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Hepatobiliary Ultrasonographic Abnormalities in Adult Patients with Sickle Cell Anaemia in Steady State in Ile-Ife, Nigeria

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Background:

Sickle cell anaemia (SCA) is associated with structural manifestations in the hepatobiliary axis. This study aimed to investigate the hepatobiliary ultrasonographic abnormalities in adult patients with sickle cell anaemia in steady state attending the Haematology clinic of a federal tertiary health institution in Ile-Ife, Nigeria.

Material/Methods:

Basic demographic data as well as right upper abdominal quadrant ultrasonography of 50 consecutive sickle cell anaemia patients were compared with those of 50 age- and sex-matched subjects with HbAA as controls.

Results:

Each of the study groups (patients and controls) comprised of 21 (42%) males and 29 (58%) females. The age range of the patients was 18–45 years with a mean (\pm SD) of 27.6 ± 7.607 years, while that of the controls was 21–43 years with a mean (\pm SD) of 28.0 ± 5.079 years ($p=0.746$). Amongst the patients, 32 (64%) had hepatomegaly, 15 (30%) cholelithiasis and 3 (6%) biliary sludge. Fourteen (28%) of the patients had normal hepatobiliary ultrasound findings. In the control group, one (2%) person had cholelithiasis, one (2%) biliary sludge, one (2%) fatty liver and none hepatomegaly. Forty-seven (94%) of the controls had normal hepatobiliary ultrasound findings. There was a statistically significant difference in the prevalence of hepatomegaly and cholelithiasis between the patients and controls (p value <0.001 for both comparisons).

Conclusions:

In this study, hepatomegaly, cholelithiasis and biliary sludge were the most common hepatobiliary ultrasound findings in patients with sickle cell anaemia. Ultrasonography is a useful tool for assessing hepatobiliary abnormalities in patients with sickle cell anaemia.

MeSH Keywords:

Abnormalities, Multiple • Anemia, Sickle Cell • Ultrasonography

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Background

Sickle cell anaemia is an autosomal recessive genetic disorder caused by a defect in the HBB gene, which codes for the haemoglobin β chain [1,2]. This leads to the production of abnormal haemoglobin chains within the red blood cell, which causes rigidity and sickling of the cell, leading to vascular occlusion and ischemia in multiple organs [3,4].

The normal human haemoglobin molecule is a heterotetramer composed of four haemoglobin chains (two α and two β) and the normal adult haemoglobin is Haemoglobin AA [3]. The abnormal genes occur as a result of glutamic acid-to-valine substitution at the sixth base position in the β haemoglobin gene on chromosome 11 [3]. Sickle cell anaemia results from the inheritance of two sickle β haemoglobin genes as HbSS [4].

Sickle cell anaemia (SCA) is particularly common among people whose ancestors come from sub-Saharan Africa, India, Saudi Arabia and Mediterranean countries. Each year about 300,000 infants are born with major haemoglobin disorders – including more than 200,000 cases of sickle-cell anaemia in Africa [5,6]. In Nigeria, by far the most populous country in the subregion, 24% of the population are carriers of the mutant gene (HbAS) and the prevalence of sickle-cell anaemia (HbSS) is about 2% [5,7–9].

Repeated vascular occlusion, chronic haemolysis with increased excretion of bilirubin and deposition of pigments, long-standing anaemia, repeated transfusions leading to iron overload and transfusional haemosiderosis, stagnation of sickled red cells in the hepatic sinusoids with sinusoidal obstruction, vascular occlusion by agglutinative thrombi, and infections, especially viral hepatitis, all contribute to the pathogenesis of the multiple hepatobiliary manifestations of sickle cell anemia [10,11]. Studies have shown that the most common structural hepatobiliary manifestations include hepatomegaly, gall bladder wall thickening, biliary sludge, cholelithiasis, choledocholithiasis and increased hepatic echogenicity [12,13].

Right Upper Quadrant Abdominal Ultrasonography is a simple, rapid, safe, non-invasive, and non-ionizing tool for assessing the hepatobiliary structural manifestations of sickle cell anemia [14]. It provides reliable and reproducible results and can be used for follow-up studies. Early identification of abnormalities in asymptomatic patients through hepatobiliary ultrasonography could aid in interventions if need be, thereby preventing or reducing the complications that otherwise would occur. This would reduce the overall morbidity and mortality associated with sickle cell anaemia. An ultrasonographic examination of sickle cell anaemia patients in steady state affords us the opportunity to evaluate the baseline features of the patients in their best state of health, and departures from the normal can be interpreted as reflecting the intrinsic consequences of the disorder itself or its chronic manifestations [13].

This study determined the usefulness of routine hepatobiliary ultrasonography for a comprehensive evaluation of patients with sickle cell anaemia.

Material and Methods

Selection of study subjects

This was a cross-sectional study that was carried out at the Haematology Clinic and Radiology Department of the institution between June 2014 and April 2015. The inclusion criteria for this study allowed for the enrolment of patients with sickle cell anaemia, having ≥ 18 years of age [Haemoglobin SS (HbSS) genotype], who were in a steady state and had given a written informed consent.

The following categories of patients were excluded from the study: patients younger than 18 years of age, patients with other haemoglobinopathies such as HbSC, HbCC, HbS B thalassaemia etc., patients in sickle cell crisis, patients who had had cholecystectomy and patients who were pregnant. A total of 100 study subjects (patients and controls)

were recruited for the study. Selection of patients for the study was by consecutive selection of fifty (50) consenting sickle cell anaemia patients. Fifty (50) age- and sex-matched subjects with HbAA who were members of staff, medical students, nursing students and blood donors at the blood bank of the institution were recruited as controls. Ethical approval was obtained from the Ethics and Research Committee of the institution.

Evaluation of study subjects

A structured questionnaire was designed for the collection of demographic and relevant clinical information. The patients were interviewed to elicit important relevant history and to ensure that they fulfil the set inclusion criteria for the study. A physical examination was conducted on the study subjects (patients and controls) including measurements of anthropometric parameters (height and weight to calculate body mass index) and an examination of the abdomen. Blood samples were collected to ascertain the haemoglobin genotype of the study subjects as well as full blood count and liver function tests.

Hepatobiliary ultrasonographic evaluation

This was done in the ultrasound room of the Radiology Department of the institution. The hepatobiliary ultrasound scan was done by the same Consultant Radiologist in all patients and controls in order to avoid inter-observer variations and differences. Patients and controls were asked to report after an overnight fast (in order to ensure adequate distension of the gallbladder for excellent cystic landmarks). A high resolution ultrasound machine in B-mode was used with a sensitive probe at a frequency of 3.5–6.5 MHz. A Mindray Real Time Ultrasound machine model DC-7 was used.

The examination was performed with the study subjects in the supine and left lateral decubitus positions to obtain an optimal view of the hepatobiliary structures. Coupling ultrasonography gel was applied over the right upper quadrant and epigastric regions of the abdomen, and the transducer placed over the same area and manoeuvred until the hepatobiliary structures were identified.

A detailed examination of the liver, gall bladder and biliary tree was carried out. Measurements of the span of the liver, the common hepatic duct and common bile duct diameters, the longitudinal and transverse dimensions of the gallbladder, gallbladder volume, gallbladder wall thickness and portal vein diameter were performed in all subjects. The liver area was scanned in multiple planes (sagittal, transverse and oblique). The liver span was defined as the liver length measured at the level of the mid-clavicular line along the long axis of the right lobe of the liver. In adults, hepatomegaly is defined as the long axis of the liver longer than 155 mm. The architecture and echogenicity of the liver were determined in comparison to the right kidney. A diffuse increase in liver echogenicity was defined as “bright liver or echogenic liver”.

The longitudinal and transverse dimensions of the gallbladder, gallbladder volume and gallbladder wall thickness

were measured either from an intercostal or subcostal window. The upper limit of normal for the gallbladder transverse diameter is 5 cm and for the longitudinal diameter 10 cm in the non-contracted state, while the normal gallbladder volume is 30–50 ml. The upper limit of normal for gallbladder wall thickness (measured from the anterior wall) is 3 mm. The common hepatic duct diameter was measured at the porta hepatis. The upper limit of normal for the common hepatic duct diameter was set at 4 mm. The diameter of the common bile duct was also measured, and it is considered to be distended when the value is greater than 7 mm. The portal vein diameter was measured at the porta hepatis. The upper limit of normal for the portal vein diameter was set at 13 mm. All measurements were made intra-luminally in millimeters. Abnormalities such as hepatomegaly, stones, polyps, sludge, folds, air, or pericholecystic fluid, gallbladder wall thickening and ascites were looked for.

B-mode parameters such as frequency, focus, gain, and tissue harmonics application were optimized by the radiologist on a case-by-case basis. Image analysis was performed visually and quantitatively. The findings obtained from the patients were compared with those of the control group.

Data analysis

The data obtained were analysed using the Statistical Package for the Social Sciences (SPSS) version 17.0 computer software package (SPSS Chicago Inc. IL U.S.A.). Descriptive statistics used included frequency tables, means and standard deviations. The statistically significant differences in the hepatobiliary ultrasonographic findings between the patients and controls were determined with appropriate statistical tests. Parametric tests, such as the t-test, were employed for comparing continuous variables, while non-parametric test, such as the chi-square (χ^2) test, for qualitative variables respectively. Correlation analysis of some variables was also done where applicable using the Pearson's correlation coefficient. A p-value of less than 0.05 was considered as statistically significant.

Study definitions

Sickle cell anaemia: Persons with Haemoglobin genotype SS (HbSS).

Normal individuals: Persons with Haemoglobin genotype AA (HbAA).

Hepatobiliary system: This consists of the liver, gallbladder and biliary tract.

Steady state: A patient with sickle cell anaemia is said to be in a steady state when there is no recent drop in the haemoglobin level and there is absence of infection, pain, acute complicating factors or acute clinical symptoms or crisis for at least three months as established by a careful history and complete physical examination [15].

Results

Each group (patients and controls) comprised of 21 (42%) males and 29 (58%) females. The ages ranged from 18–45 years with a mean (\pm SD) of 27.6 ± 7.607 years for the patients, and from 21–43 years with a mean (\pm SD) of 28.0 ± 5.079 years for the controls. The patients and controls were similar in age with $p=0.746$, as shown in Table 1.

The BMI of the patients ranged from 15.10–26.50 kg/m² with a mean (\pm SD) of 19.36 ± 2.185 , while that of the controls ranged from 18.30–32.88 kg/m² with a mean (\pm SD) of 23.56 ± 2.936 (Table 2). The mean BMI for the patients and controls were within the normal range. However, the patients had a significantly lower BMI than the control group ($p < 0.001$). Twenty-four (48%) of the patients were underweight, 1 (2%) was overweight and none was obese, whereas 6 (12%) of the controls were overweight, 3 (6%) were obese and 1 (2%) was underweight.

The hepatobiliary ultrasonographic parameters of the study subjects (patients and controls) were as shown in Table 3. The liver span ranged from 12.3–25.57 cm and 11.67–15.37 cm in the patients and controls respectively. The mean (\pm SD) liver span of the patients (16.56 ± 2.357) was significantly greater than that of the controls (13.87 ± 0.790) with $p < 0.001$.

There was a statistically significant difference in the mean (\pm SD) longitudinal diameter of the gallbladder of the patients (6.65 ± 1.285) and the controls (6.12 ± 1.277) with $p=0.042$. However, there was no significant difference in the mean gallbladder antero-posterior diameter, transverse diameter, volume and wall thickness with p values of 0.398, 0.692, 0.664 and 0.639 respectively.

The common hepatic duct could not be visualized in 7 (14%) patients as well as in 4 (8%) of the controls. There was no significant difference in the mean common bile duct diameter (Figure 1) and portal vein diameter with p values of 0.293 and 0.824 respectively.

The hepatobiliary ultrasonographic diagnosis of the study subjects (patients and controls) were as shown in Table 4. Fourteen (28%) of the patients and 47 (94%) of the controls had normal hepatobiliary ultrasound findings. Thirty-two (64%) of the patients had hepatomegaly (11 (22%) males and 21 (42%) females) but none of the controls had this finding. Twenty-two (68.75%) patients with hepatomegaly (Figure 2) were within the age range of 18–30 years, while 7 (21.87%) were within the age range of 31–35 years. Only 1 (3.13%) patient with hepatomegaly was above 40 years of age. There was no statistically significant difference in the mean (\pm SD) age of the patients with hepatomegaly (28.8 ± 6.21) when compared with patients without hepatomegaly (25.4 ± 9.42); $p=0.131$, and there was also no significant difference in the mean (\pm SD) BMI of the patients with hepatomegaly (19.06 ± 1.963) when compared with those without hepatomegaly (19.89 ± 2.503); $p=0.200$.

Fifteen (30%) of the patients had cholelithiasis; 4 (8%) were males, while 11 (22%) were females. Only 1 (2%) female control had cholelithiasis. All the patients had multiple gall

Table 1. Socio-demographic characteristics of the study subjects.

Characteristics	Patients (HbSS)			Controls (HbAA)			P-value
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)	
Sex	21 (42)	29 (58)	50 (100)	21 (42)	29 (58)	50 (100)	
Age (years)							
Range	18–43	18–45	18–45	23–43	21–35	21–43	
Mean ±SD	26.05±6.975	28.76±7.958	27.62±7.607	30.48±5.988	26.28±3.442	28.04±5.079	0.746
Age group							
18–25	14 (66.7)	9 (31)	23 (46)	6 (28.6)	18 (62.1)	24 (48)	
26–30	3 (14.3)	10 (34.5)	13 (26)	6 (28.6)	9 (31.0)	15 (30)	
31–35	2 (9.5)	6 (20.7)	8 (16)	5 (23.8)	2 (6.9)	7 (14)	
36–40	1 (4.8)	1 (3.4)	2 (4)	2 (9.5)	0 (0)	2 (4)	
41–45	1 (4.8)	3 (10.3)	4 (8)	2 (9.5)	0 (0)	2 (4)	
Marital status							
Single	18 (85.7)	22 (75.9)	40 (80)	20 (95.2)	28 (96.6)	48 (96)	
Married	3 (14.3)	7 (24.1)	10 (20)	1 (4.8)	1 (3.4)	2 (4)	
Education							
Secondary	2 (9.5)	3 (10.3)	5 (10)	1 (4.8)	1 (3.4)	2 (4)	
Post secondary	19 (90.5)	26 (89.7)	45 (90)	20 (95.2)	28 (96.6)	48 (96)	
Social Status							
Civil servant	1 (4.8)	6 (20.7)	7 (14)	11 (52.4)	14 (48.3)	25 (50)	
Trader	1 (4.8)	5 (17.2)	6 (12)	0 (0)	0 (0)	0 (0)	
Teacher	0 (0)	1 (3.4)	1 (2)	0 (0)	0 (0)	0 (0)	
Student	16 (76.2)	12 (41.4)	28 (56)	10 (47.6)	15 (51.7)	25 (50)	
Unemployed	1 (4.8)	2 (6.9)	3 (6)	0 (0)	0 (0)	0 (0)	
Artisan	2 (9.5)	3 (10.3)	5 (10)	0 (0)	0 (0)	0 (0)	

stones and the stones were mobile. The widest diameters of the stones seen in the patients ranged between 2.4–10.7 mm with a mean (\pm SD) of 6.86 \pm 2.974. The control who had cholelithiasis had a solitary mobile gallstone that measured 18.6 mm in its widest diameter. Eleven (73.3%) of the patients with cholelithiasis were within the age range of 18–30 years, while the only female control with cholelithiasis was 24 years old. Two (13.3%) of the patients with cholelithiasis were within the age range of 31–35 years, and the remaining 2 (13.3%) patients with cholelithiasis were above 40 years of age.

There was no statistically significant difference in the mean (\pm SD) age of the patients with cholelithiasis (29.6 \pm 8.32) when compared with those without cholelithiasis (26.7 \pm 7.24); $p=0.232$. There was also no significant difference in the mean (\pm SD) BMI of the patients with cholelithiasis (19.11 \pm 1.812) when compared with those without cholelithiasis (19.46 \pm 2.343); $p=0.600$. There was a statistically significant difference in the prevalence of hepatomegaly and cholelithiasis between the patients and controls (p value <0.001 for both comparisons).

Three (6%) of the patients; 1 (2%) male and 2 (4%) females had biliary sludge and this was co-existing with cholelithiasis. Only 1 (2%) male control had biliary sludge and also only 1 (2%) female control had ultrasound evidence of fatty liver. None of the patients had fatty liver. There was no statistically significant difference in the prevalence of biliary sludge and fatty liver between the patients and controls with p values of 0.307 and 0.315 respectively.

None of the study patients had choledocholithiasis or ultrasound evidence of liver cirrhosis and no focal hepatic lesion was seen. Their hepatic echogenicity, echotexture, outline, intrahepatic biliary ducts and vascular channels were all within normal limits.

Discussion

The hepatobiliary ultrasound findings from this study were similar to what had been previously reported in the literature [12,13]. The commonest findings from this study were hepatomegaly, cholelithiasis and biliary sludge.

Table 2. Anthropometric parameters of the study subjects.

Characteristics	Patients (HbSS)			Controls (HbAA)			P-value
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)	
Weight (kg)							
Range	44–76	34–74	34–76	54–80	50–82	50–82	
Mean ±SS	53.05±7.439	50.44±7.557	51.54±7.544	65.33±6.628	65.60±7.406	65.49±7.021	<0.001
Height (m)							
Range	1.54–1.77	1.5–1.72	1.5–1.77	1.6–1.79	1.53–1.77	1.53–1.79	
Mean ±SD	1.66±0.065	1.59±0.058	1.62±0.067	1.70±0.061	1.65±0.076	1.67±0.074	0.001
BMI* (kg/m²)							
Range	16.7–23.7	15.1–26.5	15.1–26.5	18.3–25.7	19.1–32.88	18.3–32.88	
Mean ±SD	18.76±1.723	19.79±2.403	19.36±2.185	22.57±1.927	24.28±3.341	23.56±2.936	<0.001
BMI* classified							
Underweight	13 (61.9)	11 (37.9)	24 (48)	1 (4.8)	0 (0)	1 (2)	
Normal	8 (38.1)	17 (58.6)	25 (50)	19 (90.5)	21 (72.4)	40 (80)	
Overweight	0 (0)	1 (3.4)	1 (2)	1 (4.8)	5 (17.2)	6 (12)	
Obese	0 (0)	0 (0)	0 (0)	0 (0)	3 (10.3)	3 (6)	

BMI – Body Mass Index.

Table 3. Hepatobiliary ultrasonographic parameters.

Parameters	Patients (HbSS)		Controls (HbAA)		P-value
	Range	Mean ±SD	Range	Mean ±SD	
Liver span (cm)	12.30–25.57	16.56±2.357	11.67–15.37	13.87±0.790	<0.001
PVD (mm)	3.10–13.00	8.14±2.052	5.20–11.50	8.22±1.533	0.824
Gall bladder dimensions					
Longitudinal (cm)	2.92–8.90	6.65±1.285	2.76–8.62	6.12±1.277	0.042
AP (cm)	1.07–3.80	2.26±0.566	1.62–3.19	2.34±0.377	0.398
Transverse (cm)	1.41–4.38	2.67±0.695	1.98–3.89	2.72±0.505	0.692
Volume (cm ³)	3.69–50.16	21.87±10.522	7.83–46.08	21.01±9.129	0.664
Wall thickness (mm)	1.20–3.00	2.04±0.470	1.20–2.80	2.01±0.324	0.639
CHDD (mm)	1.20–3.70	2.40±0.625	1.40–3.10	2.04±0.377	0.001
CBDD (mm)	1.30–6.80	3.90±1.359	2.10–5.20	3.66±0.785	0.293

PVD – portal vein diameter; AP – antero-posterior; CHDD – common hepatic duct diameter; CBDD = common bile duct diameter.

Hepatomegaly is a common finding in sickle cell anaemia, and it is largely due to extramedullary haematopoiesis in response to the chronic anaemia in this condition [3,4]. Hepatomegaly can also be due to transfusional haemosiderosis and chronic viral hepatitis from repeated blood transfusions [6,17]. However, in Nigeria, which is a malaria endemic country, frequent episodes of malaria are also a major cause of the hepatomegaly seen in these patients [17]. Malaria is the most common medical indication for hospital admission among SCA patients in Nigeria apart from sickle cell crisis [16,17].

Olaniyi et al. [17] found a prevalence of hepatomegaly of 62.2% among SCA patients in Ibadan, Nigeria. Ali et al. [13] found a prevalence of 72.6% among SCA patients in Turkey and Papadaki et al. [12] found a prevalence of 70.5% among sickle cell disease patients in Greece.

Fifty-six percent of the patients in this study had a palpable liver on clinical examination but ultrasonographic evaluation revealed a hepatomegaly prevalence of 64%. None of the controls had hepatomegaly. However, one (2%) of

Table 4. Hepatobiliary ultrasonographic diagnosis

Characteristics	Patients (HbSS)			Controls (HbAA)		
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)
Normal	9 (18)	5 (10)	14 (28)	20 (42.6)	27 (57.4)	47 (94)
Hepatomegaly	11 (22)	21 (42)	32 (64)	0 (0)	0 (0)	0 (0)
Cholelithiasis	4 (8)	11 (22)	15 (30)	0 (0)	1 (2)	1 (2)
Choledocholithiasis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Biliary sludge	1 (2)	2 (4)	3 (6)	1 (2)	0 (0)	1 (2)
Fatty liver	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)
Liver cirrhosis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)



Figure 1. Sonogram of a sickle cell anaemia patient showing the portal vein and the common bile duct as they course through the hilum of the liver. The common bile duct is anterior to the portal vein, it has a normal diameter which measures 0.17 cm. The portal vein diameter is also normal and it measures 0.82 cm.



Figure 2. Sonogram showing massive hepatomegaly in a sickle cell anaemia patient. The lower lobe of the liver (grey arrow) extends well below the lower pole of right kidney (white arrow) and the liver measures 22.3 cm in span exceeding the normal limit of 15.5 cm.

the controls who was a 24 year old female with a BMI of 24.8 kg/m² had ultrasound features of fatty liver disease. The liver span in this patient was 13.39 cm on ultrasound. None of the patients had ultrasound features of fatty liver.

Persistent hepatomegaly is one of the established markers of disease severity in SCA patients [18,19]. Olatunji et al. [20] also established that persistent hepatomegaly is an index of disease severity in patients with sickle cell anaemia in Ilorin, Nigeria. Persistent hepatomegaly in patients with SCA implies that such patients have the tendency to run a more severe clinical course than those without it, and there is a need to pay more attention to them.

Cholelithiasis is a common complication of sickle cell anaemia [21,22]. The chronic haemolysis of sickle cell anaemia predisposes patients to cholelithiasis, the world-wide prevalence of which by ultrasound examination has been reported to be 11–55% in patients with sickle cell anaemia [23]. The prevalence is low in most parts of Africa compared to the Western nations and it varies with age, gender and method of examination [24,25].

Ajayi [22] found a prevalence of cholelithiasis of 32.9% among adult sickle cell anaemia patients in Ilorin, Nigeria. Ali et al. [13] found a prevalence of 32.1% among SCA patients in Turkey and Papadaki et al. [12] found a prevalence of 20% among sickle cell disease patients in Greece.

There is a possibility that the longer average life span of patients with sickle cell anaemia may contribute to the higher prevalence of gallstones. There is no doubt that the prevalence of cholelithiasis is higher in sickle cell anaemia than in the general population. The prevalence rate of cholelithiasis in Nigerian patients with sickle cell anaemia is 4.3 to 25% compared to 0.18 to 0.8% in the general population [26,27] This can be attributed to chronic haemolysis and its consequent hyperbilirubinaemia, and is supported by the fact that most of the stones in sickle cell anaemia patients are pigment stones (Calcium bilirubinate) [28].

Another relatively common complication of sickle cell anaemia is the development of choledocholithiasis which is usually secondary to cholelithiasis, but there is also primary choledocholithiasis [29]. In this study, none of the patients had choledocholithiasis.

The differential diagnoses of an acute abdomen in SCA patients include acute cholecystitis, biliary colic with symptoms and signs of biliary tract obstruction, splenic infarction, hepatic infarction etc. Abdominal ultrasound scan should be performed to confirm biliary duct obstruction by a stone for which an elective cholecystectomy could be done, once the acute episode has subsided. Elective cholecystectomy is also indicated in patients with chronic abdominal pain in association with gallstones [30]. However, cholecystectomy in the presence of asymptomatic cholelithiasis remains controversial. Most physicians would want to wait and monitor the patient until symptoms develop. A larger longitudinal study is needed to establish the natural course of untreated gallstones.

Biliary sludge is also a common complication of sickle cell anaemia and it is due to the chronic haemolysis in these patients. Ma'aji et al. [14] found a prevalence of biliary sludge of 2.8% among children with SCA within the age range of 1–15 years in Sokoto, Nigeria. In the adult population, however, Ali et al. [13] found a prevalence of 3.6% among sickle cell anaemia patients in Turkey.

In this study, the prevalence of biliary sludge in the SCA patients was 6% (3 out of 50). Biliary sludge was also seen in a 25 year old male control with a normal BMI of 20.01 kg/m².

In a study by Hussain et al. [23], performed in Saudi Arabia, of 305 children with sickle cell anaemia 50 (16.4%) had biliary sludge and in a follow-up study of these 50 patients with biliary sludge the majority (65.7%) developed gallstones. In this study, all the three patients who had biliary sludge also had co-existing cholelithiasis, which suggests a progression of the disease from biliary sludge to the formation of gallstones.

Sickle cell anaemia patients with biliary sludge should be followed-up closely because of the risk of developing gallstones later, and those who eventually develop gallstones should be offered elective laparoscopic cholecystectomy, particularly when they are symptomatic. Again, cholecystectomy for asymptomatic patients remains controversial.

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The findings from this study should, however, be considered along with some limitations such as the absence of a long-term patient follow-up in order to re-assess the hepatobiliary findings for possible disease progression.

Conclusions

Right Upper Abdominal Quadrant Ultrasonography should be carried out routinely in all patients with sickle cell anaemia for early detection of abnormalities in their hepatobiliary system, for which they may not yet be symptomatic. In this study, hepatomegaly, cholelithiasis and biliary sludge were the most common hepatobiliary ultrasound findings in the patients with sickle cell anaemia. Persistent hepatomegaly in patients with SCA is a known marker of disease severity and therefore these patients should be followed-up closely. All the patients with biliary sludge had coexisting cholelithiasis, which supports the fact that biliary sludge is a precursor for gallstone formation. Early identification of abnormalities in asymptomatic patients through hepatobiliary ultrasonography would aid in prompt intervention if need be, thereby preventing or reducing the complications that otherwise would occur. This would reduce the overall morbidity and mortality associated with sickle cell anaemia.

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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