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Prevalence, patterns, and factors associated with abnormal lung function among children with sickle cell disease in Uganda: a cross-sectional study

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Abstract

Background Pulmonary complications are common among children with sickle cell disease (SCD). However, there is little literature on associated lung function abnormalities in Uganda. We aimed to determine the prevalence, patterns, and factors associated with abnormal lung function among children with SCD in a tertiary care hospital in Uganda.

Method A cross-sectional study was conducted among children aged 6 to 18 years at the SCD clinic (SCC) of Mulago National Super-Specialized Hospital between January 2020 and April 2021. Data on sociodemographic and clinical characteristics was collected using a standardized questionnaire. Laboratory investigations, including a complete blood count and serum lactate dehydrogenase (LDH), were done. Spirometry was performed following the ATS/ERS standards. Multivariable modified Poisson regression analysis was performed to determine factors associated with abnormal lung function.

Results A total of 332 participants were enrolled. The mean age was 11.7 ± 3.4 years, and 184 (55.4%) were female. Overall, 126 (37.9%) participants had abnormal lung function: 67/126 (53.2%) restrictive, 57/126 (45.2%) obstructive, and 2/126 (1.6%) mixed-ventilatory patterns. Factors associated with abnormal lung function were; serum LDH level > 600UL (aIRR: 1.89 95% CI: 1.2 — 7.4, $p = 0.049$), a history of acute chest syndrome (aIRR: 1.55, 95% CI: 1.06–2.25, $p = 0.024$), wasting (aIRR: 1.33, 95%CI: 1.02 — 1.72, $p = 0.032$), and use of charcoal for household cooking (aIRR: 1.49, 95% CI: 1.03–2.15, $p = 0.035$**).**

Conclusion More than one-third of children with SCD in Uganda have lung function abnormalities. Strategies to improve nutrition, reduce exposure to charcoal smoke, and monitoring serum LDH levels may be important in preventing or managing abnormal lung function in this population. The identification of reversible and irreversible airway obstruction in children with sickle cell disease also highlights the need for targeted interventions to address these specific patterns of abnormal lung function.

Keywords Sickle cell disease, Lung function, Children, Uganda

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Introduction

Sickle cell disease (SCD) is the most prevalent hereditary disorder affecting millions of people globally [1]. About 300,000 babies are born with SCD annually [2]. The majority of these births are in sub-Saharan Africa (SSA), where more than 75% of people with SCD are found; this proportion projected to increase by 2050 [3]. SCD is an important public health problem accounting for about 5% of under-five mortality in Africa [4]. In Uganda, about 20,000 babies with SCD are born each year. [5]. About 70–80% of these children die before their fifth birthday and this contributes 16.2% of all annual deaths among children less than five years in Uganda [6].

Acute and chronic pulmonary complications related to SCD, including pneumonia, acute chest syndrome (ACS), chronic hypoxaemia and pulmonary hypertension, are major causes of morbidity and mortality, contributing up to 20–30% of all-cause mortality in people with SCD [7]. Hypoxic-ischemic injuries, and embolisation from bone marrow infarcts contribute significantly to the pathogenesis of lung disorders in SCD including lung function abnormalities, interstitial lung disease, and pulmonary hypertension [8]. Lung function abnormalities such as lower lung volumes, decreased diffusion lung capacity, airway hyper-responsiveness, and hypoxemia are common in children with SCD even at a steady state [9]. Although some children with lung function abnormalities are usually asymptomatic, a significant proportion may have reduced exercise tolerance [10]. A few studies have elucidated the prevalence and pattern of abnormal lung function among children with SCD in Africa [11]. In Nigeria, a prevalence of abnormal lung function of up to 65.8% was reported [12] while in Malawi, it was 62% [13]. Reversible obstructive airway pattern has been estimated to occur in about 5–35% and restrictive pattern in 8–22% of children with SCD [14].The restrictive pattern is generally more common, however, among children less than five years, the obstructive pattern is more prevalent. Studies have also noted that obstructive patterns are more common in high-income countries while restrictive type is more prevalent in low and middle-income countries [9, 12, 13, 15]. In African-Americans, the obstructive airway pattern was noted to precede the development of restrictive airway pattern [16]. There is no data on the burden of the lung function abnormalities among children with SCD in Uganda. This study aimed to determine the prevalence, patterns and factors associated with abnormal lung function among children with SCD at a tertiary care hospital in Uganda.

Methods

Study design

This was a cross-sectional study, conducted at the Sickle Cell Clinic (SCC) of Mulago National Super-Specialized Hospital in Kampala, Uganda, between January 2020 and April 2021.

Study setting

Mulago Hospital is the largest National Referral hospital in Uganda. It also serves as a teaching hospital for Makerere University College of Health Sciences and other training institutions. The hospital has a total bed capacity of about 1500, and of these, 400 (26.7%) are for the Paediatrics section. The average number of patients seen at Mulago hospital annually is 480,000. The Department of Paediatrics and Child Health runs 8 specialized clinics including the SCC, which had an estimated 14,000 active patients at the time of the study. The clinic has about 1500 patient visits in a month, and of these, 70 are newly diagnosed patients with SCD. According to the patient register, the main reason for patients seeking care at the SCC are respiratory symptoms contributing up to 250 (16.7%) of the monthly visits. Most (75%) of the patients attending SCC are below 18 years and most come from Kampala city where the clinic is located and surrounding districts. The clinic runs from Monday to Friday (8 am – 4 pm), with an average of 40 to 70 patients per day. All patients receive cost-free standard care, including daily folic acid tablets, monthly sulfadoxine-pyrimethamine, and daily oral Phenoxymethylpenicillin (Penicillin V) for children less than five years of age. However, patients have to buy hydroxyurea, and for this reason, only about 2500 (17.8%) of the patients regularly get hydroxyurea. Investigations, including a complete blood count (CBC), chest radiography and cardiac echocardiogram, are done at the discretion of the attending clinician.

Study population

The study population were children with a confirmed diagnosis of SCD based on hemoglobin electrophoresis who attended the SCC clinic during the study period. Children who were aged 6 up to18 years and in steady state were eligible to participate in the study. A steady state was defined as the absence of emergencies like painful crises, acute chest syndrome, or acute illnesses from infections like malaria, pneumonia, or septicaemia. We excluded children with debilitating stroke and those with contraindications to spirometry.

Sample size estimation

To determine the prevalence of abnormal lung function among children aged 6 up to 18 years attending Mulago Hospital Sickle Cell Clinic, we estimated a minimum sample size of 332 children, based on a study done among children with SCD in Nigeria [12] that estimated that 68.5% of the participants had abnormal lung function. To determine the prevalence of abnormal lung function

among the participants, we used the KishLesile (1965) formula for cross sectional studies as shown below.

$$N = \frac{P(1-p)Z^2}{d^2}$$

whereby;

Z=Standard normal value corresponding to 95% Confidence Interval (1.96).

p=the prevalence of the abnormal lung function which was 68.5% in the study in Nigeria [12].

d=Absolute error between the estimated and true value=0.05 (5%).

$$N = \frac{0.685(1-0.685) * 1.96^2}{(0.05)^2}$$

N=332

To describe the factors associated with abnormal lung function among children with SCDe aged 6 up to 18years attending Mulago Hospital Sickle cell clinic, we used the Fleiss formula. assuming a 2-sided confidence level of 95% and 80% power, and based on same study in Nigeria which showed that children with previous ACS were 3.6 times more likely to have impaired lung function than those without recurrent ACS [12]. The minimum sample size was estimated to be 112 participants. Therefore, the overall sample size to address both objectives was 332.

Data collection

Data was collected using structured, researcher-administered questionnaires(supplementary file.1). Before data collection, the questionnaires were pre-tested on 10 caregivers of children with SCD to check for understanding and flow, and the necessary revisions were made. After obtaining informed consent from the caregivers and assent for children 8 years and above, the study nurse and principal investigator administered the questionnaire. The questionnaire included information on sociodemographic characteristics, respiratory symptoms, the number of hospital admissions in the previous one year, age at diagnosis of SCD, history of vaso-occlusive crises and acute chest syndrome, current medication, history of blood transfusion, history of active and/or passive tobacco smoking and cooking energy commonly used in the home. Information on the HIV sero-status was obtained from the patient's file. The study doctor did a physical examination, and this included anthropometric measurements of weight and height. The weight was measured using the SECA weighing scale while the height was measured using a stadiometer. Wasting was defined as zBMI<−2. The resting peripheral arterial oxygen saturation in room air was measured using a finger pulse oximeter with infrared light (Nonin pure SAT, United State of America).

Spirometry

The spirometry technician screened all participants for contra-indications to spirometry testing using a structured screening tool. Spirometry was performed in accordance with the American Thoracic Society/European Respiratory Society [ATS/ESR] standard protocol using the Vitalograph 6800 Pneumotrac spirometer. Briefly, the spirometer was calibrated every morning before starting the procedures. The tests were conducted in a quiet and well-ventilated room. The participants were instructed to blow into the mouthpiece as hard and as fast as they could and to continue blowing until there was no more air to exhale. After each blow, the quality of the curves was quickly assessed by the technician, and a decision was made to accept or reject it. The maneuver was repeated until three good-quality tests were obtained. The participants were then given 400 micrograms of salbutamol inhaler using a spacer, and the spirometry maneuver was repeated 15–20 min later. A maximum of 8 trials were allowed for each participant, and if a participant could not produce 3 quality tests from the 8 attempts, the test differed to another day.

Quality checks and interpretation of the spirograms was performed by two independent reviewers. All disagreements between the two reviewers were resolved by a third reviewer. The Global Lung Function Initiative [GLI 2012] reference values were used to interpret the spirometry results [6]. Spirometry patterns were classified as normal, obstructive, restrictive or mixed as shown in the table below.

Parameter	Percentage predicted	Classification
FEV1/FVC	> 70%	Normal
FEV1	> 80%	
FVC	> 80%	
FEV1/FVC	< 70%	Obstructive pattern
FEV1	< 80%	
FVC	≥ 80% or < 80%	
FEV1/FVC	≥ 70%	Restrictive pattern
FEV1	≥ 80% or < 80%	
FVC	< 80%	
FEV1/FVC	< 70%	Mixed type
FEV1	< 80%	
FVC	< 80%	

The coronavirus disease 2019 (COVID- 19) Standard Operating Procedures (SOPs) for prevention and control were observed throughout the data collection processes. All the participants were screened for signs and symptoms of COVID-19 before spirometry.However, the participants were not tested for COVID-19. This is because at the time of conducting the study, access to COVID-19

testing in the country was still low and reserved for symptomatic people and/or travelers.

Laboratory procedure

Two to three milliliters of mls venous blood were drawn into a vacutainer with clot activator under aseptic technique and transported to the laboratory in a cool box, within one hour of collection, to be analyzed for serum lactate dehydrogenase (LDH) level.

In the laboratory, the sample was immediately centrifuged for 10 min at 2000 x g, and serum was separated from the cells; the serum was then stored at -20 degrees. It was later defrosted and run in batches of 30 samples using a Cobas 6000, LDH12 reagent kit.

Data management and analysis

The principal investigator checked all the data from the questionnaires, physical examination, and laboratory tests for completeness. The spirometry test results were evaluated for quality by an independent team of three clinicians with certified training in spirometry. Data entry was done using Epidata version 3.1 and exported to STATA Version 15 for further cleaning and analysis. All hard copy data were kept under lock and key and were accessed by the principal investigator and the research assistant only. The study computers were password-protected.

Continuous data were summarized as means with standard deviation for normally distributed data and medians with and interquartile ranges for skewed data. Categorical variables were summarized as frequencies and percentages. The Chi-Square test was used to compare proportions between the categorical variables with the outcome. The Student's t-test was used to analyze continuous data.

At bivariate analysis, Poisson regression analysis with robust variance was performed to assess for factors associated with the abnormal lung function. Crude Incidence Risk Ratios (cIRR) and 95% confidence interval (CI) were reported. Variables with $p \leq 0.2$ at bivariate analysis were entered in a backward stepwise multi-variable Poisson regression analysis. Adjusted Incidence Risk Ratios (aIRRs) and the 95% CIs were reported as measure of independent association between the independent variables and abnormal lung function. A $p < 0.05$ was considered statistically significant. The goodness of fit of the model was tested using the Akaike information criterion (AIC).

Quality control

Consent and assent forms were translated into Luganda, the main language spoken in the study area. The research assistants were trained on the study protocol, data collection tools, data handling and consent process. The questionnaires were crosschecked for completeness and accuracy daily before entering the data into the database. The Spirometer was calibrated daily by the spirometry technician. The SECA weighing scale was calibrated daily before measurements were made.

Results

Participants

A total of 345 participants were recruited, with 100% response rate and of these, 184 (55%) were females. The mean age (SD) was 11.7±3.4 years. The majority 332 (96%) of the participants had valid spirograms. The details of the study profile and socio-demographics of the participants are summarized in Fig. 1 and Table 1

Prevalence and patterns of lung function abnormalities among children with SCD

A total of 126 (38%, 95% CI, 32.9–43.3) participants had abnormal lung function; 67 (20%) had restrictive, 57 (17%) had obstructive and 2 (0.6%) had mixed ventilator patterns. Of the 57 who had obstructive patterns, 30 (53%) had reversible airway obstruction, and 27(47%) had irreversible airway obstruction. (Fig. 2)

Clinical and laboratory characteristics of the study participants

Of the 332 participants, 256 (77%) were diagnosed with SCD before the age of 5 years. Sixty-one (19%) reported a history of wheezing in the previous 12 months, 26 (8%) had a history of acute chest syndrome, and 62 (19%) had low peripheral oxygen saturation (SpO2 < 92%) at the time of enrolment. Ninety-five (29%) of the participants had ever been hospitalized with acute respiratory symptoms, 56 (17%) had received a blood transfusion in the 6 months prior to enrollment, and 222 (67%) had hydroxyurea at some point during the previous year. Lactate dehydrogenase was elevated (>600 IU/litre) in 85(26%) of the participants. Details of the clinical and laboratory characteristics of the study participants are summarized in Table 2, below.

Factors associated with abnormal lung function in children with SCD

The factors that were significantly associated with abnormal lung function were; wasting (IRR: 1.33, 95% CI: 1.0 — 1.7, $p = 0.032$), a history of acute chest syndrome (aIRR: 1.55, 95%CI: 1.1 — 2.3, $p = 0.024$), $SpO_2 < 92\%$ (aIRR: 1.69, 95% CI: 1.3 — 2.2, $p < 0.001$), use of charcoal for cooking (IRR: 1.49, 95% CI: 1.1 — 2.1, $p = 0.033$), moderate serum LDH levels [between 401 and 600 U/L (aIRR: 1.99, 95% CI: 1.1 — 3.7, $p = 0.029$), and high serum LDH levels > 600 U/L (aIRR: 1.89, 95% CI: 1.0 — 3.6, $p = 0.049$)]. The details are provided in table 3.

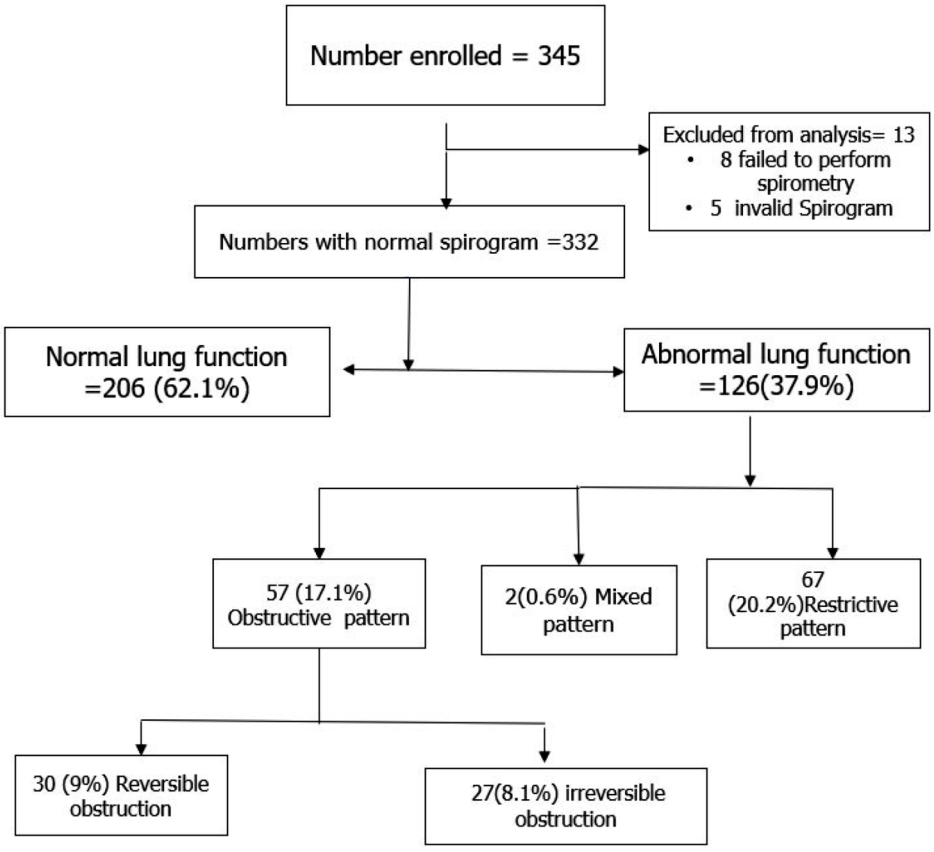

Fig. 1 Study profile

Table 1 Socio-demographic characteristics of the participants (*N* = 332

Variables	Normal (*n* = 206) (Frequency, %)	Obstructive (*n* = 57) (Frequency, %)	Restrictive (*n* = 67) (Frequency, %)	Mixed (*n* = 2) (Frequency, %)	Total (*n* = 332) (Frequency ,%)
Age (years) 6–10	89(43.2)	24(42.1)	20(29.9)	1(50.0)	134(40.4)
11–14	77(37.4)	20(35.1)	23(34.3)	0(00)	120(36.1)
15–18	40(19.4)	13(22.8)	24(35.8	1(50.0)	78(23.5)
Sex Male	94(45.6)	21(36.8)	33(49.3)	0(00)	148(44.6)
Female	112(54.4)	36(63.2)	34(50.8)	2(100)	184(55.4)
Residence Rural	54(26.2)	19(33.3)	21(31.3)	1(50.0)	95(28.6)
Urban	152(73.8)	38(66.7)	46(68.7)	1(50.0)	237(71.4)

Discussion

The prevalence of abnormal lung function among children with SCD was high. More than half of the lung function abnormalities showed a, with half of restrictive pattern. This is different from findings in developed countries that reported higher prevalence of obstructive ventilatory pattern [16]. However, our findings are similar to studies done in Africa which showed higher prevalence of restrictive ventilatory pattern in children with SCD [8, 9, 13]. This difference may suggest more severe lung disease in children in sub–Saharan Africa compared to their counterparts in high-income countries. The exact cause of lung abnormalities and disease in SCD is not clear. However, there some evidence suggesting that these could be due to increased pulmonary capillary blood volume associated with anemia [17]. Some studies have indicated that abnormal lung function could be related to the inflammation which is part of the pathophysiology of SCD, in which several cytokines like TNF, IP-10 and IL-4 are released. [18]. It is also possible that lung function abnormalities are a result of the destruction of erythrocytes freeing up haem [19], which uses nitric oxide, significantly increasing vasodilation. The subsequent compromised blood flow induces obstruction in the lung

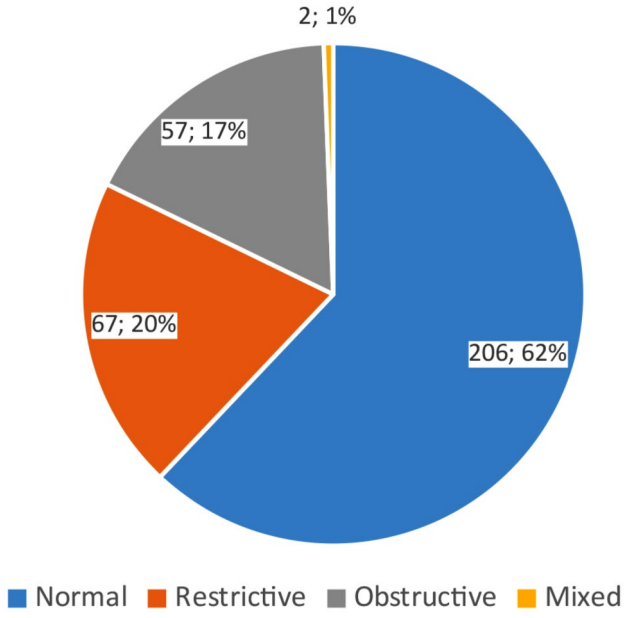

Fig. 2 Study profile

blood vessels, leading to acute chest syndrome and, in some cases, producing emboli [20]. Abnormal lung function in childhood is associated with an increased risk of chronic lung diseases like asthma and Chronic Obstructive Pulmonary Disease [21]. For children with sickle cell disease who already have a high risk of pulmonary complications like Acute Chest Syndrome, chronic hypoxaemia and pulmonary hypertension, the presence of lung function abnormalities indicates the potential likelihood of suffering from a wide range of chronic lung diseases [22]. Therefore, a high prevalence of abnormal lung function among children with SCD may indicate that a significant proportion of children with SCD will suffer a wide range of pulmonary complications throughout their life course. Early detection through screening may be associated with a reduction in the risk of chronic lung diseases and subsequent associated mortality among children with SCD.

Patterns of ventilatory abnormalities in children with SCD

The study showed that more than half of the children with lung abnormalities had restrictive ventilatory patterns. A significant proportion had obstructive patterns, and very few had a mixed type of ventilatory defect. These findings are similar to those from and study among adults with SCD in Lagos Nigeria in which more than half of the abnormal lung function were of restrictive pattern [23]. In this study, the mean forced vital capacity was reduced, inferring poor ventilation [23].A significant proportion of participants with abnormal lung function had the obstructive type, and this phenotype is thought to be due to cellular endothelial adhesion following rigidity of the cell membrane [18].

In this study, wasting increased the risk of abnormal lung function by nearly 2-folds. This observation is consistent with studies in Nigeria and the Central African Republic, which found that wasting was associated with a 2.3-4-fold increased risk of abnormal lung function [9, 11]. [24] Wasting affects the chest dimensions and the strength of the expiratory muscle, leading to poor expiratory effort. Wasting could also be a result of increased metabolic demands due to a more severe lung disease [11]. Wasting among children with SCD has also been associated with frequent and prolonged hospitalizations

Table 2 Clinical and laboratory characteristics of the participants

Variables	Normal (*n* = 206) (frequency, %)	Obstructive (*n* = 57) (Frequency, %)	Restrictive (*n* = 67) (frequency, %)	Mixed (*n* = 2) (frequency, %)	Total (*n* = 332) (Frequency, %)
Body Mass Index Z-score					
Normal	154(74.8)	44(77.2)	31(46.3)	1(50.0)	230(69.3)
Wasting	52(25.2)	13(22.8)	36(53.7)	1(50.0)	102(30.7)
History of blood transfusion within 6 months prior to enrolment	35(16.9)	4(7.0)	17(25.4)	0(00)	56(16.9)
Use of Hydroxyurea	133(64.6)	40(70.2)	48(71.6)	1(50.0)	222(66.9)
History of acute chest syndrome	11(5.3)	6(10.5)	9(13.4)	0(00)	26(7.8)
History of wheezing in the previous 12 months	30(14.6)	12(21.1)	19(28.4)	0(00)	61(18.4)
Presence of enlarged tonsils and/or nasal turbinates	76(36.9)	24(42.1)	23)34.3)	0(00)	123(37.1)
Low peripheral oxygen saturation (SpO_2) < 92%	27(13.1)	13(22.8)	22(32.8)	0(00)	62(18.7)
Serum lactate Dehydrogenase U/L					
135–225 (normal)	31(15.0)	4(7.0)	4(5.1)	0(00)	39(11.7)
226–400 (mild)	65(31.6)	17(29.8)	8(11.9)	1(50.0)	91(27.4)
401–600 (moderate)	65(31.6)	24(42.1)	27(40.3)	1(50.0)	117(35.2)
> 600 (severe)	45(21.8)	12(21.1)	28(41.7)	0(00)	85(25.6)

Underweight(wasting) < -2SD, median BMI 16.12(IOR 14.92–17.86)

Table 3 Factors associated with abnormal lung function among children with SCD (*N* = 332)

Variables	Category	Lung function (*N* = 332)		Crude IRR (95% CI)	*p* value	Adjusted IRR (95% CI)	*p*-value
		Normal (*n* = 206) ,%	Abnormal (*n* = 126) %				
Age of the child (years)		11.4 ± 3.3	12.3 ± 3.4	1.05 (1.01,1.09)	0.016	1.02(0.98,1.07)	0.196
BMI	Normal	154(74.8)	76(60.3)	1.00		1.00	
	Wasting	52(25.2)	50(39.7)	1.48(1.13,1.94)	0.004	1.33(1.02,1.72)	0.032
History of recurrent Wheezing	No	176(85.4)	95(75.4)	1.00		1.00	
	Yes	30(14.6)	31(24.6)	1.44(1.08,1.94)	0.014	1.32(0.98,1.77)	0.065
History of Acute chest syndrome	No	195(94.7)	111(88.1)	1.00		1.00	
	Yes	11(5.3)	15(11.9)	1.59(1.11,2.28)	0.012	1.55(1.06,2.25)	0.024
HIV infection/positive	No	204(99.1)	120(95.2)	1.00		1.00	
	Yes	2(0.9)	6(4.8)	2.03(1.32,3.09)	0.001	1.39(0.81,2.40)	0.228
Serum LDH (IU/L)	135–225	31(15.1)	8(6.4)	1.00		1.00	
	126–400	65(31.6)	26(20.6)	1.39(0.69,2.80)	0.353	1.48(0.76,2.40)	0.246
	401–600	65 [5, 31]	52(41.3)	2.17(1.13,4.16)	0.020	1.99(1.07,3.73)	0.029
	> 600	45(21.8)	40(31.8)	2.29(1.19,4.43)	0.013	1.89(1.00,3.56)	0.049
Use of charcoal for cooking	No	54(26.2)	105(83.2)	1.00		1.00	
	Yes	152(73.9)	21(16.7)	1.46(0.98,2.16)	0.059	1.49(1.02,214)	0.035
SpO2 (%)	< 92(abnormal)	27(13.1)	35(27.8)	1.0		1.0	
	> 92(normal)	179(86.9)	91(72.2)	1.67(1.27,2.21)	< 0.001	1.69(1.29,2.22)	< 0.001

IRR: incidence risk ratio, CI: confidence interval, BMI: body Mass Index

during which nutritional intake is limited, coupled with increased stress [25].

[25].

Children with SCD who have high LDH had almost 2-fold higher risk of having abnormal lung function compared with those with normal levels. A study done in the USA showed a weak association between high LDH and abnormal lung function, especially obstructive patterns [26]. The high levels of LDH could be due to tissue damage following haemolysis [27] which causes the release of free haem, which in turn consumes NO (nitric oxide), reducing endothelial NO bioavailability and impairing vascular functions. Lysed erythrocytes also release arginase that destroys L-arginine (converts to L-ornithine and urea). This reduces arginine availability for NO production via nitric oxide synthase (NOS). The hemolysis-induced mechanisms of NO-arginine pathway dysfunction and allergen sensitisation, in combination with innate genotypic susceptibilities, may promote interplay between the above factors in modifying SCD lung inflammation and downstream effects [28].

Children with a history of acute chest syndrome were more likely to have abnormal lung function compared to those without a history of acute chest syndrome. This is similar to a study in Nigeria, which showed that a history of ACS had 2-fold higher odds of having abnormal lung function. However, a study in the USA found no association between ACS and abnormal lung functions [16]. This variation could be that children in high-income countries have better health care than the ones in low-income countries. This may be due to poor health-seeking behavior and poverty, which hinders access to basic health care and routine medications required by a child with sickle cell disease. ACS is a common cause of acute lung disease in children with SCD [29]. The etiology of ACS is often multifactorial. The development of ACS represents a vicious cycle of lung infarction, inflammation, and atelectasis leading to ventilation–perfusion mismatch, hypoxemia, and acute increases in the pulmonary artery and right ventricular pressures [29]. At the cellular level, in the presence of low alveolar oxygen tension, abnormal rheology of the sickled red blood cells (sRBCs) facilitate adhesion to each other, leukocytes, and the vascular endothelium, resulting in vaso-occlusion and tissue hypoxia. These interactions also cause the release of inflammatory cytokines, which promote acute and chronic inflammation in the airways by being near the vasculature [29]. Patients suffering from repetitive episodes of ACS can develop scattered areas of lung fibrosis, predominantly observed in the lung bases [27]. Pulmonary fibrosis is linked to restrictive lung patterns on spirometry evaluation. This is a common finding in adults with SCD, possibly as a result of longstanding chronic inflammation of the small airways from recurrent ACS, infections, vascular infarction and extra-pulmonary restriction [30].

The study results showed that using charcoal as a cooking fuel source increases the risk of abnormal lung function. Studies show that exposure to smoke from use of charcoal during cooking is associated with systemic and pulmonary inflammation, leading to an increase in neutrophils in the broncho-alveolar fluid and blood [31]. This effect might be exaggerated in SCD due to the chronic

inflammatory state and its impact on the lung and other organs.

Low peripheral oxygen saturation (SpO2 < 92%) increased the risk of abnormal lung function by nearly 2-folds. This could be explained by the fact that children with SCD already have compromised lungs, and hypoxemia is just a manifestation of lung disease. This may also be confounded by the fact that hypoxemia is prevalent in patients with SCD during steady state, in the absence of overt cardiopulmonary illness, and during ACS or VOC crises [32]. Oxyhaemoglobin desaturation triggers HbS polymerisation, the first chain of events culminating in SCD complications [33]. Moreover, in the presence of Sleep- disordered breathing the repeated cycles of hypoxia and re-oxygenation enhances the oxidative stress and pro-inflammatory signalling pathways that contribute to SCD-related acute and chronic manifestations [34].

Strengths and limitations of the study

This study provides valuable insights into the prevalence, patterns, and associated factors of abnormal lung function in children with SCD, shedding light on an important aspect of their health. The large sample size gives it a high power. Additionally, the identification of reversible and irreversible airway obstruction patterns contributes to a deeper understanding of respiratory health in children with sickle cell disease.

However, the study had some limitations. This study had a cross-sectional design, which limits the ability to establish causality between the identified factors and abnormal lung function. Additionally, the study was carried out in an urban setting, which may limit the generalizability of the findings to other regions or populations in rural areas. Furthermore, the reliance on self-reported data for certain factors such as cooking practices and history of acute chest syndrome may introduce recall bias and affect the accuracy of the results.

Conclusion

The study showed a high prevalence of abnormal lung function among children with SCD, and this was associated with wasting, high serum LDH levels, and use of charcoal for household cooking. Strategies to improve nutrition, reduce exposure to charcoal smoke, and monitor serum LDH levels may be important in preventing or managing abnormal lung function in this population. The identification of reversible and irreversible airway obstruction in children with sickle cell disease also highlights the need for targeted interventions to address these specific patterns of abnormal lung function.

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Author contributions

Study conception and design: P.A.M; Data acquisition, Analysis and interpretation: P.A.M; H.T. A: R. N: G. F, C. B, B. O, F. B, B. K. Initial draft of the article: P. A. M; critical revision for important intellectualcontent: all authors; final approval of the version to be published: all authors; guarantor of the article: P. A. M.

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Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Makerere University School of Medicine Research and Ethics Committee (Number SOMREC 2019 – 160). Administrative clearance was obtained from Mulago National Super-Specialized Hospital. Informed written consent was obtained from the parents/guardians, and informed written assent was obtained from all children aged 8 years and above.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Disclosures

None.

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