LUNG FUNCTION ABNORMALITIES AND ASSOCIATED FACTORS AMONG CHILDREN AND ADOLESCENTS AGED 8-18 YEARS WITH SICKLE CELL ANEMIA ATTENDING SICKLE CELL CLINIC AT MUHIMBILI NATIONAL HOSPITAL

Irene K. Karamaga, MD

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LUNG FUNCTION ABNORMALITIES AND ASSOCIATED FACTORS AMONG CHILDREN AND ADOLESCENTS AGED 8-18YEARS WITH SICKLE CELL ANEMIA ATTENDING SICKLE CELL CLINIC AT MUHIMBILI NATIONAL HOSPITAL

By

Irene Kamili Karamaga

A Dissertation submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Pediatrics and Child Health) at

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for examination by Muhimbili University of Health and Allied Sciences a dissertation entitled: ‘‘Lung Function Abnormalities and Associated Factors among Children and Adolescents aged 8-18 Years with sickle cell anemia attending sickle cell clinic at Muhimbili National Hospital ’’, in(partial) fulfillment of the requirements for the degree of Master of Medicine (Pediatrics and Child Health) of Muhimbili University of Health and Allied Sciences.

_____

Dr Zawadi Edward

(**Supervisor**)

Date:_____

_____

Dr Nana Nakiddu

(**Co-supervisor**)

Date:_____

DECLARATIONANDSTATEMENTOFCOPYRIGHT

I, **Irene K. Karamaga**, declare that this dissertation is my original work and that it has not been presented and will not be presented to any other University for a similar or any other award.

Signature…….. Date…….

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DEDICATION

To my husband, Charles, and my babies, Ellie and Avi, you fill my life with joy and purpose, inspiring me to reach greater heights.

To my late Aunt Fortunata, your memory continues to inspire me.

ABSTRACT

Introduction: SCA is a chronic genetic disorder with multisystem complications that affects millions of children worldwide. One of the complications of SCA is lung function abnormalities. There have been conflicting findings on lung function among children with SCA, several demonstrating a restrictive pattern, although reports have shown that the obstructive form of the disease is the most prevalent. Despite the high prevalence of SCA globally, there is limited data on the magnitude of lung function abnormalities and associated factors among children and adolescents with SCA especially in SSA.

Broad objective: To determine the proportion of lung function abnormalities and associated factors among children and adolescents aged 8-18 years with SCA attending sickle cell clinic at Muhimbili National Hospital.

Methodology: This was a hospital-based cross-sectional study done at the SCA pediatric and adolescent outpatient clinic at MNH. An adapted structured questionnaire was used to collect data on the socio-demographic, environmental, and clinical characteristics of participants. Participants underwent physical examination and lung function assessment by spirometry. Abnormal lung function was defined as Forced Expiratory Volume in 1 second (FEV1) < 80% of the predicted value and < -1.64 of the Lower Limit of normal from the reference value. Data entry and analysis were done using Statistical Package for Social Sciences (SPSS) version 20. Continuous data were expressed as medians with respective interquartile ranges. The chi-square test was used to test for the association between categorical variables and the study outcomes. Univariable and multivariable logistic regression was used to assess for statistically significant associations with a set p-value of 0.05.

Results:A total of 306 children and adolescents with SCA aged 8–18 years were recruited into the study; many of the participants were females 53.9%. The number of children and adolescents with abnormal lung function was 70 (22.9%), with most having an obstructive pattern 28 (9.5%).The majority of the participants, 226 (82.6%), were on hydroxyurea treatment, and 22.1% were underweight. There were no factors independently associated with abnormal lung function in the multivariate regression analysis.

Conclusion: Abnormal lung function is commonamong children and adolescents attending sickle cell clinic at MNH. Noneof the studied factors was independently associated with abnormal lung function tests among children and adolescents with SCA.

Recommendations: Regular spirometry screenings may be considered an integral component of comprehensive care for children and adolescents with sickle cell anemia (SCA). Additionally, future research should include additional variables like the duration and dosage of hydroxyurea, which may potentially influence abnormal lung function.

MUHTASARI

Utangulizi: Selimundu ni tatizo sugu lenye madhara kwa mifumo mbalimbali ambalo linaathiri imamilioni ya watoto duniani kote.Kati ya changamoto za kiafya kwa selimundu ni kushindwa utendaji kazi wamapafu. Kumekuwa na matokeo yanayo tofautiana kuhusu utendaji kazi wa mapafu miongoni mwa watoto wenye selimundu, nakadhaa wakionyesha muundo wa 'obstructive', ingawa ripoti zimeonyeshakuwa aina ya 'restrictive' ndio inayoonekana zaidi. Licha ya uwingi wa selimundu duniani, kuna takwimu chache kuhusu ukubwa wakasoro za utendaji kazi wamapafu na sababu zinazohusiana miongoni mwa watoto na vijana wenye selimundu, hasa katika Afrika Kusini mwa Jangwa la Sahara.

Lengo la utafiti: Utafiti unahusu tathimin ya ukubwa wa tatizo la ufanyaji kazi wa mapafu pamoja na sababu zinazohusianamiongonimwawatotonavijanawenyeumriwamiaka 8-18 wenye SCA wanaohudhuria kliniki ya selimundu katika Hospitali ya Taifa ya Muhimbili.

Mbinu: Utafiti ulifanyika katika kliniki za watoto na vijana za SCA katika hospitali ya Muhimbili, dodoso ilitumika kukusanya taarifa kuhusu sifa za kijamii, kimazingira, na za kiafya za washiriki. Washiriki walifanyiwa uchunguzi wa mwili na tathmini ya utendaji kazi wa mapafu kwa kutumia'spirometry.Utendaji kazi wa mapafu usiowaka waidauli fafanuliwa kama Kiasi cha Hewa KinachotolewakwaSekunde Moja (FEV1) < 80% ya thamaniiliyotabiriwana< -1.64 ya Kiwango cha Chini cha kawaida. Uingizaji na uchambuziwa data ulifanyika kwa kutumia Programu ya Takwimu za Sayansi ya Jamii (SPSS) toleo la 20. Kipimo cha "Chi square" kilitumika kulinganisha kati ya viashiria vya kimakundi na utendaji kazi wa mapafu, wakati kipimo cha "t-test" kilitumika kwa viashiria endelevu.Viashiria vilivyoonyesha kuhusika zaidi na utendaji kazi wamapafu vilichanganuliwa kwa "logistic regression". Thamani ya p (p-value) chini ya 0.05 ilichukuliwa kuwa na umuhimu kitakwimu.

Matokeo: Jumla ya watotonavijana 306 wenye SCA wenyeumriwamiaka 8-18 walishirikishwakatikautafiti; wasichanawalikuwawengikwa 53.9%. Watoto na vijana wenye kasoro za utendaji kazi wa mapafu walikua 70 (22.9%), huku wengi wakiwa na 'obstructive pattern 28 (9.5%)). Wengiwawashiriki, 226 (82.6%),walikuwa kwenye matibabu ya hydroksiurea, na 22.1% walikuwa na uzito wa chini. Hakukuwa na sababu

zilizohusishwa na kasoro za utendaji kazi wa mapafu katika uchanganuzi wa ‘logistic regression’ wa vigezo mbalimbali**.**

Hitimisho: Kuna kasoro za utendaji kazi wa mapafu miongoni mwa watoto na vijana wanaohudhuria kliniki ya selimundu katika MNH. Hakuna sababu zilizochunguzwa ambazo zilihusishwa na kasoro za utendaji kazi wa mapafu miongoni mwa watoto na vijana wenye selimundu.

Mapendekezo: Uchunguziwa mara kwa mara kwa kutumia spirometri unaweza kuwa muhimu ilikuwezesha upangajiwa wagonjwa na kama sehemu ya huduma kamilifu kwa watoto na vijana wenye selimundu. Utafiti zaidi unaojumuisha sababu za ziada ambazo zinaweza kuchangia kasoro za utendaji kazi wa mapafu katika kundihilini muhimu.Aidha kuna uhitaji watafiti za muda mrefu kuchunguza ufanyaji kazi wa mapafu kwa watoto na vijana rika wenye Selimundu.

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LIST OF ABBREVIATIONS

ACS	Acute chest syndrome
FEV1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
PEF	Peak Expiratory Flow
HBSS	Hemoglobin SS
HSCT	Hematopoietic Stem Cell Transplant
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
SCA	Sickle Cell Anemia
SCLD	Sickle Cell Chronic Lung Disease
SSA	Sub-Saharan Africa

DEFINITION OF KEY TERMS

For this study, the following terms will be defined as follows:

Forced Expiratory Volume in 1 Second (FEV1): The volume of air exhaled during the first Second of a forced expiratory maneuver.

Forced Vital Capacity: The maximum volume of air exhaled forcefully after a maximal inspiration

Peak Expiratory Flow: Highest instantaneous airflow rate measured during the FVC maneuver

Abnormal lung function: Defined as Forced Expiratory Volume in 1 second (FEV1) < 80% of the predicted value and < -1.64 of the Lowe Limit of Normal.

Obstructive Pattern: Any disease that narrows the lumen of the airways, reduced FEV1, reduced FEV1: FVC.

Restrictive Pattern: Any disease that affects the capacity of the lungs to expand, reduced FEV1, normal FEV1: FVC.

1.0 INTRODUCTION

1.1 Background

1.1.1 Overview of Sickle Cell Anemia

Sickle cell anemia is a genetic disorder that occurs due to the homozygous and compound heterozygote inheritance of a mutated beta-globin gene. Specifically, a single-point mutation of GAG to GTG leads to the substitution of glutamic acid (a hydrophilic amino acid) with valine (a hydrophobic amino acid) at the 6th position of the beta-chain of hemoglobin (1). This mutated hemoglobin is known as hemoglobin S (HbS) (2). It is a multi-system disorder that has both acute and chronic complications.

1.1.2 Burden of SCA

Sickle cell anemia is widely prevalent in populations of Sub-Saharan Africa, South Asia, the Middle East, and the Mediterranean. It is considered one of the most common genetic disorder globally and in Europe it is the most common hereditary blood disorder in people of African ancestry, affecting around 14,000 people in the UK alone(3). SCA poses a significant burden in the SSA region. In Malawi for instance it is estimated that 1-3% of its population have SCA(4).

Tanzania ranks fifth globally, with 11,000 newborns born with sickle cell disease (SCD) annually, 13% of the population are carriers of the sickle cell trait (AS), and it is estimated that 8,000 children are born each year with homozygous sickle cell disease (SS). SCA accounts for 7% of all-cause mortality as well as mortality in children under five(1,6).

1.1.3 Lung Function Test in Children

Lung function tests, also known as pulmonary function tests, are a set of diagnostic and evaluative tests that assess the respiratory health and function of the lungs. These tests provide valuable information about how well the lungs are functioning, including their ability to move air in and out, the volume of air the lungs can hold, and how efficiently the lungs can exchange oxygen and carbon dioxide(7).

Spirometry is a physiological test that evaluates an individual's ability to inhale and exhale air with maximum effort, measuring parameters such as volume or flow over time. The primary measurements of interest in spirometry are the Forced Vital Capacity (FVC), which reflects the volume of air forcefully expelled during a complete expiration from a maximal inspiration, and the Forced Expiratory Volume in 1 second (FEV1), which quantifies the volume of air exhaled in the first second of the FVC maneuver(7,8). The results from a spirometry test aid in the diagnosis, follow-up, and, monitoring of respiratory disorders(8).

1.1.4 Lung function abnormalities in SCA

The primary complication that frequently necessitates hospitalization in individuals with SCAis a vaso-occlusive crisis (VOC), which arises from the occlusion of blood vessels in the bone marrow, resulting in bone infarcts and accompanying bone pain. The second leading cause of hospitalization and the most prevalent cause of mortality in individuals with SCA are pulmonary complications, namely acute chest syndrome (ACS) and chronic sickle cell lung disease (SCLD)(2, 9). Long-term complications to the lung may present as irregularities in respiratory function, interstitial lung disorder, or pulmonary hypertension(10,11).

There have been several explanations for the pathophysiology of chronic sickle cell lung disease that may present with reduced lung volume and reduced flow that progress to abnormal lung function. The presence of tissue hypoxia due to bronchoconstriction causing ventilation-perfusion mismatch and the chronic inflammatory state in SCA resulting in increased endothelial adhesion molecule expression thus ending with vaso-occlusion (12).

Reduced lung volumes (FEV1/FVC) have been demonstrated, however the prevalence of these lung function abnormalities have varied(9,10).Studies have documented obstructive pulmonary function in 5% to 35% of cases, with restrictive pulmonary function observed in 8% to 22% of cases(13). These findings highlight the variability in lung function abnormalities among children and adolescents with SCA, with a significant proportion of patients exhibiting obstructive or restrictive patterns (4,9).

1.2 Problem statement

Among the numerous complications of SCA, lung function abnormalities are prevalent among young adults and can significantly affect the quality of life and long-term prognosis of affected individuals.Acute chest syndrome is a common complication among young patients with SCA in whom recurrent acute chest events can cause injury to the vessels and eventually fibrosis with infarctions resulting in progressive lung damage in adulthood(14).

Sickle cell anemia has been shown to affect an estimated 100,000 Americans and is even more common among African Americans where approximately 1 in 365 are said to be affected. (15). With a high prevalence of SCA in SSA, there is limited information on lung function comorbidity in these patients(6).

Tanzania, a country with a low to middle-income status, experiences approximately 11,000 infants born with SCA , and it is estimated that at least 14,700 deaths of children under the age of five are attributed to SCA(1,6). Therefore, it can only be assumed that there is a significant occurrence of abnormal lung function among children with SCA.

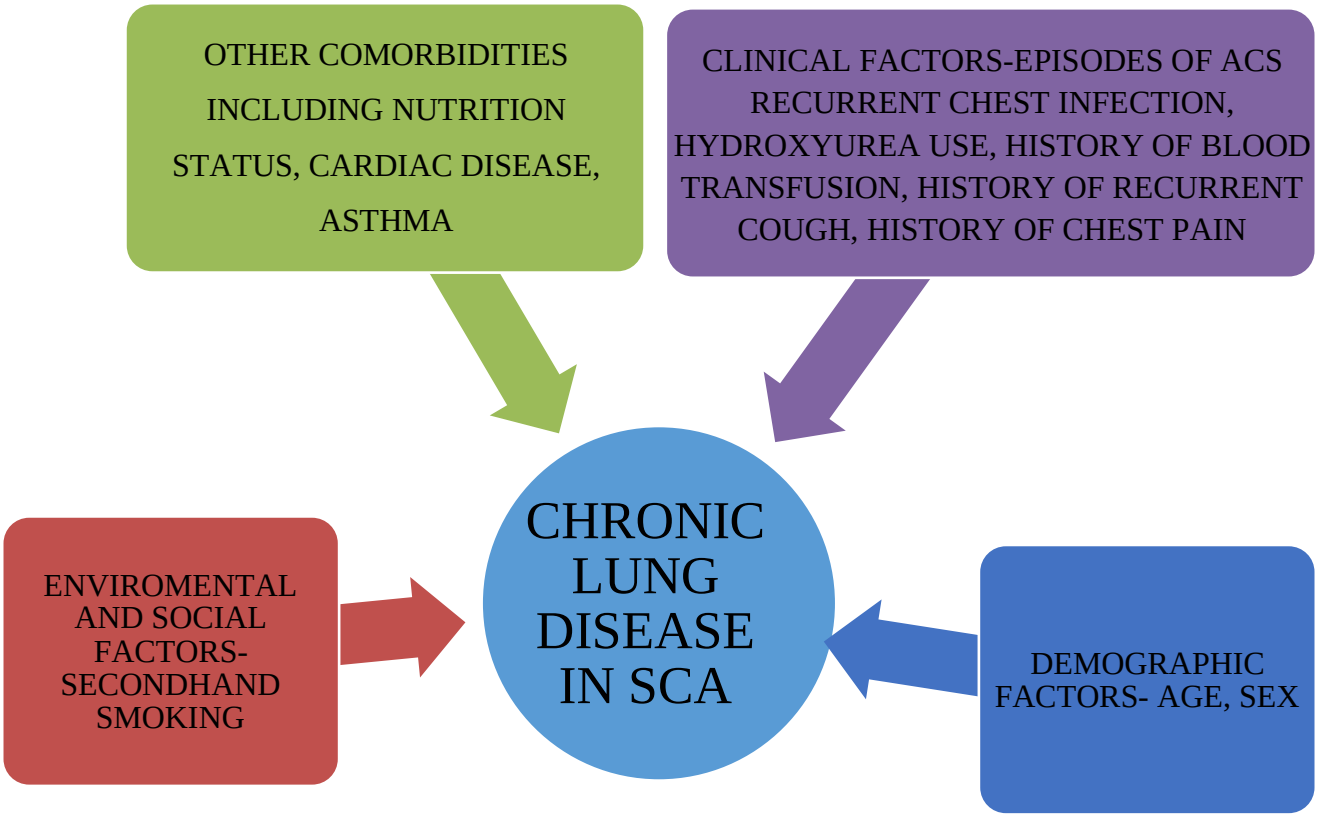
Despite the advancement of care in managing SCA in children and adolescents, there are limited data on their lung function. This aspect remains understudied, creating a knowledge gap in comprehending their respiratory health, identifying risk factors, and exploring interventions for mitigating long-term respiratory complications. This study aims to bridge the crucial gap in understanding the landscape of lung disease among children and adolescents with SCA in Tanzania.

1.3 Conceptual framework

In patients with SCA, the lungs are impacted by various pulmonary insults, including sickled RBC adherence and free fatty acids, of which repeated occurrences over time may result in chronic damage to the interstitial tissue, lung parenchyma, or blood vessels, ultimately compromising pulmonary function.

Several factors have been speculated and grouped into social demographic factors including age at diagnosis, sex, nutritional status, and clinical factors including number of admissions due to respiratory complaints, number of blood transfusions, and other factors including environmental factors like secondhand smoking. These factors can either directly or indirectly influence lung function in patients with sickle cell anemia.

Figure 1: Conceptual framework showing chronic lung disease in SCA



1.4 Rationale

Although management for children and adolescents with SCA has improved in Tanzania, there is a scarcity of data regarding lung function in the pediatric population. This knowledge gap poses challenges in comprehending their respiratory health status and identifying potential risk factors for this vulnerable population. Abnormal lung function concerns individuals with SCA and can impact their quality of life and overall health outcomes. Consequently, this study aimed to investigate the extent of lung function abnormalities and associated factors, effectively bridging this crucial gap in knowledge.

1.5 Research questions

1. What is the magnitude of lung function abnormalities among children and adolescents with SCA?
2. What are the factors associated with abnormal lung function among children and adolescents with SCA?

1.6 Objectives

1.6.1 Broad objective

To determine the proportion of children and adolescents with lung function abnormalities and associated factors among patients aged 8–18 years with SCA attending clinics at Muhimbili National Hospital.

1.6.2 Specific objectives

1. To determine the proportion of children and adolescents with lung function abnormalities among patients aged 8–18 years with SCA attending clinics at Muhimbili National Hospital.
2. To determine the clinical factors associated with lung function abnormalities among children and adolescents aged 8-18 yearswith SCA attending clinic at Muhimbili National Hospital.
3. To determine the socio-demographic factors associated with lung function abnormalities among children and adolescentsaged 8-18years with SCA attending clinic at Muhimbili National Hospital.

2.0 LITERATURE REVIEW

2.1 Lung function among children and adolescents with SCA

Lung function aberrations are commonly observed in pediatric and adolescent patients with sickle cell disease (SCD), who may exhibit a gradual decline in lung function over time (16). However, comparing findings from older studies is impeded by the utilization of diverse reference values and criteria for defining lung function abnormalities(9).

In a study done in Brazil about 11% of the participants were found to have obstructive lung disease and of those, 57% had a clinical diagnosis of asthma(17). This was consistent with Arigliani et al's study(18)which compared lung function among children with SCAin Nigeria and Europe, an obstructive pattern was more observed among the children from Europe at a prevalence of 9%.

In acase-control study in Germany, children with sickle cell disease (SCD) had statistically significantly reduced Forced Respiratory Capacity signifying a restrictive pattern of lung function among its cases when compared to the control (19).

A cross-sectional study in Egypt by Al-Biltagi et al(20) determined that 51.1%of its participants had restrictive lung disease. This was similar to a case-control study in Nigeria (21)that found 31.1% of the participants with HbSShad reduced lung volume, similarly a small cross-sectional study done in Malawi by Cook et al (4) demonstrated lung function abnormalities to be more suggestive of restrictive lung disease, despite a very small sample size.

No comparable data on lung function among children and adolescents with SCA in Tanzania exists.

2.2 Factors associated with abnormal lung function in children and adolescents with SCA

Several factors associated with abnormal lung function in children and adolescents with SCA have been described across socio-demographic clinical and environmental factors.

2.3 Socio-demographic factors

In a prospective study done in Canada, the only gender difference that was found to be statistically significant in this research was that males fared worse than females. Throughout childhood, males but not girls displayed a steady shortening of height. The growth of the spine and thoracic cage, as well as the long bones, are all at risk for multiple skeletal crises in children with SCD (22).However, this was contrary to a study in Nigeria which found sex to not be statistically significant in lung function (23).

In a study in Denmark, there was a notable impact of age on the overall lung function test among the participants with SCA as compared to those in the control group similar to findings from a cross-sectional study done in Brazil where 37.5% of the study participants above the age of 15 years had abnormal lung function.

2.4 Clinicaland environmental factors

Various disease-related factors, such as the frequency and severity of vaso-occlusive crises, the presence of acute chest syndrome (ACS), and history of acute respiratory illnesses, have been implicated in abnormal lung function among children and adolescents with SCA(24).

Studies have shown that direct correlation exists between changes in pulmonary function in sickle cell disease (SCD) and a specific type of lung injury or disease. Although radiologic and autopsy data confirm the presence of pulmonary parenchymal injury, they do not provide explanations for the underlying mechanisms responsible for this injury (25).

A case-control study done among Afro-Caribbean children with SCA revealed notable differences in lung function results between children with sickle cell disease (SCD) who were hospitalized for acute chest syndrome (ACS) episodes compared to those who did not experience ACS (26).

A prospective cohort study in Canada (15) studied the progressive lung decline in children with and without the use of hydroxyurea and the study revealed that lung function tests declined significantly in subjects, not on hydroxyurea therapy, in contrast to findings from a meta-analysis conducted by Taksande et al(9,27)

A study conducted by Cook et al. in Malawi found that the majority of participants (83%) were exposed to biomass combustion byproducts for household cooking. Also, exposure to secondhand cigarette smoking although found in participants with abnormal lung function (19.2%) there was no statistical significance from findings in both studies(P=0.49)(4)

3.0 MATERIALS AND METHODS

3.1 Study design

This was a cross-sectional analytical hospital-based study that was conducted from November 2023 to May 2024.

3.2 Study area

This study was conducted at Muhimbili National Hospital (MNH), a tertiary referral and the largest medical training hospital in Tanzania. The hospital has a bed capacity of 1500 and over, and caters to around 2000 outpatients daily, providing specialized medical care. As a teaching hospital, MNH also plays a role in providing clinical training for students from the Muhimbili University of Health and Allied Sciences (MUHAS).

Muhimbili National Hospital (MNH) serves an estimated 2000 outpatients daily. Among them, the pediatric sickle cell clinic caters to approximately 100–200 patients weekly, attending to clients aged 13 years and under. This clinic operates once a week. In contrast, the adult sickle cell clinic attends to around 5–10 adolescents aged 14 years and older, also operating once a week.

3.3 Study population

Children and adolescents with SCA (HbSS) aged 8-18 years attending sickle cell outpatient clinic at MNH within the duration of the study.

3.4 Inclusion criteria

Participants aged 8-18 years who were confirmed with SCA HbSS who gave assent and whose parents provided written consent.

3.5 Exclusion criteria

Participants who had SCA-related acute events—painful crises or acute chest syndrome—in the month before the study, patients who were clinically unwell with fever, URTI infection symptoms, or pain, and clinically known patients with asthma or congenital heart disease were excluded.

3.6 Sample size estimation

The sample size (N) was determined using the formula,

Given by

N = (Z^2 * P * (1-P)) / (E^2),

Where N represented the minimum sample size required. P denoted the magnitude of restrictive lung disease among children and adolescents in Kinshasa, DRC to be 26% (5).E represents the maximum allowable error of the study, set at 5%. Z corresponds to the standard normal distribution value at a 95% level of confidence, which is 1.96.

$$\frac{1.96^2 \times 0.268(1-0.268)}{0.05^2}$$

=295

Adjusting for a 10% anticipated non-response rate

N = n x 1/0.9 =

N =295 * 1/0.9

N = 327

The minimum sample was 327 children and adolescents with SCA.

3.7 Sampling technique

All children and adolescents attending the follow-up SCA clinic, who met the inclusion criteria were conveniently recruited into the study until the desired sample size was reached. A ratio of 20:1 (child: adolescent) was used.

3.8 Variables

The variables in this study were:

3.8.1 Dependent variables:

Lung functionabnormalities

3.8.2 Independent variables:

- Social demographic data including age, sex, level of education
- Environmental factors: exposure to secondhand cigarette smoke, use of combustible cooking stove
- Clinical profile of SCA:

- Nutrition status- BMI status
- In the past 12 months- number of hospitalizations due to respiratory complaints, number of blood transfusions.
- History of fever, weight loss, and respiratory complaints in the past year- cough, chest pain, shortness of breath, audible wheeze.
- Hydroxyurea use

3.9 Data collection methods and tools

A structured questionnaire adapted from the American Thoracic Society(7)was used to collect participants' socio-demographic and medical information. It was translated into Kiswahili before being used for a pilot study. Participants were asked about a history of chronic cough, shortness of breath, chest pain or tightness, cigarette smoking, presence of audible wheezing as well as diagnosis of SCA, use of hydroxyurea, and frequency of clinic visits as well as recent laboratory investigation results including hemoglobin levels. Participants were enrolled duringtheir scheduled clinic visits and thus disruption of clinical care was kept at a minimum.

Anthropometric measurements were taken, and weight was measured by using a calibrated weighing scale with the participants wearing light clothes and removing shoes and recorded to the nearest 10g. Height was measured using a stadiometer and the readings were recorded to the nearest 0.1cm.BMI was calculated as weight in kilograms divided by the square of height in meters. Vital signs including blood pressure, pulse rate, respiratory rate,and oxygen saturationwere measuredbefore performing a spirometry test.

Examination was performed by a research assistant, and a qualified medical doctor on all participants to identify any existing acute or chronic clinical abnormalities and assess for any emergency signs requiring emergency interventions.

Spirometer test

Lung function was assessed using a spirometer by a physiology laboratory technician from the physiology unit who was conversant in conducting spirometry. The spirometry was performed after the administration of the questionnaire.

The spirometry test was conducted using the Microlife spirometer, model PF-100, manufactured by Microlife AG Swiss Corporation. This portable, child-friendly machine complies with the 2019 American Thoracic Society (ATS) and European Respiratory Society (ERS) spirometer standards. The spirometer featured a replaceable mouthpiece (spirette), which was replaced after each test. The physiologist at MUHAS trained the principal investigator in spirometry techniques before data collection (7, 25).

Spirometry was conducted in a dedicated, quiet, well-ventilated room in a room. Spirometry was done with the participant in a standing position, erect with shoulders slightly back and chin slightly elevated. The principal investigator and research assistant instructed and demonstrated the test to the participant in the preferred language. The principal investigator and research assistant demonstrated the positioning of the mouthpiece, correct posture, rapid inspiration until full, then expiration with maximum effort until empty then inspire with maximum effort until full. Once the participant hada clear understanding of the instructions, he/she was guided into performing the maneuvers. Instructions were repeated as necessary. A minimum of three maneuvers wereallowed and the machine automatically picked the mean readingof PEF, FEV1, and FVC.

The spirometer was then connected to a computer, and the observed, FEV1, FVC, and PEF values of each participant were compared to the spirometer program, which used a color-coded system: red, yellow, and green, with red reflecting values below 80% of the predicted value. A second comparison was conducted using the reference range stipulated by the Global Lung Initiative 2012 reference values for age, height, and ethnicity(29), where the lower limit of normal (LLN) for FEV1, FVC, and FEV1/FVC is defined as $Z < -1.64$ (below the 5th percentile).

Infection prevention control was a priority during spirometry testing. Strict adherence to hand washing and the use of handsanitizers after every contact with each participant was ensured by all members of the research team.New disposable mouthpieces wereused for

eachparticipant witha minimum of 30 mouthpieces used per day. The spirometer was cleaned with a hypoallergenic sanitizer at the end of the day.

The spirometer used for testing was calibrated in the morning dailybefore conducting the testing. A control test was done at the beginning of the day before testing the participants.

3.10 Data analysis

The principal investigator performed data entry, cleaning, and analysis using the Statistical Package for Social Sciences (SPSS) version 20. For continuous variables, medians with interquartile ranges (IQR) were used. Categorical data were summarized as frequencies or proportions.

For the analysis of factors associated with abnormal lung function, Student's t-test was used for continuous variables, and Chi-square and Fisher's exact tests were used for categorical variables. Univariable and multivariable logistic regression analyses were conducted to identify factors associated with abnormal lung function.

Factors that showed an association with abnormal lung function in the univariable analysis with a p-value of less than 0.2, and those with a scientific basis from previous studies, were included in the multivariate logistic regression analysis to control for potential confounders. Any variable with a p-value of 0.05 or less was considered statistically significant.

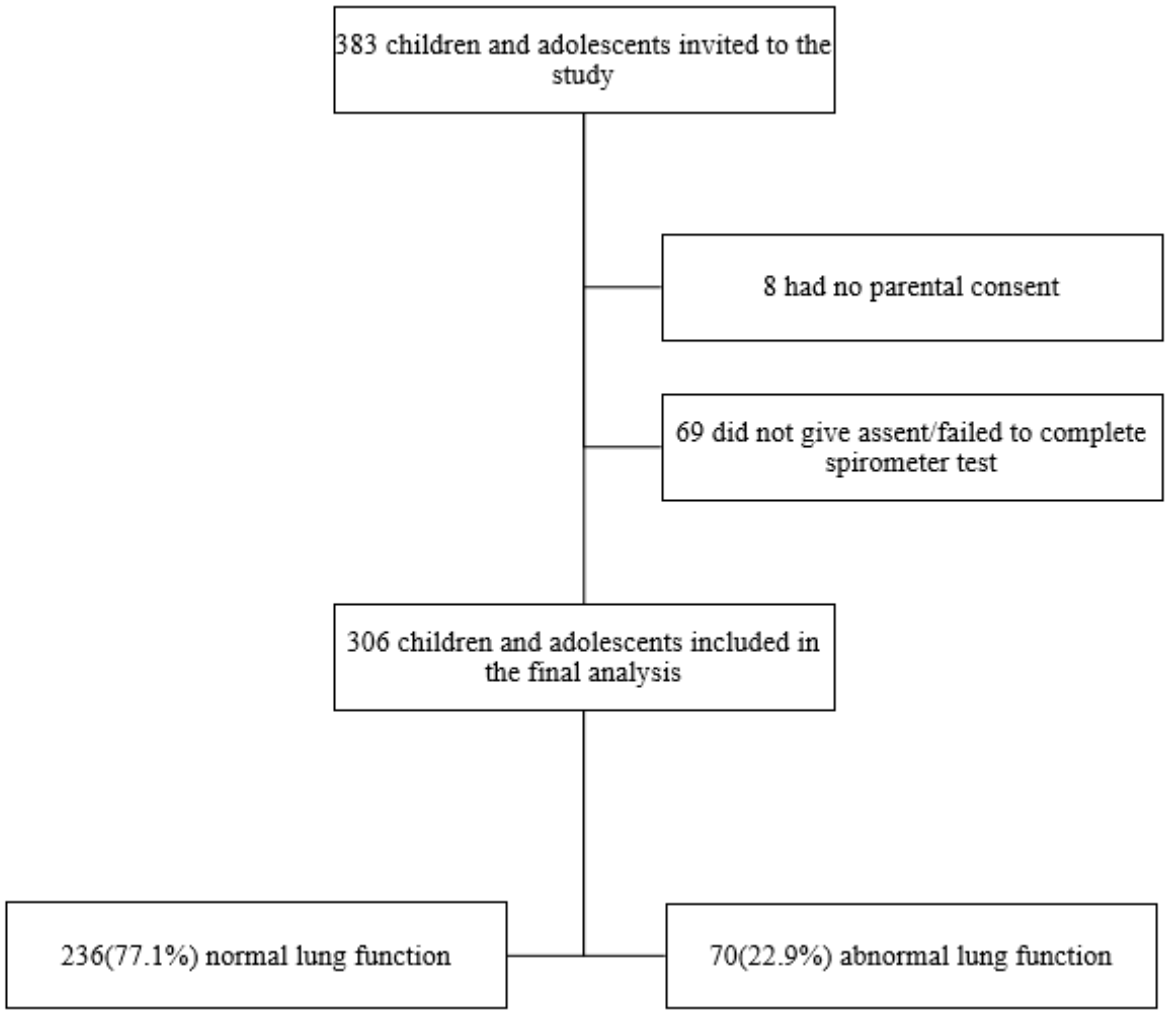
3.11 Ethical consideration

Ethical clearance from the Directorate of Research and Publications at Muhimbili University of Health and Allied Sciences (MUHAS) and the Director of Hospital Services at Muhimbili National Hospital was obtained beforethe study implementation. Participants and their parent/guardian(s) were informed about the study, and consent was obtained from parents/guardians and participants who were 18 years old. Verbal and written assent were obtained from participants aged 8-17 years after obtaining consent from their parents. Participants found to have abnormal lung function tests had their parents informed of the results and were referred to the pulmonology clinic at Muhimbili National Hospital for further evaluation.

4.0 RESULTS

A total of 383 participants were selected to participate in this study, of whom 306 met the inclusion criteria and were eventually analyzed as shown below in Figure 2.

Figure 2: Flow chart showing recruitment of study participants and results



4.1 Socio-demographiccharacteristicsoftheparticipants

Among the 306 participants, 173 (56.5%) were between 8 and 12 years old. Female participants were slightly more (56.4%), and the majority, 234 (76.5%), were in primary school. Nearly all the parents/guardians had some form of formal education with 47.4% having a primary school level of education, and 194 (63.4%) being self-employed, as shown in table 1 below.

Table 1: Study participants socio-demographiccharacteristics

Child/adolescent characteristics		**Number of participants n= 306**	**Percentage %**
Age(years)	8-12	173	56.5
	13-15	99	32.4
	16-18	34	11.1
	Median age(IQR)	12(14,17)	
Sex	Male	141	46.1
	Female	165	53.9
Level of education	Primary school	234	76.5
	Secondary school	72	23.5
Parent/guardian characteristics			
Age(years)	≤20	2	0.7
	21-34	128	41.8
	≥35	176	57.5
	Median age(IQR)	35(32-43)	0.7
Sex	Male	88	28.8
	Female	218	71.2
Occupation	Student	8	2.6
	Employed	59	19.3
	Unemployed	45	14.7
	Self-employed	194	63.4
Level of Education	Primary school	145	47.4
	Secondary school	113	36.9
	College	46	15.0
	No formal education	2	0.7

4.2 Clinical and environmental characteristicsoftheparticipants

Among the participants, 176 (57.5%) exhibited normal weight status, while 41.8% were underweight, and 0.7% were categorized as overweight. The majority of the participants, 266 (86.9%), were on hydroxyurea treatment at the time of enrollment. Twenty nine (12.7%) participants experienced admissions due to respiratory complaints within the preceding year. In comparison, 140 (45.8%) had a history of blood transfusion, among which 91 (32.4%) had a history of being transfused more than once in the past year. Most of the participants reported an absence of any respiratory symptoms over the past year. It is worth noting that 17.0% reported exposure to secondhand cigarette smoke, while exposure to charcoal stove smoke was universal among all study participants. The clinical and environmental characteristics of the study participants are summarized in Table 2 below.

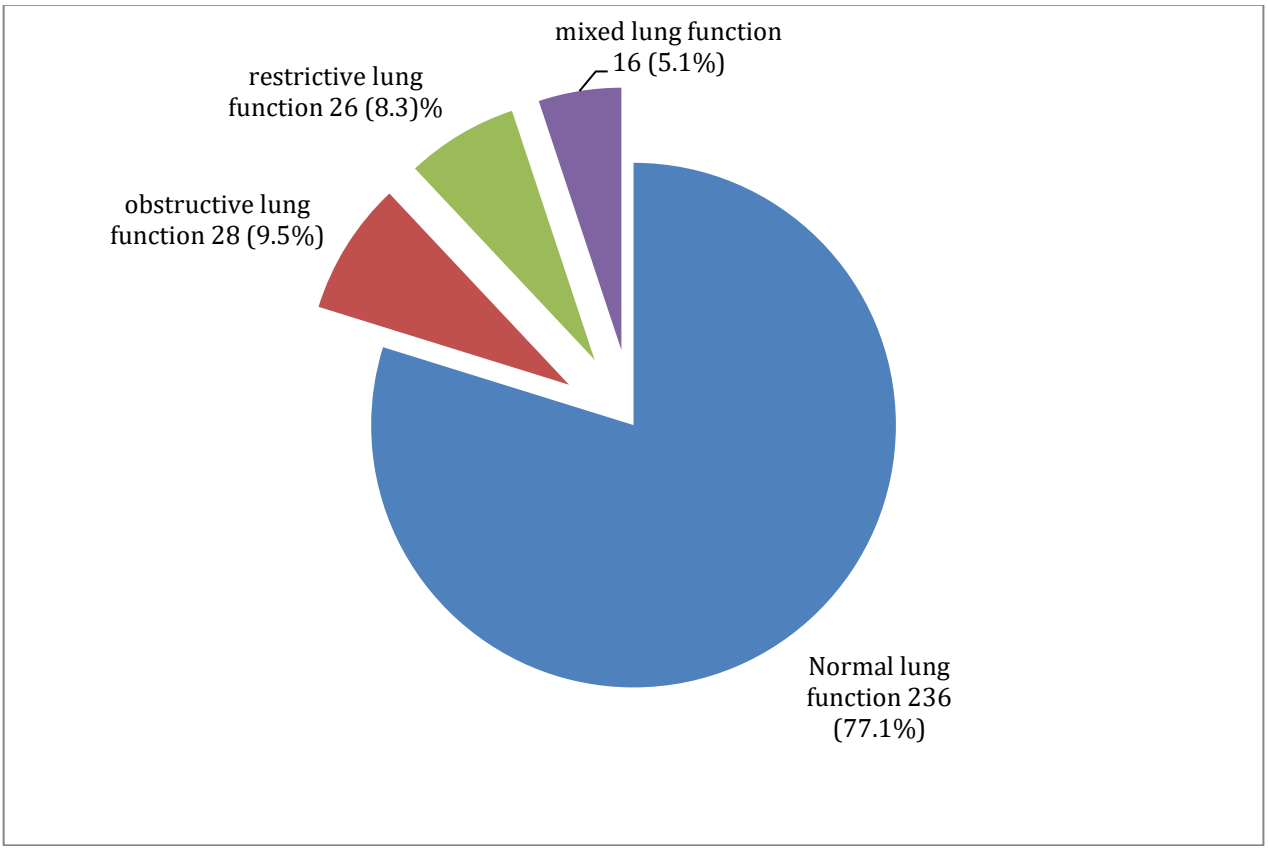
Table 2. Study participant's clinical and environmental characteristics

		Number of participants n=306	Percentage %
Nutritional status	Normal weight	176	57.5
	Underweight	128	41.8
	Overweight	2	0.7
Hydroxyurea use	Yes	266	86.9
	No	40	13.1
History of chest pain (in the past year)	Yes	51	16.7
	No	255	83.3
History of shortness of breath	Yes	19	6.2
	No	287	93.8
History of weight loss (in the past year)	Yes	46	15.0
	No	260	85.0
History of recurrent fever (in the past year)	Yes	23	7.5
	No	283	92.5
History of audible wheeze (in the past year)	Yes	4	1.3
	No	302	98.7
Admission due to respiratory complaints(in the past year)	None	267	87.3
	Yes	39	12.7
Blood transfusion (in the past year)	No	166	54.2
	Yes	140	45.8
Number of blood transfusions since diagnosis	None	166	54.2
	Once	41	13.4
	More than once	91	32.4
Exposure to secondhand cigarette smoking	Yes	52	17.0
	No	254	83.0
Use of charcoal stove in the household	Yes	306	100.0
	No	0	0.0

4.2 Prevalence of lung function abnormalities among children and adolescents with SCA

Of the 306 children included in this study, 70 (22.9%) exhibited abnormal lung function tests, as evidenced by an FEV1% below 80% of the predicted value (less than -1.64 of the lower limit of normal).Among these cases, 9.5%, 8.3%, and 5.1% presented obstructive, restrictive, and mixed spirometry patterns, respectively. Notably, none of the participants with abnormal lung function tests showed significant reversibility, defined as an increase in FEV1 exceeding 8% from baseline as shown in Figure 3.

Figure 3: Prevalence of abnormal lung function among children and adolescents with SCA



4.3 Factors associated with abnormal lung function among children and adolescents with SCA

The analysis revealed no statistically significant differences in several key factors, including age, sex, hydroxyurea use, history of cough within the past year, and exposure to passive smoking in association with abnormal lung function among children and adolescents with SCA. Table 3 summarizes these findings.

Table 3: Factors associated with abnormal lung function among children and adolescents with SCA

	NORMAL LUNG FUNCTION	ABNORMAL LUNG FUNCTION	P VALUE
Age(years)			
8-12	135(78%)	38(22%)	0.06
13-15	80(80.8%)	19(19.2%)	
16-18	21(61.8%)	13(38.2%)	
Sex			
Male	114(80.9%)	27(19.1%)	0.15
Female	122(73.9%)	43(26.1%)	
Level of education			
Primary school	186 (79.5%)	48 (20.5%)	0.07
Secondary school	50 (69.4%)	22 (30.6%)	
Hydroxyurea Use			
Yes	206(77.4%)	60(22.6%)	0.73
No	30(75.0%)	10(25.0%)	
Admissions due to Respiratory complaints(in the past year)			
None	206(77.2%)	61(22.8%)	0.97
Present	30(76.9%)	9(23.1%)	
Blood transfusion (in the past year)			
Yes	123(74.1%)	43(25.9%)	0.17
No	117(80.7%)	27(19.3%)	
History of chronic cough (in the past year)			
Yes	36(80%)	9(20%)	0.61
No	200(76.6%)	61(23.4%)	
History of chest pain/tightness (in the past year)			
Yes	40(78.4%)	11(21.6%)	0.80
No	196(76.9%)	59(23.1%)	
History of shortness of breath (in the past year)			
Yes	17(89.5%)	2(10.5%)	0.18*
No	219(76.3%)	68(23.7%)	
History of recurrent fever (in the past year)			
Yes	16 (69.6%)	7 (30.4%)	0.36*
No	220 (77.7%)	63 (22.3%)	
History of audible wheeze (in the past year)			
Yes	3(75%)	1(25%)	0.91*
No	233 (77.2%)	69 (22.8%)	
Passive smoking			
Present	42(80.8%)	10(19.2%)	0.49
Absent	194(76.4%)	60(23.6%)	
Nutritional status			
Underweight	98(77.8%)	30(22.2%)	0.63*
Normal weight	137(81.5%)	39(18.5%)	
Overweight	1(50%)	1(50%)	

*Fischer exact test

4.4 Logistic regression of factors associated with abnormal lung function among children and adolescents with SCA

In the univariable analysis, the age group 16-18 years displayed an association with reduced odds of abnormal lung function (cOR=0.45, 95% CI: 0.20-0.99, p=0.04) in comparison to the reference group (8-12 years). Nonetheless, this association did not retain significance in the multivariable analysis (aOR=0.52, 95% CI: 0.23-1.19, p=0.57). Several factors like being underweight, having a history of blood transfusion, admission due to respiratory complaints, and exposure to passive cigarette smoking demonstrated higher odds of abnormal lung function (1.16 (CI 0.49 –1.56), 1.46 (CI 0.59 – 3.01), 1.54 (CI 0.50-4.73) and 1.21 (CI 0.51–2.86), respectively). However, no notable associations were observed between all other independent variables and abnormal lung function in either univariable or multivariable analysesasshown in Table 4 below.

Table 4: Logistic regression analysis of factors associated with abnormal lung function test

		UNIVARIATE ANALYSIS			MULTIVARIATE ANALYSIS		
		cOR	**95% CI**	**P value**	**aOR**	**95%CI**	**P value**
Age(years)	8-12	*Ref*					
	13-15	1.18	0.64-2.19	0.58	1.20	0.62-2.30	0.18
	16-18	0.45	0.20-0.99	0.04	0.52	0.23-1.19	0.57
Sex	Male	*Ref*					
	Female	0.67	0.39-1.15	0.15	0.69	0.38 -1.23	0.21
BMI	Normal weight	*Ref*					
	underweight	0.930	0.64-2.33	0.79	1.16	0.49 –1.56	0.65
	overweight	0.285	0.17-4.26	0.37	0.12	0.08 -2.73	0.19
Hydroxyurea Use	Yes	*Ref*					
	No	1.14	0.52-2.47	0.73	1.20	0.41-3.48	0.76
Blood transfusion history	No	*Ref*					
	Yes	1.46	0.84-2.53	0.17	1.34	0.59 – 3.01	0.47
Admission due to respiratory complaint	No	*Ref*					
	Yes	1.01	0.45-2.25	0.97	1.54	0.50-4.73	0.44
History of cough	No	*Ref*					
	Yes	0.82	0.37-1.79	0.61	0.87	0.32-2.35	0.79
History of chest pain/tightness	No	*Ref*					
	Yes	1.09	0.52-2.26	0.80	1.04	0.32-2.34	0.79
Passive cigarette smoking	No	*Ref*					
	Yes	1.39	0.60-3.00	0.46	1.21	0.51–2.86	0.53

5.0 DISCUSSION

Lung function abnormalities among children and adolescents with SCA are prevalent and can have a substantial impact on overall well-being, quality of life and long-term prognosis. This study aimed to determine the prevalence of lung function abnormalities and associated factors among children and adolescents aged 8-18 years with SCA at MNH.We found a prevalence of 22.9% and none of the factors independently associated with abnormal lung function.

In this study, the prevalence of abnormal lung function among children and adolescents with SCA was 22.9%.These results align closely with those of Vieira et al., who identified a 23.4% prevalence of abnormal lung function in a community-based cross-sectional study in Brazil. Similarly, Kuti et al. in Nigeria reported a prevalence of 22.1%. (17,23). This consistency likely stems from comparable participant characteristics, including similar age groups, inclusion criteria, and the lung function indices (FEV1, PEF, and FVC) used for analysis. In contrast, a 2017 cross-sectional study in Nigeria reported a higher prevalence of 38% among children with SCA similar to a prospective cohort study in Italy from 2008 to 2013 which found that 30% of children and adolescents exhibited abnormal lung function. A case-control study done in Egypt showedthat 48.9% of a similar study population had abnormal lung function(3,18,20).The discrepancy in this particular study may be attributed to the use of different lung function measures, such as total lung capacity (TLC) which reflects lung capacity, and the diffusing capacity of the lungs for carbon monoxide (DLCO), which assesses gas exchange efficiency and which was estimated based on participant’s corrected hemoglobin DLCO.

The analysis revealed obstructive (9.5%), restrictive (8.3%),and mixed (5.1%) patterns of lung function test results, this could be explained by the widely evidenced proinflammatory characteristic of SCA. This inflammatory environment may drive leukocytosis, up-regulate adhesion molecules, and elevate cytokine levels, contributing to lower airway obstruction. This contrasted with the findings of Al-Biltagi et al.'s study in Egypt, where 12.2% of participants exhibited an obstructive pattern, 15.1% had a restrictive pattern, and 7.9% had a mixed pattern. Additionally, a study conducted in Nigeria revealed different results, showing a higher prevalence of restrictive patterns (30%) compared to 14% among

children from SSA compared to those from the UK (18,20).A meta-analysis and systematic review found significant variability in lung function among children and adolescents with SCA compared to adults. Obstructive patterns ranged from 4.5% to 30.9%, and restrictive patterns ranged from 2% to 30% (9). Such substantial differences can be attributed to the high heterogeneity that was observed in the review.

Observations regarding demographic factors such as gender and age did not independently correlate with abnormal lung function test results. Specifically, while 38.2% of adolescents aged 16-18 yearsexhibited abnormal lung function, no statistically significant differences were detected among various age groups. Furthermore, consistent with these results, a cross-sectional study in Brazil reported a 37.5% prevalence of abnormal lung function among participants aged 15 years and above(21). These findings echo previous studies indicating a longitudinal decline in lung function among children and adolescents with SCA(30).In this study sex was not statistically significant in lung function among children and adolescents with SCA ($p=0.15$), and this was similar to Kuti B et al. in Nigeria (23).

This study revealed that 41.8% of children and adolescents with SCA were underweight and that there was an increased odds (aOR 1.16), however there was no statistical significance aligning with the research by Cook et al. in Malawi and Yvonne et al. in Ghana and several other studies (4,31)(9). This study's findings may be influenced by anthropometric measurements such as height and weight, age, and sex, and that SCA may lower BMI but not affect lung function. Wasting among children and adolescents with SCA could potentially be attributed to the chronic illness state, making them susceptible to malnutrition(3,9). Additionally, these results align with findings from progressive longitudinal studies examining the effect of SCA on children's growth, which reveal multifactorial causes for poor growth among this population including but not limited to chronic anemia and inflammation with increased nutritional demand (32).

In a study by Biltagi et al., statistically significant clinical indicators were identified among children with abnormal lung function tests, including a history of respiratory complications, peripheral cyanosis, and lung crepitation. This aligns with the results of a prospective longitudinal study conducted by Cohen et al., which revealed that lung function abnormalities were not linked to past hospitalization rates for pain or acute pain syndrome. Additionally, they did not suggest an elevated risk in participants who experienced pain or acute chest syndrome during childhood(20,33).Despite having similar inclusion criteria and age groups, our study showed increased odds of abnormal lung function but nevertheless did not detect statistical significance in these areas. This statistical difference in findings could stem from the utilization of different methodologiesthat were not used in our study, Biltagi et al. employed additional lung function tests, including body plethysmography and induced sputum interleukin 6 (IL-6) as a marker of lung impairmentwith a sensitivity of 8 pg/ml, illustrating SCA vasculopathy on the lung resulting in airway obstruction eventually chronic obstructive lung disease(20).

Several studies have demonstrated the disease-modifying effects of hydroxyurea in patients with sickle cell anemia (SCA). It is now widely prescribed to children with SCA and has been shown to reduce leukocyte adhesion and the frequency of acute events characterized by vascular injury. Regarding lung function, previous studies have reported a slow decline among participants on hydroxyurea compared to naïve patients(2,15). Our study found that there was no statistically significant difference in lung function abnormality between participants who were on hydroxyurea and those who were not (p=0.73, CI 0.52-2.47), aligning with a meta-analysis on lung function among children and adolescents with SCA conducted by Taksande et al(9,27).The differences could be attributed to variations in the duration and dosage of hydroxyurea among study participants and the lung function parameters captured in these long-term studies.

The findings in this study showed all participants (100%) were exposed to smoke from domestic cooking, similar to findingsby Cook et al. in Malawi, where 83% of participants were exposed to biomass combustion byproducts for household cooking. This similarity can be attributed to comparable socio-economic statuses between the countries where firewood and charcoal remain widely utilized in homes. Additionally, exposure to

secondhand cigarette smoke was observed in participants with abnormal lung function(19.2%),but there was no statistical significance for abnormal lung function in the two studies (p=0.49)(4).Several studies have shown that children exposed to second-hand smoke and other air pollutants, such as indoor combustibles and cigarette smoke from household members, may experience adverse effects on lung function and growth over time. Hence the lack of significance found in our study could be attributed to the single-time assessment of lung function measured(34,35).

6.0 STRENGTHS, LIMITATIONS, CONCLUSIONS AND RECOMMENDATIONS

6.1 Strengths

This study utilized an internationally validated questionnaire that has been used in similar study settings in SSA and so ensuring the reliability and comparability of the data collected.

Also, objective lung function measurements were obtained through standard lung function assessment in this case, spirometer, conducted by a trained physiologist.

6.2 Limitations

The study participants were prone to recall bias,particularly regarding events that occurred in the preceding year such as the number of admissions due to respiratory complaints and history of blood transfusion however we were able to corroborate such information from the sickle cell passports for participants who were actively followed up in the MNH service.

While most participants consented to spirometer tests, 69 participants declined to participate for various reasons.Also, the inability to perform the bronchodilator test on all participants could underestimate the presence of reversible airway obstruction in this population. Despite these limitations, the study successfully accrued 94% of the target sample size.

6.3 Conclusion

Abnormal lung function in children and adolescents with SCA at MNH was found to be 22.9%. None of the studied factors was independently associated with abnormal lung function tests among children and adolescents with SCA.

6.4 Recommendation

Regular spirometry screenings may be considered an integral component of comprehensive care for children and adolescents with SCA addressing an important clinical issue.

Furthermore, longitudinal studies exploring lung function decline over time in children and adolescents with SCA will provide a more comprehensive understanding of the factors affecting respiratory health in children and adolescents with SCA.

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APPENDICES

Appendix 1: Investigation tools

Questionnaire in English

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

SCHOOL OF MEDICINE

QUESTIONNAIRE FOR STUDY "LUNG FUNCTION ABNORMALITIES AND ASSOCIATED FACTORS AMONG CHILDREN AND ADOLESCENTS AGED 8-18 YEARS ATTENDING SICKLE CELL CLINIC AT MUHIMBILI NATIONAL HOSPITAL."

ID number…….

PART 1: filled in by the participant

Socio-demographic data

Please circle where relevant.

1. Date of Birth……..
2. Gender: Male [1] female [2]
3. Residence: rural [1] urban [2]
4. Education level: Primary school [1] Secondary school [2] College [3] none [4]
5. Occupation: student [1] employed [2] unemployed [3] self-employed [4]

PART 2 filled out by the participant

Clinical History

1. The tendency of sickle cell clinic visits 1. Regular ( ) 2. Irregular ( )
2. Date of diagnosis……..
3. Date of Hydroxyurea initiation……
4. Hemoglobin level at the time of diagnosis…….
5. Current hemoglobin levels (if available)……and date of measurement…….
6. Is there a history of chronic cough (lasting > 2 weeks): Yes [1] No [2]

7. Is there a history of shortness of breath: Yes [1] No [2]
8. Is there a history of exercise intolerance Yes[1] No [2]
9. Is there a history of Chest Pain/ tightness: Yes [1] No [2]
10. Is there a history of weight loss: Yes [1] No [2]
11. Is there a history of recurrent fever (≥ 3 times in 6 months): Yes [1] No [2]
12. Is there a history of wheezing: yes [1] No [2]
13. Admissions due to respiratory complaints in the past year:

    ……..
14. Number of blood transfusions in the past year…….
15. Is there a history of cigarette smoking: yes [1] No [2]
16. If yes, specify the duration and number of packs per day

    ……..
17. Is there a history of passive cigarette smoking at home: Yes [1] No [2]
18. Is there a history of using the charcoal stove at home: Yes [1] No [2]

PART 3 filled by the researcher

Anthropometric measurement and physical examination:

Height (cm): ……

Weight (Kg):…….

BMI:…… BMI Z score…….

Heart rate:…… Respiratory rate:…… : SPO2:……..

Digital clubbing: yes [1] No[2]

Peripheral cyanosis: yes [1] No [2] Central cyanosis: yes [1] No [2]

Increased work of breathing: yes [1] No[2]

Presence of Rhonchi: yes[1] No[2]

Presence of crackles: yes[1] No[2]

Other Lung Findings Yes [1] NO [2]

If yes specify:

……

……

PART 4

Spirometry values

readings	FEV1	FVC	FEV1/FVC	PEF
Predicted values				
Baseline values				
Post salbutamol				

Appendix 2: Consent /assent forms

Consent in English

PERMISSION TO TAKE PART IN THE RESEARCH

***Study Title*: ABNORMAL LUNG FUNCTION AND ASSOCIATED FACTORS AMONG CHILDREN AND ADOLESCENT AGED 8-18YRS WITH SICKLE CELL ANEMIA ATTENDING SICKLE CELL CLINIC AT MNH.**

INTRODUCTION:

Hello

My name is Dr.Irene Karamaga, I am a 2nd-year resident in Pediatrics and Child Health at Muhimbili University of Health and Allied Sciences. I am a principal investigator in this study and I intend to conduct a study to determine the magnitude of lung function abnormalities among children and adolescents aged 8-18yrs with sickle cell anemia attending the sickle cell clinic at MNH.

What does this study involve? If you agree to participate in this study, the study will involve an interview whereby you will be asked questions concerning Sickle Cell Anemia. I will request your child undergo a spirometry test to determine the lung function.

What are the risks involved with taking part in this study? Participation in this study does not involve any risks, everything will be done as part of the standard care, but may involve taking some extra time answering questions and the spirometry test may be tedious.

Benefits: Feedback on your lung function result will be given on regular clinic visits, and if any abnormality is detected; the child will be sent to a specialist and will receive appropriate treatment in his/her regular visit.

Leaving the study, you may choose to stop taking part in this study at any time and for any reason. This decision will not affect your child's medical care he will continue to receive the standard medical care as required.

Cost and compensation: You will not pay for anything on participation. The cost of investigation will be covered by the principal investigator, and there will be no payments for your participation in this study

Confidentiality: Information obtained during the research will be kept confidential and it will only be accessible to the researcher. Participants will be identified by using a unique study identification number to maintain confidentiality. However, the results of your child's lung function will be shared with the attending physician to ensure the correct care is given.

Whom should you call about this study? If you have any questions about this study or need to report a study-related problem you can call Dr Irene Karamaga (0621-593696), the Principal Investigator for this study, Dr. Zawadi Edward (0754610022), the main supervisor

If you have questions about your rights as a participant, you may contact The Director of Publication and Research, at Muhimbili University of Health and Allied Sciences. Research and Publication Committee, P.O. Box 65001, Dar es Salaam, Telephone number 22 2152489

I have read/ or have had the above information read to me about the research and have been given time to ask questions. I agree for my child to take part in this study.

SIGNATURE

Parent/ Guardian ……. Date……

Researcher name…….Signature ……. Date……

Participant no:……

Appendix 3: Fomu ya ridhaa kwa mzazi/mlezi

RIDHAA YA KUSHIRIKI KWENYE UTAFITI

Namba ya utambulisho

Utangulizi:

Habari

Jina langu ni Dr.Irene Karamaga, mwanafunzi wa shahada ya uzamili ya udaktari wa watoto katika Chuo cha Sayansi Shirikishi cha Muhimbili. Ninafanya utafiti juu ya ufanyaji kazi wa mapafu kwa watoto na vijana rika wenye siko celi. Ninaomba ruhusa yako ili mtoto wako ashiriki kwenye utafiti huu.

Mada ya Utafiti: UKUBWA WA MATATIZO KATIKA UFANYAJI KAZI WA MAPAFU KWA WATOTO NA VIJANA RIKA WENYE SIKOSELI WANAOHUDHURIA KLINIKI ZA SIKOSELI KATIKA HOSPITALI YA TAIFA YA MUHIMBILI.

Dhumuni la utafiti huu: Utafiti unahusu tathimin ya viwango vya ufanyaji kazi wa mapafu ya watoto na vija rika wenye Siko Celi. Hii itasaidia katika kupanua na kuendeleza elimu juu ya matatizo y ugonjwa huu.

Utaratibu wa utafiti: Kama utakubali kushiriki katika utafiti huu,Mzazi ataulizwa maswali juu ya ugonjwa huu wa Siko Celi. Pia kumpima motto mapafu ya kwa kutumia kipimo cha spirometry.

Hasara za utafiti?: Hakuna hatari yoyote kwa mtoto, na kila kitu kitafanyika kama sehemu ya viwango vya huduma za afya. Lakini tutachukuwa mda wako kidogo kuuliza maswali na kufanya upimaji wa ufanyaji kazi wa mapafu

Faida za utafiti?: Utapata majibu ya vipimo vyako katika siku unazohudhuria kiliniki, na ikiwa tutaona shida ya ufanyaji kazi wa mapafu, mtoto ataangaliwa zaidi na madaktari bingwa na kutibiwa kwa kadri anavyo hudhuria kiliniki.

Kujiondoa katika utafiti: Ni muhimu kujua kuwa, ni hiari kushiriki kwenye utafiti huu na ikitokea kuwa umekataa mtoto wako kushiriki, mtoto wako ataendelea kupata huduma inayotakiwa bila kujali maamuzi yako kuhusiana na utafiti huu. Pia ikitokea kuwa umebadilisha mawazo na ukawa hautaki kuendelea na utafiti huu, maamuzi yako yataheshimika.

Gharama na fidia: Hautalipia kitu chochcote na gharama za vipimo zitalipwa na mtafiti mkuu.

Tafadhali kumbuka kuwa utafiti huu hautakupa garama zozote za ziada na pia hautalipwa kwa kukubali kushiriki kwenye utafiti huu.

Utunzaji wa taarifa: Tarifa za watoto wenu zitachukuliwa na kutunzwa kwa usiri mkubwa na majina ya watoto wenu hayataandikwa, na watafiti hawata eleza tarifa hizi kwa mtu mwingine yeyote bila ridhaa yako.

Ikitokea ukawa na maswali au tatizo lolote kuhusiana na utafiti huu, tafadhali wasiliana na Dr Irene Karamaga ambaye ni mtafiti wa utafiti huu kupitia namba yake ya simu 0621593696 au Dr Zawadi Edward kwa simu namba 0754610022 ambaye ni msimamizi mkuu wa utafiti huu

Kama una maswali yeyote kuhusu haki yako kama mshiriki, unaweza kuwasiliana na Mkurugenzi wa Machapisho na Utafiti, wa Chuo Kikuu cha Sayansi Shirikishi cha Muhimbili kwa anuani ifuatayo: Research and Publication Committee, P.O. Box 65001, Dar es Salaam, au simu namba 22 2152489

Ridhaa: Nimesoma na kuelewa maelezo niliyopewa kuhusiana na utafiti huu na kwa akili yangu timamu na bila kulazimishwa na mtu, nimekubali ushiriki wa mtoto wangu kwenye utafiti huu.

Sahihi: Sahihi ya Mzazi/ Mlezi wa Mtoto……. Tarehe ……

Jina na sahihi ya mtafiti ……Tarehe ……..
Mshiriki no:……

Appendix 4: Assent in English

ID NO……..

PERMISSION TO TAKE PART IN THE RESEARCH

Study Title: Lung function abnormalities and associated factors among children and adolescents aged 8-18yrs with sickle cell anemia attending sickle cell outpatient clinic at MNH.

INTRODUCTION:

Hello

My name is Dr.Irene Karamaga, I am a 2nd-year resident in Pediatrics and Child Health at Muhimbili University of Health and Allied Sciences. I am a principal investigator in this study and I am intending to conduct a study to determine the magnitude of lung function abnormalities and associated factors among children and adolescents with Sickle Cell Anemia attending the sickle cell outpatient clinic at MNH

What does this study involve? If you agree to participate in this study, the study will involve an interview whereby you will be asked questions concerning Sickle Cell Anemia. I will request your permission to screen you for lung function using spirometry.

What are the risks involved with taking part in this study? Participation in this study does not involve any risks; everything will be done as part of the standard care but may involve taking some extra time answering questions and taking a little amount of your blood from your forearm which will be a little bit painful.

Benefits: Feedback on your lung function result will be given on regular clinic visits, and if any lung function abnormality will be detected; you will be sent to a specialist and you will receive appropriate treatment in your regular CTC visit.

Leaving the study: You may choose to stop taking part in this study at any time and for any reason. This decision will not affect your medical care and you will continue to receive the

standard medical care as required.

Cost and compensation: You will not be paid for anything on participation. The cost of investigation will be covered by the principal investigator, and there will be no payments for your participation in this study

Confidentiality: Information obtained during the research will be kept confidential and it will only be accessible to the researcher. Participants will be identified by using a unique study identification number to maintain confidentiality. However, the results of your lung function will be shared with the attending physician to ensure the correct care is given.

Whom should you call about this study?

If you have any questions about this study or need to report a study-related problem you can call Irene Karamaga (0621593696) the Principal Investigator for this study, Dr. Zawadi Edward (0754610022), the main supervisor

If you have questions about your rights as a participant, you may contact The Director of Publication and Research, at Muhimbili University of Health and Allied Sciences. Research and Publication Committee, P.O. Box 65001, Dar es Salaam, Telephone number 22 2152489

I have read/ or have had the above information read to me about the research and have been given time to ask questions. I agree to be part of this study.

SIGNATURE

Child signature ……. Date……

Researcher name…….Signature ……. Date……

Participant no……

Appendix 5: Fomu ya ridhaa Kwa motto/kijana rika

Namba ya utambulisho……

Utangulizi:

Habari , Jina langu ni Dr.Irene Karamaga, mwanafunzi wa shahada ya uzamili ya udaktari wa watoto katika Chuo cha Sayansi Shirikishi cha Muhimbili. Ninafanya utafiti juu ya ukubwa wa matatizo ya ufanyaji kazi wa mapafu kwa watoto na vijana rika wenye ugonjwa Siko Celi katika hospitali ya taifa ya Muhimbili.

Mada ya Utafiti: UKUBWA WA MATATIZO KATIKA UFANYAJI KAZI WA MAPAFU KWA WATOTO NA VIJANA RIKA WENYE SIKOSELI WANAOHUDHURIA KLINIKI ZA SIKOSELI KATIKA HOSPITALI YA TAIFA YA MUHIMBILI

Dhumuni la utafiti huu: Utafiti unahusu tathimin ukubwa wa tatizo la ufanyaji kazi wa mapafu kwa watoto na vijana rika wenye Siko Seli. Hii itasaidia katika kupanua na kuendeleza elimu juu ya matatizo ya ugonjwa huu.

Utaratibu wa utafiti: Kama utakubali kushiriki katika utafiti huu, nitaomba kukuliza maswali kuhusiana na ugonjwa wa Siko Seli. Pia nitaomba kufanya kipimo cha kuaangalia ufanyaji kazi wa mapafu kwa kutumia kipimo cha spirometry.

Hasara za utafiti?: Hakuna hatari yoyote kwako, na kila kitu kitafanyika kama sehemu ya viwango vya huduma za afya. Lakini tutachukuwa mda wako kidogo kufanya kipimo cha spirometry.

Faida za utafiti?: Utapata majibu ya vipimo vyako katika siku unazohudhuria kiliniki, na ikiwa tutaona shida ya ufanyaji kazi wa mapafu, mtoto ataangaliwa zaidi na madaktari bingwa na kutibiwa kwa kadri anavyo hudhuria kiliniki.

Kujiondoa katika utafiti: Ni muhimu kujua kuwa, ni hiari kushiriki kwenye utafiti huu na ikitokea kuwa hujaridhia kushiriki, utaendelea kupata huduma unazotakiwa kupata bila kujali maamuzi yako kuhusiana na utafiti huu. Pia ikitokea kuwa umebadilisha mawazo na ukawa hautaki kuendelea na utafiti huu, maamuzi yako yataheshimika.

Gharama na fidia: Hautalipia kitu chochcote na gharama za vipimo zitalipwa na mtafiti mkuu.

Tafadhali kumbuka kuwa utafiti huu hautakupa garama zozote za ziada na pia hautalipwa kwa kukubali kushiriki kwenye utafiti huu.

Utunzaji wa taarifa: Taarifa zako zitachukuliwa na kutunzwa kwa usiri mkubwa na majina yako hayataandikwa, na watafiti hawata eleza tarifa hizi kwa mtu mwingine yeyote bila ridhaa yako.

Ikitokea ukawa na maswali au tatizo lolote kuhusiana na utafiti huu, tafadhali wasiliana na Dr Irene Karamaga ambaye ni mtafiti wa utafiti huu kupitia namba yake ya simu 0621593696 au Dr Zawadi Edward kwa simu namba 0754610022 ambaye ni msimamizi mkuu wa utafiti huu .

Kama una maswali yeyote kuhusu haki yako kama mshiriki, unaweza kuwasiliana na Mkurugenzi wa Machapisho na Utafiti, wa Chuo Kikuu cha Sayansi Shirikishi cha Muhimbili kwa anuani ifuatayo: Research and Publication Committee, P.O. Box 65001, Dar es Salaam, au simu namba 22 2152489

Ridhaa: Nimesoma na kuelewa maelezo niliyopewa kuhusiana na utafiti huu na kwa akili yangu timamu na bila kulazimishwa na mtu, nimekubali kushiriki kwenye utafiti huu.

Sahihi

Sahihi ya Mtoto……. Tarehe ……

Jina na sahihi ya mtafiti …….Tarehe ……..

Mshiriki no:……

Appendix 6: Ethical clearance

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATIONS

Ref. No.DA.282/298/01.C/ Date:

23/10/2023 MUHAS-REC-10-2023-1953
IRENE KARAMAGA
College of Medicine
MUHAS

RE: **APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: LUNG FUNCTION ABNORMALITIES AND ASSOCIATED FACTORS AMONG CHILDREN AND ADOLESCENTS AGED 8-18YEARS WITH SICKLE CELL ANEMIA ATTENDING SICKLE CELL CLINIC AT MUHIMBILI NATIONAL HOSPITAL**

Reference is made to the above heading.
I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects' research.
APPROVAL DATE: 23/10/2023
EXPIRATION DATE OF APPROVAL: 23/10/2024

STUDY DESCRIPTION:
Purpose:

The purpose of this cross-sectional study is to determine the prevalence of lung function abnormalities and associated factors among children and adolescents aged 8-18 years with sickle cell anemia attending sickle cell clinic at Muhimbili National Hospital

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2015015.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain Data Transfer Agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain Material Transfer Agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country.
8. Apply for and obtain permission to publish the results from National Institute for Medical Research. The application should be before submitting to a publisher and not concurrently through the email publications@nimr.or.tz.
9. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
10. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
11. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.

Dr. Nahya Salim Masoud,
Chairperson, MUHAS Research and Ethics Committee

Appendix 7: Permission letter

THE UNITED REFUBLIC OF TANZANI

MINISTF Y OF HEALTH

MUHIMBILI NO TIONAL HOSPITAL

In reply please quote;

Ref. No. MNH/CRTCU/Perm/2023/54† Date: 03rd November, 2023

Head of Department Pediatrics and Child Health
Noted; 13.11.2023
Muhimbili National Hospital Upanga & Mloganzila

RE: PERMISSION TO COLLECT DATA AT MNH

Name of student	Irene Karamaga
	Lung function abnormalities and associated factors among children and adolescents aged 8-18 years with Sickle Cell Anemia Attending Sickle cell Clinic at MNH".
Institution	Muhimbili University of Health and Allied Sciences
Supervisor	Nana Nakiddu (MUHAS)
Co — Supervisor	Dr. Zawadi Edward
Period	03rd November, 2023 to 28th February, 2024

Approval has been, granted to the above principal investigators to collect data at MNH. Dissemination of study findings at MNH shall be overseen by Dr. Zawadi Edward (MNH) supervisor.

Kindly ensure the named principal investigator abide to the ethical principles And other conditions of the research approval

Sincerely,

Dr. Deus Buma
For: Head of Clinical Research, Training and Consultancy Unit

P.O. Box 65000 DAR-ES-S

cc DMS
cc Dr. Zawadi Edward
cc Irene Karamaga

Upanga West Kalonga Street Plot No 0180/1† P.O. BOX 65000, Dar es Salaam, Tanania Telephone +255-22-2151317 6, Felephone +2e5-22 2151351-2
Email: info@mnh or tz, Website: www.mnh or tz.

Appendix 8: Turnitin

turnitin

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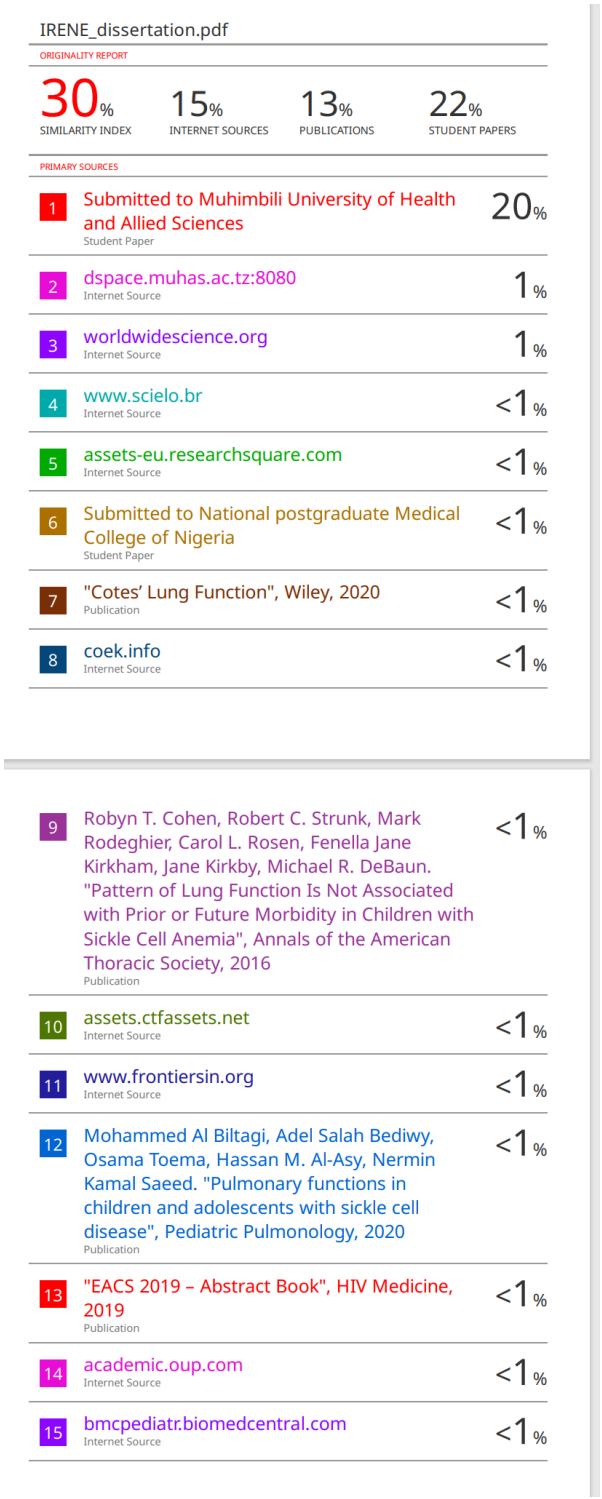


LUNG FUNCTION ABNORMALITIES AND ASSOCIATED FACTORS AMONG CHILDREN AND ADOLESCENTS AGED 8-18 YEARS WITH SICKLE CELL ANEMIA ATTENDING SICKLE CELL CLINIC AT MUHIMBILI NATIONAL HOSPITAL

Irene K. Karamaga, MD

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Appendix 9: Plagiarism



IRENE_dissertation.pdf

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