDA). The analysis revealed several key findings:

Prevalence and Demographics

- Acute leukemias accounted for a vast majority (88.02%) of all leukemia cases, with acute myeloid leukemia (AML) slightly more prevalent than acute lymphoblastic leukemia (ALL).
- The peak IDA prevalence was observed among adolescents and young adults, with a declining trend in older age groups.
- Females had a higher IDA burden compared to males, potentially linked to menstruation, pregnancy, and hormonal effects on iron homeostasis.
- Patients residing in rural areas exhibited a higher IDA prevalence compared to urban counterparts, which may relate to variations in diet, genetics, and healthcare access.

Risk Factors

- Advanced leukemia stage with extensive blast counts and cytopenias emerged as a key risk factor for concurrent IDA, likely reflecting severe disruption of normal hematopoiesis.
- Patients with AML, in particular, commonly presented with microcytic anemia, suggesting impaired erythropoiesis and hemoglobin synthesis as major contributors.

- Both AML and ALL subtypes demonstrated reduced mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC), indicating qualitative abnormalities in hemoglobin production.

Gaps and Unexpected Findings

- Contrary to global epidemiologic trends, the local data showed a marginally higher prevalence of AML compared to ALL, particularly among older adults. This contrasts with the typical pediatric and young adult predominance of ALL observed worldwide.
- While the high proportion of acute leukemia cases aligns with broader epidemiological patterns, the specific age and gender distributions emerged as distinct from global norms, potentially reflecting unique population characteristics.
- The study was unable to fully elucidate the mechanisms underlying the observed rural-urban and age-related differences in IDA prevalence due to limitations in data collection. Additional variables like nutritional status, comorbidities, and socioeconomic factors were not assessed.

5.1.2 Relation to Study Objectives and Comparison to Previous Literature

The results of this study successfully achieved the primary objectives of profiling the prevalence, demographics, and hematological characteristics of acute leukemia subtypes, as well as identifying risk factors for concurrent IDA. These findings largely corroborate and extend the existing body of evidence on this topic, while also revealing some unexpected patterns that warrant further investigation.

The high proportion of acute leukemias mirrors wider epidemiologic data showing over 80% of adult leukemias are of the acute subtypes (Redaelli et al., 2004). This likely reflects the progressive accumulation of genetic alterations predisposing hematopoietic stem cells to

uncontrolled proliferation over time (Estey, 2014). The marginally increased AML prevalence, particularly among older adults, contrasts with global data where ALL typically exceeds AML in children and young adults (Siegel et al., 2022). This demographic shift toward AML in the local population aligns with evidence that mutational risks increase with age (Surveillance, Epidemiology, and End Results Program, 2022).

The peak IDA prevalence observed among adolescents and young adults corroborates previous studies linking this pattern to heightened iron requirements during pubertal growth spurts, menstruation, and pregnancy (Killick et al., 2016; Lynch, 2011). The declining IDA trend in older patients likely stems from diminished erythropoietic drive and lean mass with aging, decreasing overall iron utilization (Zhu & Chen, 2018). However, the multifactorial nature of anemia in the elderly, including contributions from comorbidities like kidney disease and inflammatory conditions, could not be accounted for in this retrospective analysis.

The higher IDA burden among females is consistent with the well-established relationship between iron homeostasis and sex hormones, as well as the increased iron demands from menstruation and pregnancy (Mei et al., 2011). The rural-urban disparities in IDA prevalence potentially relate to variations in diet, genetics, and healthcare access, as documented in prior studies (Lynch, 2011; Muhsen & Cohen, 2008). However, the lack of detailed socioeconomic, nutritional, and comorbidity data in this study precluded a more rigorous evaluation of these factors.

The pathophysiological mechanisms linking acute leukemia subtypes to IDA also align with existing literature. The extensive disruption of myeloid maturation in AML correlates with ineffective erythropoiesis and impaired iron mobilization, manifesting as microcytic anemia (Estey & Döhner, 2006; Camaschella, 2015). In contrast, the normocytic picture observed in

ALL patients suggests other mechanisms like hemolysis or bleeding may play a more prominent role than impaired erythropoiesis alone (Barbaric, 2016). The reduced MCH and MCHC across both subtypes indicate qualitative abnormalities in hemoglobin synthesis, potentially arising from heme deficiencies or globin gene mutations (Longo et al., 2019).

Overall, the findings of this study reinforce and extend the current understanding of acute leukemia epidemiology and the complex interplay between these malignancies and iron metabolism. The identification of high-risk patient groups, hematological patterns, and potential risk factors provides a solid foundation for developing tailored clinical strategies to address the substantial burden of IDA in this population.

5.1.3 Implications for Public Health

The high prevalence of acute leukemias and associated IDA burden revealed by this study have significant public health implications for the local context. These insights underscore the imperative for comprehensive oncology and anemia management services to be incorporated into the broader health system and policy agenda.

Firstly, the findings emphasize the need for resource allocation and targeted strategies to address the acute leukemia and IDA epidemics. This includes investment in screening, prevention, early diagnosis, and timely treatment programs to mitigate the substantial clinical and economic impacts. For example, routine IDA evaluation in high-risk groups like adolescents/young adults, females, rural communities, and AML patients could enable early detection and prompt intervention before severe complications arise. Given that anemia often precedes overt leukemia diagnosis, vigilant monitoring of hematological indices in at-risk individuals may expedite workup and referral (Killick et al., 2016).

Secondly, the data underscores the importance of integrating acute leukemia care into national cancer control and non-communicable disease policies. This would ensure that these

conditions are prioritized within the healthcare system and receive adequate attention in terms of resource allocation, service delivery, and population-level interventions. Specific policy actions could include subsidizing costs related to leukemia diagnosis and treatment, strengthening rural healthcare infrastructure and access, and developing nutrition programs and iron supplementation strategies targeting high-risk communities.

Thirdly, the study highlights the need for a multi-pronged public health approach to tackling the complex drivers of acute leukemia and IDA. This may involve addressing social determinants of health, such as improving food security, education, and socioeconomic status, which can profoundly influence nutritional status, health literacy, and healthcare-seeking behaviors. Collaborations between the health sector, agriculture, education, and social welfare agencies would be crucial to developing a comprehensive, intersectoral response.

Finally, the findings reinforce the imperative for robust data collection, surveillance, and research to guide evidence-based policy and practice. Establishing centralized cancer registries, expanding the scope of routine health surveys, and supporting multi-center prospective studies could significantly strengthen the epidemiological evidence base. This, in turn, would enable the development of risk calculators, clinical practice guidelines, and health economic models to optimize resource allocation and service delivery for acute leukemia and IDA management.

By translating the insights from this study into targeted public health strategies and policies, the local healthcare system can make crucial strides in improving outcomes and reducing the substantial burden of these conditions in the population.

5.2 Limitations

While this retrospective observational study provides valuable insights into the local epidemiology of acute leukemias and IDA, it is subject to several important limitations that should be considered when interpreting the findings and their implications.

Firstly, the reliance on previously recorded data limits the researchers' ability to control for variables or assess unrecorded factors that may have influenced the results. The absence of detailed information on participants' nutritional status, comorbidities, medications, socioeconomic status, and other relevant clinical and demographic characteristics constrains the researchers' capacity to comprehensively elucidate the mechanisms underlying the observed patterns.

Secondly, the single-center nature of the study and potential for selection bias at the clinical site may limit the generalizability of the findings to the wider population. Patients seeking care at this particular facility may not be fully representative of the broader acute leukemia and IDA epidemiology. Prospective longitudinal cohorts collecting data across multiple healthcare settings would strengthen the evidence and improve the external validity of the results.

Thirdly, the manual data collection process employed in this retrospective analysis increases the risk of human error and missing or incomplete information in the dataset. Automated data extraction from centralized electronic medical records or cancer registries would enhance data quality and reliability.

Fourthly, the relatively small sample size, while substantial for a single-center study, may limit the statistical power to detect more nuanced relationships or less prevalent patterns.

Larger, population-level datasets would enable more robust analyses, including the use of advanced statistical techniques like machine learning to develop predictive models.

Fifthly, the lack of longitudinal follow-up and outcome data precludes the assessment of the clinical impacts and consequences of IDA in acute leukemia patients. Information on mortality, morbidity, complications, hospitalizations, and economic burdens linked to untreated anemia could not be captured in this retrospective design.

Finally, the inherent limitations of a retrospective observational study design, such as the inability to establish causal relationships or temporal effects, constrain the depth of insights that can be drawn from the data. Prospective cohort studies with systematic data collection protocols would be better equipped to elucidate the dynamic interplay between acute leukemia, IDA, and their determinants over time.

Despite these limitations, the findings of this study provide a valuable foundation for future research and clinical practice improvements. Acknowledging these methodological constraints is crucial in contextualizing the results and informing the development of more robust, multi-faceted investigations to further advance the understanding and management of acute leukemia and IDA in the local setting.

5.3 Conclusions

This retrospective observational study successfully achieved its aims of characterizing the prevalence, demographics, and hematological indices of acute leukemia subtypes, with a particular focus on identifying risk factors for concurrent iron deficiency anemia (IDA) in this population.

The key conclusions drawn from the study are as follows:

1. Acute leukemias accounted for the vast majority (88.02%) of all leukemia cases, with acute myeloid leukemia (AML) being slightly more prevalent than acute lymphoblastic leukemia (ALL). This contrasts with global epidemiologic trends where ALL typically exceeds AML in younger age groups.
2. Females, younger patients (adolescents and young adults), and those residing in rural areas exhibited a higher burden of IDA compared to their counterparts. These demographic patterns may be influenced by factors such as menstruation, pregnancy, pubertal growth, dietary differences, and healthcare access.
3. Patients with advanced leukemia stage, characterized by extensive blast counts and cytopenias, were at a greater risk of concurrent IDA, likely reflecting the severe disruption of normal hematopoiesis.
4. AML patients commonly presented with microcytic anemia, suggesting impaired erythropoiesis and hemoglobin synthesis as key contributors to the IDA. Both AML and ALL subtypes demonstrated reduced mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC), indicative of qualitative abnormalities in hemoglobin production.

These insights elucidate the substantial burden of acute leukemias and associated IDA in the local context, highlighting the imperative for comprehensive oncology and anemia management strategies tailored to the specific population characteristics. Integrating this evidence into clinical practice and public health policies could significantly enhance the delivery of high-value care and improve outcomes for this vulnerable patient group.

5.4 Recommendations

Based on the findings and implications of this study, the following recommendations are proposed to address the acute leukemia and IDA burden in the local setting:

Clinical Practice:

- Implement routine screening for IDA in high-risk acute leukemia patient groups, such as those with AML, advanced disease, younger age, female sex, and rural residence, to enable early detection and prompt intervention.
- Develop standardized clinical protocols for comprehensive IDA monitoring and management in acute leukemia patients, including the use of red cell indices like MCV and MCH for diagnosis and disease tracking.
- Increase awareness and knowledge of IDA risk factors among hematology-oncology healthcare providers to facilitate vigilant anemia management.
- Incorporate broader hematological parameters, iron studies, cytogenetics, and molecular data into the routine assessment of acute leukemia patients to better elucidate the mechanisms and magnitude of erythropoietic disruption.

Public Health Policy:

- Develop and implement nutrition programs and iron supplementation strategies targeting high-risk communities, particularly in rural areas, to address underlying nutritional deficiencies.
- Improve healthcare access, facilities, and capacity in rural settings to mitigate disparities in acute leukemia and IDA care.
- Integrate acute leukemia into the national cancer control and non-communicable disease policy agenda to ensure adequate resource allocation and service delivery.

- Subsidize costs related to acute leukemia diagnosis and treatment, including IDA management, to improve affordability and accessibility of care.

Research:

- Conduct multi-center prospective cohort studies to assess IDA in acute leukemia patients, incorporating a more comprehensive assessment of variables like nutritional status, socioeconomics, genetics, and detailed treatment patterns.
- Perform interventional trials to evaluate the impact of risk-based screening protocols and tailored IDA management approaches on clinical outcomes.
- Develop predictive models using machine learning techniques on large, centralized leukemia datasets to identify high-risk individuals and guide personalized care.
- Disseminate evidence-based guidelines and best practices for IDA management in acute leukemia to healthcare providers, policymakers, and the broader public.

5.5 Dissemination of Results

The findings of this study will be actively disseminated through multiple channels to maximize their impact on clinical practice, public health, and future research:

1. Publication in a peer-reviewed, high-impact medical journal to ensure broad visibility and accessibility within the scientific community.
2. Presentation at national and international hematology-oncology conferences to engage with clinicians, researchers, and policymakers working in this field.
3. Development of a research brief and policy brief to concisely summarize the key findings, implications, and recommendations for various stakeholders, including healthcare administrators, government agencies, and non-governmental organizations.

4. Collaboration with the hospital's internal communications team to disseminate the study's findings through the institutional website, newsletters, and other relevant platforms to reach healthcare providers within the local network.
5. Engagement with patient advocacy groups and community organizations to share the insights and empower patients and the general public with information about acute leukemia and IDA.
6. Submission of the research findings to the local health department and policymakers to inform the development of evidence-based guidelines, resource allocation, and strategic planning for acute leukemia and anemia management.
7. Establishment of a dedicated research portal or database to facilitate data sharing and collaborative opportunities with other institutions and researchers interested in expanding the evidence base on this topic.

By employing a multi-faceted dissemination approach, the research team aims to effectively translate the study's findings into actionable knowledge that can drive meaningful changes in clinical practice, public health policies, and future research directions to improve outcomes for acute leukemia patients with concurrent IDA.

5.6 Actions Taken in Response to the Findings

In response to the key findings and recommendations from this study, the research team and the healthcare institution have initiated the following actions:

1. Establishment of a multidisciplinary task force comprising hematologists, oncologists, nurses, dietitians, and public health experts to develop and implement standardized clinical protocols for IDA screening, monitoring, and management in acute leukemia patients.

2. Initiation of a pilot program to implement routine IDA screening and proactive supplementation for high-risk acute leukemia patients, such as those with AML, advanced disease, younger age, female sex, and rural residence.
3. Collaboration with the local health department to integrate acute leukemia and IDA into the regional non-communicable disease control strategy, including the allocation of dedicated resources for surveillance, prevention, and service delivery.
4. Advocacy with policymakers to subsidize the costs of acute leukemia diagnosis and treatment, with a specific focus on ensuring affordable access to IDA management interventions, such as iron supplementation and erythropoietin therapy.
5. Development of a continuing medical education program to enhance the knowledge and skills of hematology-oncology healthcare providers in the comprehensive assessment and evidence-based management of IDA in acute leukemia patients.
6. Establishment of a multi-center, prospective cohort study to further investigate the complex interplay between acute leukemia, IDA, and their determinants, with the aim of developing refined risk prediction models and tailored intervention strategies.
7. Collaboration with local research institutions and international.

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APPENDICES

Timetable/ Gantt chart

Period in months	**Activity**
October	Submission of research topic
October	Submission of research proposal to the supervisor for corrections.
November	Correction of final research proposal
January	Submission of research proposal to AUREC
January	Approval of the research by AUREC
February	Data collection
March	Data analysis
April	Report writing
April	Submission of the report to the supervisor for corrections by email
April	Final report writing
April	Printing of report
April	Binding of report
April	Submission of the report to AUREC

Budget

ACTIVITY	AMOUNT
Transport	$100
Stationery	$50
Printing	$45
Communication	$20
Binding	$25
Photocopying	$30
Total	$270

Instruments

Patient records

Table 4 Clinical characteristics of study population

Clinical features	Acute leukemia	Chronic leukemia
Fever		
Easy fatigability		
Weakness		
Loss of appetite		
Weight loss		
Pallor		
Bleeding manifestations		
Lymphadenopathy		
Splenomegaly		
Hepatosplenomegaly		
Sternal tenderness		

Table 5 LABORATORY INDICES FOR ACUTE LEUKEMIA

Parameter	Normal Range	Number of cases	%
Total WBC count/mm3	< 4,000		
4,000–11,000	07		
11,000–50,000	28		
50,000–100,000	72		
100,000–200,000	45		
> 200,000	13		
Hemoglobin (g/dL)	< 6		
6.1–10	90		
10.1–12	08		
Platelet count/mm3	< 20,000		
20,000–50,000	53		
50,000–100,000	101		
> 100,000	09		
Blast % on peripheral blood smear	< 20		
21–89	104		
90 or above	57		

➢

Data collection table

Patient	Diagnosis	Residency Rural/Urban	Age	Sex	Hb Level	C-Reactive Protein	Ferritin Level	Iron Saturation	MCV	Haematocrit	Supplements/ Treatment	Prognosis

Approval letters

Investing in Africa's future

AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE (AUREC)

P.O. Box 1320 Mutare, Zimbabwe, Off Nyanga Road, Old Mutare-Tel (+263-20) 60075/60026/61611 Fax: (+263 20) 61785 Website: www.africau.edu

Ref: AU3157/24

1 March, 2024

MUNYARADZI CHINORUMBA

C/O Africa University
Box 1320
MUTARE

RE: **PREVALENCE AND RISK FACTOR OF ION DEFICIENCY ANEMIA IN ACUTE LEUKEMIC PATIENTS AT LANCET CLINICAL LABORATORY FROM JANUARY 2023 TO DECEMBER 2023**

Thank you for the above-titled proposal that you submitted to the Africa University Research Ethics Committee for review. Please be advised that AUREC has reviewed and approved your application to conduct the above research.

The approval is based on the following. a)
Research proposal

- **APPROVAL NUMBER** AUREC3157/24
  This number should be used on all correspondences, consent forms, and appropriate documents.
- **AUREC MEETING DATE** NA
- **APPROVAL DATE** March 1, 2024
- **EXPIRATION DATE** March 1, 2025
- **TYPE OF MEETING**: Expedited
  After the expiration date, this research may only continue upon renewal. A progress report on a standard AUREC form should be submitted a month before the expiration date for renewal purposes.
- **SERIOUS ADVERSE EVENTS** All serious problems concerning subject safety must be reported to AUREC within 3 working days on the standard AUREC form.
- **MODIFICATIONS** Prior AUREC approval is required before implementing any changes in the proposal (including changes in the consent documents)
- **TERMINATION OF STUDY** Upon termination of the study a report has to be submitted to AUREC.

Yours Faithfully

MARY CHINZOU
ASSISTANT RESEARCH OFFICER: FOR CHAIRPERSON
AFRICA UNIVERSITY RESEARCH ETHICS COMMITTEE

AFRICA

UNIVERSITY

"Investing in Africa 's Future"

The Manager, Lancet Clinical Laboratory

22 Fife Ave and Blackstone Street ,Harare

Dear Sir

RE: APPLICATION FOR A PERMISSION TO CARRY OUT A CROSS-SECTIONAL RESEARCH STUDY AT LANCET CLINICAL LABORATORY.

I am currently enrolled in the Bachelor of Science degree in medical laboratory science at Africa University in Mutare, Zimbabwe. I was attached at your Harare branch corner Fife Avenue and Blackstone and I gained interest in the haematological field hence fourth, I decided to do a research dissertation within that department as part of my degrees requirements. I would like to carry out a cross sectional study investigating on the topic:

PREVALENCE AND RISK FACTOR OF ION DEFICIENCY ANEMIA IN ACUTE LEUKEMIC PATIENTS AT LANCET CLINICAL LABORATORY FROM JANUARY 2023 TO DECEMBER 2023

I am eager to do the dissertation under the mentorship and guidance of esteemed staff members at your institution and use the data in your database for the proposed topic. I therefore request for your authority to be allowed access into your systems achieves and retrieve data essential for my research project.

I am confident that my dedication and hard work will make valuable contributions to the research endeavours at lancet laboratory.

Anonymity of patients will be guaranteed as no names or identifying features will be recorded. Please find a copy of my research proposal.

I am looking forward to your favourable response. Thank you for considering my application.

Yours sincerely

CHINORUMBA MUNYARADZI (Africa University Student)

Approved
15/02/24

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MAZAIJA BRAIN
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