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The Prevalence of Cholelithiasis in Nigerians with Sickle Cell Disease as Diagnosed by Ultrasound

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Authors' contributions

This work was carried out in collaboration between all authors. Authors CAA and AOA designed the study, author CAA performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors CAA, AOA and OMA managed the analyses of the study. All authors managed the literature searches, read and approved the final manuscript.

Original Research Article

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ABSTRACT

Aim: To determine the prevalence of cholelithiasis in Nigerians with sickle cell disease in steady state, using ultrasonography.
Study Design: A prospective cross-sectional study.
Place and Duration of Study: Haematology Clinic, University of Benin Teaching Hospital, Benin City and Sickle Cell Centre, Benin City, Nigeria between July and December 2011.
Methodology: The study population was made up of non-pregnant sickle cell disease patients not in crisis and who have not had cholecystectomy. They were confirmed to have sickle cell disease through haemoglobin electrophoresis. All the patients were examined with a B-mode ultrasound machine with a curvilinear multifrequency transducer 2.5-7.5MHZ after an overnight or at least six hour fast. Calculi were diagnosed if highly echogenic structures, with acoustic shadowing were detected in the lumen of the gallbladder.
Results: There were 79 females and 71 males, aged between 10 months and 51 years. Of the 150 patients, 140 were homozygous for sickle cell disease (HbSS), while the remaining 10 were heterozygous for sickle cell disease (HbSC). The prevalence of

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cholelithiasis was 16.0%. It was related to age, sex and haemoglobin genotype. There was progressive increase in cholelithiasis with age which was more pronounced in the third and fourth decades. Cholelithiasis was also significantly more commonly seen in the HbSS group 23 (16.4%) out of 140 patients compared with the HbSC group 1 (10.0%) out of 10 patients. Cholelithiasis did not correlate with sex, although it was more commonly observed in females. The youngest patient with gall stones in this study was 2 years.

Conclusion: The prevalence of cholelithiasis in Nigerians with sickle cell disease was 16.0% and it was related to age and haemoglobin genotype.

Keywords: Cholelithiasis; sickle cell disease; gallbladder; ultrasound; Nigeria.

1. INTRODUCTION

Sickle cell haemoglobin [HbS] is the most important structural abnormality of the haemoglobin chain and sickle cell disease is one of the most common inherited haemoglobinopathies [1,2]. This disease is believed to have originated in malaria endemic West Africa where it has the highest prevalence, but it is also present in black Americans of African ancestry, Indian and Eastern Mediterranean region [3-5].

The prevalence of sickle cell trait in sub-Sahara Africa is as high as 30%, while the prevalence of sickle cell disease in Nigeria has been reported as 1-2% of the population [6-8].

Sickle cell disease (SCD) can occur as homozygous form (HbSS) or heterozygous form, such as HbSC, or HbSD among many other heterozygous variants.

The homozygous variant HbSS, has the severest clinical manifestations of any of the sickle cell variants and one of the most common clinical manifestation of sickle cell disease is anaemia due to chronic haemolysis secondary to repeated sickling [1,2,9]

Cholelithiasis is common in sickle cell disease due to persistent and accelerated haemolysis associated with multiple blood transfusions. Pigmented gallstones are predominantly formed in sickle cell disease due to the increased bilirubin excretion and precipitation resulting in bilirubinate crystals which is primordial to the formation of the pigmented gallstones [2,10].

Cholelithiasis is found more commonly in patients older than 10 years and in all the pathologies, it is directly related to the severity of sickle cell disease and to the intensity of the haemolysis [10,11]. The prevalence of cholelithiasis is high in patients with sickle cell disease and increases progressively with age, affecting 11-13% of children and has been found to be as high as 32% in adults [12-14]. It is also well established that majority of sickle cell disease patients with biliary sludge eventually develop gallstones [15-17].

Recommendation of elective cholecystectomy for sickle cell patients with asymptomatic gall stones is increasing because of increasing longevity of sickle cell patients, significant complications of even asymptomatic cholelithiasis and to eliminate the diagnostic confusions which may arise between acute cholecystitis and sickle cell hepatobiliary crisis [18-20]

Real time ultrasonography is a standard screening procedure and the first line imaging modality of choice in the assessment of the biliary tract.

The aim of this study was to assess the prevalence of cholelithiasis in Nigerians with sickle cell disease using ultrasonography.

2. MATERIALS AND METHODS

This was a prospective study of the prevalence of cholelithiasis as diagnosed by abdominal ultrasound scan of 150 consecutive confirmed sickle cell disease patients of all ages on routine follow up at the University of Benin Teaching Hospital (UBTH), Benin City and the Benin City Sickle Cell Disease Centre over a six month period.

These patients were confirmed to have sickle cell disease through haemoglobin electrophoresis.

The study population was made up of non-pregnant sickle cell disease patients not in crisis and who have not had cholecystectomy.

The study protocol was approved by the ethical committee of the teaching hospital. All the patients were examined with a B- mode ultrasound: Titan (Sonosite Inc, USA 2004) machine with a curvilinear multifrequency transducer 2.5-7.5MHZ. The procedure was explained to the patients and all patients were examined after an overnight or at least six hour fast.

Calculi were diagnosed if highly echogenic structures, with acoustic shadowing were detected in the lumen of the gallbladder.

Data analysis was done using SPSS version 16.0 statistical package.

Statistical test was considered significant at p-values ≤0.05.

3. RESULT

One hundred and fifty confirmed sickle cell disease patients aged 10 months to 51 years were studied. The mean age of the study population was 15.24±10.58 years. The largest number of patients was in the age group 0-10 years, which was 65 (43.3%) out of 150 patients. One hundred and forty (93.3%) of the patients were homozygous HbSS while the remaining 10 (6.7%) were heterozygous HbSC. There were 71(47.3%) and 79 (52.7%) males and females respectively.

Cholelithiasis was reported in 24 patients, giving a prevalence of 16.0% Fig. 1.

This was more commonly seen in the HbSS group, 23 (16.4%)] out of 140 patients than in the HbSC group, 1 (10.0%) out of 10 patients and was statistically significant ($p<0.0001$) Tables 1 and 2.

Furthermore, cholelithiasis was reported in 3 (4.6%), 5 (11.1%), 8 (30.8%), 3 (42.9%), 4 (57.1%) patients in the age groups 0-10, 11-20, 21-30, 31-40, and >40 years respectively Table 1. The prevalence of cholelithiasis was found to increase with increasing age and was statistically significant ($p=0.003$) Fig. 2. Gallstone was seen in 14 (17.7%) of 79 female

patients which was more than that reported in male sickle cell disease patients, 10 (14.4%), but was not statistically significant (p=0.701).

Table 1. Prevalence of cholelithiasis in 150 sickle cell disease patients according to age, sex and haemoglobin genotype

Age (years)	No of patients	No with cholelithiasis				
		HbSS 140 (93.3%)	HbSC 10(6.7%)	Male 71(47.3%)	Female 79(52.7%)	Overall 150
1-10	65(43.3%)	3(4.6%)	0	2(3.1%)	1(1.5%)	3(4.6%)
11-20	45(30.0%)	5(11.1%)	0	2(4.4%)	3(6.7%)	5(11.1%)
21-30	26(17.3%)	8(30.8%)	0	3(11.5%)	5(19.2%)	8(30.8%)
31-40	7(4.7%)	3(42.9%)	1(6.1%)	1(6.1%)	3(42.9%)	4(57.1%)
>40	7(4.7%)	4(57.1%)	0	2(28.6%)	2(28.6%)	4(57.1%)
Total	150(100%)	23(16.4%)	1(10.0%)	10(14.1%)	14(17.7%)	24(16.0%)

Table 2. Test of significance of age, haematological genotype and sex

Variable	Chi-square	P-value
Age	7.9	0.003
Genotype	11.130	< 0.0001
Sex	0.147	0.701

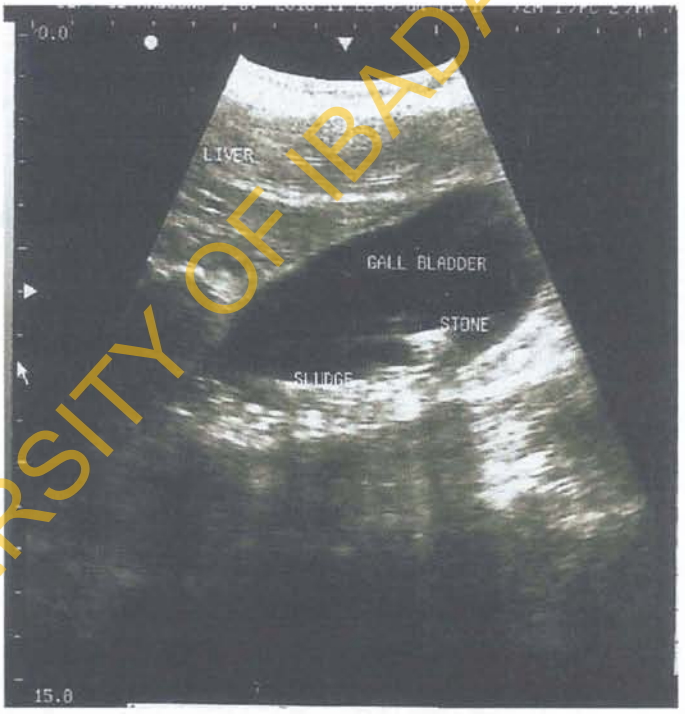

Fig. 1. Longitudinal sonogram of the gall bladder with a stone showing acoustic shadowing and biliary sludge

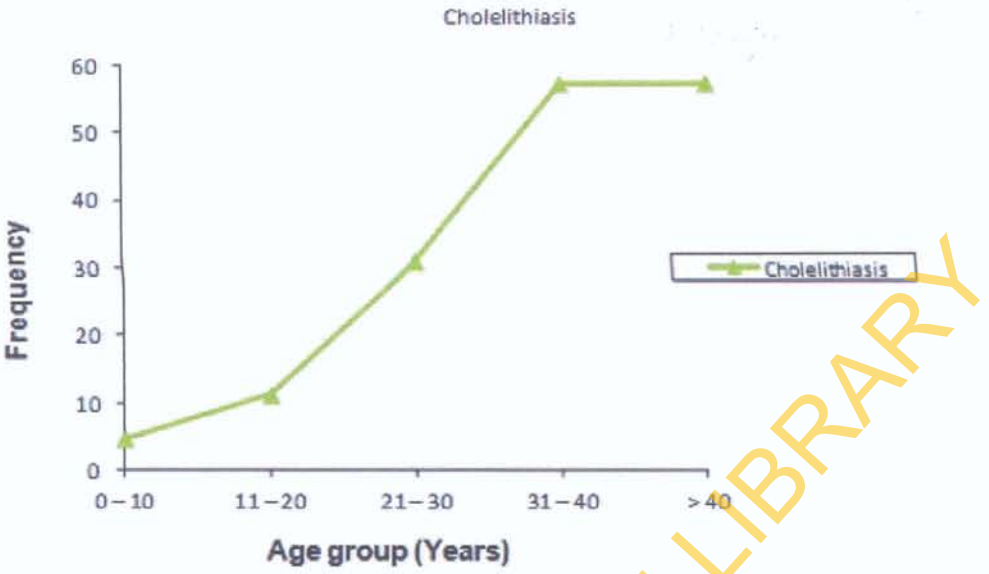

Fig. 2. Graph showing increse in the prevalence of cholelithiasis with age

4. DISCUSSION

There is wide variation in the ultrasonic prevalence of cholelithiasis among sicklers as previously reported [12,13,21,22]. This variation may be attributable to the different age groups, selection of distinct populations, gender, inclusion of symptomatic patients and imaging modalitis used in these studies [12,13,23].

Bond et al. [21] reported the prevalence of cholelithiasis to be 58% and 17% in HbSS and HbSC group respectively. This was among 95 patients aged 10 to 65 years from the United Kingdom who were examined by ultrasound. Webb et al. [13] however reported a 13% prevalence of cholelithiasis in 226 Jamaican sickle cell disease children aged 5 to 13 years who were examined by abdominal ultrasound. In another study, Attalla [12] reported 11% prevalence of cholelithiasis in 90 Sudanese sickle cell disease patients aged 6 months to 16 years who were also examined by ultrasound. A low prevalence of cholelithiasis of 6% in patients younger than 15 years who were examined by oral cholecystography was reported by Akinyanju and Ladapo in Nigeria [12]. This is similar to the 5% prevalence of cholelithiasis observed by Akamaguna et al. [23] among sickle cell disease patients at the university of Benin teaching hospital Nigeria using oral cholecystography

Cholelithiasis was observed in 24 (16.0%) of 150 patients in the current study. This was made up of 23 (16.4%) and 1 (10.0%) of patients in the HbSS and HbSC groups respectively. This finding was statistically significant and correlated with haemoglobin genotype with a p value of 0.0001. The prevalence in this study is less than that obtained by Durosimi MA et al. [24], who reported 24.2% among 18 to 56 years old Nigerian with sickle cell disease. They also observed that earlier studies from Africa had lower prevalence of less than 10%, which could be due to the predominant adult age group in their study and greater sensitivity of cholecystosonography.

Gallstone was reported in a boy with HBSS as young as 2 years of age in this study. This finding was similar to the study among Saudi children where the youngest patient with gall stones was 3 years old [25] but much younger than the report of 51/2 year old boy as the youngest in an earlier study by Akamaguna et al. [23] in the same environment . Although the current report of 4.6% incidence of cholelithiasis is significantly lower in the 0-10 years age group compared with the older age groups; it was however, similar to the report by Nzeh and Adedoyin [26] where the prevalence of cholelithiasis was 4.2% among HbSS Nigerians children between 2 months and 16 years of age. Furthermore, there was progressive increase in the prevalence of cholelithiasis with age, which was more pronounced in the third and fourth decades. This was also statistically significant (p value=0.003).

This finding was comparable to the findings by Webb et al. [13] but significantly less than the findings by Bond et al. [21]. The reason for the higher prevalence of cholelithiasis in the report by Bond et al. [21] may be due to the higher age group (10-64 years) in their study group compared to the majority of patients 65 (43.3%) of 150 patients between 10 months and 10 years of age in this study; however, the prevalence of cholelithiasis has been shown to increase with age in this and previous studies [12,14,21,27].

Furthermore, the prevalence of cholelithiasis in this study was higher than that reported by Akamaguna et al. [23] at the university of Benin teaching hospital. This low prevalence may be attributed to the paediatric age group and to the less sensitive diagnostic method of oral cholecystography used in their study.

Thus the prevalence of cholelithiasis in our current report correlated significantly with haemoglobin genotype and age to a large extent. However, the prevalence of cholelithiasis did not correlate with gender.

With the very early incidence of gallstone seen in a 2 year old, in this study, it will be necessary for sickle cell disease patients to be routinely screened for cholelithiasis as early as less than 10 years of age and this is further supported by the report in a previous study of about four fold higher prevalence of cholelithiasis among SCD patients compared with the general Nigerian population [28].

Elective laparoscopic cholecystomy procedure has been found to be safer than emergency procedure to prevent potential complications of biliary colics, acute cholecystitis and choledocholithiasis which leads to major risks, discomfort and longer hospital stay [29,30]. Therefore this is recommended for sicklers of all ages to prevent the risk of requiring an emergency cholecystectomy procedure as the incidence of gall stones and its complications increase with increasing age [18,19,20,29].

5. CONCLUSION

The prevalence of cholelithiasis in Nigerians with sickle cell disease was found to be 16%. It increases with increasing age and significantly more common in the homozygous SCD compared with the heterozygous cases.

CONSENT

A prospective cross sectional study design was used and approval was given by the Ethics and Research Committee of the University of Benin Teaching Hospital, Benin City, Edo

State, Nigeria. Participants and parents/guardians of minors also gave their consent for the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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