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### Prevalence of cholelithiasis in Nigerians with sickle cell disease

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#### Summary

Gall bladder ultrasonography was performed on 157 fasting patients (mainly adults) with sickle cell disease (133 SS and 24 SC) with a view to establishing the prevalence of cholelithiasis in Nigerian 'sicklers'. There were 82 females and 75 males whose ages ranged from 9 to 60 years (mean 34.5). Gallstones were demonstrated in 38 patients, giving an overall prevalence of 24.2% (22.6% in SS and 33.3% in SC). Their ages ranged from 18 to 56 years (mean 37.0) in HbS+C patients and 10-34 (mean 22.0) in SS patients. All the patients except one were asymptomatic. Autopsy confirmed gallstones in two SS patients who died of unrelated problems. The higher prevalence obtained in this study (24.2%) compared with the prevalence (< 10%) in earlier studies from Africa could be due to the predominantly adult age group screened and the greater sensitivity of cholecystosonography.

#### Résumé

Cent cinquante-sept patients à jeûne (en majorité des adultes) ont subi l'ultrasonographie de la vessie au moyen du SCD (133 SS et 24 SC) afin d'établir l'incidence de la cholélithiase chez les Nigérians qui souffrent de la drépanocytose. Il y avait 82 patientes et 75 patients de 9 à 60 ans ( $\bar{x}$  34.5). Nous avons relevé l'incidence des calculies chez 38 patients, ce qui donne un total de 24.2% (22.6% pour SS et 33.3% pour SC). L'âge des patients HbS+C qui souffrent de calculies varie entre 18 et 56 ans ( $\bar{x}$  37.0) et 10–34 ans ( $\bar{x}$  22.0) chez les patients SS. Tous les patients sauf un étaient asymptomatiques. L'autopsie a confirmé la présence des calculies chez deux patients SS atteints de drépanocytose que sont morts de maladies différentes. La plus forte incidence obtenue dans cette étude (24.2%) par rapport à la faible incidence (moins 10%) dans des études antérieures en Afrique serait la conséquence de la majorité des adultes étudiés et la plus forte sensibilité de la cholécystosonographie.

#### Introduction

Cholelithiasis is a known complication of chronic haemolytic disorders such as sickle cell disease (SCD). It is usually asymptomatic, although occasionally patients may present with symptoms of biliary obstruction that may necessitate cholecystectomy as recently experienced by two of our patients with sickle cell anaemia (SCA). Gall-stone in SCD is largely due to the chronic hyperbilirubinaemia and the resultant excretion and precipitation of bilirubin (pigment) stones in the biliary system [1]. Although the prevalence of homozygous sickle cell disease (HbSS) is as high as 2% in this country [2], the reported prevalence (4-9%) of cholelithiasis in these patients was rather low [3,4]. This is in contrast with the prevalence of 25-70% reported from Jamaica and North America [5-11].

The present study was designed to reexamine the incidence of gallstones amongst our largely adult patients (mean age 34.5 years) at Ibadan as it is known that incidence of cholelithiasis in SCD increases with age [8–9]. The data could then be compared with the previous reports from studies that were done mainly on children and young adults [1,3]. A grey scale ultrasonography was used since this is

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non-invasive, safer for all patients including deeply jaundiced and pregnant ones and more importantly, it is also very sensitive in detecting biliary calculi [9,12,13].

#### Patients and methods

The study was conducted on 157 patients with confirmed SCD (133 SS and 24 SC). There were 82 females and 75 males with ages ranging from 9 to 60 years (mean 34.5). Twenty-two (14.0%) of the patients (20 SS and 2 SC) were aged  $\leq 14$ years. All the patients except one were asymptomatic. The procedure was explained to the patients and/or their parents or guardians and due consent was obtained in each case. Blood samples were analysed for haematocrit, reticulocyte counts, serum bilirubin and alkaline phosphatase. A Phillips sono Diagnostic R1000 ultrasound (Endhoven, The Netherlands) with a 2.5 mHz transducer was used for scanning. The scans were performed before breakfast in the morning to prevent gall bladder contraction.

The patients were usually scanned in the supine position and longitudinal, transverse and oblique scans of the right hypochondrium were made. Apart from these routine views, scans were sometimes obtained with the patients sitting erect or lying obliquely. Scanning in these latter positions was very useful in resolving septae within the gall bladder from shadows around the gall bladder area that may mimic gallstones. Ultrasonograms were considered positive for gallstones when discrete, strongly refractive and mobile echoes were seen within the gall bladder with acoustic shadows behind them.

#### Results

Cholelithiasis (Fig. 1) was demonstrated in 38 patients (30 SS and 8 SC) giving an overall prevalence of 24.2%. Sludge was present in 5 cases (3 SS and 2 SC) and a phyrigian cap deformity in one (SS).

The prevalence of cholelithiasis in SS patients was 22.6% (30/133); and 20.0% (4/20) in those aged 14 and below, and 30.8% (8/26) in patients aged 25 years and over.

The oldest of the SS patients (60 years) had no gallstones (Fig. 2). Thirty-three per cent of



Fig. 1. (a) Oblique scan of the gall bladder. Note a single calculus with an accompanying acoustic shadow. (b) Scan through the subcostal region liver and gall bladder. Note the calculi within the gall bladder with accompanying acoustic shadow. (c) Long scan of the liver and gall bladder. Note the multiple calculi with accompanying acoustic shadows.



Fig. 2. Cholelithiasis in sickle cell disease: age distribution. ( $\Box$ ) SS screened, ( $\blacksquare$ ) SS with cholelithiasis, ( $\blacksquare$ ) SC screened, and ( $\boxtimes$ ) SC with cholelithiasis.

the SC patients with ages ranging from 18 to 56 years (means 37.0) had demonstrable gallstones and 50% of them were aged  $\ge$  30 years (Fig. 2). The presence of gallstones had little or no effect on both the haematological and biochemical parameters.

The only symptomatic patient (a 15-year-old HbS boy) presented with abdominal pain, pruritus and nausea, all of 6 weeks duration. Physical and laboratory examinations were consistent with a diagnosis of cholelithiasis. He was deeply jaundiced with tender hepatomegaly 6 cm below the costal margin and an epigastric tenderness. Bilirubin was 44.6 mg/dl (conjugated 36.2 mg/dl) and alkaline phosphatase was 80 IU/l. Urine revealed bilirubin, normal urobilinogen but no bile salt. Two other HbSS patients died of unrelated problems and gallstones were found at autopsy.

#### Discussion

A review of the literature shows that the incidence of cholelithiasis is very low in most parts of Africa [14–17]. In a review of 1386 autopsies in Lagos, Parnis [14] found a prevalence of 0.8%, while only 0.18% was obtained in a similar study at Ibadan by DaRocha-Afodu and Adesola [15] involving 5529 cases. This is in contrast with 15–20% from autopsy reports in Western Europe [18]. Consumption of low-fibre and cholesterol rich foods by the

Western nations is believed to be responsible for the differences noted between these nations and the poorer countries of Africa and Asia [19].

Prevalence of cholelithiasis in patients with SCD had also been found to be much lower in this country than in the North American patients; dietary factors are probably responsible [19]. Studies from this part of the world have revealed frequencies of gallstones in homozygous SS patients varying from 4.4 to 25%. These studies were conducted largely on children and young adults within the age range 2-35 years (mean 19.5) [3,4,20]. The findings were in contrast with reports from North America where the prevalence of gallstones in children under the age of 18 years has been reported to vary from 17 to 55% and could be as high as 70% in those aged 30 years and above [8,9,11,21].

The prevalence of 22.6% obtained for SS patients in the present study is similar to that of 25% reported by Akamaguna [20] who also used ultrasonography, although his patients were mainly children (mean age 16 years). Our figure is much higher than those of Akinyanju [3] and Adekile [4] (4.4–9%). The greater sensitivity of cholecystosonography over contrast cholecystography (used by Akinyanju) is most likely responsible for the lower figure he obtained since his patients were fairly old (mean age 19.5 years). The very low prevalence of 4.4% obtained by Adekile despite the fact

that ultrasonography was used could be due to the large proportion of younger patients (mean age 9.5 years). The present study is in agreement with the previous reports that gallstones in SCD generally increases with age [3,5,8,9,20]. Twenty per cent of our patients aged 14 years and below had gallstones, in contrast with 30.8% of those aged 25 years and above.

The frequency of gallstones in SC patients in this study was 33.3% (8/24) and it also increased with age. This is consistent with the report by River *et al.* [22] in which 83.3% of his six SC patients with gallstones were aged 40 years and above. There was no previous report of cholelithiasis in SC patients from this country [23].

Abdominal vaso-occlusive crisis is a common manifestation of SCD. It is usually mild but it may be quite severe, simulating 'acute surgical abdomen'. Differential diagnosis would include peptic ulcer, splenic infarction, hepatic infarction, acute cholecystitis, biliary colic with signs and symptoms of biliary tract obstruction as seen in one of our patients in this study. Management of 'acute abdomen' in SCD patients is essentially conservative with analgesia and intravenous fluid administration. Plain abdominal radiographs and ultrasound examination of the biliary system should be taken to rule out perforated viscous and/or bile duct obstruction. If due to biliary tract disease, elective cholecystectomy could be done once the acute episode subsides. Elective cholecystectomy is also indicated in patients with chronic upper abdominal pain in association with gallstones [11]. However, cholecystectomy in the presence of asymptomatic cholelithiasis remains controversial. Most physicians would want to wait and monitor the patients until symptoms develop [11].

The present study shows that cholelithiasis in Nigerians with SCD is not as rare as previously reported [23] (especially in older patients) but the prevalence is still lower than those reported in North American patients [11]. Diet appears to be the most important contributory factor since patients with sickle cell disease are of the same racial extraction.

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