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Risk factors associated with tonsillar hypertrophy in sickle cell patients followed at the Centre for Mixed Medicine and Sickle Cell Anaemia in Kinshasa

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ABSTRACT

Introduction

Sickle cell disease is the most common genetic disorder worldwide, primarily affecting individuals of African, Mediterranean, and Asian descent. Previous studies have reported that patients with sickle cell disease are predisposed to tonsillar hypertrophy as a result of compensatory immune responses to functional asplenia and recurrent infections.

Purpose

The main objective of this study was to determine the frequency of tonsillar hypertrophy in sickle cell patients followed at our centre and to identify the associated risk factors.

Methods

This was a cross-sectional analytical study conducted at the *Centre for Mixed Medicine and Sickle Cell Anaemia* (CMMASS), Kinshasa, from September 2022 to February 2023. The sample comprised homozygous SS sickle cell patients aged six years and above who were followed up at CMMASS. The size of the palatine tonsils was assessed according to Friedman's criteria. Data were analysed using IBM Statistical Package for the Social Sciences (SPSS) version 26.0. Associations between variables were tested using the chi-square test, with statistical significance set at $p < 0.05$.

Results

A total of 123 patients with sickle cell disease participated in the study, with a median age of 15 years (range: 6–50 years). Females accounted for 58.5% of participants. The prevalence of tonsillar hypertrophy was 57.7%. Treatment without hydroxyurea (adjusted OR = 10.53 [1.74–63.59]; $p = 0.010$), presence of jaundice (adjusted OR = 4.21 [1.33–13.39]; $p = 0.015$), and haemoglobin ≤ 7.9 g/dL (adjusted OR = 7.55 [2.85–19.99]; $p = 0.001$) were identified as factors significantly associated with tonsillar hypertrophy among sickle cell patients.

Conclusions

Tonsillar hypertrophy is common among sickle cell patients in our setting. Addressing the associated risk factors identified in this study could help reduce its frequency.

INTRODUCTION

Tonsillar hypertrophy is an abnormal enlargement of the palatine tonsils, which are lymphoid organs located in the oropharynx (Friedman et al., 2017). Friedman and Brodsky classified palatine tonsils according to their size and the degree to which they occupy the oropharyngeal space, which often determines their clinical presentation. However, in some cases, this hypertrophy remains asymptomatic (Friedman et al., 2017; Powell et al., 2010). The aetiopathogenesis of tonsillar hypertrophy remains unclear. The two most popular hypotheses at present are the deleterious effects of pollution and an inflammatory state of the upper airways (François, 2009).

Studies of otorhinolaryngological (ENT) complications associated with sickle cell disease have revealed a predisposition of sickle cell patients to tonsillar hypertrophy, due to a compensatory immune response to their functional asplenia (Opoku-Buabeng et al., 2012; Adekanye et al., 2023; Góis et al., 2017; Salles et al., 2009; Abou-Elhamd, 2011).

Sickle cell disease is an autosomal recessive genetic disorder caused by the synthesis of abnormal haemoglobin (HbS). It is common in Africa and South Asia (Mario et al., 2016; Brandow & Liem, 2022; Piel et al., 2013). The disease is characterised by chronic tissue hypoxia, which may be aggravated by tonsillar hypertrophy responsible for obstructive sleep apnoea syndrome (Sundd et al., 2018; Dzon et al., 2019). Therefore, patients with sickle cell disease require careful ENT monitoring to prevent severe complications such as sensorineural hearing loss (Yalombe et al., 2025; Stuart & Smith, 2019) and stroke (Wali et al., 2000).

The prevalence of tonsillar hypertrophy in sickle cell disease has been estimated at 93.1% in Ghana (Opoku-Buabeng et al., 2012) and 41.6% in Nigeria (Adekanye et al., 2023). However, in the Democratic Republic of the Congo (DRC), data on tonsillar hypertrophy among patients with sickle cell disease are almost non-existent. This gap motivated the present study, which aimed to describe the characteristics of the palatine tonsils in sickle cell patients, determine their frequency, and identify factors associated with tonsillar hypertrophy in our setting.

METHODS

Type, Setting, and Period of Study

This was a cross-sectional analytical study conducted at the *Centre for Mixed Medicine and Sickle Cell Anaemia* (CMMASS) in Kinshasa over a six-month period, from 1 September 2022 to 28 February 2023. The study population consisted of all sickle cell patients followed up at CMMASS during the study period who were aged six years or older.

All SS homozygous sickle cell patients whose status had been confirmed by haemoglobin electrophoresis and who had provided direct or indirect written informed consent (via their guardian) were included in the study. The sample was one of convenience due to the absence of local prevalence data.

Variables of Interest

The variables of interest included sociodemographic characteristics (age, sex, educational level, occupation, religion, and residence), clinical characteristics (symptoms, medical history, ENT examination), and paraclinical parameters (haemoglobin level).

Data Collection Technique

Data for this study were collected in the hospital setting using patient consultation and registration records, and then recorded on a pre-established data collection form. Sociodemographic data and medical history were obtained through interviews, while ENT examinations were conducted using instruments such as the RIESTER otoscope, the BISTOS EYESCOPE BT-410 headlamp, ear and nasal speculums, and tongue depressors to assess the oropharynx.

Operational Definitions of Variables

Sickle cell crises included vaso-occlusive, haemolytic, and infectious crises.

Tonsillar hypertrophy was defined as an increase in the volume of the tonsils assessed according to Friedman's classification:

- **Grade 0:** The uvula and tonsillar pillars are fully visible.
- **Grade 1:** The tonsils are contained within the tonsillar compartment.

- **Grade 2:** The tonsils protrude beyond the tonsillar pillars.
- **Grade 3:** The tonsils protrude well beyond the pillars but do not meet at the midline.
- **Grade 4:** The tonsils meet at the level of the uvula.

"Good health" was defined as the ability of a person with sickle cell disease to independently meet their basic needs. The urban zone included all residences in Kinshasa located within the districts of Lukunga, Funa, and Mont Amba, while the urban–rural zone included those located in the Tshangu district.

Statistical Analysis

Data were entered and coded using EpiData, then exported to SPSS version 26.0 for statistical analysis. Quantitative variables were summarised using measures of central tendency and dispersion (median, mean, standard deviation), while qualitative variables were summarised as frequencies and percentages. The association between two variables was assessed using the chi-square test. A multivariate logistic regression model was employed to identify independent determinants of tonsillar hypertrophy, with odds ratios (ORs) and 95% confidence intervals (CIs) calculated after adjusting for confounding factors. Statistical significance was set at $p < 0.05$.

Ethical Considerations

The study protocol was approved by the National Ethics Committee under approval number ESP/CE/111/2022. Authorisation was also obtained from the heads of the *Institute for Health Sciences Research* (IRSS) and the CMMASS. The study was conducted in compliance with ethical standards and professional conduct.

RESULTS

Sociodemographic Characteristics of Patients

The sociodemographic characteristics of the 123 sickle cell patients included in this study are presented in **Table 1**. Females predominated (58.5%), and the median age was 15 years, with an age range of 6–50 years.

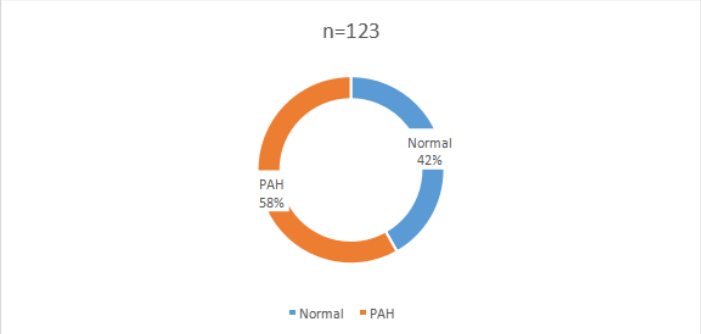
Table 1:
Patient characteristics

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	51	41.5
	Female	72	58.5
Age group (years)	6–17	74	60.1
	18–29	38	30.9
	30–41	7	5.7
	≥ 42	4	3.3
Median age	15 years		
Residence	Urban	79	64.2
	Urban–rural	44	35.8
Level of education	No formal education	14	11.4
	Primary	75	61.0
	Secondary	26	21.1
	University	8	6.5
Religion	Catholic	15	12.2
	Evangelical	83	67.5
	Protestant	12	9.7
	Other	13	10.6

Frequency of Tonsillar Hypertrophy

Figure 1 shows that the frequency of tonsillar hypertrophy among sickle cell patients was **57.7%**.

Figure 1:
Frequency of tonsillar hypertrophy in sickle cell disease patients



Clinical Features

As shown in **Table 2**, snoring during sleep was the most frequent symptom, reported by 50.4% of patients.

Table 2:
Patients' complaints

Variable	Frequency (n)	Percentage (%)
Dysphagia	16	13.0
Dyspnoea	21	17.1
Sleep snoring	62	50.4
Mouth breathing	27	22.0
Insomnia	31	25.2
Daytime sleepiness	19	15.0
Headaches	13	10.6
Halitosis	2	1.6

Variable	Frequency (n)	Percentage (%)
Rhinorrhoea	8	6.5
Earache	13	10.6
Hearing loss	16	13.0

ENT Examination

Table 3 shows that **57.7%** of patients presented with enlarged tonsils of various grades according to Friedman's criteria. Grade 2 tonsils accounted for more than half of the enlarged cases.

Table 3:
Friedman's classification of palatine tonsils on oropharyngeal examination

Friedman score	Right tonsil n (%)	Left tonsil n (%)
Grade 0	52 (42.3)	52 (42.3)
Grade 1	8 (6.5)	11 (8.9)
Grade 2	41 (33.3)	37 (30.1)
Grade 3	20 (16.3)	21 (17.1)
Grade 4	2 (1.6)	2 (1.6)

Table 4 shows that tympanic dullness and nasal mucosal pallor were significantly more frequent among patients with tonsillar hypertrophy.

Table 4:
Other physical ENT findings

Examination	Parameter	Without hypertrophy *n (%)*	With hypertrophy *n (%)*	*p*-value
Otoscopy	Normal	47 (38.2)	38 (73.1)	
	Tympanic dullness	76 (61.8)	14 (26.9)	< 0.001
Rhinoscopy	Normal	73 (59.3)	46 (88.5)	
	Pallor of mucosa	50 (40.7)	6 (11.5)	< 0.001

Factors Associated With Tonsillar Hypertrophy in Sickle Cell Patients

Sociodemographic factors such as age, sex, and residence, as well as clinical factors such as transfusions, jaundice, frequency of crises, haemoglobin level, and hydroxyurea treatment, were examined for their relationship with tonsillar hypertrophy.

After univariate analysis, female gender, presence of jaundice, previous transfusions, frequent crises (≥3 per year), low haemoglobin (≤7.9 g/dL), and absence of hydroxyurea treatment were statistically significant. In the multivariate model, only the presence of jaundice, low haemoglobin level, and treatment without hydroxyurea remained independently associated with tonsillar hypertrophy **(Table 5)**.

Table 5:
Factors associated with tonsillar hypertrophy

Variable	Univariate analysis		Multivariate analysis	
	p-value	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)
Gender (Female)	0.029	2.40 (1.09–5.25)	0.124	2.18 (0.81–5.88)
Presence of jaundice	<0.001	5.88 (2.19–15.81)	0.015	4.21 (1.33–13.39)
Previous transfusions	0.001	3.92 (1.69–9.08)	0.461	1.53 (0.49–4.71)
≥3 crises per year	0.001	5.24 (1.96–13.99)	0.132	2.50 (0.76–8.22)
Hb ≤ 7.9 g/dL	<0.001	9.04 (3.67–22.30)	<0.001	7.55 (2.85–19.99)
No hydroxyurea	0.013	7.54 (1.55–36.81)	0.010	10.53 (1.74–63.59)

DISCUSSION

Frequency of Tonsillar Hypertrophy

In the present study, 57.7% of sickle cell patients exhibited various grades of palatine tonsil enlargement according to Friedman's classification. This finding aligns with that of Abou-Elhamd (2011), who reported a 55% prevalence in the Middle East. The palatine tonsils, as part of Waldeyer's lymphoid ring, play an important immunological role in defending the upper aerodigestive tract. Recurrent infections in sickle cell disease are believed to contribute to hypertrophy, which may further aggravate tissue hypoxia and trigger crises (Adekanye et al., 2023; Góis et al., 2017; Salles et al., 2009).

Sickle cell patients are also predisposed to tonsillar hypertrophy due to a compensatory immune response to functional asplenia (Opoku-Buabeng et al., 2012; Sundd et al., 2018). Opoku-Buabeng et al. (2012) in Ghana found a much higher prevalence (over 90%), though their study included only children aged 2–13 years, who are generally more prone to ENT disorders. In contrast, Adekanye et al. (2023) in Nigeria found a prevalence of 41.6% using similar criteria.

Despite variations in prevalence, all studies indicate a significantly higher frequency of tonsillar hypertrophy in sickle cell patients than in the general population. In our series, Friedman's grade 2 tonsils were most common, consistent with Opoku-Buabeng's (2012) findings. More than half of our patients presented with sleep snoring, likely resulting from upper airway obstruction by enlarged tonsils. Tonsillar hypertrophy can contribute to obstructive

sleep apnoea, worsening chronic hypoxia in sickle cell patients (Salles et al., 2009; Dzon et al., 2019).

Determinants of Tonsillar Hypertrophy

Treatment without hydroxyurea increased the likelihood of tonsillar hypertrophy approximately elevenfold. Hydroxyurea has been shown to increase foetal haemoglobin (HbF) production, reducing HbS polymerisation, vaso-occlusive crises, transfusion frequency, and infection risk (Brandow & Liem, 2022b; Elendu et al., 2023; Meier, 2018; Pace et al., 2021). Functional asplenia, a proposed mechanism of hypertrophy, can be mitigated by hydroxyurea's beneficial effects—supporting its protective role observed in this study.

Low haemoglobin (≤7.9 g/dL) increased the risk eightfold. Persistent anaemia may reflect functional asplenia and chronic hypoxia, predisposing patients to infection and tonsillar hypertrophy (Adekanye et al., 2023; Sundd et al., 2018). Although sickle cell patients tolerate lower haemoglobin levels, further drops due to splenic sequestration or infection can cause severe asthenia and dyspnoea, requiring transfusion. Conversely, excessively high haemoglobin may increase viscosity and precipitate crises (Brandow & Liem, 2022b).

Jaundice quadrupled the risk of tonsillar hypertrophy. Elendu et al. (2023) identified jaundice as a frequent manifestation of sickle cell disease linked to haemolytic anaemia and elevated bilirubin (>10 mg/dL or >20 mmol/L). The causal relationship between jaundice and tonsillar hypertrophy remains unclear, warranting further case–control studies comparing jaundiced and non-jaundiced sickle cell patients.

Strengths and Limitations

This study is the first in the DRC to explore the relationship between sickle cell disease and tonsillar hypertrophy. However, limited financial resources restricted the inclusion of certain biological and biochemical analyses that could have clarified some associations, such as between jaundice and tonsillar hypertrophy.

CONCLUSION

More than half of the sickle cell patients in this study presented with tonsillar hypertrophy, most commonly Friedman grade 2. Treatment without hydroxyurea, haemoglobin ≤7.9 g/dL, and persistent jaundice were significantly associated factors. Addressing these factors through multidisciplinary care and enhanced access to hydroxyurea may help reduce the frequency of tonsillar hypertrophy. Public health initiatives focused on patient education and the free distribution of hydroxyurea are strongly recommended.

Authors' Contributions: Honoré Ngoyi Yalombe and Dieudonné Tshipukane Nyembue developed the study protocol. Honoré Ngoyi Yalombe and Sarah Ntumba contributed to data collection and study design. Honoré Ngoyi Yalombe drafted the first version of the manuscript with contributions from Yasmin Kamin Tshingamb, Hilaire Kabala Kalala, and Dieudonné Tshipukane Nyembue. Hilaire Kabala Kalala performed the statistical analyses. All authors read and approved the final version.

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Ethical Approval: Nil required.

Conflicts of Interest: None declared.

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