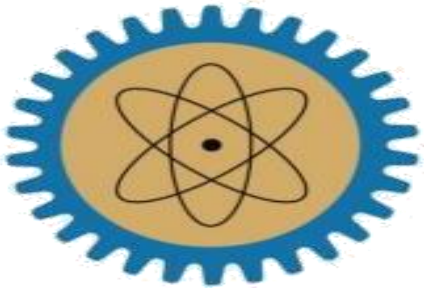

FACULTY OF HEALTH SCIENCES

DEPARTMENT OF INTERNAL MEDICINE

FINAL YEAR PROJECT

PREVALENCE AND FACTORS ASSOCIATED WITH ABNORMAL LUNG FUNCTION AMONG ADOLESCENTS AND ADULTS AGED 12 YEARS AND ABOVE WITH SICKLE CELL DISEASE IN EASTERN UGANDA: A CROSS-SECTIONAL STUDY

By

ACHIRO KEVIN BU/GS23/MMM/1

A DISSERTATION SUBMITTED TO THE FACULTY OF HEALTH SCIENCES IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE

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ABSTRACT

Background: Sickle Cell Disease (SCD) is the most prevalent genetic condition in the world caused by a mutation in the beta-globin gene. The lungs are among the progressively damaged organs by this condition. The majority of research conducted in Africa is restricted to younger individuals with SCD, and yet there is a downward trajectory in lung function with age. Due to advancements in care, many young people with SCD are living into adulthood, and therefore, it's critical to comprehend the anomalies in lung function that these individuals experience.

Aim: This study aimed to determine the prevalence, patterns, and factors associated with abnormal lung function among adolescents and adults aged 12 years and above with SCD in Eastern Uganda.

Methods: This was a hospital-based cross-sectional study conducted among 228 individuals with SCD aged ≥12 years attending the Sickle Cell Clinic (SCC) at Mbale Regional Referral Hospital (MRRH). The inclusion criteria were individuals with SCD aged 12 years and above who provided informed consent or assent, as appropriate. Exclusion criteria included those who were critically ill, had musculoskeletal disorders capable of influencing lung function, verified cases of pneumonia, pulmonary tuberculosis, or any other respiratory illness being treated or diagnosed at the time of enrollment. Lung function was assessed using spirometry. Sociodemographic and clinical data were collected using a pretested questionnaire. Data were analysed using R version 4.5.2. Descriptive statistics summarised participant characteristics and spirometric patterns. Prevalence was estimated with 95% confidence intervals, and logistic regression was used to identify factors associated with abnormal lung function. ORs, aORs, 95% confidence intervals, and p-values were reported; $p < 0.05$ was considered statistically significant.

Results

Of 228 enrolled participants, 218 with valid spirometry were analysed. The median age was 17 years (IQR 14–22), 53.2% were male, 70.6% had a history of recurrent acute chest syndrome, and 92.7% were receiving hydroxyurea therapy. The prevalence of abnormal lung function was 47.2% (103/218; 95% CI: 40.7–53.9%). Restrictive lung pattern was the most common abnormality **(**48.5%**),** followed by obstructive pattern with reversibility **(**26.2%**)**.

In multivariable analysis, Haemoglobin levels showed the strongest association, with moderate anaemia (aOR 6.04, 95% CI 2.26 to 16.15, $p < 0.001$) and severe anaemia (aOR 13.99, 95% CI 4.98 to 39.28, $p < 0.001$) having higher odds than mild or normal haemoglobin. Each additional year of age was associated with 9% higher odds of abnormal lung function (aOR 1.09, 95% CI 1.02 to 1.17, $p = 0.009$; likelihood ratio test for age $p = 0.007$) and non-use of hydroxyurea (aOR: 3.54; 95% CI: 1.01–12.49; $p = 0.049$) were independently associated with abnormal lung function.

Conclusion

Adolescents and adults with SCD frequently have impaired lung function, with a restrictive spirometric pattern being the most common. Significant predictors included growing older, anaemia, and non-use of hydroxyurea. Pulmonary outcomes may be improved by routine lung function evaluation, proper management of anaemia, and optimisation of disease-modifying treatment.

DECLARATION

I, **ACHIRO KEVIN (BU/GS23/MMM/1)**, declare that the research work presented in this dissertation for the award of a degree of master of Medicine in Internal Medicine of Busitema University, entitled- Prevalence and factors associated with abnormal lung function among adolescents and adults with sickle cell disease in Eastern Uganda-A cross sectional study, is entirely my own original work with no submissions to other academic institutions for any awards whatsoever. However, I have included works from other authors and provided proper citations and references to acknowledge their contributions.

ACHIRO Kevin

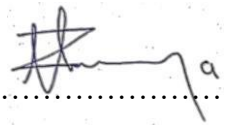
Signature  …….

APPROVAL

We have supervised Dr. Achiro Kevin, and we have given the go-ahead for this study to be advanced to the next stage as she works on her research dissertation, which is titled "Prevalence and factors associated with abnormal lung function among adolescents and adults with sickle cell disease in Eastern Uganda: A cross-sectional study."

Signature……  ……

Dr KATURAMU Richard, MBChB, MMed, INTERNAL MEDICINE (MUK) MSc (LSHTM)

Signature……  ……

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DEDICATION

This study is dedicated to my beloved father, Mr. Otto Michael Gulamali, who has consistently provided me with both financial and emotional support.

ACKNOWLEDGEMENT

My sincere gratitude goes out to Associate Professor David Mukunya and Dr Richard Katuramu, my supervisors. To my dedicated research assistants, Miss Deborah Namatome, Mr Wanzaala Perez, Mr Isaac Pitua, and the nursing team at the sickle cell clinic, Mr Jasper Odur and the complete laboratory team, God bless you abundantly.

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ACRONYMS

ACS	Acute Chest Syndrome
BMI	Body Mass Index
BUFH-REC	Busitema University Faculty of Health Sciences Research and Ethics Committee
CRD	Chronic Respiratory Disease
DALY	Disability-Adjusted Life Years
DLCO	Diffusing capacity of the lungs for carbon monoxide
ECG	Electrocardiogram
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HB	Hemoglobin
HBS/B^0	Sickle Beta-Thalassemia
HBSC	Haemoglobin SC Disease
HBSS	Sickle Cell Anaemia
HRQOL	Health-Related Quality of Life
MRC	Modified Medical Research Council
MRRH	Mbale Regional Referral Hospital
MRRH-REC	Mbale Regional Referral Hospital Research and Ethics Committee
MOH	Ministry of Health
RA	Research Assistant
RFT	Renal Function Test
SCA	Sickle Cell Anaemia
SCC	Sickle Cell Clinic
SCD	Sickle Cell Disease
SCT	Sickle Cell Trait
SSA	Sub-Saharan Africa
SPO_2	Peripheral Capillary Oxygen Saturation
T	Thymine
WHO	World Health Organisation

OPERATIONAL DEFINITIONS

Abnormal lung function: Derangements in pulmonary function tests, which can be restrictive, obstructive with or without irreversibility, and mixed patterns by spirometry

Acute Chest Syndrome: A complication of sickle cell disease that is marked by a recent pulmonary infiltrate seen on imaging. Clinically, it can be identified through symptoms such as cough, rapid breathing, fever, chest discomfort, low oxygen levels, and wheezing.

Adolescent: Defined as a person in the second decade of life, aged 10 to 19 years.

Adult: A person aged 20 years or older.

FEV1: The volume of air a person forcefully exhales during the first second of a forced expiratory manoeuvre after the deepest inhalation

FVC: The total volume of air that can be forcibly exhaled after maximal inspiration.

Irreversible obstruction: post-bronchodilator FEV1/FVC% ratio <70%. Less than a 12% increase following bronchodilator administration.

Mixed pattern: Defined as FEV_1 <80% of the predicted value, FVC <80% of the predicted value, and FEV_1/FVC <70%**.**

Obstructive Lung Disease: Forced Expiratory Volume in 1 second (FEV1) / Forced Vital Capacity (FVC)<0.70(70%)

Recurrent episodes of Acute Chest Syndrome: 3 or more episodes within the preceding 12 months, confirmed by medical records or by the patient.

Restrictive lung disease: Forced Vital Capacity (FVC)<80% predicted. FEV1/FVC ≥ 0.70

Reversible obstruction: post-bronchodilator increases in FEV1 of 12% or more

Sickle Cell Anaemia: Sickle cell anaemia refers to the homozygous form of sickle cell disease

(HbSS), where a person inherits two sickle cell genes (one from each parent). It is the most severe type of sickle cell disease.

Sickle cell crisis: An acute episode or exacerbation of sickle cell disease characterised by the development of one or more disease-related complications that may result from vaso-occlusion, increased haemolysis, acute anaemia, or sequestration of sickled red blood cells. Sickle cell crises include vaso-occlusive (painful) crisis, aplastic crisis, splenic or hepatic sequestration crisis, hyperhaemolytic crisis, and other acute complications such as acute chest syndrome.

Sickle cell disease (SCD): A collection of genetic blood conditions, confirmed by Hb electrophoresis, marked by the presence of an unusual type of haemoglobin known as haemoglobin S in red blood cells. It comprises different genotypes, which include: HbSS, HbSC, and HbS/β-thalassemia.

Sickle cell trait: Sickle cell trait (SCT) was defined as a hereditary condition where an individual receives one normal haemoglobin gene (HbA) and one abnormal sickle haemoglobin gene (HbS).

Steady-state: This was defined as a state in which the patient was clinically stable without acute complications of sickle cell disease, such as Vaso-occlusive crisis or infections, for at least 2 to 4 weeks before recruitment and had not received recent blood transfusions within the last 3 months.

CHAPTER ONE:

1.0 INTRODUCTION

1.1 Background

Sickle cell disease (SCD) is a group of inherited haemoglobin disorders caused by the presence of haemoglobin S (HbS). HbS results from a single-nucleotide substitution in the β-globin gene that replaces glutamic acid with valine at the sixth position of the β-globin chain (Kato et al., 2018; Sundd et al., 2019). The disease occurs when the HbS mutation is inherited in the homozygous state (HbSS) or in combination with another abnormal β-globin gene, such as haemoglobin C or β-thalassaemia (Chatzidavid et al., 2024; Kato et al., 2018). In contrast, individuals with the Sickle Cell Trait (SCT) inherit one normal haemoglobin A gene and one HbS gene and are generally asymptomatic, with limited clinical manifestations (Brown et al., 2023).

Recent global estimates indicate that the number of individuals living with SCD increased from approximately 5.5 million in 2000 to 7.7 million in 2021, representing a substantial increase in the global disease burden (Thomson et al., 2023). Over 100,000 people in the United States suffer from this common genetic disorder, and of these, about 90% are Black and 10% are Hispanic (Paula Tanabe et al., 2019). It is associated with reduced life expectancy and quality of life, with vaso-occlusion, hemolytic anaemia, and vasculopathy as the main mechanisms of disease. In Africa, the mortality rate for children <5 years of age ranges from 50% to 80% (Mulumba & Wilson, 2015).

The greatest burden of SCD occurs in sub-Saharan Africa. The high prevalence of the sickle cell gene in malaria-endemic regions is partly attributed to the survival advantage associated with SCT against severe malaria (Hsu et al., 2018; Wastnedge et al., 2018).

Uganda is among the countries with a substantial burden of SCD. National newborn screening

data have shown marked geographical variation in the prevalence of Sickle Cell Trait (SCT) and disease. The prevalence of SCT among newborns in Uganda has been estimated at approximately 13%, while the prevalence of SCD is approximately 0.7–0.8% nationally (Ndeezi et al., 2016; Schaefer et al., 2016). Regional analyses of Uganda's national newborn screening programme have demonstrated that several districts in Eastern Uganda have a high prevalence of SCT**,** with some areas reporting prevalences above 20% (Hernandez et al., 2021). More recently, data from the Ugandan Sickle Pan-African Research Consortium registry showed that Mbale Regional Referral Hospital contributed 16.9% of the 5,655 patients enrolled across four major sickle cell treatment sites between June 2022 and October 2023(Nsubuga et al., 2024). These findings support the classification of Eastern Uganda as a high-burden setting and provide an epidemiological basis for investigating SCD-related complications in this region.

Although advances in early diagnosis, introduction of hydroxyurea therapy, and comprehensive care have improved survival, SCD remains associated with considerable morbidity and premature mortality, particularly in low-resource settings where access to newborn screening, preventive interventions, and specialised care is limited (Hsu et al., 2018; Mcgann et al., 2017).

SCD results in impairments across multiple systems, with lung complications being a significant factor in morbidity and mortality. The lungs are commonly affected by both acute and chronic complications of SCD. Pulmonary complications include acute chest syndrome, pulmonary hypertension, venous thromboembolism, asthma and recurrent wheezing, sleep-disordered breathing, and abnormalities in pulmonary function (Mehari & Klings, 2016; Pervaiz et al., 2021). These lung abnormalities are responsible for 20% to 30% of SCD mortality (David et al., 2018). Due to their high vascularisation, the lungs are more vulnerable to damage from hypoxia and ischemia, and they are more likely to develop pneumonias and

other lung conditions (Pervaiz et al., 2021).

Studies have reported varying prevalences of abnormal lung function among individuals with SCD. In Brazil, Vieira et al. reported abnormal lung function among 23.4% of children with SCD aged 8–15 years (Vieira et al., 2016). Another cross-sectional study in Africa, involving 56 adult patients at a tertiary hospital in Lagos, Nigeria, found that 18.9% of adult individuals with sickle cell anaemia had chronic lung disease, and this number rises with age (Fawibe et al., 2010). In Uganda, Aol et al. (2024) reported abnormal lung function in 37.9% of children and adolescents aged 6–18 years attending a tertiary SCD clinic (Aol et al., 2024).

Despite the substantial burden of SCD in Eastern Uganda, there is limited information on the prevalence, spirometric patterns, and factors associated with abnormal lung function among adolescents and adults with SCD in the region. The available Ugandan study focused on younger populations and was conducted in an urban tertiary-care setting (Aol et al., 2024). This lack of evidence hindered clinicians' and health planners' ability to recognise patients at greater risk, provide suitable pulmonary monitoring, and create tailored strategies for preventing and managing pulmonary complications.

1.2 Problem Statement

More people with Sickle Cell Disease (SCD) are living longer due to factors like improved access to healthcare, the introduction of hydroxyurea for all individuals with SCD and increased awareness among the general population. SCD has evolved from a deadly pediatric condition to a chronic adult illness marked by progressive multiorgan failure (Thein et al., 2017). However, little is known about the lung function abnormalities among older individuals with SCD. Additionally, lung function declines with age in the general population, so understanding the lung function of older individuals with SCD is crucial.

Pulmonary complications, including acute chest syndrome, pulmonary vascular disease, and abnormalities in lung function, contribute substantially to morbidity and may contribute to premature mortality among individuals with SCD (Brandow & Liem, 2022; McGann et al., 2017; Pervaiz et al., 2021).

Evidence from Uganda demonstrates that abnormal lung function is common among children and adolescents with SCD. A cross-sectional study involving 332 participants aged 6–18 years at Mulago National Referral Hospital reported abnormal lung function in 37.9% of participants (Aol et al., 2024). However, this study was conducted in a tertiary urban setting and mainly involved younger individuals with SCD. Its findings may not be directly generalisable to older adolescents and adults receiving care in Eastern Uganda because lung function may change with increasing age and because differences in disease severity, healthcare access, environmental exposures, and clinical management may influence pulmonary outcomes.

In Eastern Uganda, there is limited data on the prevalence, spirometric patterns, and factors associated with abnormal lung function among adolescents and adults with SCD despite the substantial burden of SCD in the region. In particular, no published study was identified that had evaluated lung function among adolescents and adults aged 12 years and above attending

the Sickle Cell Clinic (SCC) at Mbale Regional Referral Hospital (MRRH). Consequently, the magnitude and patterns of abnormal lung function and the factors associated with these abnormalities in this population were unknown. Therefore, this study aimed to determine the prevalence and patterns of abnormal lung function, and identify factors associated with it, among adolescents and adults aged 12 years and above attending the SCC at MRRH.

1.3 Study Objectives

1.3.1 General Objectives

To determine the prevalence, patterns, and factors associated with abnormal lung function among adolescents and adults aged 12 years and above with sickle cell disease (SCD) attending the Sickle Cell Clinic (SCC) at Mbale Regional Referral Hospital (MRRH).

1.3.2 Specific Objectives

i. To determine the prevalence and patterns of abnormal lung function among adolescents and adults aged 12 years and above with SCD attending the SCC at MRRH.

ii. To describe the factors associated with abnormal lung function among adolescents and adults aged 12 years and above with SCD attending the SCC at MRRH.

1.4 Research Questions

i. What is the prevalence, and what are the patterns of abnormal lung function among adolescents and adults aged 12 years and above with sickle cell disease(SCD) attending the Sickle Cell Clinic (SCC) at Mbale Regional Referral Hospital (MRRH)?

ii. Which factors are associated with abnormal lung function among adolescents and adults aged 12 years and above with SCD attending the SCC at MRRH?

1.5 Justification

Sickle Cell Disease (SCD) is associated with progressive multi-organ damage, and pulmonary

complications contribute substantially to morbidity, reduced quality of life, and premature mortality. Eastern Uganda is an important setting for this study because national newborn screening data have demonstrated a high prevalence of sickle cell trait (SCT) in several districts within the region, with some areas reporting prevalences above 20%. However, there is limited evidence on the burden and patterns of abnormal lung function among adolescents and adults with SCD receiving care in Eastern Uganda.

Most available studies have focused on children and younger adolescents and have largely been conducted in urban tertiary-care settings. Consequently, the prevalence, patterns, and factors associated with abnormal lung function among older adolescents and adults attending the Mbale Regional Referral Hospital Sickle Cell Clinic were not well understood. Since pulmonary impairment may progress with age and cumulative disease-related organ injury, local evidence is needed to characterise lung function in this population.

Identifying abnormal lung function may have important implications for patient management. Spirometry can detect pulmonary impairment, including restrictive, obstructive, and mixed ventilatory patterns, even when respiratory symptoms are mild or absent. Identification of these abnormalities may enable clinicians to undertake further clinical evaluation, investigate potentially reversible or treatable causes, provide appropriate treatment or referral, and prioritise patients who require closer respiratory monitoring. The identification of factors associated with abnormal lung function may also support risk stratification and help clinicians target preventive and disease-modifying interventions, including optimisation of hydroxyurea therapy and management of modifiable risk factors.

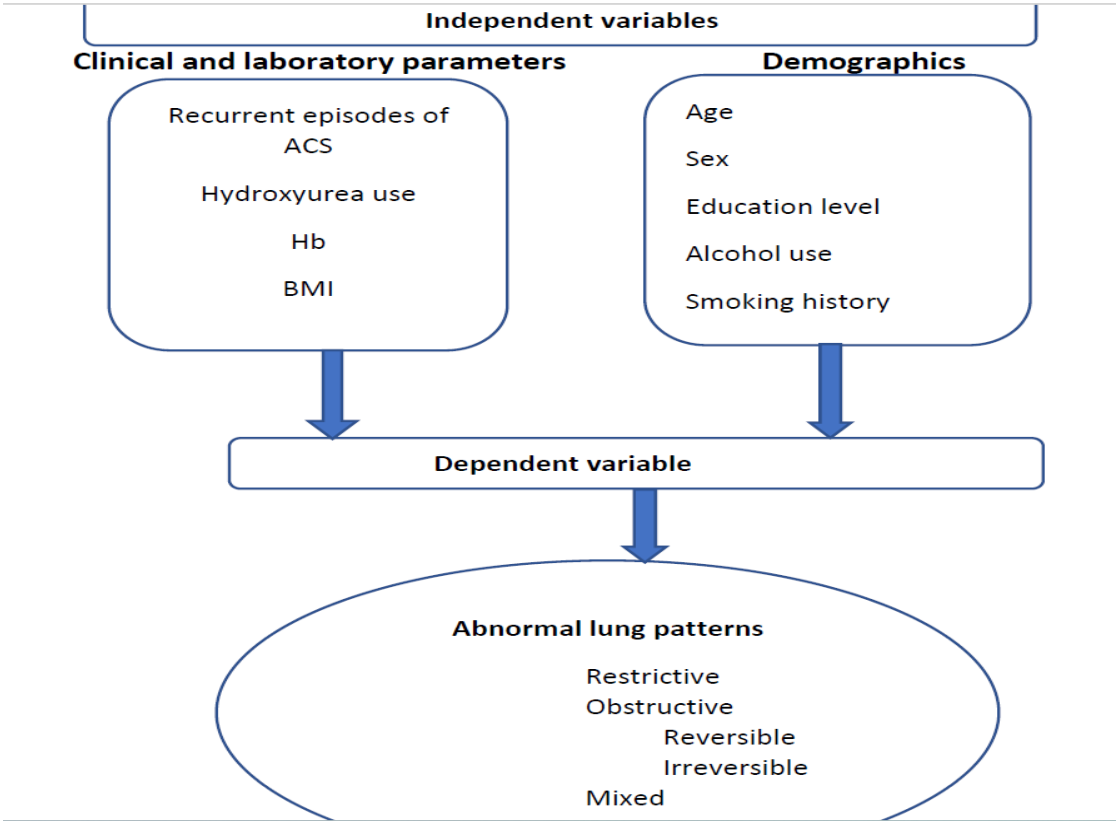
The findings of this study will provide local evidence to support the integration of targeted lung function assessment into comprehensive SCD care, particularly among patients at increased risk of pulmonary impairment. Earlier identification and appropriate management of respiratory abnormalities may help reduce respiratory symptoms and complications, preserve

functional capacity, improve quality of life, and potentially reduce SCD-related morbidity.

The findings may also guide future clinical protocols, resource allocation, and research on long-term pulmonary outcomes among individuals with SCD in Uganda.

1.6 Conceptual Framework

Figure 1: Conceptual Framework



The independent and dependent variables are described in this conceptual framework. In this study, three domains were thought to have an impact on lung function. These were:

Clinical and Laboratory Characteristics

Recurrent episodes of Acute Chest Syndrome (ACS)

Recurrent episodes of acute chest syndrome are associated with small airway damage, development of pulmonary fibrosis predominantly in the lung bases, impaired ventilation-perfusion matching, and sustained inflammatory responses mediated by cytokines such as IP-10, IL-5, IL-13, and TNF-α**.** The cumulative effect of all this is chronic lung disease.

Body Mass Index (BMI)

Both high and low BMIs can affect lung function in various ways. A high BMI, particularly due to excess fat deposition around the chest and abdomen, can negatively impact respiration in several ways. Excess fat can limit chest wall expansion, leading to decreased lung volumes; abdominal fat pushes up the diaphragm, limiting its downward movement, which lowers forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1)**.** Obese people are more prone to obstructive sleep apnoea and asthma-like symptoms.

Being underweight reduces respiratory muscle strength, including the intercostal muscles and diaphragm, which impairs normal ventilation. Being underweight is also associated with an impaired immune system, which can lead to recurrent respiratory infections that can affect overall lung function over time. Low BMI is often associated with chronic conditions like sickle cell disease, and often correlates with poorer lung function.

Hydroxyurea Use

Hydroxyurea treatment in individuals with sickle cell disease (SCD) has been associated with improved lung function, mainly by decreasing pulmonary complications such as acute chest syndrome (ACS), which plays a key role in long-term respiratory impairment. By preventing recurrent lung injury and fibrosis, hydroxyurea helps slow the progressive decline in lung function. Additionally, it has been shown to lower tricuspid regurgitant velocity—a marker of pulmonary hypertension—indicating enhanced pulmonary vascular function, improved oxygenation, and reduced shortness of breath during physical activity. Hydroxyurea also lowers white blood cell counts and curbs chronic inflammation, thereby reducing lung damage caused by sickled red blood cells and inflammatory processes.

Hemoglobin Levels

In SCD**,** haemoglobin levels have a direct and significant impact on lung function. Lower haemoglobin levels contribute to impaired oxygen delivery, inflammation, and damage to the pulmonary system.

Oxygen Saturation (SpO_2)

The sufficiency of pulmonary gas exchange is reflected in oxygen saturation. Reduced SpO_2 has been linked to higher disease severity in SCD and may be a sign of underlying pulmonary dysfunction. Poor lung function impairs Oxygen uptake in the alveoli and distribution through the pulmonary vasculature, resulting in reduced SpO_2.

Demographic Characteristics

Age

Growing older may be linked to cumulative lung damage and a gradual deterioration of lung function. This is compounded by the natural deterioration of lung function that comes with ageing.

Sex

Sex influences lung function in several ways, including anatomical, hormonal, and physiological variations. For example, males have larger lungs than females, even when matched for age and sex, hence higher lung volumes than females. Estrogen and progesterone affect airway reactivity, especially during pregnancy and growth spurts. These differences may influence the prevalence and pattern of lung function abnormalities.

Smoking History

Smoking contributes to airway inflammation and airflow limitation, directly affecting the alveoli and airways and causing airway narrowing, which impairs gas exchange and increases

the risk of obstructive airway diseases.

Alcohol Use

Chronic alcohol use can lead to a weakened immune system, hence increased susceptibility to infections like Klebsiella-associated pneumonia. Alcohol intake is also associated with poor nutrition, hence affecting lung function in the long run.

Education status

Education status may influence health-seeking behaviour, health literacy, and exposure to environmental risk factors, which can indirectly affect respiratory health outcomes.

1.7 Scope of the Study

1.7.1 Content Scope

Only adults and adolescents with SCD who were 12 years of age or older and enrolled in the Mbale regional referral sickle cell clinic were included in the study. In-depth counselling and assessment, appropriate history taking and examination, and the option to withdraw from the study at any point were all provided to the participants. Individuals found to have abnormal lung function were referred for additional testing and treatment.

1.7.2 Time Scope

Between October 2025 and March 2026, the study was carried out over a period of six months.

CHAPTER TWO:

2.0 LITERATURE REVIEW

2.1 Introduction

This chapter reviews the existing literature on Sickle Cell Disease (SCD) and lung function abnormalities, with emphasis on the prevalence, patterns, and factors associated with abnormal lung function among adolescents and adults with SCD. The chapter discusses the definition and classification of SCD, pulmonary complications and their pathophysiology, the burden of lung function abnormalities among individuals with SCD, patterns of abnormal lung function, and factors associated with impaired lung function.

The literature reviewed was obtained from a range of electronic databases, including PubMed, Google Scholar, and ResearchGate, as well as reports from the World Health Organisation (WHO) and the Uganda Ministry of Health, along with other relevant scientific sources. The focus was on peer-reviewed articles, systematic reviews, and research relevant to Africa and similar contexts concerning the study population. This body of literature establishes the scientific basis for the study and highlights the existing knowledge gaps regarding lung function challenges in adolescents and adults with SCD in Eastern Uganda.

2.2 Definition of sickle cell Disease and subtypes

Sickle Cell Disease (SCD) refers to a group of inherited haemoglobin disorders characterised by the presence of haemoglobin S (HbS) (Kato et al., 2018). It comprises several genotypes that vary in clinical severity and manifestations. When a person inherits one normal hemoglobin A gene and one hemoglobin S gene, they develop the sickle cell trait (HbAS). Individuals with the sickle cell trait are generally asymptomatic and do not have sickle cell disease (Brown et al., 2023). This genetic alteration causes reduced or nonexistent production of normal beta-globin and can be inherited homozygously or in conjunction with a thalassemic

mutation on the other beta-globin allele (Chatzidavid et al., 2024).

Sickle cell anaemia (HbSS), which is caused by the inheritance of two hemoglobin S genes, is the most prevalent and severe type of SCD. Other clinically important forms of SCD arise from coinheritance of haemoglobin S with other abnormal β-globin variants, including haemoglobin C (HbSC), haemoglobin D (HbSD), haemoglobin E (HbSE), haemoglobin O- Arab (HbSO-Arab), and β-thalassemia mutations (HbS/β^0-thalassemia and HbS/β^+-thalassemia) (Sachdev et al., 2021). Disease severity varies according to genotype. Individuals with HbSS and HbS/β^0-thalassemia generally experience the most severe clinical manifestations, while those with HbSC disease and HbS/β^+-thalassemia often have a milder clinical course. However, substantial variability in disease severity exists even among individuals with the same genotype (Onimoe & Rotz, 2020).

2.3 Burden of sickle cell disease

SCD is a major global public health concern, with the greatest burden occurring in sub-Saharan Africa. In 2021, an estimated 7.74 million people were living with SCD worldwide, and approximately 515,000 babies were born with the condition. Nearly 80% of people living with SCD reside in sub-Saharan Africa (World Health Organisation, 2025; Thomson et al., 2023).

The number of people living with SCD globally increased from an estimated 5.46 million in 2000 to 7.74 million in 2021. This represents a 41.4% increase in the number of people living with SCD**,** and this increase has been attributed mainly to population growth and improved survival among individuals with SCD (Thomson et al., 2023).

SCD contributes substantially to morbidity and premature mortality, particularly in low- and middle-income countries where access to newborn screening, preventive interventions, comprehensive care, and disease-modifying treatment may be limited (Mcgann et al., 2017; World Health Organisation, 2025). In 2021, SCD was associated with an estimated 34,400

cause-specific deaths globally. However, when deaths related to conditions associated with SCD were considered, the estimated total mortality burden was approximately 376,000 deaths (Thomson et al., 2023).

In West African countries like Ghana and Nigeria, the trait affects about 15% to 30% of the general population, while on the other hand, the prevalence of SCD is much higher in East African nations, especially Uganda, at over 45%, with substantial regional variations (Afolayan & Jolayemi, 2011).

Sub-Saharan Africa accounts for more than 75% of the global burden of SCA, with alarmingly high rates of early death due to lack of healthcare resources coupled with inadequate knowledge and sensitisation in both the public and medical domains(McGann et al., 2017).13.3% of children in Uganda have the sickle cell trait, and 0.7% have SCD (Ndeezi et al., 2016). Several districts in Eastern Uganda have reported sickle cell trait prevalences exceeding 20%, indicating a high frequency of the sickle cell gene in parts of the region (Hernandez et al., 2021).

Eastern Uganda is a high-burden region for SCD. Earlier surveys had reported sickle cell trait prevalences ranging from approximately 20% to 28% in the Mbale and Sironko area, indicating a high frequency of the sickle cell gene in this region (Okwi et al., 2010). More recently, data from the Ugandan Sickle Pan-African Research Consortium registry showed that Mbale Regional Referral Hospital contributed 16.9% of the 5,655 patients enrolled across four major sickle cell treatment sites between June 2022 and October 2023 (Nsubuga et al., 2024). These findings demonstrate a substantial local burden of SCD and highlight the importance of strengthening evidence on disease-related complications among patients receiving care at MRRH.

2.4 Complications of sickle cell disease

SCD affects multiple organs, such as the heart, brain, and kidneys. Older patients experience complications like leg ulcers as well as chronic issues related to the kidneys, heart, and lungs. (Mcgann et al., 2017). The SCD genotype is one of the factors that influences the severity of clinical complications (Gardner et al., 2016). Compared to people with Hb SC or HbS with mild β thalassemia, patients with homozygous sickle cell anaemia (HbSS) and HbS paired with severe β thalassemia had more severe anaemia and a more complicated clinical course (Elmariah et al., 2014).

Pulmonary complications are important contributors to morbidity among individuals with SCD. These complications include acute chest syndrome, pulmonary hypertension, venous thromboembolism, asthma and recurrent wheezing, sleep-disordered breathing, and abnormalities in pulmonary function (Brandow & Liem, 2022; Pervaiz et al., 2021)**.**

Sudden clinical events resulting from tissue ischemia and infarction are the primary consequences of SCD, with pain being the most common symptom. Over time, recurrent episodes of ischemia-reperfusion injury and hemolysis's aftereffects result in a chronic inflammatory state and aberrant blood vessels, which exacerbate the organs' continuous damage (Sachdev et al., 2021).

Increased morbidity and death are linked to cardiopulmonary disease in individuals with SCD (Brandow & Liem, 2022).

2.5 Prevalence of Lung functional abnormalities in individuals with sickle cell disease

A hospital-based cross-sectional study in a Nigerian tertiary hospital found the prevalence of abnormal lung function at 40.7% among children with Sickle cell Disease (Odeyemi et al., 2022). A cross-sectional study in Ugandan children with SCD at Mulago National Referral Hospital found the prevalence of abnormal lung function at 37.9% (Aol et al., 2024). A cross-

sectional research study of 56 adult individuals with SCD at a major hospital in Lagos, Nigeria, found that 18.9% of these adults had chronic lung disease, which was more common with increasing age (Fawibe et al., 2010). In a prospective cross-sectional study conducted in South Africa with 25 sickle cell individuals between the ages of 6 and 16, Owusu et al. found that pulmonary function impairments were at 47% (Owusu et al., 2024).

2.6 Patterns of Lung functional abnormalities in individuals with sickle cell disease

Abnormal lung function in individuals with Sickle Cell Disease (SCD) may present as restrictive, obstructive, or mixed ventilatory patterns (Brandow & Liem, 2022)**.** The distribution of these patterns varies across studies and may be influenced by age, disease severity, respiratory comorbidities, and the methods used to interpret pulmonary function tests (Desai et al., 2022).

Several studies carried out in Malawi, Nigeria, and the Central African Republic have shown that restrictive impairment is the main lung function abnormality found by spirometry in Africa, especially in lower-income nations (Ahmed et al., 2024; Cook et al., 2013) .In a hospital-based cross-sectional study, Odeyemi et al. looked at individuals with SCD at a tertiary hospital in Ogbomoso, Nigeria, who were six years of age or older. According to the results, 40.7% of the individuals had aberrant lung function, with the restrictive pattern being the most common problem (Odeyemi et al., 2022). Similarly, the Ugandan study by Aol et al. (2024) found that restrictive abnormalities accounted for more than half of the abnormal spirometry findings among children and adolescents with SCD (Aol et al., 2024)**.**

It has, however, been noted that children with SCD who may experience asthma-like symptoms and airway hyperreactivity are more likely to have obstructive abnormalities. According to pulmonary function testing (PFT), 16% of children and 8% of adults with SCD have obstructive lung disease, while up to 28% of adults and only 7% of children have

restrictive lung disease (Cohen et al., 2015).

The majority of children and adolescents with SCD who have either normal or obstructive patterns on spirometry come from high-income nations (Koumbourlis, 2014). The adult population with SCD studied had a low incidence of obstructive abnormalities (Dosunmu et al., 2013).

2.7 Factors associated with abnormal pulmonary function

2.7.1 Recurrent episodes of Acute Chest Syndrome

There are few prior studies on the relationship between prior Acute Chest Syndrome (ACS) episodes and abnormal lung function; however, in a Nigerian/UK study with 250 participants, a history of ACS was linked to lower FEV_1 (-0.41 z) and FVC (-0.35 z) even after adjustment, as well as increased ventilation heterogeneity on multiple-breath washout (Ahmed et al., 2024).

According to large cross-sectional research, blockage is more common in children (~15–20%), while restriction is more common in adults (27–74%) (Desai et al., 2022).

Additionally, a cross-sectional study in Brazil found a connection between restrictive spirometric anomalies and a history of ACS (Maioli et al., 2016).

Another study found an association between restrictive damage and a higher frequency of ACS, which can be explained, at least in part, by chronic hemolysis and repeated episodes of intermittent vascular occlusion, which lead to tissue damage (Lunt et al., 2014).

In a retrospective study conducted at Kitgum General Hospital among children with sickle cell anaemia, an ACS prevalence of 27.8% was reported. Age was significantly associated with the occurrence of ACS (Omara et al., 2025).

Due to difficulty in obtaining a clear history and diagnostic challenges, ACS can be difficult to diagnose in sub-Saharan Africa, where SCD is very common. However, a cross-sectional study in Ghana found that patients experiencing three or more crises in the past year, primarily of the

vaso-occlusive type, had lower per cent predicted values for forced vital capacity (FVC) compared to those who had two or fewer crises annually (65.9% predicted versus 75.0% predicted, respectively; p=0.180) (Dei-Adomakoh et al., 2019).

2.7.2 Hydroxyurea use in sickle cell disease

Adult recipients of allogeneic hematopoietic stem cell transplants at three French tertiary care facilities participated in a retrospective, observational, multicenter matched case-control study, and it was found that children treated with hydroxyurea had significantly greater FEV_1 and FVC values, as well as lower rates of lung function (Alcazer et al., 2019). It has been demonstrated that hydroxyurea greatly lowers the chance of having ACS by about 50% (Desai et al., 2022).

Evidence from a comprehensive review and meta-analysis indicates that hydroxyurea use is associated with decreased tricuspid regurgitant velocities, a noninvasive indicator of improved pulmonary hemodynamics (Khargekar et al., 2024).

In an open-label global study involving 606 children aged 1 to 10 years across four clinical settings in Sub-Saharan Africa, hydroxyurea use was associated with a lower incidence of vaso-occlusive events, infections, malaria, transfusion requirements, and mortality. This highlights how important it is to increase access to this treatment in low-income communities (Tshilolo et al., 2019).

There was no discernible difference in the presence or absence of asthma, wheezing, or abnormal pulmonary function among patients receiving various treatments, including hydroxyurea, in a single-centre, cross-sectional study involving 70 SCD patients and controls between the ages of 6 and 18 (Angel et al., 2020).

In a cross-sectional analytical study conducted, 76 clinically stable adult patients with Hb-SS who had never received hydroxyurea were compared with 76 matched controls without sickle

cell disease. The levels of Hb, urea, and free plasma haemoglobin were notably linked to a reduced FEV1% predicted, less than 80% (Dei-Adomakoh et al., 2019).

2.7.3 Body Mass Index

In a cross-sectional study conducted in Lagos, Nigeria, 233 children with sickle cell anaemia (SCA) (mean age 9 ± 4 years; 60.9% boys) were found to be shorter, lighter, and more likely to be undernourished than their HB AA counterparts (Esezobor et al., 2016). 113 SCD patients and matched controls participated in another cross-sectional study at a Nigerian tertiary hospital. The results showed that individuals with SCD had considerably worse body mass index (BMI) than their non-SCD counterparts. Furthermore, abnormal lung function was prevalent among these individuals with SCD, occurring in 40.7% of cases, with the restrictive pattern being the most frequently observed, affecting 28.3% of the participants in the study (Odeyemi et al., 2022).

2.7.4 Abnormal Hb concentration

Hb concentration was positively correlated with FEV1 and FVC, while White Cell Count and age were negatively correlated with FVC and FEV1, according to a case-control study conducted at Lagos University Teaching Hospital in Nigeria with 245 SCD patients and 216 age- and gender-matched non-SCD controls (Ozoh & Olufunto, 2019). Low haemoglobin levels contribute to lower FEV_1, which is a major predictor of death (Liem et al., 2019). Lower haemoglobin was linked to reduced lung function (lower FEV_2, FVC), as well as a higher likelihood of restrictive patterns and pulmonary hypertension, according to a systematic review (Taksande et al., 2021).

2.8 Pathophysiology of abnormal lung function

As explained in this section, the many variant genotypes of SCD (double heterozygous states or SCA with modifying genes) have a similar pathophysiology.

Over the past 70 years, researchers have identified three primary biological mechanisms that contribute to disease progression: hemolysis-related endothelial dysfunction, vaso-occlusion, and HbS polymerisation. A fourth process that has been discovered more recently is sterile inflammation (Sundd et al., 2019).

The main pathogenic mechanism causing ischemia, inflammation, vascular proliferation, endothelial dysfunction, and oxidative stress in people with SCD is the frequent occurrence of vaso-occlusive episodes (Olutogun et al., 2018).

The primary causes of pulmonary complications in SCD include chronic hemolysis, endothelial dysfunction, inflammation, and recurrent vaso-occlusion. Haemoglobin S polymerisation in deoxygenated conditions causes red blood cells to become hard and sickled, blocking the pulmonary microvasculature and resulting in recurrent episodes of ischemia-reperfusion injury (Kato et al., 2018).

Inflammation, endothelial activation, and tissue damage are all caused by recurrent vaso-occlusive episodes in the lungs. These processes may cause pulmonary vascular remodeling, poor gas exchange, and a gradual decline in lung function over time (Sundd et al., 2019). Recurrent pulmonary injury may contribute to impaired gas exchange and progressive abnormalities in lung function (Brandow & Liem, 2022; Pace et al., 2021).

Chronic hemolysis contributes further through the release of cell-free haemoglobin, which scavenges nitric oxide, leading to endothelial dysfunction and increased pulmonary vascular resistance. These mechanisms are implicated in the development of pulmonary hypertension, a recognised complication of SCD (Potoka & Gladwin, 2015).

In addition, repeated episodes of ACS and pulmonary infections can cause chronic lung injury, fibrosis, and restrictive ventilatory defects. Persistent inflammation and repeated pulmonary insults may therefore contribute to the development of abnormal lung function patterns,

including restrictive, obstructive, and mixed ventilatory abnormalities observed among individuals with SCD (Brandow & Liem, 2022; Pace et al., 2021).

CHAPTER THREE:

3.0 METHODOLOGY

3.1 Study Design

This was a hospital-based cross-sectional study among individuals with sickle cell disease (SCD) aged 12 years and above attending Mbale Regional Referral Hospital (MRRH) Sickle Cell Clinic (SCC).

3.2 Study setting

The study was conducted at the SCC of MRRH, located in Mbale City, approximately 220 km east of Kampala, Uganda's capital city. MRRH is a regional referral hospital that serves as a teaching hospital for Busitema University, an internship training centre, and a referral facility for Eastern Uganda.

The hospital serves a large catchment population from the districts of Eastern Uganda and neighbouring regions. The SCC provides specialised outpatient care to children, adolescents, and adults with SCD and is staffed by paediatricians, medical officers, senior house officers, intern doctors and other members of the multidisciplinary healthcare team involved in patient care. The clinic operates once weekly, every Wednesday, and attends to approximately 150 patients, making it an important centre for the management of SCD in Eastern Uganda.

Patients attending the clinic receive routine follow-up and clinical assessment, including evaluation for symptoms and complications of sickle cell disease. Common services provided include clinical review, counselling, health education, prescription and monitoring of medications, laboratory investigations, management of acute and chronic complications, and referral to other specialist services when indicated. Hydroxyurea is prescribed as part of routine disease-modifying care for eligible patients; however, its use may depend on clinical eligibility, treatment availability, patient acceptance, and adherence.

Common complications managed among the individuals with SCD include vaso-occlusive pain episodes, anaemia, acute chest syndrome, infections, and other disease-related complications.

Routine lung-function screening using spirometry was not part of the standard clinical services offered at the clinic during the study period. Therefore, the study provided an opportunity to determine the burden and patterns of abnormal lung function among patients attending the clinic.

The choice of this study site was based on the high burden of SCD in the region and the availability of a dedicated SCC that provides continuous follow-up care to patients with SCD.

3.3 Study Population

Adolescents and adults living with SCD aged 12 years and above who received care at Mbale Regional Referral Hospital Sickle Cell Clinic between October 2025 and March 2026

3.3.1 Target population

All adolescents and adults living with SCD aged 12 years and above in Uganda.

3.3.2 Accessible population

Adolescents and adults living with SCD aged 12 years and above receiving care from the Mbale Regional Referral Sickle Cell Clinic.

3.4 Selection criteria

3.4.1 Inclusion criteria

i. Adolescents and adults aged 12 years and above with SCD confirmed by Hb electrophoresis

ii. Those who consented to take part in the study.

3.4.2 Exclusion criteria

i. Adolescents and adults with SCD aged 12 years and above who were critically ill, for spirometry to be carried out.

ii. Adolescents and adults with SCD aged 12 years and above who had musculoskeletal disorders capable of influencing spirometry results.

iii. Adolescents and adults with SCD aged 12 years and above who had verified cases of pneumonia, pulmonary tuberculosis, or any other respiratory illness being treated or diagnosed at the time of enrollment.

3.5 Sample size

The sample size was derived using the Kish-Leslie formula as stated below.

$$n = \frac{Z^2 pq}{d^2}$$

Where:

n=Sample size

Z-score for the desired confidence interval (1.96 for a 95% confidence interval)

P- Assumed true population prevalence;

q = complement of p(1-p)

d- Margin of error (0.05)

The sample size for objective 1 (Prevalence of abnormal lung function)

Calculated using a similar study with similar age groups that reported a prevalence of 18.9% for abnormal lung function (Fawibe et al., 2010).

Substituting into the formular

$$n = \frac{3.8416^2 \times 0.189 \times 0.811}{0.05^2}$$

n = 235.54

n is approximately 236 participants

Sample size for objective 1(Patterns of abnormal lung function): Calculated using a prevalence of 18.8% for restrictive pattern,9.4% for obstructive pattern, and 0% for mixed pattern. This was based on a hospital-based analytical cross-sectional study in Kenya (Olewe et al., 2024). This gave a sample size of 235,33,0 respectively.

The sample size for Objective 2

To describe the factors associated with abnormal lung function, the prevalence of previous episodes of ACS of 8% was used based on a cross-sectional study done at a tertiary hospital in Uganda by Aol et al, giving a sample size of 113 participants (Aol et al., 2024).

From a hospital-based cross-sectional study that was carried out to determine the lung function of children and adolescents with SCD at Jaramogi Oginga Odinga Hospital in Kenya, which reported a prevalence of 91% for wasting (Olewe et al., 2024) was used to give a sample size of 125.

A final sample size of 228 participants was considered practically equivalent and feasible within the available study period.

3.5.1 Sampling procedure

All individuals aged 12 and older diagnosed with sickle cell disease (SCD) and receiving treatment at the Mbale Regional Referral Sickle Cell Clinic (SCC) were included in the study. Before the start of recruitment, Research Assistants (RAs) reviewed the clinic register and identified individuals with SCD aged 12 years and older who were expected to attend the clinic. The register review was used only to identify potentially eligible patients and to facilitate

recruitment planning; enrolment was not conducted directly from the register. On each clinic day, Research assistants approached all individuals aged 12 and older after they had arrived at the SCC and screened them individually to determine their eligibility for participation before consultation. Eligibility was determined using the study inclusion and exclusion criteria. Eligible patients were provided with information about the study, and written informed consent was obtained before enrolment. For participants below the legal age of consent, assent and parental or guardian consent were obtained in accordance with the approved study protocol.

Consecutive sampling was used to enroll all eligible and consenting individuals with SCD aged 12 years and above who attended the Mbale Regional Referral Hospital Sickle Cell Clinic during the study period, until the required sample size of 228 was reached.

To prevent repeat enrolment, each participant was assigned a unique study identification number at the time of enrolment. This identification number was recorded in the participant enrolment log and was used consistently on the interview questionnaire and haemoglobin estimation form. Before enrolling a patient, the RAs cross-checked the patient's clinic identification number against the enrolment log to determine whether the patient had previously participated. Patients whose clinic identification numbers were already recorded in the enrolment log were not enrolled again. The enrolment log was reviewed regularly by the research team to identify and resolve any potential duplicate records. A screening log was maintained to document all patients assessed for eligibility, including the date of screening, age, sex, eligibility status, and the reason for ineligibility or refusal to participate. This information was used to describe the recruitment process and assess the potential for selection bias. Patients who declined participation or were ineligible were not replaced individually; instead, consecutive recruitment continued among subsequently attending eligible patients until the required sample size was achieved. The recruitment procedures were designed to minimize disruption to routine patient care. Eligibility screening and enrolment were conducted

before or after clinical consultation, as appropriate, without interfering with the delivery of routine services.

3.5.2 Study variables

Dependent variables

The dependent variables were the abnormal lung patterns, which included: restrictive, obstructive, which was either reversible or irreversible, and mixed patterns on spirometry.

Independent variables

The independent variables comprised clinical and laboratory parameters, which included**:** Recurrent episodes of Acute Chest Syndrome, Hydroxyurea use, Hb, and BMI. The demographics included: Age, Sex, Education status, Alcohol consumption and Smoking history.

3.5.3 Data collection tools

Data were collected using a structured, pretested questionnaire; the modified Medical Research Council (mMRC) Questionnaire for assessment of respiratory symptoms; a Spirolab spirometer for pulmonary function testing; a Haemocue Hb 301 System for haemoglobin estimation; a SECA weighing scale for weight measurement; and a stadiometer for height measurement. The Global Lung Initiative (GLI) reference values were used to interpret spirometry.

3.5.4 Data Collection Procedures

The study data were collected by the principal investigator and two research assistants (RAs), who were certified clinical officers with diplomas.

To guarantee the consistency and quality of the data collected, the RAs were trained on the study protocol, participant recruitment, informed consent procedures, questionnaire administration, anthropometric measurements, haemoglobin estimation, and spirometry

procedures before the start of data collection.

The data collection tools were pretested among 22 patients with sickle cell disease attending the Mbale Regional Referral Hospital Sickle Cell Clinic who met the study inclusion criteria but were not included in the final study sample. Feedback from the pretest was used to refine the questionnaire and improve the clarity of the study tools.

Eligible participants were consecutively recruited during routine clinic visits to the Mbale Regional Referral Hospital Sickle Cell Clinic. The study objectives, procedures, potential risks, and benefits were explained to all eligible participants. Written informed consent was obtained from participants aged 18 years and above. For participants aged 12–17 years, written consent was obtained from parents or guardians, and assent was obtained from the adolescents before enrolment.

Following enrolment, participants were assigned unique study identification numbers to ensure confidentiality. Socio-demographic and clinical information were collected using a structured pretested questionnaire. Thereafter, respiratory symptoms were assessed using the Medical Research Council (MRC) Questionnaire. Physical examination, anthropometric measurements, haemoglobin estimation, pulse oximetry, and spirometry were then performed according to standard operating procedures. Completed questionnaires were reviewed daily by the principal investigator for completeness and consistency before data entry.

3.6 Measurement of variables

Socio-demographic variables collected included age, sex, residence, education level, occupation, smoking history, and alcohol consumption. Clinical variables included history of recurrent acute chest syndrome, hydroxyurea use, respiratory symptoms, haemoglobin level, oxygen saturation, and body mass index (BMI).

Respiratory symptoms were assessed using the Medical Research Council (MRC)

Questionnaire. Weight was measured using a SECA weighing scale and height using a stadiometer. BMI was calculated as weight in kilograms divided by height in metres squared (kg/m²). Participants with a BMI below 18.5 kg/m² were classified as underweight, while those with a BMI of 25 kg/m² or above were classified as overweight.

Hemoglobin levels

A HemoCue HB 301 System was used for point-of-care testing to determine the Hb levels. A qualified nurse used a swab and a lancet to perform a venepuncture using conventional sterile technique. To avoid clotting, 1 to 2 mL was taken from a peripheral vein and placed in an EDTA vacutainer. To guarantee uniform distribution, the EDTA tube would be gently shaken. A tiny drop of the sample was then collected using the Haemocue microcuvette, which was then placed inside the Haemocue hemoglobin analyzer. After reading the absorbance, the device would show the hemoglobin concentration in grams per deciliter.

The Haemocue 301 system was factory calibrated for quality control; nevertheless, regular checks with Haemocue-provided control cuvettes were performed at regular intervals to guarantee accuracy. Control tests were performed for internal quality control either before to patient testing or upon opening a fresh batch of cuvettes. For external quality control, the Lancet Laboratory, an outside laboratory, was consulted for each of the thirty samples. The RAs received training on proper microcuvette filling, including preventing bubbles, overfilling or underfilling, and keeping the cuvettes at room temperature, as part of operator quality control.

Spirometry

To ascertain the pulmonary function pattern, spirometry was performed. A Spirolab spirometer produced by Medical International Research (MIR), USA, was used. The spirometer was calibrated and checked according to the manufacturer's instructions before data collection. A

calibration check was performed using a 3-L calibration syringe in accordance with the American Thoracic Society/European Respiratory Society (ATS/ERS) standards. The calibration was considered acceptable when the measured volume was within ±3% of the 3-L syringe volume. Spirometry was conducted by the principal investigator who had received training on participant preparation, standardised spirometry techniques, equipment operation, recognition of acceptable manoeuvres, and spirometry quality-control procedures. Before the test, the procedure was explained to each participant using simple and understandable language. The participant was informed that the test required a maximal inhalation followed by a rapid, forceful, and sustained exhalation until no more air could be expelled. The principal investigator demonstrated the correct spirometry manoeuvre before testing. Participants were allowed to ask questions and were given an opportunity to perform practice attempts to become familiar with the procedure before the recorded manoeuvres were obtained. The patients were instructed to sit up straight, with their feet on the ground and their legs uncrossed. After the patient's nose was occluded, the mouthpiece was inserted into their mouth, and they were told to firmly close their lips around it. After that, the patient was instructed to inhale as deeply as possible and exhale as quickly and forcefully as possible until their lungs were empty. Standardised verbal encouragement was provided throughout the expiratory manoeuvre to promote maximal effort and completion of the test. At least three repetitions of the test would be conducted. Additional attempts were allowed when the initial manoeuvres did not meet the required acceptability or reproducibility criteria. The test could not be repeated eight times in a row by patients. The acceptability and reproducibility of the spirometry manoeuvres were assessed using ATS/ERS quality-control criteria. A qualified clinician reviewed the results before final classification. The acceptable grades were A, B and C. Spirometry results that did not meet the required quality criteria were excluded from the final analysis. To check for reversibility, a 400-mcg salbutamol inhaler was used. The test was

done after a 15-minute interval from the initial dose. Bronchodilator responsiveness was assessed by comparing the post-bronchodilator FEV_1 with the baseline FEV_1. An increase in FEV_1 of at least 12% from the baseline value was considered evidence of significant bronchodilator responsiveness**.** A change in FEV_1 of less than 12% from the baseline value was classified as the absence of significant bronchodilator responsiveness. However, the absence of bronchodilator responsiveness was not considered diagnostic of chronic obstructive pulmonary disease (COPD), and the presence of bronchodilator responsiveness alone was not considered diagnostic of asthma. The diagnosis of asthma or COPD requires interpretation of spirometry findings together with the patient's clinical history, symptoms, physical examination, and, where appropriate, additional investigations. Participants with abnormal spirometry findings or clinically suspected respiratory disease were referred to a physician for further clinical assessment and appropriate management. For interpretation quality control, GLI 2012 reference values for age, sex, height, and ethnicity were used as stated below. A qualified clinician reviewed the results to confirm acceptability and reproducibility before classification. The results were stated as normal, restrictive, obstructive with reversibility, obstructive without reversibility, or mixed patterns.

Figure 2: GLI 2012 reference values for spirometry

Parameter	Percentage predicted	Classification
FEV_1/FVC	≥ 0.70	Normal
FEV_1	≥ 80%	
FVC	≥ 80%	
$FEF_{25–75\%}$	≥ 65%	
FEV_1/FVC	< 0.70	Obstructive pattern
FEV_1	≥ 80%	
FVC	≥ 80% or ≥ 20%	
FEV_1/FVC	≥ 0.70	Restrictive pattern
FEV_1	≥ 80% or < 80%	
FVC	< 80%	
FEV_1/FVC	< 0.70	Mixed pattern
FEV_1	< 80%	
FVC	< 80%	

3.7 Data management and analysis

3.7.1 Data management

A unique serial number was given to each participant for the questionnaire. The questionnaires were stored in a safe place, and their completeness was confirmed by a second check. The data were recorded using the double-entry method and input into a password-protected computer to ensure correctness.

3.7.2 Data Analysis

Data were exported from REDCap into Microsoft Excel for cleaning and analysed in R version 4.5.2 using the tidyverse, gtsummary, and broom packages. Continuous variables were assessed for normality using the Shapiro–Wilk test and visual inspection of histograms and Q–Q plots. Because most continuous variables were non-normally distributed, they are summarised as medians with interquartile ranges (IQR), while categorical variables are presented as frequencies and percentages. Missing data in independent variables (<5%) were handled using median imputation for continuous variables and mode imputation for categorical variables; participants with missing outcome data were excluded from analysis.

For objectives 1 and 2, the prevalence of abnormal lung function was calculated as the proportion of participants with any spirometric abnormality and presented with 95% confidence intervals using the Wilson score method. Patterns of abnormal lung function were summarised as frequencies and proportions across restrictive, obstructive, and mixed categories.

For objective 2, factors associated with abnormal lung function were assessed using logistic regression. Candidate predictors were first examined in bivariate analyses to generate crude odds ratios (ORs) with 95% confidence intervals. For ordered categorical variables, tests for trend were performed by modelling categories as ordinal scores in logistic regression. Variables with $p < 0.2$ were considered for multivariable logistic regression. The final model was fitted using maximum-likelihood logistic regression, with adjusted odds ratios (aORs), 95% confidence intervals, and p-values reported. Model adequacy was assessed using McFadden's pseudo-R-squared, Akaike Information Criterion (AIC), and variance inflation factors to evaluate multicollinearity. All statistical tests were two-sided, with $p < 0.05$ considered statistically significant.

3.8 Data quality control

RAs who were well-trained by the principal investigator were used for data collection. These RAs were diploma-holding clinical officers. The inclusion and exclusion criteria were carefully followed. A well-tested questionnaire was used. The principal investigator supervised the completion of the questionnaires to ensure they were accurately and thoroughly filled out.

3.9 Validity of data collection instruments

Ten per cent of the sample size that met the study's inclusion criteria underwent a pretest of the instruments. This was done to evaluate consistency, and before data collection began, any questionnaire items that needed to be modified were revised.

3.10 Reliability of data collection instruments

To ensure reliability, standardisation of the equipment, regular calibration logs, and the formal training of the clinical research assistants.

3.11 Ethical consideration

Ethical consideration was sought from BUFH-REC, award number BUFHS-2025-85. For all participants aged 12 years to 17 years, consent was obtained from their parents or guardians while they provided assent before participating in the study. Those 18 years and above provided informed consent before being enrolled in the study. Those who were found to have markedly deranged pulmonary functional test results on spirometry were referred to a paediatrician or physician for further follow-up and care. Administrative approval was also obtained from Mbale RRH.

3.12 Data Dissemination Plan

A reputable journal will publish copies of the study's findings and recommendations. Copies will be sent to the Faculty of Health Sciences Research and Ethics Committee at Busitema University (BUFHSREC). Copies will also be sent to Mbale Regional Referral Hospital (MRRH).

CHAPTER FOUR:

4.0 RESULTS AND DISCUSSION

4.1 Results

4.1.1 Study Flow and Participant Characteristics

A total of 228 participants were enrolled over 6 consecutive months of rolling clinic visits, of whom 218 (95.6%) had valid spirometry data and were included in the final analysis. Ten participants were excluded due to missing or uninterpretable spirometry results. The median age was 17.0 years (IQR 14.0–22.0). A total of 113/218 (51.8%) were adolescents aged 12–17 years, and 116/218 (53.2%) were male. Alcohol use was reported by 10/218 participants (4.6%), while smoking was reported by 2/218 participants (0.9%).

A history of recurrent acute chest syndrome (ACS) episodes was reported by 154/218 participants (70.6%), while 202/218 participants (92.7%) were receiving hydroxyurea. The median haemoglobin concentration was 7.6 g/dL (IQR: 6.6–9.6 g/dL). Overall, 71 of the 218 participants (32.6%) had severe anaemia, defined as a haemoglobin concentration of <7 g/dL. A total of 130/218 participants (59.6%) were underweight, and the median BMI was 17.7 kg/m² (IQR: 15.8–19.8). On the mMRC dyspnea scale, 80/218 (36.7%) were Grade 0 (minimal dyspnea), while 58/218 (26.6%) were Grade 3. Smoking history was excluded from the logistic regression analysis because there were zero outcome events in one exposure category.

Figure 3: Study flow diagram

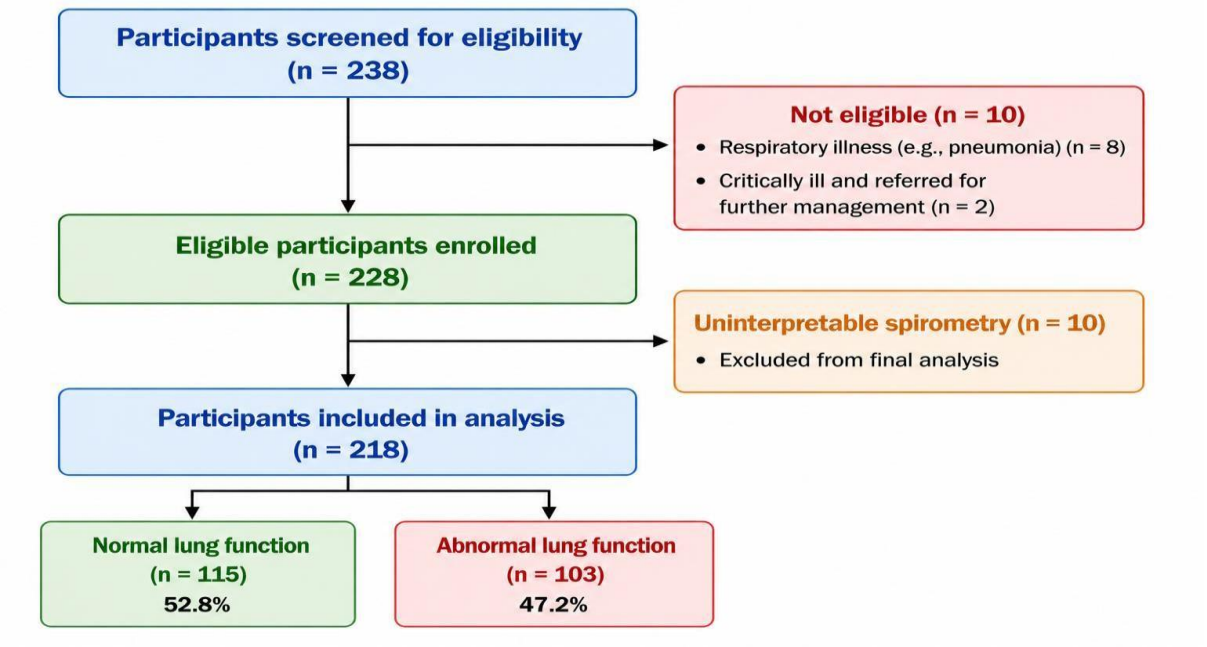


Table 1: Socio-demographic and clinical characteristics of study participants (N=218)

Variable	Category	n (%) or Summary
Total		218 (100.0)
Age (years)	Median (IQR)	17.0 (14.0–22.0)
Age category	12–17 (Adolescent)	113 (51.8)
	18–29	94 (43.1)
	30–39	9 (4.1)
	40+	2 (0.9)
Sex	Male	116 (53.2)
	Female	102 (46.8)
Alcohol use	No	208 (95.4)
	Yes	10 (4.6)
Smoking history	No	216 (99.1)
	Yes	2 (0.9)
History of recurrent ACS	No	64 (29.4)
	Yes	154 (70.6)
Hydroxyurea use	No	16 (7.3)
	Yes	202 (92.7)
Haemoglobin (g/dL)	Median (IQR)	7.6 (6.6–9.6)
Hemoglobin category	Severe anaemia (<7)	71 (32.6)
	Moderate anaemia (7–9.9)	99 (45.4)
	Mild anaemia (10–11.9)	42 (19.3)
	Normal (≥12)	6 (2.8)
BMI (kg/m²)	Median (IQR)	17.7 (15.8–19.8)
BMI category	Underweight (<18.5)	130 (59.6)
	Normal (18.5–24.9)	84 (38.5)
	Overweight (25–29.9)	2 (0.9)
	Obese (≥30)	2 (0.9)

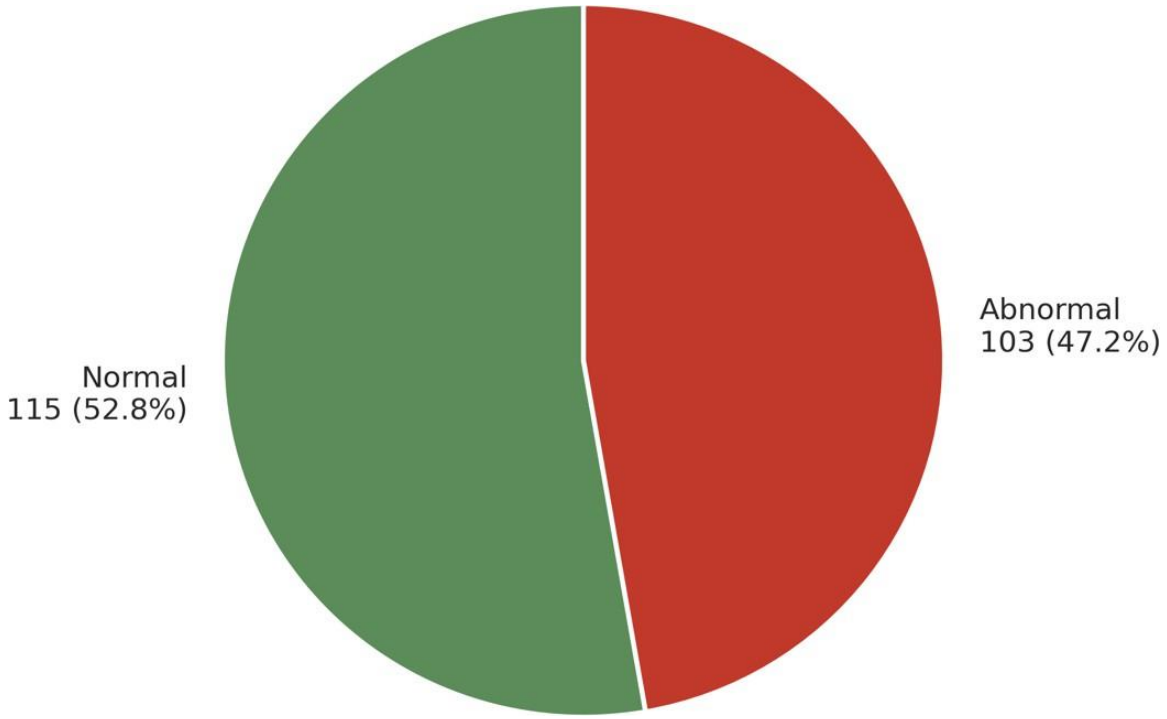
Oxygen saturation (%)	Median (IQR)	96.0 (94.0–98.0)
SpO2 category	Normal (≥95%)	161 (73.9)
	Low (<95%)	57 (26.1)
SCD age at diagnosis (years)	Median (IQR)	5.0 (3.0–7.0)
mMRC dyspnea grade	Grade 0	80 (36.7)
	Grade 1	38 (17.4)
	Grade 2	28 (12.8)
	Grade 3	58 (26.6)
	Grade 4	14 (6.4)

ACS = Acute Chest Syndrome; BMI = Body Mass Index; IQR = Interquartile Range; mMRC = Modified Medical Research Council; SCD = Sickle Cell Disease; SpO2 = Peripheral Oxygen Saturation

4.1.2 Prevalence of Abnormal Lung Function

Abnormal lung function was identified in 103 of 218 participants, yielding a prevalence of 47.2% (95% CI: 40.7–53.9%). The distribution of normal and abnormal lung function is presented in Figure 4.

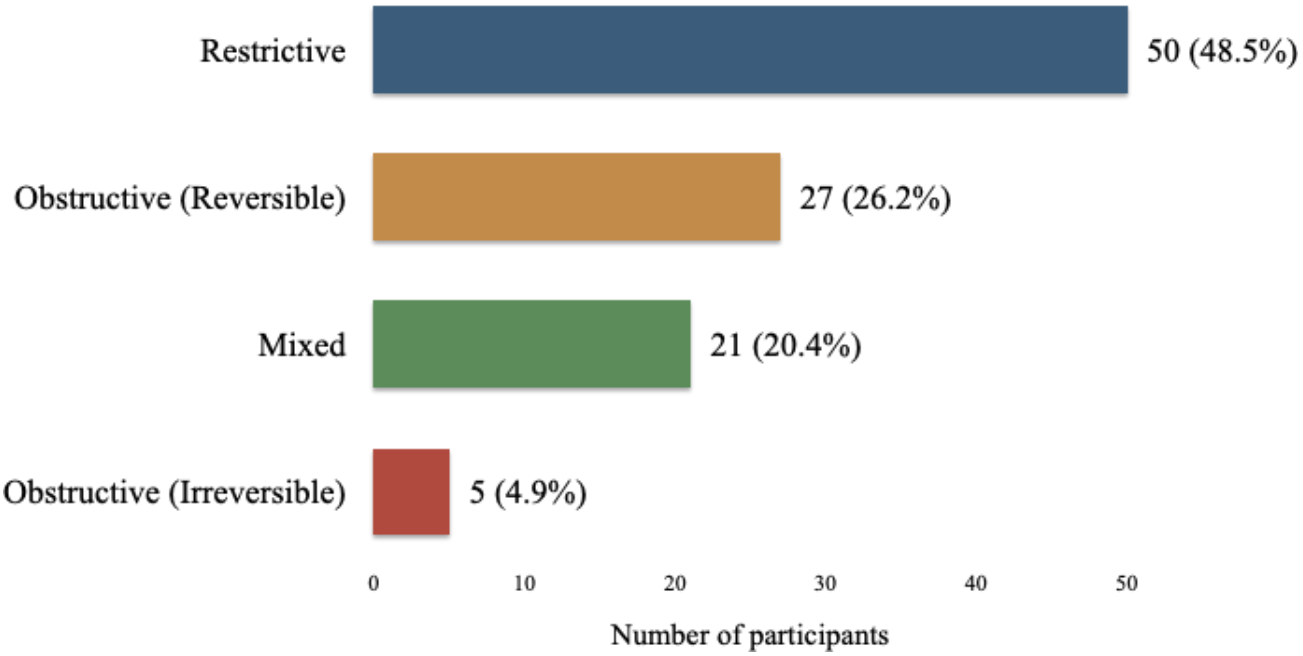
Figure 4 : Prevalence of abnormal lung function among adolescents and adults with SCD aged 12 years and above attending Mbale Regional Referral Hospital sickle cell clinic (N=218)



4.1.3 Spirometric Patterns of Abnormal Lung Function

Among the 103 participants with abnormal lung function, the restrictive pattern was the most common, occurring in 50/103 (48.5%), followed by the obstructive pattern with reversibility in 27/103 (26.2%). The distribution of patterns is illustrated in Figure 5

Figure 5: Patterns of abnormal lung function among SCD individuals with spirometric abnormalities (n=103)



4.1.4 Factors Associated with Abnormal Lung Function

In the bivariable analysis, the following factors were statistically significant with abnormal lung function: age and Hb level

Age

In bivariable analysis, increasing age and lower haemoglobin were significantly associated with abnormal lung function. Participants with abnormal lung function were older than those with normal lung function (median 19.0 years, IQR 16.0 to 25.0 versus median 16.0 years, IQR 13.0 to 20.0), and each additional year of age was associated with 11% higher odds of abnormal lung function (cOR 1.11, 95% CI 1.06 to 1.17, $p < 0.001$).

Haemoglobin

Compared to participants with mild or normal haemoglobin (≥ 10 g/dL), those with moderate anaemia (7–9.9 g/dL) had over five-fold higher odds of abnormal lung function (cOR 5.29, 95% CI: 2.17–12.93, $p < 0.001$), and those with severe anaemia (< 7 g/dL) had over thirteen-

fold higher odds (cOR 13.05, 95% CI: 5.06–33.61, p < 0.001) and these were statistically significant. A test for linear trend across the three ordered haemoglobin categories confirmed a strong dose-response relationship, with the odds of abnormal lung function increasing by approximately 3.3-fold for each step up the anaemia severity ladder (OR per category step = 3.32, 95% CI: 2.16–5.12, p for trend < 0.001).

Other variables were not statistically significant, as shown in Table 2 below

Table 2: Bivariate analysis of factors associated with abnormal lung function (N = 218)

Variable	Category	Normal (n = 115) n (%)	Abnormal (n = 103) n (%)	cOR (95% CI)	p-value
Sex	Male	61 (53.0)	55 (53.4)	Ref	—
	Female	54 (47.0)	48 (46.6)	0.99 (0.58–1.68)	0.958
Age(years)	Median (IQR)	16.0(13.0-20.0)	19.0(16.0-25.0)	1.11(1.06-1.17)	**<0.001**
ACS history	No	39 (33.9)	25 (24.3)	Ref	—
	Yes	76 (66.1)	78 (75.7)	1.60 (0.88–2.90)	0.120
Hydroxyurea use	Yes	110 (95.7)	92 (89.3)	Ref	—
	No	5 (4.3)	11 (10.7)	2.63 (0.88–7.85)	0.083
Hb category	Mild/Normal (≥ 10)	41 (35.7)	7 (6.8)	Ref	—
	Moderate (7–9.9)	52 (45.2)	47 (45.6)	5.29 (2.17–12.93)	**< 0.001**
	Severe (< 7)	22 (19.1)	49 (47.6)	13.05 (5.06–33.61)	**< 0.001**
BMI category	Underweight	74 (64.3)	56 (54.4)	Ref	—
	Normal/Overweight	41 (35.7)	47 (45.6)	1.51 (0.88–2.61)	0.135
SpO_2 category	Normal (≥ 95%)	89 (77.4)	72 (69.9)	Ref	—
	Low (< 95%)	26 (22.6)	31 (30.1)	1.47 (0.80–2.70)	0.210
Alcohol use	No	112 (97.4)	96 (93.2)	Ref	—
	Yes	3 (2.6)	7 (6.8)	2.72 (0.69–10.82)	0.155
Smoking	No	115 (100.0)	101 (98.1)	Ref	—
	Yes	0 (0.0)	2 (1.9)	—	—
Education status	Educated	113 (98.3)	97 (94.2)	Ref	—
	Uneducated	2 (1.7)	6 (5.8)	3.49 (0.69–17.72)	0.131
mMRC grade	0–1	69 (60.0)	49 (47.6)	Ref	—
	2–4	46 (40.0)	54 (52.4)	1.65 (0.97–2.83)	0.067

ACS = Acute Chest Syndrome; BMI = Body Mass Index; mMRC = Modified Medical Research Council; SCD = Sickle Cell Disease; SpO2 = Peripheral Oxygen Saturation

Multivariable logistic regression

In multivariable logistic regression adjusting for age, haemoglobin category, Recurrent episodes of acute chest syndrome, hydroxyurea use, BMI, alcohol use, and education status, haemoglobin category and increasing age remained independently associated with abnormal lung function. Haemoglobin showed the strongest association, with moderate anaemia (aOR 6.04, 95% CI 2.26 to 16.15, $p < 0.001$) and severe anaemia (aOR 13.99, 95% CI 4.98 to 39.28, $p < 0.001$) having higher odds than mild or normal haemoglobin. Each additional year of age was associated with 9% higher odds of abnormal lung function (aOR 1.09, 95% CI 1.02 to 1.17, $p = 0.009$; likelihood ratio test for age $p = 0.007$). After adjustment, non-use of hydroxyurea was independently associated with three-and-a-half-fold higher odds of abnormal lung function compared to current users (aOR 3.54, 95% CI: 1.01–12.49, $p = 0.049$). No independent associations were observed for acute chest syndrome history, BMI, alcohol use, and education status, and the model showed adequate fit (pseudo $R^2 = 0.197$; AIC = 262.1) (Table 3).

Table 3: Multivariable logistic regression of factors independently associated with abnormal lung function (N = 218)

Variable	Category	aOR (95% CI)	p-value
Age(years)	Per 1-year increase	1.09(1.02-1.17)	**0.009**
Hb category	Mild/Normal (≥ 10)	Ref	—
	Moderate (7–9.9)	6.04 (2.26–16.15)	**< 0.001**
	Severe (< 7)	13.99 (4.98–39.28)	**< 0.001**
ACS history	No	Ref	—
	Yes	1.36 (0.67–2.75)	0.305
Hydroxyurea use	Yes	Ref	—
	No	3.54 (1.01–12.49)	**0.049**
BMI category	Underweight	Ref	—
	Normal/Overweight	1.43 (0.71–2.89)	0.320
Alcohol use	No	Ref	—
	Yes	2.18 (0.47–10.04)	0.319
Education status	Educated	Ref	—
	Uneducated	4.28 (0.63–29.04)	0.137
mMRC grade	0–1	Ref	—
	2–4	1.33 (0.70–2.53)	0.386

ACS = Acute Chest Syndrome; BMI = Body Mass Index; mMRC = Modified Medical Research Council; SCD = Sickle Cell Disease; SpO2 = Peripheral Oxygen Saturation

4.2 Discussion

4.2.1 Prevalence of Abnormal Lung Function

In this hospital-based cross-sectional study, we found that 47.2% (95% CI: 40.7–53.9%) of adolescents and adults with Sickle Cell Disease (SCD) had abnormal lung function, suggesting that almost half of these individuals had spirometry abnormalities.

The increased prevalence in our study could be attributed to the inclusion of adults, who have experienced a longer duration of chronic haemolysis, repeated vaso-occlusive episodes, pulmonary infections, and acute chest syndrome, all of which can lead to ongoing lung damage over time. In addition to these factors, the physiologic age-related decline in lung function also contributes to the higher prevalence of lung function abnormalities in adult individuals with SCD.

The prevalence of abnormal lung function in our study was comparable to the 40.7% reported in a hospital-based cross-sectional study in a Nigerian tertiary hospital (Odeyemi et al., 2022). But higher than the 37.9% observed in a cross-sectional study in Ugandan children with SCD at Mulago National Referral Hospital (Aol et al., 2024) and the results from a descriptive hospital-based cross-sectional Kenyan study where 28% of children and adolescents with sickle cell disease exhibited abnormal lung function (Olewe et al., 2024).

However, our study's prevalence is lower compared to the 64% prevalence reported in a hospital-based cross-sectional study conducted among adults with sickle cell disease in Nigeria (Collins Ahamefule et al., 2025) and the 70.4% reported in an analytical cross-sectional study among adults with sickle cell anaemia attending the Ghana Institute of Clinical Genetics in Accra, Ghana (Dei-Adomakoh et al., 2019).

The lower prevalence observed in this study compared with the adult studies from Nigeria and Ghana may partly reflect differences in the age distribution of participants, disease severity,

access to care, and treatment practices. In addition, the use of different spirometry reference equations and definitions of abnormal lung function may affect prevalence estimates and limit direct comparisons across studies

4.2.2 Patterns of abnormal lung function

Among participants with abnormal lung function, the most prevalent abnormality was the restrictive pattern, occurring in 48.5% of cases, followed by the obstructive pattern with significant bronchodilator reversibility noted in 26.2%.

The higher prevalence of restrictive defects within adult cohorts may be attributed to several compounding pathophysiological mechanisms. Recurrent episodes of pulmonary vaso-occlusion, acute chest syndrome (ACS), and localised lung infarctions induce chronic, low-grade tissue inflammation, progressively leading to pulmonary fibrosis and parenchymal scarring (Brandow & Liem, 2022; Pervaiz et al., 2021).

The predominance of restrictive abnormalities may not only reflect cumulative pulmonary injury from SCD itself. However, it may also be influenced by environmental exposures, particularly biomass fuel smoke and recurrent respiratory infections, which are very common in low-income countries, as demonstrated by the cross-sectional Ugandan study (Aol et al., 2024).

This finding of restrictive pattern predominance is consistent with findings from several studies conducted in Africa and elsewhere. A cross-sectional study conducted at a tertiary hospital in central Uganda similarly reported that restrictive abnormalities accounted for over half of all abnormal spirometry patterns (Aol et al., 2024). Studies from Ghana, Nigeria and Kenya have identified restrictive physiology as the dominant pulmonary manifestation in SCD (Dei-Adomakoh et al., 2019; Odeyemi et al., 2022; Olewe et al., 2024).

The presence of reversible obstruction in over one-quarter of affected participants in our study

may reflect coexisting airway hyper-responsiveness or asthma-like disease, which has been increasingly recognised in patients with SCD. Cohen et al. highlighted that airway obstruction and airway hyper-responsiveness are common pulmonary manifestations of SCD and may occur independently of classical asthma (Cohen et al., 2015).

In a prospective longitudinal study of children with sickle cell disease in the United States, it was demonstrated that airway inflammation in SCD differs from classical allergic asthma and is characterised predominantly by neutrophilic and monocytic inflammatory pathways. The authors further proposed that this heightened inflammatory state may underlie the high prevalence of airway obstruction and airway hyper-responsiveness observed in patients with SCD, even in the absence of asthma (De et al., 2019).

Studies involving children and adolescents with sickle cell disease frequently report substantial rates of obstructive lung abnormalities, supporting the concept that airway disease may represent an early manifestation of pulmonary involvement in SCD. In a multicenter cohort of children with sickle cell anaemia conducted in the United States, Robyn Cohen et al. found that obstructive abnormalities were more than twice as common as restrictive abnormalities (16% versus 7%) (Cohen et al., 2016). Similarly, in a cohort study among children and young adults with SCD at King's College Hospital, London, United Kingdom, a distinct phenotype of younger patients characterised by obstructive lung disease and bronchodilator reversibility was observed, whereas restrictive abnormalities were more common among older participants (Lunt et al., 2018)

The differences in the distribution of spirometric patterns across studies may be related to variation in age, disease severity, SCD genotype, respiratory comorbidities, spirometry reference equations, and criteria used to classify pulmonary abnormalities (Dei-Adomakoh et al., 2019; Odeyemi et al., 2022). Both of the aforementioned studies were cohort studies

conducted in high-income nations. The prevalence of obstructive lung function abnormalities observed in research from these countries may be due to factors such as earlier identification, improved survival rates, regular pulmonary monitoring, and a greater awareness of asthma and airway hyper-responsiveness in patients with sickle cell disease.

In contrast, studies from sub-Saharan Africa often identify restrictive abnormalities as the primary pattern, which may be attributed to accumulated lung damage from recurrent acute chest syndrome, delayed diagnosis, limited access to comprehensive care for SCD, and variations in study populations and spirometry techniques.

4.2.3 Factors associated with abnormal lung function

In our study, we found that haemoglobin level was the strongest predictor of abnormal lung function. This finding is consistent with the known pathophysiology of SCD. Severe anaemia reflects more pronounced haemolysis and disease severity. Chronic haemolysis leads to nitric oxide depletion, endothelial dysfunction, oxidative stress, and vasculopathy, all of which contribute to pulmonary vascular injury and parenchymal lung damage. Lower haemoglobin concentrations also reduce oxygen-carrying capacity, increasing tissue hypoxia and promoting recurrent vaso-occlusive events within the pulmonary microcirculation.

Similar associations between anaemia severity and impaired lung function have been reported in several studies, where lower haemoglobin levels correlated with reduced forced vital capacity (FVC) and forced expiratory volume in one second (FEV1). In a cross-sectional study among adults with SCA in Nigeria, lower lung function indices were observed alongside chronic anaemia and disease burden (Musa et al., 2017)

However, other studies, including a cross-sectional study from Ghana, found no significant independent association between steady-state haemoglobin levels and lung function indices (Dei-Adomakoh et al., 2019)

A multicenter prospective cohort study of children with sickle cell anaemia in the United States found that haemoglobin concentration was not an independent predictor of pulmonary function decline (Willen et al., 2018). Nevertheless, our findings reinforce the importance of optimising haemoglobin levels as part of comprehensive SCD management.

We also observed a significant correlation between advancing age and abnormal lung function, indicating that as patients age, lung function abnormalities increase. This finding is biologically plausible and consistent with previous studies. This finding may reflect the cumulative effects of chronic haemolysis, recurrent vaso-occlusion, acute chest syndrome, pulmonary infections, and progressive organ injury over time (Brandow & Liem, 2022; Pervaiz et al., 2021)**.**

In a cross-sectional study conducted at Mulago National Referral Hospital involving 332 children with sickle cell disease, the researchers indicated that ongoing respiratory issues, such as acute chest syndrome, hemolysis, and chronic inflammation, play a role in the gradual deterioration of lung health, which may worsen as the children grow older (Aol et al., 2024).

Similarly, in an analytical cross-sectional study among adults with sickle cell anaemia in Ghana, a higher prevalence of abnormal pulmonary findings was observed in adults compared with paediatric populations, suggesting that pulmonary complications accumulate over time, resulting in progressive lung damage (Dei-Adomakoh et al., 2019).

Our findings are also consistent with reports from Nigeria, from a hospital-based cross-sectional study where Odeyemi et al. found a prevalence of abnormal lung function of 40.7% with a statistical relationship to increasing age (Odeyemi et al., 2022)

However, because this was a cross-sectional study, the observed association does not establish that increasing age caused abnormal lung function.

Non-use of hydroxyurea emerged as an independent predictor of abnormal lung function. After statistically controlling for the effect of haemoglobin, the protective association of hydroxyurea use with preserved lung function became apparent, consistent with its established role in reducing vaso-occlusive episodes and acute chest syndrome (ACS).

Hydroxyurea exerts its role through several mechanisms, including increasing fetal haemoglobin levels, reducing haemolysis, decreasing the frequency of vaso-occlusive crises and ACS and reducing the need for blood transfusions and hospitalisations, hence improving overall clinical outcomes in individuals with SCD (Rankine-Mullings & Nevitt, 2022; Ware et al., 2017). Through these mechanisms, hydroxyurea may slow the progression of chronic lung injury (Pervaiz et al., 2021).

Similar studies have suggested that patients receiving hydroxyurea experience slower declines in pulmonary function compared with untreated patients. Hydroxyurea reduces SCD complications that contribute to pulmonary injury (Aol et al., 2024).

In contrast, a large prospective multicenter cohort study conducted among children with sickle cell anaemia in the United States found no independent association between hydroxyurea therapy and the rate of lung function decline (Willen et al., 2018).

Given that over 90% of participants in our study were receiving hydroxyurea, the observed association may underestimate the true protective effect of the drug. Nonetheless, our findings provide further support for expanding access to hydroxyurea therapy in SCD populations.

The lack of an independent association between recurrent ACS and abnormal lung function in our study was somewhat unexpected, given the established role of ACS in the pathogenesis of chronic sickle cell lung disease. Although participants with recurrent ACS had 44–60% higher odds of abnormal lung function, this association did not remain statistically significant after adjustment for potential confounders. The lack of statistical significance may be due to limited

statistical power, misclassification of self-reported ACS episodes, variation in episode severity, or the high prevalence of hydroxyurea use in the cohort, which may have attenuated the effect of ACS on pulmonary outcomes.

Our findings differ from those reported in a hospital-based cross-sectional study among 332 Ugandan children with SCD attending Mulago National Referral Hospital. In their study, a history of ACS remained independently associated with abnormal lung function after multivariable analysis (aIRR 1.55, 95% CI: 1.06–2.25, p = 0.024), indicating that children with a history of ACS were 55% more likely to have abnormal lung function than those without ACS (Aol et al., 2024).

Similarly, Adegoke et al., in a cross-sectional study among Nigerian children with sickle cell anaemia, found that previous ACS was an independent predictor of impaired lung function. Children with a history of ACS were 3.6 times more likely to have impaired lung function than those without ACS, and this association remained significant after multivariable analysis (OR 5.8, 95% CI: 1.1–5.8, p = 0.03) (Adegoke et al., 2018).

A prospective cross-sectional study by Knight-Madden et al. of young adults with SCD in Jamaica demonstrated that participants with recurrent ACS had significantly lower FVC, FEV_1, and total lung capacity than those with one or no ACS episodes. Furthermore, lung function progressively worsened with increasing numbers of ACS episodes, suggesting a cumulative effect of recurrent pulmonary injury on long-term respiratory function (Knight-Madden et al., 2010).

Given the well-established role of ACS in the pathogenesis of chronic lung disease in individuals with SCD, the observed positive trend remains biologically plausible and clinically relevant.

Body mass index

In our study, BMI was not significantly associated with abnormal lung function, although participants with normal or overweight BMI had higher odds of abnormal lung function than underweight participants; the association was not statistically significant in either the crude analysis or the adjusted analysis. This finding may partly be explained by the limited variability in BMI within the study population, as most participants were underweight and very few were overweight or obese. Consequently, the small number of participants in the higher BMI categories may have reduced the statistical power and precision needed to detect a significant association. In addition, low BMI may be associated with reduced muscle mass and respiratory muscle strength, while excess body weight may affect chest-wall mechanics and lung volumes (Peters & Dixon, 2019)**.** However, these mechanisms were not directly assessed in our study.

Studies among individuals with SCD have also demonstrated that BMI may not fully capture differences in body composition, as alterations in fat-free mass, muscle mass, and other nutritional indicators may occur independently of BMI (Nartey et al., 2021).

Therefore, the absence of a statistically significant association should not be interpreted as evidence that nutritional status does not influence lung function; rather, it may indicate that BMI alone was insufficient to capture this relationship in the study population.

4.3 Study strengths and limitations

4.3.1 Strengths of the study

This study had several strengths.

i. Standardised and validated tools, including spirometry interpreted using Global Lung Initiative reference values, were used to ensure accurate assessment of lung function

ii. Objective measurements of lung function and haemoglobin concentration were obtained using calibrated equipment with established quality-control procedures.

iii. The relatively large sample size and inclusion of both adolescents and adults enhanced the generalizability of the findings.

4.3.2 Limitations

i. The cross-sectional study design did not allow the temporal relationship between the associated factors and abnormal lung function to be established. Therefore, the observed associations should not be interpreted as causal relationships

ii. Additional pulmonary investigations, including diffusion capacity testing and advanced chest imaging, were not performed. Therefore, subtle abnormalities in gas transfer, pulmonary vascular disease, or structural lung abnormalities may not have been detected. In addition, the absence of comprehensive imaging may have limited the ability to exclude all coexisting pulmonary or chest conditions that could influence lung-function results.

iii. Information on previous episodes of acute chest syndrome was obtained from participant or caregiver reports and available clinical records. This may have introduced recall bias or misclassification, particularly where the number, timing, or severity of previous episodes was not consistently documented.

iv. SCD genotype-specific analysis was not performed. Therefore, differences in lung-function abnormalities across SCD genotypes could not be assessed, and genotype may have remained an unmeasured source of confounding.

v. This study did not evaluate serum lactate dehydrogenase (LDH) levels or exposure to smoke from charcoal and other cooking fuels in households. As a result, it was not possible to determine whether there was a correlation between elevated LDH levels and household smoke exposure with abnormal lung function in the study population, which had been previously reported by Aol et al. The exclusion of these factors restricted the

study's capacity to confirm findings from the Mulago National Referral Hospital population and to analyze potentially modifiable environmental risk factors related to pulmonary impairment in individuals with sickle cell disease.

vi. The application of Global Lung Function Initiative (GLI) reference equations to a Ugandan population was another limitation noted. While the GLI equations offer standardised reference values for a wide range of ages and account for factors such as age, sex, and height, their accuracy for all Sub-Saharan African populations has not been fully confirmed. The differences between the reference group and the study group could lead to a poor fit and potential misclassification of certain participants, especially adolescents. As a result, the observed prevalence and trends of abnormal lung function should be analysed with this limitation in mind. Future research should examine how well the GLI reference equations perform within Ugandan populations and seek to establish or confirm appropriate local spirometry reference values.

CHAPTER FIVE: CONCLUSIONS, RECOMMENDATIONS AND FURTHER RESEARCH

5.1 Conclusions

Abnormal lung function was common among adolescents and adults aged 12 years and above with sickle cell disease (SCD) attending the Mbale Regional Referral Hospital Sickle Cell Clinic (MRRH). The restrictive spirometry pattern was predominant.

Increasing age, moderate and severe anaemia, and non-use of hydroxyurea were independently associated with abnormal lung function. These findings identify clinical characteristics that may help clinicians recognise patients who could benefit from closer respiratory assessment.

Because this was a hospital-based cross-sectional study, the observed associations do not establish causality and may not be generalizable to all individuals with SCD in Uganda. The findings provide local evidence on the prevalence, patterns, and factors associated with abnormal lung function and may inform the development and evaluation of targeted approaches to respiratory assessment within sickle cell care.

5.2 Recommendations

Based on the findings of this study, the following recommendations are made:

i. **Targeted respiratory assessment:** Healthcare providers at the Mbale Regional Referral Hospital (MRRH) Sickle Cell Clinic (SCC)should strengthen routine assessment of respiratory symptoms and clinical risk factors, particularly among older individuals with Sickle Cell Disease (SCD) and those with moderate or severe anaemia. Patients with respiratory symptoms, abnormal clinical findings, or other clinical indications should be prioritised for spirometry or further respiratory evaluation.

ii. **Risk-based use of spirometry:** Routine spirometry for every patient with SCD may not currently be feasible in a resource-limited setting because it requires functioning equipment, regular calibration, trained personnel, adequate testing time, quality-control procedures, and access to further diagnostic assessment. A phased, targeted approach may therefore be more practical. Spirometry could initially be prioritised for patients with persistent respiratory symptoms, recurrent acute chest syndrome(ACS), unexplained exercise limitation, low oxygen saturation, or other clinical features suggestive of pulmonary involvement.

iii. **Clinical follow-up of abnormal findings:** Patients identified with abnormal spirometry findings should undergo further clinical assessment to determine possible underlying causes and should be referred for appropriate management when indicated. Abnormal spirometry findings should not be interpreted as a definitive diagnosis without clinical correlation and, where necessary, additional investigations.

iv. **Optimisation of comprehensive SCD care:** Given the observed association between non-use of hydroxyurea and abnormal lung function, healthcare providers should assess barriers to hydroxyurea use and support appropriate access, prescribing, adherence, and monitoring in accordance with established SCD treatment guidelines. However, the present study does not establish that hydroxyurea use prevents lung-function abnormalities.

5.3 Areas for further research

i. Prospective cohort studies are needed to determine the temporal relationship between recurrent acute chest syndrome and decline in lung function among patients with sickle cell disease.

ii. Longitudinal studies should evaluate the rate of lung function decline over time and identify predictors of progressive pulmonary impairment.

iii. To properly describe pulmonary abnormalities in this population, studies utilising comprehensive pulmonary function testing, including lung volumes and diffusion capacity assessments, are required.

iv. Multi-centre studies involving different regions of Uganda should be conducted to determine the national burden and patterns of abnormal lung function among patients with sickle cell disease.

v. Future studies should explore the influence of impaired lung function on quality of life, hospitalisation rates, exercise ability, and death among people with sickle cell disease.

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APPENDICES

Appendix 1: Study Timeline (Gantt Chart)

	2025									2026		
Activity	Apr	May	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar
Proposal Development and Submission												
Research Approval Process												
Pretesting and Checklist												
Training of Research Assistants												
Data Collection, entry and Analysis												
Development of Manuscript												
Defense												

Appendix 2: Study Budget

Category	Item Description	Quantity	Unit Cost (UGX)	Total Cost (UGX)
Stationery	Pens (2 boxes)	2	8,000	16,000
Stationery	Duplicating papers (5 reams)	5	20,000	100,000
Stationery	Punching machine	2	15,000	30,000
Stationery	Stapling machine	1	15,000	15,000
Stationery	Handbooks	3	20,000	60,000
Stationery	Box files	5	8,000	40,000
Stationery	Ink pad	2	5,000	10,000
Secretarial Services	Flash disk	1	40,000	40,000
Secretarial Services	Typing and printing	Lump sum	-	1,000,000
Secretarial Services	Photocopying	Lump sum	-	500,000
Communication	Modem	1	120,000	120,000
Communication	Internet subscription	3 months	100,000	300,000
Communication	Airtime	Lump sum	-	50,000
Ethics and Administration	IRB fees	Lump sum	-	100,000
Ethics and Administration	Questionnaire pretesting	Lump sum	-	50,000
Investigations and Equipment	Haemocue and microcuvettes	1 set	-	1,100,000
Investigations and Equipment	Salbutamol inhaler	50	30,000	1,500,000
Investigations and Equipment	Stadiometer	1	150,000	150,000
Investigations and Equipment	Weighing scale	1	60,000	60,000
Investigations and Equipment	Pulse oximeter	1	80,000	80,000
Investigations and Equipment	Spirometer mouthpieces	250	5,000	1,250,000
Investigations and Equipment	Spirometer filters	250	2,000	500,000
Research Personnel	Research assistants (4)	4	400,000	1,600,000
Data Analysis	Statistical analysis	Lump sum	-	1,000,000
Report Writing	Report writing	Lump sum	-	500,000
Report Writing	Typing	Lump sum	-	50,000
Report Writing	Printing	Lump sum	-	50,000
Report Writing	Photocopying	Lump sum	-	50,000
Dissemination	Report dissemination	Lump sum	-	500,000
Grand Total				9,271,000

Appendix 3: Consent to Participate in the Study (English)

Appendix 4: Consent to Participate in the Study-English

STUDY TITLE: PREVALENCE AND FACTORS ASSOCIATED WITH ABNORMAL LUNG FUNCTION AMONG PEOPLE WITH SICKLE CELL DISEASE IN EASTERN UGANDA: A CROSS-SECTIONAL STUDY

Study No. [ ] IP No. [ ]

Investigators:

1. Dr Achiro Kevin -Principal Investigator (Student)
2. Dr Katuramu Richard-Investigator (Supervisor)
3. Assoc. Professor-Mukunya David -Investigator (Supervisor)

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Background and Rationale for the study

Am Doctor Achiro Kevin, second year resident in the Department of Internal Medicine, Busitema University Faculty of Health Sciences. I am conducting a study that will look at the Prevalence of abnormal lung function and associated factors among sickle cell disease patients aged 12 years and above Mbale RRH.

Sickle cell disease is a multisystemic disease that affects almost all systems in the body and the lungs being highly vascularized is prone to Vaso occlusive events, studies on lung function in

the setting of sickle cell disease is limited and there is no available data on lung function among sickle cell patients aged 12 years and above in our setting.

Lung complications can lead to loss in school and work days. These lung complications can also lead to morbidity or even mortality among these patients.

The study aims to determine the lung function of sickle cell patients aged 12 years and above attending Mbale Regional Referral Sickle Cell clinic

It will also determine the factors associated with abnormal lung function amongst sickle cell patients aged 12 years and above attending Mbale Regional Referral hospital sickle cell clinic.

Doing this study will contribute to the improvement in the patient care for sickle cell disease patients

You have been kindly invited to participate in the study because you receive care from Mbale Regional Referral Sickle Cell Clinic. If you decide to take part in the study, the following will take place with your cooperation:

Procedures

a) A medical interview where several questions will be asked about your medical history, including current complaints, past remarkable surgical and medical history, and family history
b) A complete physical examination will be carried out. The whole process may take around 45 minutes
c) Height and weight will be measured, and the BMI will be calculated
d) A finger prick will be done to the participant's ring finger tip to draw blood. At the tip of a haemocule, one to two drops of whole blood (10–20 microliters) will be applied, and the Hb will be read off the machine.
e) Spirometry will be performed

Your rights as a participant

Recruitment is voluntary; decline to participate in the study carries **NO** penalty whatsoever. Once recruited, you reserve the right to withdraw from the study, and withdrawal will **NOT** affect your work/ job in any way.

Risks and discomfort

Participation in this study is not expected to expose you to any serious risks. However, some procedures, such as blood collection and breathing tests, may cause minor and temporary discomfort. These effects are usually short-lived and resolve on their own. Trained health workers will be available to support you and ensure your safety throughout the study. We shall only spend about 60 minutes of your time. The procedures above may involve the following risks and discomfort

a) Drawing blood from your vein may cause you some pain and discomfort. The small amount of blood will not significantly reduce your blood levels and is not associated with any health risks.
b) There is a small risk of infection involved in drawing blood; however, all the necessary precautions will be taken to avoid the associated risk.
c) While performing the spirometry, you may feel dizzy, lightheaded, or tired from breathing in and out so deeply, or even cough, however, you need not worry as this is short-lived.
d) Because the on-call medical staff will have access to your blood test data to provide you with better care for your disease, participating in this study may result in a little bit of privacy loss. Your study records, however, will be treated with utmost confidentiality.

All data will be classified and kept in a cupboard with a locker. It is only I who will have access, and the other study participants who are directly participating. Publications arising from this study will not contain any personal information about individuals.

Benefits of participating in the study

a) Enhanced medical care

b) Early recognition of lung pathology and early management to reduce the complications associated with abnormal lung function

a) c)You will receive free laboratory check-ups and spirometry that will enhance the care you will be receiving.

Confidentiality

Because the on-call medical staff will have access to your blood test data to provide you with better care for your disease, participating in this study may result in a little bit of privacy loss. Your study records, however, will be treated with utmost confidentiality. All data will be classified and kept in a cupboard with a locker.It is only I who will have access and the other study participants who are directly participating. Publications arising from this study will not contain any personal information about individuals.

Cost of participation

There are no costs involved whatsoever in agreeing to participate in the study

Compensation for participation in the study: For agreeing to participate in the study, you will not receive any payment; however, you will be offered some benefits, as listed above. Additionally, you will be given a drink in appreciation for your time spent and for agreeing to participate in the study.

Questions about the study:

If there are any questions, concerns, or complaints about the study that you would like to ask, you could ask them right away or later using this contact: Dr. Katuramu Richard on mobile Number (0701154444 or 0787641051).

Questions about your rights as a participant

If there are any questions regarding your rights as a result of participating in this study, you can direct them to the chairman of the Busitema University Faculty of Health Sciences Research and Ethics Committee

Dr Katuramu Richard on telephone number 0787641051

Statement of voluntariness:

Participation in this study is entirely voluntary. You are free to decide whether or not to take part. If you choose to participate, you do so out of your own free will and not because of any pressure, influence, or obligation. You have the right to refuse to participate or to withdraw from the study at any stage without giving a reason. Choosing not to participate or deciding to withdraw will not affect the quality of medical care or services you receive at the hospital, and you will not lose any of your rights or benefits as a patient

Dissemination of results:

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You get feedback on findings and progress of the study, and any new information that affects the study or data that has clinical relevance to research participants (including incidental findings) will be made available to you and the hospital administrators.

Busitema University Faculty of Health Sciences Research and Ethics Committee will receive their copies as well.

Ethical approval:

The study has been approved by Busitema University Faculty of Health Sciences Research Ethics Committee (BUFREC), which is an accredited Ugandan-based REC

STATEMENT OF CONSENT

Study No..... **IP No**.....

..... has described to me what is going to be done,

the risks, the benefits involved, and my rights regarding this study. I understand that my decision to participate in this study will not alter my usual medical care. In the use of this information, my identity will be concealed. I am aware that I may withdraw at any time. I understand that by signing this form, I do not waive any of my legal rights but merely indicate that I have been informed about the research study in which I am voluntarily agreeing to participate. A copy of this form will be provided to me.

Name .....

Signature/thumb print of participant .....Date .....

Name.....Signature of witness (if applicable).....Date.....

Name .....

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Signature of interviewer/Person obtaining informed consent .....Date .....

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Appendix 4: Consent to Participate in the Study (Lumasaba)

ETITULO KY'ESOMI: OBWENE N'EBISOLE EBIFUNYIRWAHO KU KUTAKORA BULAYI KW'EMIBIRA MU BANTU ABALINA ENDWARA YA SICKLE CELL MU BUKIIKA BWA UGANDA: KIKUSOMI KY'OKUKWATANGA EMIRIMO EKIRAIRWE

Sitoidi No. ____ IP No. _____

Abashomi ba Sitoidi:

1. Dr Achiro Kevin – Omulabhalasi Mukulu (Omwana wa Eddunda)
2. Dr Katuramu Richard – Omulabhalasi wa Sitoidi (Omusomesa)
3. Assoc. Prof. Mukunya David – Omulabhalasi wa Sitoidi (Omusomesa)

BUSITEMA UNIVERSITY FACULTY OF HEALTH SCIENCES APPROVED VALID UNTIL 28 SEP 2026 RESEARCH & ETHICS COMMITTEE P. O. BOX 1460, MBALE

Obulambula n'Obuteekateeka bwa Sitoid

i

Nze niko Dr Achiro Kevin, nze ndi mu mwaka gwa bbiri mu Department ya Internal Medicine, Busitema University Faculty of Health Sciences. Nsobola okutandika sitoidi egy'okusemaliza okulambula obubala bwa umwova ogusadiza (abnormal) ne ebintu ebikawuikiriza mu bantu

abali na sickle cell disease abazahakuliddwa okumala emyaka 12 okusobola okusuliriza mu MbaleRRH.

Sickle cell disease signa endwadde eyosokolamu ebifuula ebingi muruumi gwa muntu, ate umwova guliko endwadde ez'okunutizibwa (vaso-occlusive events), naye sitoidi ku bumanyi bwa lung function ng'oli mu sickle cell disease kuliko banene nnyo, era tetulina data mu ggwanga ku bantu abali na SCD abazahakuliddwa emyaka 12 oba eddene.

Obulwadde bwa mwova busobola okukusembayo ebisoma oba enkole eby'ekiyitirivu, era kye kisinga okukyampa oba okuwalibwa mu bantu abaali na SCD.

Obulimba bw'Omulamwa: Okugezesa obumanyi bwa mwova mu bantu abali na SCD abazahakuliddwa emyaka 12 okusobola okuva mu Mbale Regional Referral Sickle Cell Clinic Okukulemberamu ne ebintu ebikawuikiriza mu budde bwa mwova mu bantu abali na SCD abazahakuliddwa emyaka 12 okusobola okuva mu Mbale RRH Sickle Cell Clinic. Okutandika sitoidi kuno kutaaga okuteekateeka mu kwongera obujjanjabi obuli ku bantu abali na SCD.

Munyweebwa ekirabo okujja okuva mu nito mugyenye kuno kubanga muno mugya jjukibwa olushemezi ku Mbale Sickle Cell Clinic. Ssinga mweyagala kujja mu sitoidi eno, bino bingi bigenda kukukolebwa n'okwetaba kwammwe:

Emirimu:

a) Okusomesa ku nzikiza y'obujjanjabi, okulabirirwa ebifo ebigamba ku mbeera y'obujjanjabi, ebisanyizo eby'obujjanjabi, n'omukaayiro gwa family.

b) Okuzuulirwa kw'omubiri kwonna kukolebwako – bino byetaaga obudde bwa akawungeezi ka 45 amaminisa.

c) Okuyingira obunene n'obulemu, okulaba BMI.

d) Okudda ekimuli ku kitwe ky'omutwe (finger prick) okutonda eddagala eri omuntu. Ekitundu

1 oba 2 droppa za blood (10–20 µL) zijja kusikibwa ku haemocue, era hemoglobin kyijja kuggyibwa.

e) Spirometry ejja kukolebwawo.

Amanagiriro go ng'omutabani wa Sitoidi

Okutandikiranga kweru ku mutwe gwo, obuteeka mu sitoidi tebujja kukulembera kintu kyonna. Ssinga okusalawo okutandika, olina akakwate kamala ku sitoidi, era okumalawo tebijja kutuukiriza n'obuva.

Enkoma n'okukazoza:

Sitoidi eno tetizikiriza nnyingi eri ggwe. Waliwo ekiseera kya 60 amaminisa. Ebirimu bino:

a) Okuttayo omuwangwa gw'eddiro ogw'okukola ebirungo, genda kuba ku mutima gumu, kale treat.

b) Waliwo obulabe obuto bw'okutonda blood, era bwenkima tezigenda kuyitako kintu.

c) Ensobi y'okutonda droppa kwiikira, naye tulina ebyokulondawo ebyokka eby'okujja tezikwasaganya
ensobi.

d) Eby'okukola spirometry osobola okuba akoofu mu mutwe, okunyooma oba okwefulumya, naye tusuubira nga kiba kiddugavu.

4) Abalambwa abasooka okuzuula data ya ebibaddewo ku blood test bagenyi wansi yaffe, era eno ye privacy ezo. Obujulizi bwammwe bujja kusibwa mu kitabo era kikolebwa mu locker. Nze ndeeba data, abantu abalala abatabadde mu sitoidi basomesa. Publikations tezijja kuba n'ebintu bya buli muntu.

Eby'obulamu byo n'obuyambi:

a) Obujjanjabi bweyongedde

b) Okuzuula embeera ya mwova nga bwe kisusse, okutandika okufumba kwekulwanyisa

c) Weyangibwa obulungi mu laboritori n'okusomba spirometry ku buntu.

Obuvunaanyizibwa bwa Privacy:

Data emisanyizo gy'obusolo businziira ku blood test gulina tone, naye data yako yabadde eiffe mu weetaaga. Bayera mu kitabo kyasooka kikattibwa mu locker. Nze bwefuna okuba mu mutuufu. Publikations tezijja kuba ne bweyalefala mmwe.

Endadde eby'ensimbi:

Waliwo ensimbi zonna, oba pendwa kulwana nayo – tewali ky'osomba.

Okubonyezebwa:

Okhukhwama mu bukhafu buno, tikhu khumwikhila sente yosi; khane okhulonda khukhwama mu bukhafu buno wakhwaba n'obulayi obukhasi bwalondolwamo wuli, era wakhu khusindikilwa kumwa kamalwa ka khukhwama khu masikhani.

9/17/2025

Version II

Ebibuuzo ku sitoidi:

Ssinga waliwo ebibuuzo, osobola kubibuuzibwa kati oba okusooka ggwe wakusanga: Dr Katuramu Richard ku no. 0701154444 oba 0787641051.

Ku ddembe lyo:

Ssinga waliwo ebibuuzo ebikwatagana n'ebirungi byo okukozesebwa mu sitioidi, osobola kusaba ebirungi ku chairman wa BUFREC:

Dr Katuramu Richard ku 0787641051.

Ebiragiriro byo:

Okujja mu sitoidi eno kubeera ekiragala era osobola kusimbukira wakati. Otandike okumala ekiseera kyonna olina ennono.

Okumulula eibbi:

Okyusibwa ku bisanyizo n'enjawulo za sitoidi, na buli nkuru eny'uwaaza. Buli data ebirala eya klinika, jakyusibwa fue wamu n'ekitongole era ekitongole kyakukolako.

Okusuubirwa kwa Ethics:

Sitoidi enyweeyongerwemu ne BUFREC, Uganda.

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EKY'OKUTEESA OKW'ENTANDIKO

Sitoidi No. _____ IP No. ____,

_____ategeza nze kye kijja kukolebwa, enkiiko, ebyembi

n'obuvunaanyizibwa. Ntegedde nti.siteidi okugenda obulungi tebikyusa bujjanjabi bwange obwa bulijjo. Mu ky'okuteesa kino, erinnya lyange terijjakwogera. Ntegezezza nti osobola kusimbula ekiseera kyonna. Ntegezezza nti nteeka kasigazza wange tekwonya pulisa zange era kwekyusa siteidi. Amplastice wano.

Erinnya .....

Signature/thumb print ya mutabani .....Date..... Erinnya wa musango (ssinga alipo) ..... Signature/thumbprint..... Date ..... Erinnya wa onouku no kufunamu consent .....

Signature .....Date .....

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Appendix 5: Consent to Participate in the Study (Luganda)

OKUKIRIZA OKW'OKUTWALA MU KUNOONYEREZA

ERINNYA LY'OKUNOONYEREZA: OBUNGI N'EBINTU EBIGENDANA N'OBUTAKORA BULUNGI KW'EBIBUMBA BY'OKUSINGA OMUKKA MU BANTU ABALINA OBULWADDE BWA SICKLE CELL MU BUVANJUBA BWA UGANDA: EKITUNZI KY'OKUNOONYEREZA EKITALAZE KU LUSEGERE LUMU.

Enamba y'Okunoonyereza: _____IP No: _____

Abanoonyereza:

1. Dr Achiro Kevin – Omunoonyereza Omukulu (Omuyizi)
2. Dr Katuramu Richard – Omunoonyereza (Omugoberera)
3. Assoc. Prof. Mukunya David – Omunoonyereza (Omugoberera)

1

Version II 9/17/2025

Enkola n'Enteekateeka y'Okunoonyereza

Nze Dr Achiro Kevin, ndi omuyizi wa mwaka ogw'okubiri mu Department y'Internal Medicine, Faculty of Health Sciences eya Busitema University. Nkolera okunoonyereza kuno okulaba ku bubonero bw'okulemererwa kw'empiyo n'ebintu ebigenda ne kyo mu bantu abali waggulu w'emyaka 12 abali ne sickle cell disease e Mbale Regional Referral Hospital. Sickle cell disease ye ndwadde etta ensolo zonna z'omubiri, era empyeyo olw'okuba eyeyongera okutambuza omusaayi esobola okulumba ennyo. Mu Uganda tetulina bujulizi bulungi ku mbeera y'empiyo mu bantu ba sickle cell disease abatandise emyaka 12, era kino kye tugenda okunoonyerezaako. Obuzibu bw'empiyo buyinza okuleetera okuvundira kw'amasomo, okukosa emirimu n'okusobola n'okufa.

Tugenderera okulaba obulungi bw'empiyo mu bakugu abanoonyerezebwaako, era n'okulaba ebiyinza okukitwala.

Owewandiisiddwa olw'okuba oyambibwa mu ddwaaliro lya Mbale Sickle Cell Clinic. Ssinga okkiriza okwetaba mu kunoonyereza kuno, bino byebigenda kukolebwa:

Ebinaakolebwa:

a) Okulambulwa n'okubuuza ku mbeera yo ey'obulamu – okubuuzibwa ebibuuzo ku bulwadde bwo, ebyakuddako, eby'eddembe ly'obufumbo.

b) Okukebera omubiri gwo gwonna – kigenda kumala akaseera ka ddakika 45.

c) Okupimibwa obuwanvu n'obuzito, era BMI ejja kubalibwa.

d) Okukolebwa akamwa ku munwe ogw'obusawo, okuwandiika omusaayi omutono (10–20

microliters) ku Haemocue, era ebivudde mu musaayi bijja kusomwa.

e) Okukola spirometry – okulaba obulamu bw'empiyo yo.

Ebintu byo nga Mwettabye

- Okwetaba kwa buwa nga bw'oyagala.
- Okugaana okwetaba tekikosa budde bwo ku ddwaaliro.
- Osobola okukyuka n'ova mu kunoonyereza bino nga buweereza.
- Ebigenda okukolebwa si bya bulabe bungi.

Obusoomoozi Buyinza Okuvaamu:

a) Okukola ku musaayi kuyinza okuleetera akubala, naye tekikosa nnyo omusaayi.

b) Waliwo akasoomoozi akatono k'ensiri, naye tusobola okukozesa ebikwekateeko eby'okugikuuma.

c) Spirometry eyinza okutwala obunnyogovu, okufuna akavuvu, oba okukolokota, naye bino biba bya kaseera katono.

d) Abakozi b'eddwaaliro balina okufuna ku byava mu musaayi gwo okumanya engeri

y'okujjanjaba, era bino biyinza okutwala akawandiiko ako'biseera. Naye ebyawandiikibwa bijja kubeerawo mu kyama, biggaliddwa, era byetaggibwa byokka.

Ebifuna okuva mu kunoonyereza:

a) Obujjanjabi obw'omulembe.

b) Okuzuula obulwadde bw'empiyo nga tebunnafuna buzibu.

c) Wofuna ku bwereere laboratory check-ups n'okukola spirometry.

Ebikwata ku Kyama:

Data yonna egenda kukuumibwa mu kyama, mu kabati akaggalwako, era eraba nze n'abantu abakola ku kunoonyereza kwokka. Ebinafulumizibwa mu bitabo tebinaabangaamu mannya go.

Ebyenfuna:

- Okukkiriza okwetaba mu kunoonyereza kuno tojja kufuna mpeera yonna; naye ojja kufuna eby'obufuzi ebimu, nga bwe bisookeddwa waggulu, era ojja okuweebwa ekinywero nga kye kisasu olw'ebbanga lyo l'osudde n'okukkiriza okwetaba mu kunoonyereza kuno.

Okubuuza ku Kunoonyereza:

- Ssinga olina ebibuuzo, osobola kubibuza kati oba okuyita ku Dr Katuramu Richard: 0701154444 / 0787641051.
- Ssinga olina ebibuuzo ku ddembe lyo nga mutabani, oyinza okwogera ne Ssentebe wa Research and Ethics Committee e Busitema University: Dr Katuramu Richard ku 0787641051.

Okukiriza kwa Bwa Nfuna:

- Okwetaba kwa buwa – osobola okukyuka buli kaseera nga toyonoona.
- Ebivudde mu kunoonyereza bijja kuba bikusimbulwako, era n'ebinaaba ne makulu ku ddagala bijja kusasulwa.

Okukkirizibwa kwa Ethics:

- Kunoonyereza kuno kwakkiriziddwa Busitema University Faculty of Health Sciences Research and Ethics Committee (BUFREC), ekitongole ekirambika mu Uganda.

OKW'OKUKKIRIZA

Enamba ya Sitoidi: _____IP No: _____

_____ansinzidde ku kunnyonnyola eby'okukolebwa, obulabe, ebiganyulo, n'ebisembayo ku ddembe lyange. Ntegedde nti okwetaba kwange tekikyusa kujjanjabwa kwange okwa bulijjo. Erinnya lyange lijja kukweka. Ntegedde nti osobola okuleka okwetaba buli kaseera. Ntegedde nti okuteeka omukono wange kuno si kulagisa nti nzibiddwa ddembe lyange, wabula nti nkoze kino nga mazima era nga nkozeddwako ennyonnyola. Ndigenda kufuna akopi ak'akusaako

Erinnya ly'Omwetabye: _____

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Omukono / obuko obuliko agalamu: _____ Olunaku: ___

Erinnya ly'omujulizi (ssinga aliko): _____

Omukono: _____ Olunaku: _

Erinnya ly'Omutwala Obukkakafu: _____

Omukono: _____ Olunaku: _

Appendix 6: Assent to Participate in the Study (English)

STUDY TITLE: PREVALENCE AND FACTORS ASSOCIATED WITH ABNORMAL LUNG FUNCTION AMONG PEOPLE WITH SICKLE CELL DISEASE IN EASTERN UGANDA: A CROSS-SECTIONAL STUDY

Study No. [ ] IP No. [ ]

Investigators:

1) Dr Achiro Kevin -Principal Investigator (Student)

2) Dr Katuramu Richard-Investigator (Supervisor)

3) Assoc. Professor-Mukunya David -Investigator (Supervisor)

Background and Rationale for the study

Am Doctor Achiro Kevin, second year resident in the Department of Internal Medicine, Busitema University Faculty of Health Sciences. I am conducting a study that will look at the Prevalence of abnormal lung function and associated factors among sickle cell disease patients aged 12 years and above Mbale RRH.

Sickle cell disease is a multisystemic disease that affects almost all systems in the body and the lungs being highly vascularized is prone to Vaso occlusive events, studies on lung function in the setting of sickle cell disease is limited and there is no available data on lung function among sickle cell patients aged 12 years and above in our setting.

Lung complications can lead to loss in school and work days. These lung complications can also lead to morbidity or even mortality among these patients.

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The study aims to determine the lung function of sickle cell patients aged 12 years and above attending Mbale Regional Referral Sickle Cell clinic

It will also determine the factors associated with abnormal lung function amongst sickle cell patients aged 12 years and above attending Mbale Regional Referral hospital sickle cell clinic.

Doing this study will contribute to the improvement in the patient care for sickle cell disease patients.

You have been kindly invited to participate in the study because you receive care from Mbale Regional Referral Sickle Cell Clinic. If you decide to take part in the study, the following will take place with your cooperation:

Procedures

f) A medical interview where several questions will be asked about your medical history, including current complaints, past remarkable surgical and medical history, and family history
g) A complete physical examination will be carried out. The whole process may take around 45 minutes
h) Height and weight will be measured, and the BMI will be calculated
i) A finger prick will be done to the participant's ring finger tip to draw blood. At the tip of a haemocule, one to two drops of whole blood (10–20 microliters) will be applied, and the Hb will be read off the machine.
j) Spirometry will be performed

Your rights as a participant

Recruitment is voluntary; decline to participate in the study carries **NO** penalty whatsoever. Once recruited, you reserve the right to withdraw from the study, and withdrawal will **NOT** affect your work/ job in any way.

Risks and discomfort

This study poses no serious risks to you. But we shall only spend about 60 minutes of your time. The procedures above may involve the following risks and discomfort

e) Drawing blood from your vein may cause you some pain and discomfort. The small amount of blood will not significantly reduce your blood levels and is not associated with any health risks.
f) There is a small risk of infection involved in drawing blood; however, all the necessary precautions will be taken to avoid the associated risk.
g) While performing the spirometry, you may feel dizzy, lightheaded, or tired from breathing in and out so deeply, or even cough, however, you need not worry as this is short-lived.
h) Because the on-call medical staff will have access to your blood test data to provide you with better care for your disease, participating in this study may result in a little bit of privacy loss. Your study records, however, will be treated with utmost confidentiality. Alldata will be classified and kept in a cupboard with a locker. It is only I who will have access, and the other study participants who are directly participating. Publications arising from this study will not contain any personal information about individuals.

Benefits of participating in the study

c) Enhanced medical care
d) Early recognition of lung pathology and early management to reduce the complications associated with abnormal lung function

b) c)You will receive free laboratory check-ups and spirometry that will enhance the care you will be receiving.

Confidentiality: Because the on-call medical staff will have access to your blood test data to provide you with better care for your disease, participating in this study may result in a little bit of privacy loss. Your study records, however, will be treated with utmost confidentiality. All data will be classified and kept in a cupboard with a locker.it is only I who will have access and the other study participants who are directly participating. Publications arising from this study will not contain any personal information about individuals.

Cost of participation

There are no costs involved whatsoever in agreeing to participate in the study

Compensation for participation in the study: For agreeing to participate in the study, you will not receive any payment; however, you will be offered some benefits, as listed above. Additionally, you will be given a drink in appreciation for your time spent and for agreeing to participate in the study.

Questions about the study:

If there are any questions, concerns, or complaints about the study that you would like to ask, you could ask them right away or later using this contact: Dr. Katuramu Richard on mobile Number (0701154444 or 0787641051).

Questions about your rights as a participant

If there are any questions regarding your rights as a result of participating in this study, you can direct them to the chairman of the Busitema University Faculty of Health Sciences Research and Ethics Committee

Dr Katuramu Richard on telephone number 0787641051

Statement of voluntariness:

Participation in this study is voluntary, and you may join on your own free will. You also have the right to withdraw from the study at any time without penalty.

Dissemination of results:

You get feedback on findings and progress of the study, and any new information that affects the study or data that has clinical relevance to research participants (including incidental findings) will be made available to you and the hospital administrators.

Ethical approval:

The study has been approved by Busitema University Faculty of Health Sciences Research Ethics Committee (BUFREC), which is an accredited Ugandan-based REC

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Statement of Assent

I have been told what the study is about, and I understand what will happen if I choose to join. I know I can ask questions and that I can stop at any time if I change my mind. No one will be upset with me. I agree to be part of this study.

Name of Participant (Child/Minor): _____

Signature/Thumbprint: _____ **Date:** _____

Statement of Permission (Parent or Guardian)

I have read (or been told about) this study, and I understand the purpose, procedures, risks, and benefits. I give permission for my child to take part in this study. I understand that participation is voluntary, and I reserve the right to withdraw my child at any time.

Name of Parent/Guardian: _____ **Signature:** _ **Date:** _____

_____

Name of Witness: _____

Signature: _____ **Date:** _____

Name of Person Obtaining Assent: _____ **Signature:** . **Date:**

_____

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Appendix 7: Assent to participate in the study (Lumasaba)

ETITULO KY'ESOMI:

Obwene n'ebisole ebirina enyakha ku kutakora bulayi kw'emibira mu bantu abalina endwara ya Sickle Cell mu Bukiika bwa Uganda: Kikusomi ky'ekirairwe.

Enamba y'Omusomo: _____ **Enamba ya IP:** _____

Basuubizi b'esomi:

1. **Dk. Achiro Kevin** – Omusomozi omukulu (Omuyizi)
2. **Dk. Katuramu Richard** – Omusomi (Omulabirizi)
3. **Asos. Prof. Mukunya David** – Omusomi (Omulabirizi)

Enkalo n'Ensonga Y'Esomi

Ndi Dk. Achiro Kevin, omuyizi ow'omwaka ogw'okubiri mu kitongole ky'abasawo b'eby'omunda ku Busitema University mu Faculty y'eby'obulamu. Ndi kukola okusomi okulondoola obwene bw'abantu abalina endwara ya sickle cell abaali wamu n'obutakora bulungi kw'emibira okuva ku myaka 12 okutuka waggulu ku ddwaliro lya Mbale Regional Referral Hospital.

Endwara ya sickle cell etta ebifo bingi mu mubiri, era emirambo gya munda (emibira) gikosebwa nyo olw'okubaire nga gikwatibwako nyo omusaayi. Ebizibu ku mibira biyinza okukosa okusoma kw'abayizi oba emirimu gy'abakulu. Wabula mu kitundu kyaffe tewali

kusomi kwa ddala kwakoleddwa ku mibira mu bantu balina sickle cell okuva ku myaka 12 okutuka waggulu.

Esomi lino ligenderera okumanya engeri emirambo gya munda gy'ekola mu bantu balina sickle cell era liramula ebigenderako ku kutakora bulungi kw'emibira. Kino kijja kuyamba mu kwongera ku mutindo gw'okujanjaba abo abalina sickle cell.

Ompakasa oyingire mu kusomi kubanga ofunira obujanjabi ku ddwaliro lya Mbale Sickle Cell Clinic. Bw'osiima okwetaba, bino byebijja kubaawo:

Enkola ezijja okukolebwa

a) Tukubuuza ebibuuzo ebikwata ku byafaayo byo eby'obulamu.

b) Tukukola ku mubiri wonna (physical examination) nga bitwala akaseera ka ddakiika 45.

c) Tukupima obuwanvu n'obuzito okukola BMI.

d) Tukukolako akawundo ku munwe okufuna omusaayi ogutono okulinganiza Hb.

e) Tukukola spirometry (okupima obusobozi bw'emibira gy'okussa).

Eddembe ly'omwetabye

Okwetaba kwa kwegasa. Okugaana okwetaba tekikuleetera buzibu bwonna. Era bw'osiima okwetaba, osobola okulekayo ku lw'okwagala kwo nga tekikosa mirimu gyo.

Obulabe n'okutabanguka

Obulabe obunene tebuli. Wabula, ebimu ku bino bijja kubaamu obutabanguka:

- Akawundo ka munwe kayinza okutwala akawuubaalo
- Osobola okuwulira obuzibu, obutabanguka nga okukaluubirira n'okwesittala ng'okukola spirometry
- Akabongeko k'obukaba (privacy) kasobola okukosebwa kubanga abajjanjabi bajja kulaba ku mikutu gyo egifunyeemu ebyava mu musaayi Wabula, ebyo byonna bijja kukwatibwa mu kyama, era ebifaananyi byo tebijja kumanyibwa mu kusomooza kwaffe.

Ebifo by'okuganyulwa mu kusomi

- Ojja kufunira obujanjabi obulungi
- Ojja okumanyibwa mangu oba olina obuzibu ku mubira
- Ojja kufunira okukebera kwa lab ne spirometry ku bwereere

Obukakafu bw'ebiwandiiko byo

Ebyafaayo byo bijja kukuumibwa mu kyama n'obukuumi obugumivu. Wano mbyonna bijja kubikwatibwa na kyama n'ekisumuluzo. Si muntu mulala ajja kuba n'obukugu ku byo wabula nze omusomi n'abalala abetaba.

Omugaso g'okwetaba

- Okhukhwama mu bukhafu buno, tikhu khumwikhila sente yosi; khane okhulonda khukhwama mu bukhafu buno wakhwaba n'obulayi obukhasi bwalondolwamo wuli, era wakhu khusindikilwa kumwa kamalwa ka khukhwama khu masikhani.Tewali mpa abo ogenda okuwaayo

Ebibuuzo ku kusomi

Bw'oba n'ekibuuzo kyonna ku kusomi, osobola okukibuza kati oba oluvannyuma:

Dk. Katuramu Richard ku: **0701-154444 oba 0787-641051 Ebibuuzo ku ddembe lyo**

Bw'oba n'ebibuuzo ku ddembe lyo nga omwetabye mu kusomi, osobola okubibuulira ssentebe wa **Busitema University Faculty of Health Sciences Research Ethics Committee** – Dk. Katuramu Richard ku **0787-641051**

Okusiima okw'obwennyini

Okwetaba kwa kwegasa. Ojja kwesalirawo wekka. Era osobola okukoma okwetaba buli kaseera nga tosóbezeddwa.

Okumanyisa ebyava mu kusomi

Ojja kufunira ebyava mu kusomi n'obubaka obumpya obuyinza okukukosa, n'okumanyisa eddwaliro ku bya mugaso.

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Okukkirizibwa okw'obwanakyewa

Esomi lino lyakkiriziddwa **BUFREC** (Busitema University Faculty of Health Sciences Research Ethics Committee)

Okukkiriza

Nnyumiziddwa ku kusomi kuno, era nkitegedde ebigenda okukolebwa ssinga nsalawo okwetaba. Mmanyi nti nsobola okubuuza ebibuuzo era nsobola okukoma buli kaseera. Nsiimye okwetaba mu kusomi kuno.

Erinnya ly'Omwana: _____

Omukono/Obulago: _____ **Olunaku:** _____

Okukkiriza kwa Muzzadde/Omulera

Nsomye (oba banyumiziddwa) ku kusomi kuno, era nkitegedde ebigendererwa, engeri gy'ekolebwa, obulabe n'emigaso. Nsiimye omwana wange okwetaba. Nkitegedde nti kwegesa era nsobola okukomya buli kaseera.

Erinnya lya Muzzadde/Omulera: _____ **Omukono:** _____ **Olunaku:** _____

Erinnya ly'Omugezi Omukono: (Witness): _____

Olunaku: _____

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Erinnya ly'Omutwala Omukono: **Assent:**

Olunaku: _____

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Appendix 8: Assent to participate in the study (Luganda)

ERINNYA LY'EBY'OKUNOONYEREZA:OBUNGI N'EBINTU EBIFAANANAKO EBIKWATAGANA N'OBUTAKOLA BULUNGI KW'EBY'OBULAMU BW'AMANNYO G'OKUSSA MU BANTU ABALINA OBULWADDE BWA SICKLE CELL MU BUVANJUBA BWA UGANDA: OKUNOONYEREZA OKUSINGA KU LUSEGERE LUMU.

Namba y'Okunoonyereza: _____ **Namba ya IP:** _____

Abanoonyereza:

1. **Dk. Achiro Kevin** – Omukulembeze w'okunoonyereza (Omuyizi)
2. **Dk. Katuramu Richard** – Omunoonyereza (Omugoberera)
3. **Asosoweeta Prof. Mukunya David** – Omunoonyereza (Omugoberera)

Ennyanjula n'Ensonga y'Okunoonyereza

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Nze **Dk. Achiro Kevin**, omuyizi wa mwaka ogw'okubiri mu kitongole ky'eby'obulamu munda ku Busitema University Faculty of Health Sciences. Nkozesa okunoonyereza okugenderera

okumanya obungi bw'abantu abalina obuzibu bw'emibira egy'okussa mu bantu abalina sickle cell okuva ku myaka 12 waggulu ku Ddwaliro lya Mbale Regional Referral.

Obulwadde bwa sickle cell bwekosa emibiri mingi mu mubiri, era ebibumba by'amannyo g'okussa (emibira) bisobola okwongera okukosebwa olw'ensonga z'omusaayi okubeera nga gufunama. Mu Uganda ebikolebwa ku mbeera y'emibira mu balwadde ba sickle cell bakyali bitono, ate n'amawulire ku bantu abava ku myaka 12 waggulu tebaliiko.

Okunoonyereza kuno kugenderera okumanya engeri amannyo g'okussa bwe gakola mu balwadde ba sickle cell n'ebintu ebirina enjawulo ebikwatagana n'obutakola bulungi kw'emibira. Kino kijja kuyamba mu kunoonyereza okwongera ku mutindo gw'okusooka okukolako ku balwadde ba sickle cell.

Olekeddwaamu okusaba okwetaba mu kunoonyereza kuno kubanga ofunira obujanjabi okuva ku Ddwaliro lya Mbale Sickle Cell Clinic. Bwe nosalawo okwetaba, bino bye bijja okukolebwa:

Ebikolebwa

a) Tukubuuza ebibuuzo ku mbeera y'obulamu bwo—ebyafaayo byo eby'obulwadde, ebisobola okubeera mu maka, n'ebigambibwa eby'omubiri.

b) Tukulongoosa (physical examination) ku mubiri gwo gwonna—kino kijja kutwala

ddakiika 45.

c) Tukupima obuwanvu n'obuzito, tukubala BMI.

d) Tukukwata ku munwe okufuna omusaayi omutono okumanya hemoglobin (Hb).

e) Tukukola spirometry – okukebera engeri gy'oyitamu omukka.

Eddaala ly'eddembe lyo

Okwetaba kwa buwaze. Tewali kusasulwa oba musango gwonna ogukuweebwa bw'osalawo okugaana. Bw'osaba okulekulira okwetaba, ekyo tekikukosa.

Obulabe obusoboka n'obutabanguko

Okunoonyereza kuno tekulina bulabe bunene. Wabula osobola:

- Okuluma mu munwe wakati w'okufuna omusaayi
- Okwesittala oba okuwulira otatadde olumu bw'okukola spirometry

- Okuviirako okufiirwa akaseera k'obwama w'obusaba bw'eby'obulamu (privacy), naye tukukakasa nti amawulire go gakumibwa mu kyama ennyo

Emigaso gy'okwetaba

- Ojja kufunira obujanjabi obulungi
- Ojja kumanyibwa bw'olina obuzibu ku mubiri gwo ogw'amannyo g'okussa
- Ojja kufunira okukebera kwa lab ne spirometry ku bwereere

Ekyama ku bifuniddwa

Amawulire g'okunoonyereza gano gakumibwa mu nkola ya kyama. Gajja kukuumibwa mu kabati akaggaddwako. Nze n'abanoonyereza abakwatibwako bokka be bajja kuba nabo. Tewajja kubaawo kufulumya linnya lyo mu byonna ebinaava mu kunoonyereza kuno.

Ensasaana y'okwetaba

Tewali nsimbi zisasulwa. Wabula, emigaso gy'oyinza okufuna giri waggulu.

Okubuuza ku kunoonyereza

Bw'oba n'ekibuuzo kyonna, osobola okukibuuza kati oba oluvannyuma:

Dk. Katuramu Richard ku **0701 154444 / 0787 641051**

Okubuuza ku ddembe lyo

Okubuuza ku ddembe lyo nga omwetabye mu kunoonyereza, osobola okukikubira ku Ssentebe wa **BUFREC** – Busitema University Faculty of Health Sciences Research and Ethics Committee

Dk. Katuramu Richard – 0787 641051

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Ekwatirizo y'okwetaba kwa buwaze

Okwetaba kwa buwaze. Osalawo wekka. Osobola n'okulekulira buli kaseera nga tosobezeddwa.

Okuweebwa ebivudde mu kunoonyereza

Ojja kufunira ebyava mu kunoonyereza, n'obubaka obupya obuyinza okukukosa, n'eby'amugaso eri abalala, birimanyisibwa gy'oli n'abakulira eddwaliro.

Okukkirizibwa kw'Ekibiina kya Bufrec

Okunoonyereza kuno kwakkiriziddwa **BUFREC** – Busitema University Faculty of Health Sciences Research Ethics Committee.

Okukkiriza

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Bannyumizza kunoonyereza kuno, era ntegedde ebigenda okukolebwa ssinga nsiima okwetaba. Mmanyi nti nsobola okubuuza ebibuuzo era nsobola n'okulekulira buli kaseera. Nsiimye okwetaba mu kunoonyereza kuno.

Erinnya ly'Omwana:

_____

Omukono/Obulago: _____ _ Olunaku: _____

Okukkiriza kwa Muzzadde/Omulera

Nsomye oba bannyumizza ku kunoonyereza kuno, era ntegedde ensonga, ebikolebwa, obulabe n'emigaso. Nsiimye omwana wange okwetaba. Kitegeerekeka nti kwegesa era nnyinza n'okumulekulira buli kaseera.

Erinnya lya Muzzadde/Omulera: ____

_____ Omukono: _____ Olunaku:

_____

Erinnya ly'Omugezi Omukono: **(Witness):**

_____

Olunaku: _____

_____

Erinnya ly'Omutwala Omukono: **Assent:**

_____

Olunaku: _____

Appendix 9: Data collection tool

DEMOGRAPHICS AND RELEVANT HISTORY

I) Patient ID Number (PID):			
Initials:			
III) Gender:	☐ Male ☐ Female	IV) Date of Birth	___/___/___
Age:	___ Years ___ Months	Age at SCD Diagnosis	___ Years ___ Months
VII) Tribe (ethnic group)		VIII) Religion	
IX) Education status	☐ Educated	☐ Uneducated	
X) History of alcohol consumption		☐ Yes ☐ No	
XI) History of smoking		☐ Yes ☐ No	
XII) Recurrent episodes of ACS		☐ Yes ☐ No	
XIII) Hydroxyurea use		☐ Yes ☐ No	
2. RESIDENCE INFORMATION			
District:		County (Municipality):	
Sub-County (Division):		Parish (Ward):	

Version II 9/17/2025

Village (Cell):		Household Head's Name:	
Phone No. (if any):		Nearest Health Centre:	
3. GENERAL EXAMINATION			
Temperature:	____ °C	Pulse rate:	____ bpm
Respiratory rate:	____ breaths/min	Oxygen saturation:	____ %
Blood pressure:	____ / ____ mmHg	Height:	____ m
Weight:	____ kg	BMI:	____ kg/m²
Hb	Result		
Spirometry	Result		

Appendix 10: mMRC Dyspnea

Not troubled by breathlessness except with strenuous exercise	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Short of breath when hurrying	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Short of breath when walking up a slight hill	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Walking slower than people of the same age on the ground level because of breathlessness	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Walking slower than people of the same age on the ground level because of breathlessness	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Have to stop for breath when walking at my own pace	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Stop to breathe after walking about 100 yards (100 metres) on the level	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Stop to breathe after walking for a few minutes on level ground	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Too breathless to leave the house	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Breathless when dressing	Not at all ☐	Some of the time ☐	Most of the time ☐	All of the time ☐
Breathless when undressing	Not at all	Some of the time	Most of the time ☐	All of the time

Appendix 11: Clearance form

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FACULTY OF HEALTH SCIENCES' REC

28/09/2025
To: Kevin Achiro
kevinotto447@gmail.com

Review Type: Initial Review

Re:BUFHS-2025-85: PREVALANCE AN FACTORS ASSOCIATED WITH ABNORMAL LUNG FUNCTION AMONG PEOPLE WITH SICKLE CELL DISEASE

I am pleased to inform you that at the **10th** convened meeting on **11/09/2025**, the Busitema University Faculty of Health Sciences REC meeting voted to approve the above referenced application.
Approval of the research is for the period of **28/09/2025** to **28/09/2026.**

As Principal Investigator of the research, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the protocol or the consent form must be submitted to the REC for re-review and approval **prior** to the activation of the changes.
3. Reports of unanticipated problems involving risks to participants or any new information which could change the risk benefit: ratio must be submitted to the REC.
4. Only approved consent forms are to be used in the enrollment of participants. All consent forms signed by participants and/or witnesses should be retained on file. The REC may conduct audits of all study records, and consent documentation may be part of such audits.
5. Continuing review application must be submitted to the REC **eight weeks** prior to the expiration date of **28/09/2026** in order to continue the study beyond the approved period. Failure to submit a continuing review application in a timely fashion may result in suspension or termination of the study.
6. The REC application number assigned to the research should be cited in any correspondence with the REC of record.
7. You are required to register the research protocol with the Uganda National Council for Science and Technology (UNCST) for final clearance to undertake the study in Uganda.

The following is the list of all documents approved in this application by Busitema University Faculty of Health Sciences REC:

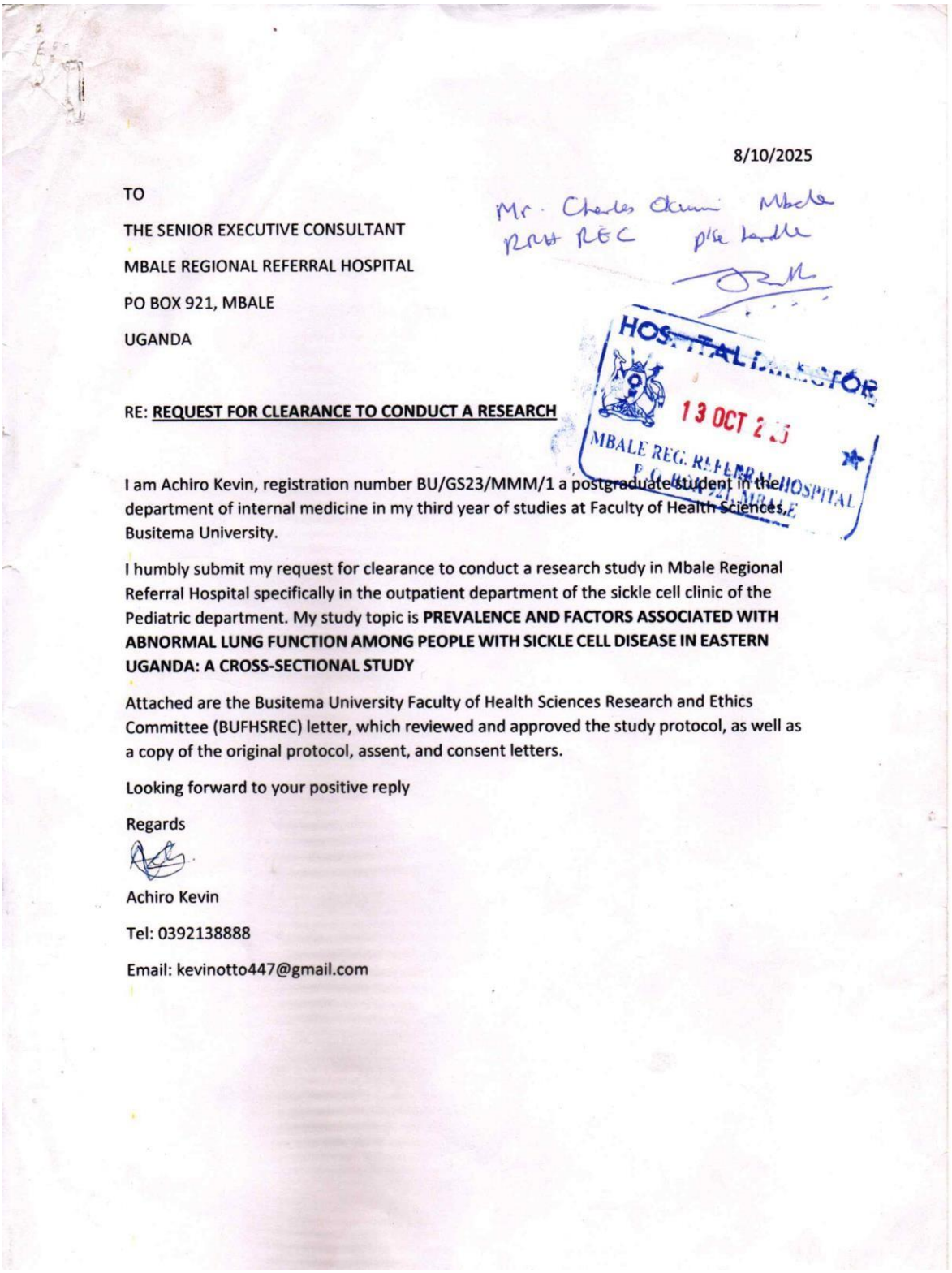
No.	Document Title	Language	Version Number	Version Date

1	Data collection tools	English	version 11	2025-09-26
2	Track changes	English	track changes version 2	2025-09-26
3	Letter to the REC/IACUC Chairperson	English	Letter to REC Version 11	2025-09-26
4	Informed consent form for the recruitment of research participants	English	pdf	2025-08-04
5	Data collection tools	English	pdf	2025-08-04
6	Protocol	English	pdf	2025--04

Yours sincerely,

Richard Katuramu
For: Busitema University Faculty of Health Sciences REC

Appendix 12: Administrative clearance letter, Mbale Regional Referral Hospital(MRRH)



8/10/2025

TO

THE SENIOR EXECUTIVE CONSULTANT

MBALE REGIONAL REFERRAL HOSPITAL

PO BOX 921, MBALE

UGANDA

Mr. Charles Okumu Mbale
RRH REC pls handle

HOSPITAL DIRECTOR
13 OCT 2025
MBALE REG. REFERRAL HOSPITAL
P.O. BOX 921, MBALE

RE: **REQUEST FOR CLEARANCE TO CONDUCT A RESEARCH**

I am Achiro Kevin, registration number BU/GS23/MMM/1 a postgraduate student in the department of internal medicine in my third year of studies at Faculty of Health Sciences, Busitema University.

I humbly submit my request for clearance to conduct a research study in Mbale Regional Referral Hospital specifically in the outpatient department of the sickle cell clinic of the Pediatric department. My study topic is **PREVALENCE AND FACTORS ASSOCIATED WITH ABNORMAL LUNG FUNCTION AMONG PEOPLE WITH SICKLE CELL DISEASE IN EASTERN UGANDA: A CROSS-SECTIONAL STUDY**

Attached are the Busitema University Faculty of Health Sciences Research and Ethics Committee (BUFHSREC) letter, which reviewed and approved the study protocol, as well as a copy of the original protocol, assent, and consent letters.

Looking forward to your positive reply

Regards

Achiro Kevin

Tel: 0392138888

Email: kevinotto447@gmail.com