ULTRASOUND FINDINGS IN THE GALLBLADDER OF ADULT SICKLE CELL ANAEMIA AND SEX-AGE MATCHED NON SICKLE CELL ANAEMIA PATIENTS AT NATIONAL HOSPITAL ABUJA: AN ANALYTIC CROSS SECTIONAL STUDY

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ABSTRACT

Background: **Sickle Cell Anaemia (SCA), a hereditary hemoglobinopathy prevalent in sub-Saharan Africa, is associated with chronic haemolysis that predisposes patients to pigment gallstones. While gallbladder complications are common in SCA, especially in resource-limited regions, adult-targeted screening remains infrequent.**

Objective: **To evaluate gallbladder morphology in adults with SCA using ultrasonography and compare these findings with healthy, age- and sex-matched non-SCA in relation to their anthropometry parameters.**

Methods: **In this hospital-based analytic cross sectional study, 160 confirmed adult SCA patients and 160 age and sex-matched healthy controls underwent standardized gallbladder ultrasound. Parameters assessed included gallbladder volume, gallbladder wall thickness, and presence of stones in gallbladder. The examination was performed after atleast 6 hours fasting using a 3.5-5.0MHZ curvilinear array probe of a Mindray DC-N3-PRO ultrasound machine. The data obtained was analysed with SPSS version 20.0 using Student T-Test, p-value and Spearman or Karl-Pearson's correlation coefficient where appropriate, and the results were presented in tables where necessary. The significant findings identified were highlighted.**

Results: **The prevalence of cholelithiasis among the sickle cell anaemia subjects in this study was 20%, while the prevalence of cholelithiasis among the controls was 7.5%. Sickle cell anaemia subjects had significantly higher mean gallbladder volume ($31.9\pm1.2cm^2$) compared to the healthy controls ($23.2\pm1.4cm^2$), ($P<0.001$).**

Conclusion: **Adults living with SCA exhibit significantly higher rates of cholelithiasis and enlarged gallbladder volumes. Routine ultrasound screening should be integrated into adult SCA management in Nigeria to facilitate early intervention.**

Keywords: Sickle cell anaemia, Gallstones, Gallbladder ultrasound, Nigeria

INTRODUCTION

Sickle Cell Anaemia (SCA) is a monogenic disorder caused by a point mutation in the β-globin gene, which substitutes valine for glutamic acid at the sixth codon. This substitution results in the production of haemoglobin S (HbS), which polymerizes under deoxygenated conditions, causing erythrocyte deformation and rigidity. These distorted cells obstruct microcirculation and undergo premature destruction, triggering a cascade of vaso-occlusive crises, chronic hemolysis, and multi-organ damage.[1,2]

Globally, Nigeria remains at the epicentre of SCA, accounting for over 30% of affected births worldwide, with an estimated 150,000 neonates born annually with the homozygous form (HbSS).[3] Despite growing awareness, the systemic complications of SCA in adulthood, particularly in hepatobiliary systems, remain underexplored in sub-Saharan Africa. Chronic intravascular hemolysis generates high levels of unconjugated bilirubin, a key substrate in the formation of pigment gallstones, especially in patients who have not undergone splenectomy or hydroxyurea therapy.[4] Although gallstones can remain asymptomatic, their potential complications, including cholecystitis, biliary colic, pancreatitis, and even sepsis, present significant risks, particularly in SCA patients who are often medically fragile. Yet in many low-resource settings, gallbladder evaluation is only performed after symptomatic crisis or during unrelated scans. There is an urgent need for proactive, non-invasive screening

strategies in SCA patients to detect and manage gallbladder pathology early.[5]

Ultrasonography is ideally suited for this role. Its affordability, absence of ionising radiation, and real-time evaluation make it a frontline tool in gallbladder imaging, especially in regions where CT and MRI are often unavailable or cost-prohibitive. Prior studies from Nigerian cities including Enugu and Kano have identified an elevated prevalence of cholelithiasis among adult and paediatric SCA patients.[6,7] However, findings remain inconsistent, and the literature is particularly sparse regarding ultrasonographic gallbladder profiles in northern and central Nigeria.

This study addresses this gap by evaluating gallbladder morphology in adult SCA patients attending National Hospital Abuja, a major referral centre, using a standardized sonographic protocol. By comparing SCA cases with age and sex- matched controls, this study provides insight into the burden of gallbladder disease in this high-risk population and reinforces the case for routine screening.

MATERIALS AND METHODS

This analytic cross-sectional study was conducted at the Radiology Department of the National Hospital Abuja over a six-month period. The study population comprised 160 adults (≥18 years) with confirmed HbSS in steady state defined as being free from acute crisis and transfusion for at least four weeks.

An equal number of healthy controls matched for age and sex, and without a history of haemoglobinopathy or hepatobiliary disease, were recruited from outpatient clinics and hospital staff. All participants gave written informed consent. Ultrasound scans were conducted using a Mindray DC-40 machine equipped with a 3.5–5.0 MHz curvilinear transducer. Each participant underwent a fasting abdominal scan after at least six hours of food abstinence.

Sample size determination

Using the Fischer's formula[8]:

$N=Z^2pq/d^2$

Where:

N=the desire sample size.

Z=the standard normal deviation, usually set at 1.96, which correspond to the 95% confidence level.

P= the proportion in the target population estimated to have a particular characteristic.

q= 1-P

d=degree of accuracy desired, set at 0.05.

Using the prevalence rate of 16% for gallbladder stones in SCA patients, the proportion (P) is 0.16

With these values, the required sample size (N_s) for this study is

$= (1.96)^2 (0.16) (1-0.16)/ (0.05)^2$.

N=152

The sample size value was rounded up to 160 to make up for any error of attrition.

Hence 160 adult SCA Patients and 160 age and sex matched adult non SCA healthy controls were recruited for this study.

Sampling technique

Using the common ellipsoid formula[9], the gall bladder volume in cubic centimetres was obtained as stated below for each subject:

$V = \pi/6(L \times W H)$[10]

Where the constant $\pi/6 = 0.52387$

The body surface area (BSA) of subjects were calculated from weight and height using the Mosteller formula[11]

BSA (m^2) = [height (m) x weight (kg)/3600]1/2

Gallbladder wall thickness was measured in centimetres (cm) from the inner to the outer wall of the gallbladder in the transverse axis.

The gallbladder parameters evaluated included gallbladder volume, gallbladder wall thickness, with values greater than 3 mm considered indicative of thickening, and the presence of gallstones, defined as hyperechoic foci with posterior acoustic shadowing. Additionally, the scans assessed for gallbladder contractility, which was inferred based on the degree of fullness following the fasting period.

Ethical approval

Clearance from the ethical committee of the hospital was obtained. The cases and the controls were examined after an informed consent was obtained from all subjects following thorough explanation of the study objectives and method of examination.

Risk

There was no anticipated ethical issue because ionizing radiation was not utilized. Ultrasonography was a safe procedure.

Cost

No additional cost was accrued for the patients as the investigations were part of their normal clinical evaluations. However, completion of the data sheet and ultrasound examination took about 45minutes of the patients' time.

Confidentiality
All Information disclosed by the subjects and the ultrasound scan results were treated with utmost confidentiality.

Data collection
Anthropometric and sociodemographic data were collected and correlated with sonographic findings. Statistical analysis was performed using SPSS version 20.0. The results were presented in tables. Categorical variables were compared using Chi-square tests, and continuous variables using Student's t-tests. Pearson correlation assessed associations between gallbladder volume and patients' characteristics. Significance was set at p/ </ 0.05.

RESULTS

The study enrolled 320 participants. Demographics showed proper age and sex matching, with a mean age of 27.3/ ±/ 9.4 years across both groups. This is demonstrated in Table 1. There was no statistically significant difference in BMI or BSA between cases and controls as demostrated in table 1. However, both BMI and BSA demonstrates statistical significance as shown in Table 3

Gallbladder morphology
The mean fasting gallbladder volume was significantly higher among SCA patients (31.9 ± 2.0cm³) compared to the control group (23.2±1.4cm³; p <0.001). However, there was no statistically significant difference in gallbladder wall thickness between the groups, with measurements of 0.24 ± 0.1 cm in SCA patients and 0.23 ± 0.1 cm in controls (p = 0.214).

Prevalence of gallstones
Gallstones were detected in 32 (20%) of the SCA patients, compared to 12 (7.5%) of the sex and age-matched control group, representing a statistically significant difference (p < 0.001). Notably, among those with gallstones, female patients were disproportionately affected, with 21 females and 11 males presenting with cholelithiasis.

Correlates of gallbladder volume
Pearson correlation analysis revealed moderate correlation and significant associations (p-value) between gallbladder volume and body surface area (r = 0.735, p < 0.001), age (r = 0.757, p = 0.047), and body mass index (r = 0.526, p < 0.001). Sex demonstrated a weaker correlation and non-significant association (r = 0.122, p = 0.125). These findings suggest that gallbladder volume is influenced not only by the underlying hemolytic process but also by individual variations in body habitus.

There were no significant differences in age, height, weight, BMI, or BSA between the SCA cases and control group, confirming adequate matching.

Table 1: Sociodemographic and anthropometric characteristics of SCA cases and controls

Parameter	Overall (n = 320) Mean±SD	SCA Cases (n = 160) Mean±SD	Controls (n = 160) Mean±SD	P-value
Age (years)	27.3±9.4	27.4±9.7	27.1±9.0	0.794
Sex				0.432
Male	173(54.1%)	90(56.2%)	83(51.9%)	
Female	147(45.9%)	70(43.8%)	77(48.1%)	
Height (m)	1.7±0.1	1.7±0.1	1.6±0.1	0.082
Weight (kg)	58.6±7.2	58.6±7.3	58.5±7.1	0.909
BMI (kg/m²)	20.4±2.4	20.3±2.8	20.5±1.9	0.441
BSA (m²)	1.7±0.1	1.7±0.2	1.7±0.1	0.480

***Abbreviations: SCA** – Sickle Cell Anaemia; **BMI** – Body Mass Index; **BSA** – Body Surface Area; **SD** – Standard Deviation; **cm³** – ; m² – **Square metres**; **kg** – Kilograms; **m** – Metres.*

Table 2: Gallbladder characteristics of adult SCA cases and controls

Parameter	Overall (n = 320) Mean±SD	SCA Cases (n = 160) Mean±SD	Controls (n = 160) Mean±SD	P-value
Gallbladder Volume (cm³)	27.8±0.9	31.9±1.2	23.2±1.4	<0.001*
Gallbladder Wall Thickness (cm)	0.23 ± 0.04	0.24 ± 0.1	0.23 ± 0.1	0.809
Gallbladder stone				<0.001*
Present	32(10.0%)	32(20.0%)	0(0.0%)	
Absent	288(90.0%)	128(80.0%)	160(100.0%)	

**Statistically significant at 95% confidence level.*
***Abbreviations: SCA** – Sickle Cell Anaemia; **p** – Probability value; **%** – Percentage.*

The mean fasting gallbladder volume was notably higher among SCA patients (31.9 cm^3) compared to controls (23.2 cm^3), suggesting possible functional or pathological gallbladder changes in SCA. Gallbladder wall thickness showed minimal variation between groups and remained within normal limits.

in adult SCA patients. Of the one hundred and sixty SCA patients examined, 32 (20%) had gallbladder calculi; the prevalence of gallbladder calculi which was seen in 21 females was nearly twice that of males in 11 cases. This suggests a significant relationship between gender and the presence of gallbladder calculi.

Table 3: Correlation of fasting gallbladder volume with sociodemographic and anthropometric characteristics

Variable	Correlation Coefficient (r)	p-value
Gallbladder Volume with Age	0.757	0.047*
Gallbladder Volume with Sex	0.122	0.125
Gallbladder Volume with BMI	0.526	< 0.001*
Gallbladder Volume with BSA	0.735	< 0.001*

**Statistically significant at 95% confidence level.*

***Abbreviations: BSA** – Body Surface Area; **BMI** – Body Mass Index; **r** – Pearson correlation coefficient; **p** – Probability value.*

Gallbladder stones were significantly more prevalent in SCA patients (20.0%) compared to controls (7.5%), with a highly significant chi-square result ($p < 0.001$). This supports the well-documented association between chronic haemolysis in SCA and pigment gallstone formation (Table 4).

The observed 20% gallstone prevalence is consistent with earlier studies conducted in Nigeria and Ghana, which reported prevalence rates between 15% and 25% in adults with HbSS.[6,12] These findings likely reflect a shared pathophysiological mechanism: the ongoing

Table 4: Comparison of mean gallbladder volume and wall thickness between SCA cases and controls

Variable	SCA Cases (n = 160) Mean ± SD	Controls (n = 160) Mean ± SD	t-value	p-value
Gallbladder Volume (cm^3)	31.9 ± 1.2	23.2 ± 1.4	4.686	< 0.001*
Gallbladder Wall Thickness (cm)	0.24 ± 0.10	0.23 ± 0.01	0.267	0.789

**Statistically significant at 95% confidence level.*

***Abbreviations: SCA** – Sickle Cell Anaemia; **SD** – Standard Deviation; **cm^3** – Cubic centimetres; **cm** – Centimetres; **t** – t-statistic; **p** – Probability value.*

Fasting gallbladder volume showed moderate positive correlations and strong association (p-value) with age ($r = 0.757$; $p = 0.047$), BSA ($r = 0.735$; $p < 0.001$), and BMI ($r = 0.526$; $p < 0.001$). These associations were statistically significant, indicating that gallbladder volume tends to increase with these parameters. The weakest correlation was with sex ($r = 0.122$; $p = 0.125$).

SCA patients had a significantly larger mean fasting gallbladder volume compared to controls ($p < 0.001$), indicating a meaningful difference. However, there was no significant difference in gallbladder wall thickness between the groups ($p = 0.789$).

Discussion

This study investigated the gallbladder of three hundred and twenty (320), age and sex matched SCA cases and the controls in fasting state. The results reinforce the growing body of evidence that gallbladder stones and increased gallbladder volume are significant features

hemolysis in SCA releases heme-derived bilirubin into bile, increasing its saturation and promoting pigment stone formation.[13]

Our results also confirmed the presence of enlarged gallbladder volumes in the SCA group. This is consistent with studies suggesting that sickle cell-related autonomic dysfunction can impair gallbladder motility, leading to bile stasis and distension.[14] Gallbladder hypocontractility, when combined with viscous bile laden with pigment, forms a nidus for sludge and eventually gallstones.

Female predominance among those with gallstones mirrors global epidemiological data, where hormonal factors, particularly estrogen-induced changes in bile cholesterol content, may elevate risk.[15]

Ultrasound remains the imaging modality of choice for screening due to its portability, safety, and

affordability. In light of these findings, proactive annual abdominal ultrasounds should be integrated into standard adult SCA care, particularly as patients in Nigeria now live longer due to improved disease management and access to hydroxyurea.[16]

Limitations

This was a single-centre study, which may limit generalizability across the broader Nigerian population. We did not measure liver function tests or bilirubin levels to correlate with imaging findings. Additionally, gallstone composition was not analysed biochemically. Long-term outcomes, such as the progression of sludge to symptomatic cholelithiasis, were not assessed due to the cross-sectional nature of the study. The implication of increased gallbladder volume is unknown.

Recommendations

We recommend that adult SCA patients undergo annual fasting abdominal ultrasound to evaluate gallbladder morphology.

Furthermore, multicentre studies incorporating biochemical data and longitudinal follow-up should be conducted.

Policy-makers should prioritize gallbladder screening as part of comprehensive sickle cell care in Nigeria.
Future research should consider analysis of variables such as BMI, BSA and Age in respect to the presence of gallbladder calculi, which may yield findings that will enrich the study.The implication of increased gallbladder volume should also be a subject for future research

Conflict of Interest

The authors declare no conflicts of interest.

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CONCLUSION

Adult patients with Sickle Cell Anaemia demonstrate significantly elevated rates of gallstones and increased gallbladder volume. These findings emphasize the importance of routine sonographic screening, even in asymptomatic individuals.

Integrating abdominal ultrasound into routine annual evaluation of adult SCA patients may reduce morbidity, enable elective interventions, and improve quality of life.

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