Original Article

Demographics of Tonsillar Hypertrophy among Sickle Cell Disease Patients in Calabar

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Abstract

Background: Sickle cell disease (SCD) is the most common genetic disorder, with Africa bearing the highest burden. In this cohort study, sickle cell subjects are immunocompromised and predisposed to recurrent infections and tonsillar hypertrophy, especially in children. Subsequently, tonsillar hypertrophy leads to sleep-disordered breathing (SDB) with resulting hypoxemia, hypercapnia, and acidosis, raising the risk of HbS polymerization and, consequently, vaso-occlusive phenomena and other complications. **Aims:** This study aimed to compare tonsillar hypertrophy between sickle cell patients and controls. **Materials and Methods:** A cross-sectional descriptive study was conducted at, University of Calabar Teaching Hospital, Calabar from September 2019 to September 2021. The cohort of the study was an SCD patient confirmed using hemoglobin electrophoresis at the hematology laboratory of University of Calaabr teaching hospital and recruited via the adult and pediatric hematology unit of University of Calabar teaching hospital, and Calabar sickle cell club. The data were analyzed using Microsoft Excel and IBM Statistical Package and Service Solution (SPSS) version 22. **Results:** Using Brodsky's grading, the prevalence of grade 3 and 4 hypertrophic tonsils in sickle cell subjects was 41.6% but 17.3% in control. The age range of 0–25 years was the most frequently affected with the peak at 0–5 years. The males among the sickle cell subjects were slightly more affected than the females (M: F =1.2:1), while the females were slightly more in the control (M: F =1:1.1). **Conclusions:** Hypertrophic tonsils affect control and SCD, but the obstructive grades are commoner in genotypes SCD- Sickle cell disease Haemoglobin SS, SC and AA.

Keywords: *Hypertrophy, Nigeria, sickle cell disease, tonsil*

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Introduction

Sickle cell disease (SCD) is a heterogeneous group of chronic autosomal recessive structural hemoglobin disorder.[1]

The sickle cell gene is inherited either in homozygous form as hemoglobin S (HbS): the most severe phenotype, or a compound heterozygous state with either a normal hemoglobin AS or a variance hemoglobin genes SC, SE, and HbS/B-thalassemia.[2]

SCD is the most common genetic disorder worldwide. The data on the global prevalence of diseases estimated that 20–25 million people worldwide have SCA.[3] About 12–15 million affected people are in sub-Saharan Africa.[3] Nigeria bears the highest burden. An estimated 2–3% of Nigerians have sickle cell anemia[4,5] out of an estimated population of over 200 million, while an estimated 20–30% of the population carry the sickle cell gene. In Nigeria, more than 150,000 children are born with the disease annually, while 4 million people are said to have sickle cell trait.[5] The disease burden differs from

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one geographical region to another.[3,6] Nwogoh *et al.* reported a prevalence rate of 2.4% in Benin, South-South Nigeria,[4] while a similar study by Jude *et al.* reported a prevalence of 3.7% in a multicenter study in Nigeria.[7]

The clinical spectrum of presentation varies from steady state, acute (crisis) to chronic complications affecting all parts of the body, characterized by progressive damage in several organs. SCD is considered one of the most severe monogenic diseases.[8]

The steady state is the crisis-free period extending from at least 3 weeks since the last clinical event and 3 months since the blood transfusion to at least one week before the start of a new clinical event.[9]

The crises are acute exacerbations of the symptoms of SCD. These include four clinical spectra: vaso-occlusive, aplastic, acute sequestration, and hemolytic crisis. Bacterial infections are the leading cause of morbidity and mortality in SCD. It results from hyposplenism, a disorder in the activation of the compliment system, micronutrient deficiency, and tissue ischemia.[10]

Adenotonsillar hypertrophy (ATH) is a term used to describe adenoid vegetation and palatine tonsil enlargement. Its etiology is yet to be fully elucidated, but acute or recurring chronic inflammation seems to be a precipitating factor. Children subjected to these processes usually exhibit an abnormal growth of cervical and pharyngeal lymphoid tissues.[11]

Hypertrophy of the adenoids and tonsils seems more frequent and tends to extend in SCD children, with resultant recurrent pharyngitis. Three hypotheses are suggested for the association between ATH and SCD: compensation for autosplenectomy, recurrent upper airway infection due to failed opsonization of pathogenic bacteria, and the function of pharyngeal and palatine tonsils as hematopoietic centers due to hemolysis.[12]

ATH can lead to sleep-disordered breathing (SDB), varying from snoring to obstructive sleep apnea syndrome. This results in hypoxemia, hypercapnia, and acidosis, raising the risk of HbS polymerization and, consequently, vaso-occlusive phenomena and other complications, such as transient ischemic attacks and cerebrovascular accident.[12,13] There is a high prevalence (55%)[14] of obstructive tonsillar hypertrophy in children and adolescents with SCD.[14] Previous studies documented that tonsillectomy reduced the pain crisis in sickle cell anemia.[14]

This study aimed to assess tonsillar hypertrophy among SCD and control subjects.

Materials and Methods

Study design

The study is a cross-sectional descriptive study conducted at University of Calabar Teaching Hospital Calabar from September 2019 to September 2021.

Methodology

The cohorts of the study were SCD patients confirmed using hemoglobin electrophoresis at the hematology laboratory of University of Calabar teaching hospital. SCD patients were recruited via the adult and pediatric hematology unit of the University of Calabar teaching hospital, also through Calabar sickle cell club. The controls were apparently healthy children and adults with confirmed hemoglobin AA and AS. The study population information of age, sex, body mass index, sickle cell crisis, and obstructive sleep-disordered symptoms was collected with a structural questionnaire after obtaining informed consent from adult participants, the parents, or guardians of young children, and assent from children above 7 years.

The ear, nose, and throat examination of the participants was performed at the ENT Clinic of the Hospital by a single otolaryngologist to reduce human error. The headlamp, disposable and Lac's tongue depressors, and video oropharyngoscope were used for the examination. Tonsil size was estimated using Brodsky's criteria.[14] Hyperemic or exudative tonsils were excluded from the study. In addition, some clinical photographs were taken for the purpose of publication [Figures 3-7].

The Health Research Ethics Committee (HREC) of the University of Calabar Teaching Hospital gave ethical approval (UCTH/HREC/33/674) for the study.

Sample size

$$n = \frac{Pqz^2}{d^2}$$

n = sample size

P = prevalence

Z = 1.96 (95% confidence interval)

d = desire of accuracy (0.04)

$$\frac{0.023 \times 0.977 \times (1.96)^2}{.(0.04)^2}$$

0.08632459 = 54 + Attrition of 80 = 154

0.0016

Selection criteria

A total of 300 structural interviewee questionnaires were distributed among participants, 150 each. The controls

with complete information were 110, while the total number of SCD patients was 101. Inclusion criteria are confirmed SCD patients, both adults and pediatrics, and apparently, healthy individuals are the controls. Exclusion criteria are those without confirmed and validated sickle cell reports, seropositive individuals, lymphoid morbidity, and children with craniofacial anomalies, upper airway infections, and previous history of tonsillectomy.

Data analysis

Quantitative data were analyzed using IBM Statistical Product and Service Solution version 22, Chi-square at a 5% significance level was used to test for association between SCD and tonsillar hypertrophy.

Results

The socio-demographic information of our study population is displayed in Table 1. The total number of participants was 211 consisting of 101 SCD and 110 controls with an age range from 1 to 65 years [Table 1 and Figure 1]. We classified tonsillar hypertrophy using Brodsky's criteria[14] [Tables 2-4 and Figure 2a and b]. Using age distribution among the SCD subjects, grade 3 was most common among ages 0–5 years, grade 4 was most frequent among 11–15 years, grade 2 tops the list among 16–20 years, and grade 1 was mostly between 21 and 25 years [Figure 2a and b].

Comparing the grading between control and SCD subjects, grade 1 was 52.7% in the control and 10.9% in SCD subjects. Grade 2 tonsillar hypertrophy was 30.0% in control and 47.5% in SCD. The prevalence of grade 3 was nearly equal in control and SCD subjects at 15.5% and 17.3%, respectively. There is a marked difference in the frequency of grade 4 tonsillar hypertrophy between SCD subjects with 41.6% and 1.8% in control [Tables 3 and 4].

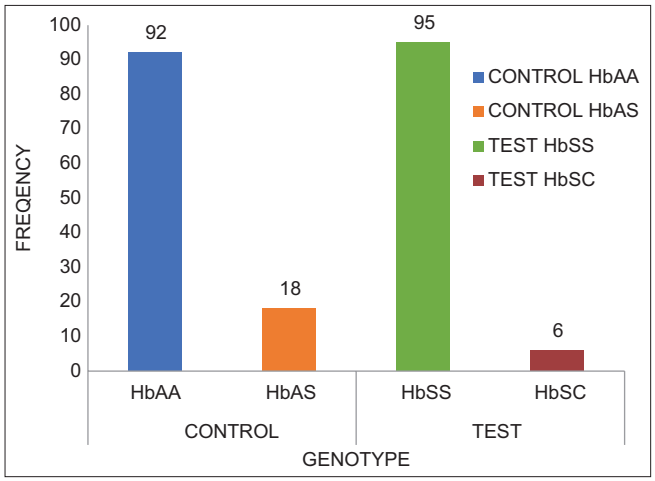

Figure 1: Number of SCD and control participants

There was no statistical significance in gender distribution among SCD patients and controls. Males are more affected than females in grade 1 in both SCD patients and control. Females are more in grades

Table 1: Socio-demographic characteristics of control and SCD

Variable	Frequency (%)		χ^2	*P*
	Control	Test		
Age				
0–5	8 (7.27)	14 (13.86)	27.236	0.268
6–10	3 (2.73)	17 (16.83)		
11–15	1 (0.91)	18 (17.82)		
16–20	3 (2.73)	17 (16.83)		
21–25	64 (58.18)	17 (16.83)		
26–30	13 (11.82)	11 (10.89)		
31–35	6 (5.45)	2 (1.98)		
36–40	10 (9.09)	4 (3.96)		
>40	2 (1.82)	1 (0.99)		
Total	110	101		
Sex				
Male	53 (48.18)	55 (54.46)	1.577	0.209
Female	57 (51.82)	46 (45.54)		
Total	110 (100.00)	101 (100.00)		
Tribe				
Efik	19 (17.27)	23 (22.77)	24.817	0.209
Ibibio	15 (13.64)	10 (9.90)		
Igbo	16 (14.55)	16 (15.84)		
Hausa	1 (0.91)	0 (0.00)		
Yoruba	1 (0.91)	3 (2.97)		
Others	58 (52.73)	49 (48.51)		
Education				
None	0 (0.00)	4 (3.96)	10.200	0.598
Primary	9 (8.18)	25 (24.75)		
Secondary	16 (14.55)	29 (28.71)		
Tertiary	79 (71.82)	37 (36.63)		
Others	6 (5.45)	6 (5.94)		
Occupation				
Business	4 (3.64)	4 (3.96)	2.857	0.875
Civil service	10 (9.09)	17 (16.83)		
Student	90 (81.82)	78 (77.23)		
Unemployed	6 (5.45)	2 (1.98)		

Table 2: Tonsillar classification according to Brodsky's criteria[13]

Grade	Size of tonsils
0	Palatine tonsils located inside the tonsillar fossa
1	Tonsils located beyond the tonsillar fossa occupying <25% of oropharyngeal air space
2	Tonsils located beyond the tonsillar fossa occupying >25% and <50% of oropharyngeal air space
3	Tonsils located beyond the tonsillar fossa occupying >50% and <75% of oropharyngeal air space
4	Tonsils located beyond the tonsillar fossa occupying >75% of oropharyngeal air space

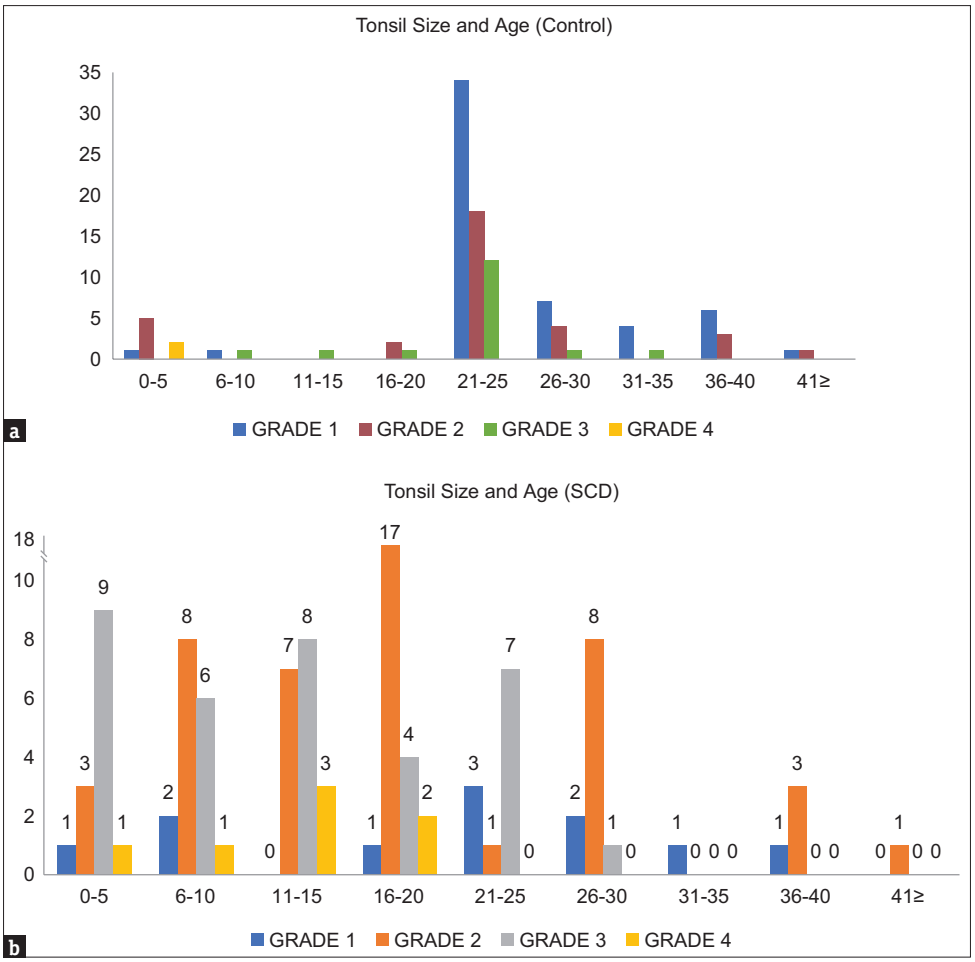

Figure 2: (a) Age distribution of Brodsky's grading of tonsils of the control (AA and AS). (b) Age distribution of Brodsky's grading of tonsils of SCD subjects. 11 SCD subjects had grade 1, 48 with grade 2, 35 with grade 3, and 7 with grade 4

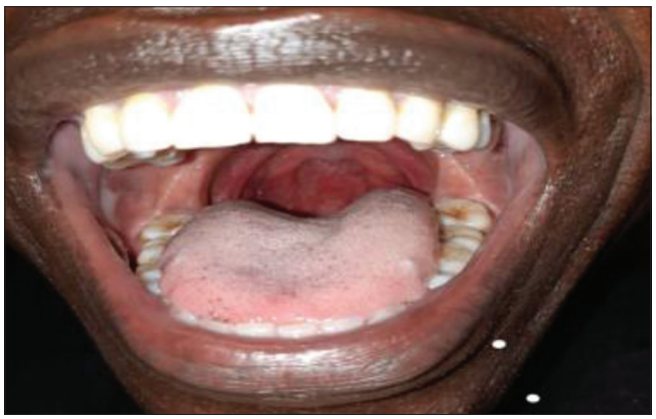

Figure 3: 57-year-old AS with grade 1 tonsillar hypertrophy

2 and 3 among both SCD patients and controls. Grade 4 was more among males of SCD patients, and none were in control [Table 4]. Overall, there was slight male preponderance among the sickle cell subjects, M: F =1.2:1, while that of control was M: F =1:1.1 [Table 4].

Table 3: Tonsil hypertrophy between control and test

Tonsil size	Control *n*=110 (%)	Test *n*=101 (%)	Total *n*=211 (%)
Grade 1	58 (52.7)	11 (10.9)	69 (32.7)
Grade 2	33 (30.0)	48 (47.5)	82 (38.9)
Grade 3	17 (15.5)	35 (34.7)	52 (24.6)
Grade 4	2 (1.8)	7 (6.9)	9 (4.3)
Total	110 (100)	101 (100)	211
Statistic	χ^2=8.749	*P*=0.461	

Discussion

Hypertrophic tonsils cut across both children and adult SCD participants in our study population but are the most prevalent among the age range of 0–5 years. Other studies in the literature reported that ATH ranges from 2 to 6 years, and after this age, there is an involution process of the lymphoid tissue in the pharynx.[8,15-18] However, we noted a significantly high percentage of tonsil hypertrophy among the SCD up to the age of 30 years.

The proportion of SCD patients with tonsillar hypertrophy in our study was male, although the sex

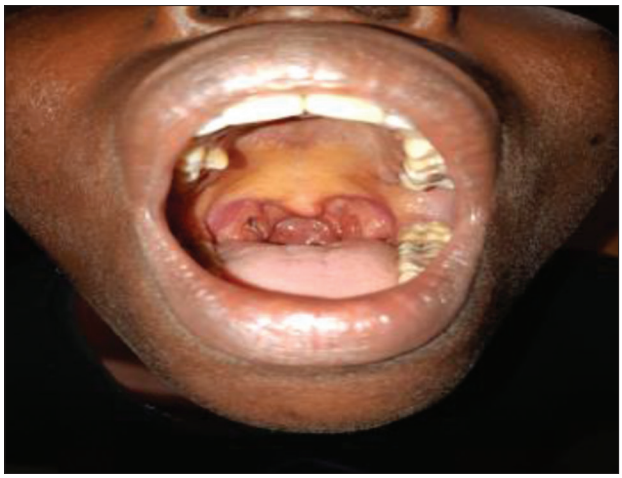

Figure 4: 19-year-old SS with grade 2 tonsillar hypertrophy

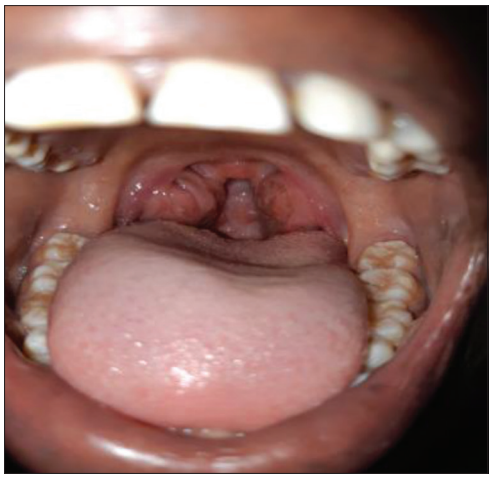

Figure 5: 21-year-old SS with grade 3 tonsillar hypertrophy

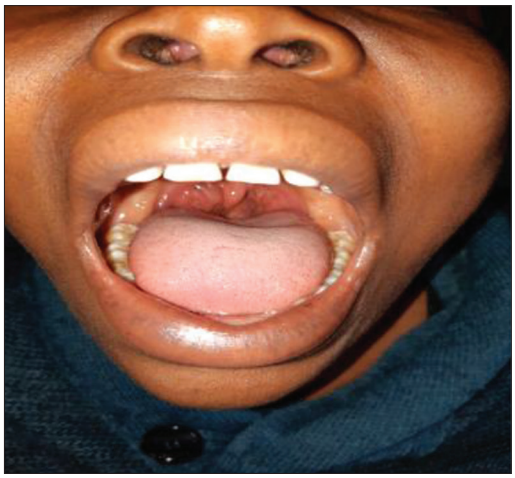

Figure 6: 17-year-old SS with grade 3 tonsillar hypertrophy

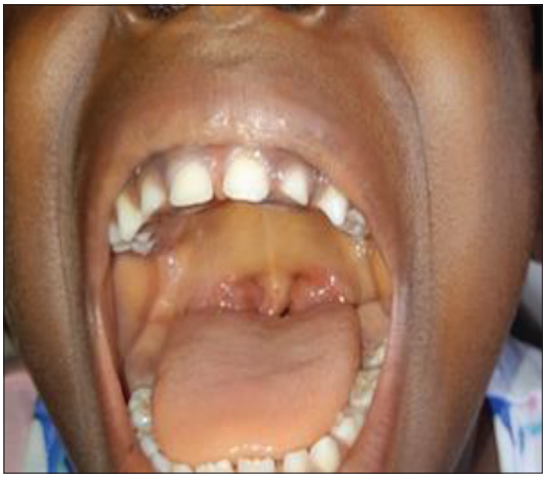

Figure 7: 3-year-old SS child with grade 4 tonsillar hypertrophy

Table 4: Association between tonsil size and sex

Tonsil size	Control		Test	
	Male (%)	Female (%)	Male (%)	Female (%)
Grade 1	33 (62.26)	25 (43.86)	9 (16.36)	2 (4.35)
Grade 2	14 (26.42)	19 (33.33)	22 (40.00)	26 (56.52)
Grade 3	6 (11.32)	11 (19.30)	18 (32.73)	17 (36.96)
Grade 4	0 (0.00)	2 (3.51)	6 (10.91)	1 (2.17)
Total	53 (100.00)	57 (100.00)	55 (100.00)	46 (100.00)
Statistic	χ^2=5.193	*P*=0.158	χ^2=7.647	*P*=0.054

Hypertrophic tonsil of Grades 3 and 4 is highest among SCD males (43.6%), and females accounted for 39.1%, while 11.3% of control males had grade 3 and 4 tonsillar hypertrophy and female counterparts with 22.8%

prevalence was not statistically significant. Our result agreed with the results of studies conducted by Felix *et al.*[19] and Inoshita *et al.*[20] who reported that ATH had a similar prevalence between males and females.[19,20]

Ajulo *et al.*[21] (1994) in the United Kingdom, Ijaduola *et al.*[22] (1987) in Ibadan (Nigeria), Madden *et al.*[23] (1989) in Toluene in the USA, and Salles *et al.*[24] (2009) in Salvador (Brazil) in their studies reported that tonsillar hypertrophy was more frequent in SCD. Opoku *et al.*[14] (2012) in Ghana reported 93.1% of grade 1–4 and 6.9% of grade 0 tonsillar hypertrophy. In our study, the control and SCD patients had various degrees of tonsillar hypertrophy, but we did not record any grade 0. The proportion of SCD patients with obstructive tonsillar hypertrophy in our study although high (48.5%), however is lower than the 55.3% reported by Salles *et al.* (2009) among SCD patients in Brazil,[14] Grade 3 tonsillar hypertrophy is 34.7% in this study, similar to that of Opoku *et al.*[14] of 34.6% in Ghana. In contrast to the study of Opoku *et al.*,[14] which documented 24.2% of grade 2 hypertrophy, we reported 47.3% among the SCD. In the control group, Brodsky's grade 1 was the most frequent (52.7%) documented in this study, contrary to the 5% reported by Opoku *et al.*[14]

Some studies reported a marked reduction in the rate of pain crisis in sickle cell anemia after tonsillectomy. We counseled all the subjects with obstructive tonsils in this

study for tonsillectomy, but only a few (two of 101 SCD patients) underwent tonsillectomy because of financial constraints. The two SCD patients who had tonsillectomy reported a significant reduction in sickle cell crisis after tonsillectomy. In fact, in the last 2 years after tonsillectomy none of them had been admitted to the hospital.

This study showed that both control and SCD had various degrees of TH, but the SCD subjects suffered more of higher Brodsky's tonsillar grades, which can lead to airway obstruction, eating difficulty, and sickle cell crisis and its complications.

We recommend that future studies assess the medical and economic impacts of tonsillar hypertrophy and that the National Health Insurance Scheme take over the financial burden of the operation of these individuals.

Limitations

This study did not assess the size of adenoids, if hypertrophied along with tonsils could worsen SDB and further worsen the sickle cell crisis.

Declaration of patient consent

The authors certify that appropriate consent was obtained from all the patients. In the consent form, the patient had given his/her consent for his/her/image and other clinical information to be published in this article. The patients were informed that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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