

Sonographic Evaluation of Some Abdominal Organs in Sickle Cell Disease Patients in a Tertiary Health Institution in Northeastern Nigeria

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Abstract

Background: Sonographic evaluation of abdominal organs is an important work up in managing sickle cell disease (SCD) patients. This study aimed at evaluating abdominal organs by sonography among SCD patients. **Methodology:** A cross-sectional study was carried out in Maiduguri, Nigeria from April 2014 to July 2015. Two hundred and fifty-two patients participated in the study, with 126 controls and 126 SCD patients. There were 131 (52%) males, and 121 (48%) females, with age range 3–38 years. Measurements were done using ultrasound machine with probe frequencies ranging from 1–4MHz and 4–9MHz in supine, right and left oblique positions for optimum visualization of the abdominal organs. **Results:** Participants within the age range of 10–15 years had the highest frequency with 88 (34.9%), followed by those within the age group of 17–23 years with 86 (34.1%), and the least were those within the age group of 30 years and above with 8 (3.2%). Hepatomegaly was found in 53 (75.7%), and increased echogenicity of the liver was found in 50 (94.3%) of the SCD patients, $P = 0.000$. Gallstones were found in 45 (17.9%), gallbladder sludge was found in 51 (21.4%) and thickened gallbladder wall was found in 84 (33.3%) of the SCD patients, $P = 0.000$. Autosplenectomy was found in 45 (17.9%), splenomegaly in 63 (24.9%), and calcified spleen in 18 (8.7%) of the SCD patients, $P = 0.000$. Enlarged kidneys in SCD patients were found in 61 (98.4%) and 63 (98.4%) on the right and left kidneys, respectively. Shrunken kidneys were found in 5 (2.0%) and 4 (1.6%) of the SCD patients on the right and left kidneys, respectively, $P = 0.000$. **Conclusion:** Abdominal sonography in SCD patients revealed varied remarkable changes in the size, echotexture, intraluminal deposits and wall thickness in the liver, gallbladder, kidneys, and spleen.

Keywords: Abdominal organ, sickle cell disease, sonography

INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder in which there is an alteration in the normal globin chain. It is characterized by red blood cells (RBCs) with abnormal hemoglobin resulting in rigid sickling of the cell, leading to vascular occlusion, and ischemia in multiple organs.^[1] It is associated with pathologic consequences of chronic and life-long illnesses. Patients with SCD often have different forms of sickle cell crises.^[2] It is a common genetic condition that is global and particularly common among people from sub-Saharan Africa, India, Saudi Arabia, and Mediterranean countries.^[3] The prevalence of SCD in countries of West Africa like Ghana and Nigeria, range between 15% and 30%.^[1,2,4] This disease is still prevalent in

Northeast Nigeria, due to ignorance, limited exposure to health education and access to health-care facilities. Prominent organ involvement are often the liver, spleen, and kidneys and they respond to SCD by dimensional and parenchyma changes,^[2] while there may be a stone formation in the gallbladder (GB) and changes in its wall thickness. There is a need to develop models of care appropriate to the management of SCD in sub-Saharan Africa which will be based on constant monitoring, early detection of crises, and early presentation to the specialist

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Received: 13-02-2017 Accepted: 01-06-2017 Available Online: 28-03-2018

Access this article online

Quick Response Code:



Website:
www.jmuonline.org

DOI:
10.4103/JMU.JMU_5_17

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How to cite this article: Luntsi G, Eze CU, Ahmadu MS, Bukar AA, Ochie K. Sonographic evaluation of some abdominal organs in sickle cell disease patients in a tertiary health institution in Northeastern Nigeria. J Med Ultrasound 2018;26:31-6.

treatment centers. Early monitoring and detection can be enhanced by ultrasonography of the liver, spleen, kidneys, and the gallbladder. Ultrasonography is a simple, noninvasive, affordable, and easily accessible imaging modality. Regional variations in organ size and parenchymal echotexture among SCD patients exist in different publications. No such study has been documented in our locality to the best of the researchers' knowledge. This study was aimed at evaluating some abdominal organs (liver, GB, kidneys, and the spleen) in SCD patients in Maiduguri, Northeastern, Nigeria using ultrasonography.

METHODOLOGY

A cross-sectional study was conducted from April 2014 to July 2015 using a convenience sampling technique. Two hundred and fifty-two participants comprising 131 (52%) males and 121 (48%) females with age range of 3–38 years were involved in the study. Ethical clearance was obtained from the Ethical Committee of the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Borno State, Nigeria, while informed consent was obtained from the patients and/or from their parent/guardian if they were minors before the study. A total of 126 SCD patients confirmed to have homozygous hemoglobin were purposively selected from the sickle cell clinic of UMTH. Furthermore, 126 age-matched controls (volunteers) with confirmed normal hemoglobin (HbAA)^[2,5-7] were also enlisted in the study.

Recruitment of patients

SCD patients were recruited from the hematology department of UMTH. The hematology department of UMTH runs clinics for SCD patients on Tuesdays and Thursdays for children and adults, respectively. All the patients that consented to participate in the study were scheduled for an abdominal scan in the radiology department based on convenience. Abdominal ultrasound scan findings, demographic data, anthropometric measurements, and their records/files were reviewed for evidence of laboratory investigations such as Hb electrophoresis, previous surgeries (splenectomy, and/or cholecystectomy), and recorded on a data capture sheet.

Equipment

A real-time ultrasound machine General Electric; Lp5 Pro- Europe; model number: 5415172, was used for the study. Curvilinear probe with frequencies ranging from 1–4 MHz and 4–9 MHz was used to evaluate the abdominal organs. The equipment was validated for quality performance by the departmental medical physicist before the measurements. The choice of the probe was to give adequate penetration and resolution of intraperitoneal and retroperitoneal abdominal organs in both pediatrics and adult patients. Using the available freeze-frame capability, all measurements were done using the electronic clippers of the ultrasound machine. Height and weight measuring scale (Surgifriend Medicals England) which was periodically checked for accuracy and calibration was used to measure the height and weight of the patients. Patients stood upright for measurement of their height with the head in Frankfurt positioned and weight after removing their shoes. Body

mass index (kg/m^2), was computed using weight (in kg), divided by height (in m^2).

Scanning technique

All the patients fasted overnight or at least for 6 h before being scanned. No subject had undergone any surgery at the time of the scan. The examinations were performed with the patients in the supine position for comfort and to obtain optimal views of the liver, GB, the kidneys and the spleen. Right and left oblique positions were used as alternate positions if the organs were not clearly visualized in the supine position.

The liver span was measured in the right lobe with the longitudinal center of the right kidney in the plane of imaging. Liver parenchyma was assessed for echotextural and focal abnormalities. Hepatomegaly was defined if the long axis of the liver was >150 mm.^[1,8,9] The gallbladder, its wall thickness, and content were also assessed.

The long axis of the spleen was measured at the level of the hilum. When the spleen was not visualized in its position, it was defined as autosplenectomy,^[2,5,10] when the long axis of the spleen was >130 mm in adults, it was defined as splenomegaly, while a shrunken spleen was defined in adults when the long axis of the organ was <50 mm. The spleen was also assessed for parenchymal echotextural changes and focal abnormalities.^[2,9]

The length of the kidneys was obtained by measuring the bipolar length (long axis) of the kidneys. The upper limits for normal right and left kidneys sizes were 128 mm and 130 mm, for adults, respectively.^[8-10] The kidneys were considered abnormally echogenic if the renal cortex was equal to or more echogenic than adjacent spleen or liver.^[8,11] Renal corticomedullary differentiation was considered abnormal when the cortex was difficult to visually distinguish from the medulla. Kidneys were also assessed for the presence of renal calculi, cysts, or other focal parenchymal abnormalities. The measurements obtained from the study group were compared with those obtained from the control group. Evaluation of the echotexture of the organs was done subjectively in gradation of the echo textural changes in accordance with the grading pattern of Shetty *et al.*,^[11] who categorized the echogenicity of abdominal organs starting from the diaphragm being more echogenic than the pancreas, the pancreas is more echogenic than the spleen, the spleen is more echogenic than the liver and the liver is more echogenic than the kidneys.

Data were analyzed using Statistical Package for Social Sciences version 20.0 (IBM SPSS (2011), Version 20.0. Armonk, NY: IBM Corp.), where descriptive statistics, such as the mean, standard deviation, and paired sample *t*-test, was used for analysis and $P < 0.05$ was considered statistically significant.

RESULTS

There were 131 (52%) males and 121 (48%) females, with age ranged from 3 to 38 years (mean age of 18.8 ± 6.3). No patient

had undergone any surgery or had any clinical signs of acute sickle crisis as at the time of ultrasonography scan.

Patients within the age group of 10–16 years had the highest frequency of 88 (34.9%), followed by those within the age group of 17–23 years with 86 (34.1%), while patients with age range >30 years were least with 8 (3.2%). $P = 0.43$, as shown in Table 1.

The sonographic finding on the liver showed normal liver span among 137 (54.4%) patients, and hepatomegaly was found among 70 (27.8%) patients. A total of 53 (21.0%) SCD patients had increased liver echotexture and 40 (15.9%) SCD patients had coarse liver echotexture, and 40 (15.9%) had coarse liver echotexture. $P = 0.000$, as shown in Table 2.

This study found gallstone (gallbladder calculi/cholelithiasis) in 45 (17.9%) SCD patients, GB sludge in 54 (21.4%) SCD patients and 87 (34.5%) SCD patients had thickened GB wall. $P = 0.000$, as shown in Table 3.

Sixty-three (24.9%) patients had splenomegaly and 45 (17.9%) had auto splenectomy (absent/not visualized spleen) among the studied patients. Increased echotexture, was found among 15

(7.25%) patients and 18 (8.7%) patients had calcified spleen. $P = 0.000$, as shown in Table 4.

Enlarged kidneys were found among 62 (24.6%) patients on the right, and 64 (25.4%) patients on the left. A total of 56 (22.2%) and 70 (27.8%) patients had increased renal echogenicity on the right and left kidneys, respectively. $P = 0.000$, as shown in Table 5.

There was a significant difference in organ sizes among SCD patients compared with the controls ($P < 0.05$) as shown in Table 6.

DISCUSSION

SCD is a genetic disorder in which there is an alteration in the normal globin chain that results in the production of abnormal hemoglobin chains within the RBC, which causes sickling of the cell, leading to vascular occlusion and ischemia in multiple organs.^[8] These cause different changes in the organs which may vary with race and ethnicity, some of which may have long-term complications to abdominal organs, such as the liver, kidneys, spleen, and the gallbladder and others.^[12] Ultrasound is a simple, affordable, and easily accessible imaging modality that plays an important role in early detection of these changes for further management and follow-up of SCD patients. Participants in this study with age range of 10–16

Table 1: Demographic characteristics of the participants

Variable	Participants group		Total	P
	Control	Sickle cell		
Gender				
Female	51 (42.1%)	70 (57.9%)	121 (48.0%)	
Male	75 (57.3%)	56 (42.7%)	131 (52.0%)	0.017
Age group (years)				
<10	7 (41.2%)	10 (58.8%)	17 (6.7%)	
10-16	38 (43.2%)	50 (56.8%)	88 (34.9%)	0.434
17-23	48 (55.8%)	38 (44.2%)	86 (34.1%)	
24-30	29 (54.7%)	24 (45.3%)	53 (21.0%)	
>30	4 (50.0%)	4 (50.0%)	8 (3.2%)	
BMI group (kg/m ²)				
Underweight (<18.5)	33 (35.9%)	59 (64.1%)	92 (36.5%)	
Normal (18.5-24.9)	71 (54.6%)	59 (45.4%)	130 (51.6%)	0.002
Overweight (25.0-29.9)	21 (85.0%)	3 (15.0%)	24 (9.5%)	
Obese (>30.0)	6 (100.0%)	0 (0.00%)	6 (2.4%)	

BMI=Body mass index (kg/m²) (National Obesity Observatory, 2009)^[19]

Table 2: Sonographic findings in the Liver of Participants

Variable	Participant group		Total	P
	Control	Sickle cell		
Liver span category				
Normal	109 (79.6%)	28 (20.4%)	137 (54.4%)	0.000
Upper limit normal	0 (0.0%)	45 (100.0%)	45 (17.9%)	
Hepatomegaly	17 (24.3%)	53 (75.7%)	70 (27.8%)	
Echogenicity of liver				
Increased	3 (5.7%)	50 (94.3%)	53 (21.0%)	
Coarse	2 (5.0%)	38 (95.0%)	40 (15.9%)	0.000
Decreased	0 (0.0%)	2 (100.0%)	2 (0.8%)	
Normal	121 (77.1%)	36 (22.9%)	157 (62.3%)	

Table 3: Sonographic findings in the Gall bladder of Participants

Variable	Participant group		Total	P
	Control	Sickle cell		
Gallbladder content				
Gall stones	0 (0.0%)	45 (100.0%)	45 (17.9%)	
Sludge	3 (5.6%)	51 (94.4%)	54 (21.4%)	
Empty	123 (80.4%)	30 (19.6%)	153 (60.7%)	0.000
Total	126 (50%)	126 (50%)	252 (100%)	
Gallbladder Wall Thickness				
Normal	123 (48.8%)	42 (16.7%)	165 (65.5%)	
Thickened gallbladder wall	3 (1.2%)	84 (33.3%)	87 (34.5%)	0.000
Total	126 (50%)	126 (50%)	252 (100%)	

Table 4: Sonographic findings in the spleen of participants

Variable	Participant group		Total	P
	Control	Sickle cell		
Spleen				
Auto splenectomy	0 (0.0%)	45 (100.0%)	45 (17.9%)	
Normal	126 (90.2%)	18 (9.8%)	144 (57.2%)	0.000
Splenomegaly	0 (0.0%)	63 (100.0%)	63 (24.9%)	
Echogenicity of spleen				
Increased	3 (16.7%)	15 (83.3%)	18 (8.7%)	
Coarse	0 (0.0%)	30 (100.0%)	30 (14.5%)	0.000
Calcified Spleen	0 (0.0%)	18 (100.0%)	18 (8.7%)	
Normal	123 (87.2%)	18 (12.8%)	141 (68.1%)	

years and 17–23 years had the highest preponderance of SCD complications. These findings are comparable to previous studies,^[1,9,12] who had similar findings among SCD patients within these age groups. These findings support the early onset of the disease in teenage age.

Hepatomegaly was the most predominant findings in the liver of SCD patients in this study. Previous researchers^[1,9,12] had reported similar findings. The liver is generally affected by a number of complications due to the SCD and its treatment, in addition to the vascular complications from the sickling process, multiple transfusions often place SCD patients at the risk of viral infections such as hepatitis B and C, iron overload, and combined with the effects of chronic hemolysis, all of which may contribute to the development of liver disease. Infiltrative and granulomatous diseases, infections, malignancy, and other hematologic diseases may also cause hepatomegaly.^[9,12]

Increased echogenicity of the liver was found in 53 (21%) of SCD patients. These findings are similar to findings from previous studies.^[8,12] These differences may be due to the

socioeconomic status of the patient, lifestyle, and diet as these may also affect the echogenicity of the liver. Several features of liver histology in patients with SCD may contribute to brightening liver echo like hemosiderin pigment, periportal fibrosis, and distention of the sinusoid with sickle cell.^[12]

Gallstones were found in 45 (17.9%) of SCD patients in this study. Previous studies^[12-14] had similar findings and reported a progressive age-related increase in the prevalence of gallstones, however, higher prevalence was reported by Balci *et al.*,^[8] Gumiero *et al.*,^[14] and Billa *et al.*^[15] These variations may be attributable to the inclusion of different age groups, race, symptomatic patients, diet, access to and availability of diagnostic and therapeutic agents and other health services which may be inadequate in most developing countries like Nigeria.

Gallbladder sludge was found in 51 (94.4%) sickle cell disease patients in this study. Previous studies^[8,12] had reported similar findings. Most of the patients with biliary sludge may eventually develop gallstones, however not in all cases.^[16]

This study found thickened gallbladder wall in 84 (33.3%) SCD patients. These findings were higher than those reported by previous researchers.^[1,16] This may be due to the condition of the GB at the time of the scan, as normally filled GB will best demonstrate thickened GB wall.

This study found 18 (9.8%) SCD patients with normal spleen. It should be noted that sonographic normal findings on the spleen among the sickle cell patients do not rule out the presence of other complications such as intravascular sickling and other complications may not be sonographically visible at the time of scan, and the technique is also operator dependent.

Splenomegaly in this study was found in 63 (24.9%) of the patients with SCD. Several studies have reported splenomegaly as a common abdominal manifestation among SCD patients.^[2,3,8,12] Splenomegaly appears in the first year of life and should be suspected in children if the spleen is more than 1.25 times longer than the adjacent normal kidney,^[17,18] and this may persist into the third and fourth decades of life.^[12] A common splenic complication is the sequestration

Table 5: Sonographic findings in the right and left kidneys of participants

Variable	Participant group		Total	P
	Control	Sickle cell		
Right Kidney (RK) size				
Normal	125 (67.6%)	60 (32.4%)	185 (73.4%)	
Enlarged	1 (1.6%)	61 (98.4%)	62 (24.6%)	0.000
Shrunken	0 (0.0%)	5 (100.0%)	5 (2.0%)	
Echogenicity of RK				
Normal	126 (66.3%)	64 (33.7%)	190 (75.4%)	
Increased	0 (0.0%)	56 (100.0%)	56 (22.2%)	0.000
Decreased	0 (0.0%)	6 (100.0%)	6 (2.4%)	
Left Kidney (LK) size				
Normal	125 (67.9%)	59 (32.1%)	184 (73.0%)	
Enlarged	1 (1.6%)	63 (98.4%)	64 (25.4%)	0.000
Shrunken	0 (0.0%)	4 (100.0%)	4 (1.6%)	
Echogenicity of LK				
Normal	126 (69.2%)	56 (30.8%)	182 (72.2%)	0.000
Increased	0 (0.0%)	70 (100.0%)	70 (27.8%)	

Table 6: Difference in the mean response from the two participant groups

Variable	Participant group	n	Mean	Std. deviation	Std. error mean	Df	P
Liver span	Control group	126	0.2698	0.68601	0.06111	250	0.000**
	Sickle cell group	126	1.1984	0.77995	0.06948		
Gallbladder Wall thickness	Control group	126	1.0238	0.15306	0.01364	250	0.000**
	Sickle cell group	126	1.6667	0.47329	0.04216		
Spleen size	Control group	126	1.0000	0.00000	0.00000	250	0.007*
	Sickle cell group	126	0.8254	0.71643	0.06382		
Right Kidney (RK) size	Control group	126	1.0079	0.08909	0.00794	250	0.000**
	Sickle cell group	126	1.5635	0.57266	0.05102		
Left Kidney (LK) size	Control group	126	1.0079	0.08909	0.00794	250	0.000**
	Sickle cell group	126	1.5635	0.55851	0.04976		

*Indicates $P < 0.05$; ** $P < 0.005$

syndrome, which is believed to be the cause of splenomegaly in SCD patients. It consists of a rapid pooling of blood within the spleen; the blood pooling may be larger than expected for a child or adult with sickle cell anemia, resulting in intravascular volume depletion which may progress rapidly to cardiovascular collapse and death.^[9] Other diseases that may cause splenomegaly include infectious or granulomatous disease, malignancy, congestive conditions, and other hematologic diseases.^[17,19,20]

Autosplenectomy in this study was found in 45 (17.9%) of the SCD patients. None of our participants had undergone any surgery at the time of the scan. Previous studies^[2,3,8,17] have reported auto splenectomy as a common finding among SCD patients. These findings could be due to the tortuous vasculature of the spleen that favors sickling of RBCs and as a consequence, splenic infarctions are very common. Repeated multiple infarctions with time may progress to auto splenectomy.

The study found 15 (83.3%) SCD patients with increased echotexture of the spleen and 30 (14.5%) with coarse echotexture of the spleen, while 18 (8.7%) had calcification of the spleen which was either amorphous or punctuate. Similar findings were reported in previous studies.^[2,8,12,17] This could probably be due to the similar methodology used in the studies.

This study found 60 (32.4%) and 59 (32.1%) SCD patients with normal right and left kidneys. Mohanty *et al.*,^[12] had similar findings. It should be noted that sonographic normal findings of the kidneys among the SCD patients do not rule out the presence of other complications like intravascular sickling which may not be sonographically visible. However, it is also highly operator dependent.

Enlarged right and left kidneys were found in 61 (98.4%) and 63 (98.4%) SCD patients, respectively. Previous studies,^[9,10,12,19] had similar results. The etiology of renal enlargement in sickle cell patients is unknown.^[5] However, enlargement of sickle cell kidneys has been attributed to vascular dilatation, engorgement of vessels, glomerular hypertrophy, increased renal blood volume, and interstitial edema.^[6,19]

Shrunken kidneys have been reported by previous studies,^[9,12] among SCD patients, findings from this study are consistent with the findings from previous studies where a reduction in renal size in patients in their fifth decade of life have been reported.^[12] This could be attributed to sickle cell nephropathy, a chronic condition that may progress to end-stage renal disease as part of renal complications in SCD.

Increased renal echogenicity among SCD patients was 56 (22.2%) and 70 (27.8%) on the right and left kidneys, respectively. Diffuse increase in reflectivity on renal sonography in patients with the SCD has been reported in previous studies.^[6,11,12,19] The cause and significance of this entity are unknown; however, renal papillary necrosis, high concentrations of iron deposits within tubular epithelial cells, focal scarring and interstitial fibrosis in vasa recta

system, glomerular hypertrophy, and renal sclerosis have been suggested as factors that may cause increased renal echogenicity. Medullary hyperechogenicity has also been reported in many conditions, including hypercalciuria, medullary sponge kidney, hyperparathyroidism, and papillary necrosis.^[10,19]

In general, there was an increase in organ sizes among SCD patients compared to that of the controls ($P < 0.05$). These findings agree with the result from the previous studies,^[2,9] who found a significant difference between the organ sizes among the control group and that of the SCD patients ($P < 0.05$). These enlarged organs could also be due to decreased immunity among SCD patients making them susceptible to acute complications of the SCD resulting to enlargement of their organs. Sequestration syndrome has been reported as a reason for enlargement of the spleen. This result in rapid pooling of blood within the spleen, which becomes larger than normal for a child or adult with SCD.

Limitations of the study

Abdominal sonographic findings were not specific, as no biopsy or any other imaging modality was used to confirm sonographic findings.

This was a single center study and the sample size was not large enough; this was because most of our recruited patients did not turn up for the scheduled scan.

CONCLUSION

Assessment of abdominal organs such as the liver, gallbladder, spleen, and kidneys by ultrasound among SCD patients in this study has revealed a varied remarkable changes in these organ size, echotexture, intraluminal deposits and wall thickness among the studied patients. Abdominal sonography is an easy, affordable, readily available, accurate, and non-invasive diagnostic tool for early detection of organ changes for further management and follow-up of SCD patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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