Renal Complications of Sickle Cell Anemia in Zaria, Nigeria: An Ultrasonographic Assessment

Philip Oluleke Ibinaiye, Aliyu Ahmadu Babadoko[1], Rasheed Yusuf[2], Abdul-Aziz Hassan[1]

Departments of Radiology, [1]Hematology and Blood Transfusion, [2]Chemical Pathology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

Correspondence: Dr. Philip Oluleke Ibinaiye, Department of Radiology, ABU Teaching Hospital, Zaria, Nigeria. E-mail: olurad@yahoo.co.uk

ABSTRACT

Background: Vaso-occlusion in the kidney is a capillary phenomenon. Renal medullary hyperosmolalrity and low oxygen tension encourage the maximum formation of sickled red cells. In addition, the glomerular loops constitute an aggregating point for the sickled red cells with subsequent obstruction to the blood flow. These factors, together with the large volume of blood flowing through the kidneys make renal complications inevitable in sickle cell anemia (SCA). **Aim:** The purpose of this prospective study was to report the renal sonographic findings of a sample of patients with hemoglobin electrophoretic pattern consistent with sickle cell anemia **Materials and Methods:** A cross-sectional prospective study of 74 patients with the diagnosis of SCA, as documented by electrophoresis and who attended the adult sickle cell clinic, Hematology Department of the Ahmadu Bello University Teaching Hospital, Zaria, Nigeria and 20 age-matched controls with a normal hemoglobin (HbAA) phenotype and with no history of renal disease, was carried out between April and December, 2010. None of the patients had any clinical evidence of acute sickle episode (crisis) at the time of ultrasonographic examination. B-mode ultrasonography with Aloka SSD-3500 was used to assess the kidneys. The hematological parameters were determined by multiparameter analyzer Sysmex XT 2000i, whereas creatinine and urea of the patients were also analyzed using the Selectra XL chemistry autoanalyzer. **Results:** Renal size of the study group was compared with that of the control group and it showed a significant increase in the adult patients with SCA (P<0.05). The mean right renal length in the study group and control group was 10.65±0.97 cm and 9.95±0.80 cm (P<0.001), respectively, whereas the mean left renal length in the study group and control group was 10.70±1.02 cm and 10.00±0.66 cm (P<0.001), respectively. Statistical relationships between renal length and some hematological indices (packed cell volume (PCV), red blood cell count, and reticulocyte count) showed no correlation but renal length was positively correlated with reticulocyte count, especially high reticulocyte count. Other findings documented and discussed include echogenicity of renal parenchyma, hydronephrosis, and papillary necrosis. **Conclusion:** Renal ultrasound imaging of patients with SCA showed a high incidence of renal abnormalities.

Key words: Renal complications; sickle cell anemia; ultrasonographic assessment

Introduction

Since the earliest clinical and pathological descriptions of sickle cell disease by Herrick[1] and Sydenstricker *et al.*[2] in 1910 and 1923, respectively, renal complications have been noted.

Sickle cell disease is a group of genetic disorders caused by an alteration in the molecular structure of hemoglobin.[3]

Access this article online	
Quick Response Code:	Website: www.wajradiology.org
	DOI: 10.4103/1115-1474.117906

More especially, this disease involves the possession of two abnormal allelomorphic genes related to the formation of hemoglobin, at least one of which is the sickle cell gene.[3] Sickle cell disease includes sickle cell anemia (SCA), sickle cell hemoglobin-C disease (HbSC), sickle cell thalassemia (HbS/βthal), and sickle cell O-Arab disease (HbS/O-Arab). SCA is the condition resulting from the inheritance of two sickle genes (HbSS) and it is the most severe of these disorders.[3]

Repeated vaso-occlusion accounts for the majority of the clinical manifestations of the disease.[4,5] The most common renal complications include renal enlargement, a diffuse increase in reflectivity throughout the kidney, and widespread confluent or focal increase in reflectivity confined to the renal medulla.[5,6] The purpose of this prospective study was to report the renal sonographic findings of a sample of patients with hemoglobin electrophoretic pattern consistent with SCA.

Materials and Methods

A cross-sectional prospective study of 74 patients with the diagnosis of SCA, as documented by electrophoresis and who attended the adult sickle cell clinic, Hematology Department of the Ahmadu Bello University Teaching Hospital, Zaria, Nigeria and 20 age-matched controls with a normal hemoglobin (HbAA) genotype and with no history of renal disease, was carried out between April and December, 2010. Their age ranged from 10 to 52 years (mean age: 23.2±5.3 years). None of the patients had any clinical evidence of acute sickle cell episode (crisis) at the time of ultrasonographic examination.

Approval for the study was granted by the ethical committee of the Ahmadu Bello University Teaching Hospital, Zaria. All the participants provided informed written consent.

B-mode ultrasonography with Aloka SSD-3500 ultrasound diagnostic equipment with a variable frequency probe at 2-5 MHz was used to assess the kidneys. The examination was performed with the patient in the supine, right, and left oblique positions to obtain an optimal view of the kidneys. Measurement of the kidneys was performed in all patients by obtaining the length, transverse diameter, anterior-posterior (AP) diameter, and parenchymal thickness in centimeters. The measurements obtained from the study group were compared with those obtained from the control group and also with the hematological parameters. The parenchyma of the kidneys was evaluated by two radiologists, and the ultrasonographic appearance of the organ was described by consensus. An increase in reflectivity throughout the kidney and poor cortico-medullary differentiation were defined as diffusely increased renal echogenicity. A high reflective renal medulla with a normal renal cortex was defined as medullary hyperechogenicity. 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 hematological parameters were determined by the multiparameter analyzer Sysmex XT 2000i, whereas the creatinine, electrolytes, and urea of patients were also analyzed using Seletra XL chemistry autoanalyzer.

Statistical analysis

The data was analyzed using SPSS software version 17 (SPSS Inc., Chicago) for statistical analysis. Renal length was expressed as mean±standard deviation (SD). We report Pearson correlation coefficient for investigating the relation between renal length in the two groups and renal length with hematological parameters by using *t*–test; $P<0.05$ was considered as a statistically significant value. Other ultrasound renal abnormality findings were expressed as percentages of SCA patients.

Results

The mean age of all subjects was 23.2±5.3 years (range: 10-52 years), consisting of 43 males and 51 females.

Renal size in the study group was compared with that of the control group and was found to show a significant increase [Table 1]. The mean right renal length in the study group and control group was 10.65±0.97 cm and 9.95±0.80 cm ($P<0.001$), respectively, whereas the mean left renal length in the study group and control group was 10.70±1.02 cm and 10.00±0.66 cm ($P<0.001$), respectively. The mean right renal AP diameter in the study group and control group was 4.45±0.54 cm and 4.01±0.30 cm ($P<0.001$), respectively, whereas the mean left renal AP diameter in the study group and control group was 4.65±0.47 cm and 4.17±0.47 cm ($P<0.001$), respectively. The mean right renal transverse diameter in the study group and control group was 7.11±0.73 cm and 6.00±0.49 cm ($P<0.001$), respectively, whereas the mean left renal transverse diameter in the study group and control group was 7.17±0.76 cm and 6.07±0.51 cm ($P<0.001$) respectively. The mean right renal parenchymal thickness in study group and control group was 1.90±0.26 cm and 1.50±0.12 cm ($P<0.001$), respectively, whereas the mean left renal parenchymal thickness in the study group and control group was 1.95±0.19 cm and 1.55±0.14 cm ($P<0.001$), respectively. However, all the three patients above 50 years had reduced renal size when compared with four patients of the control group who were also above 50 years.

Statistical relationships between renal length and some hematological indices (PCV, red blood cell count, and reticulocyte count) showed no correlation but renal length was

Table 1: Assessment of kidney size in patients and controls

Study parameter	Study group *n*=74				Control group *n*=20				Level of significance	
	Right kidney		Left kidney		Right kidney		Left kidney			
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Right	Left
Length (cm)	8.5-13.4	10.65±0.97	8.3-14.2	10.70±1.02	8.6-11.3	9.95±0.80	8.8.8-11.4	10.00±0.66	<0.000111	<0.0001
Anterior posterior diameter (cm)	3.4-5.7	4.50±0.54	3.2-5.7	4.65±0.47	3.6-4.6	4.01±0.30	3.5-5.6	4.17±0.47	<0.0001	<0.0001
Transverse diameter (cm)	5.7-8.8	7.11±0.73	4.8-8.6	7.17±0.76	5.0-6.9	6.00±0.49	5.2-7.0	6.07±0.51	<0.0001	<0.0001
Parenchymal thickness (cm)	1.2-2.7	1.90±0.26	1.5-2.5	1.95±0.19	1.3-1.7	1.50±0.12	1.3-1.9	1.55±0.14	<0.0001	<0.0001

positively correlated with reticulocyte count, especially high reticulocyte count ($P<0.0001$). The mean values of creatinine were 82.67 μmol/L and 76 μmol/L in the study and control groups, respectively, and the mean difference between the two groups was statistically significant with a P value of 0.016. However, there was no evident correlation between the renal length and biochemical indices like urea and creatinine (r values of 0.14 and 0.03; P values of 0.23 and 0.81, respectively).

Medullary and diffuse renal hyperechogenicity was observed in 14 (18.9%) and 7 (9.5%) patients, respectively [Figure 1]. Ultrasound findings consistent with renal papillary necrosis, viz a viz multiple round or triangular cystic spaces communicating with the collecting system in the medullary region without dilated renal pelvis was observed in one patient [Figure 2]; the intravenous urogram [Figure 3] confirmed papillary necrosis in this patient. A left hydronephrosis was noted in one patient.

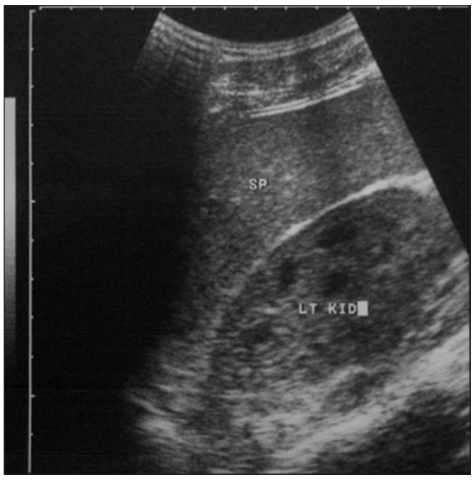

Figure 1: Ultrasound image of the kidney shows diffuse increase in renal echotexture similar to that of the adjacent liver, in a 38-year-old female patient with sickle cell anemia

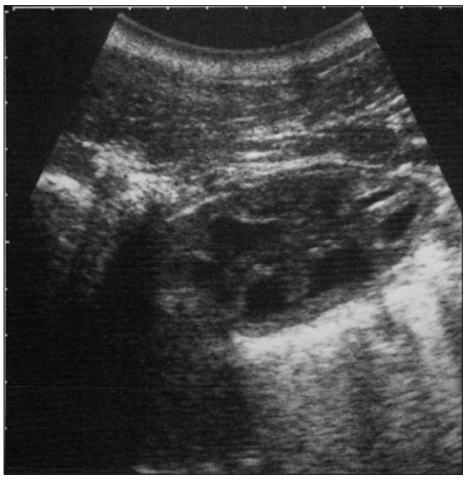

Figure 2: Ultrasound image of the kidney shows triangular fluid-filled cavities within renal papillae that communicate with collecting system in an 18-year-old male patient with sickle cell anemia; renal pelvis is not dilated

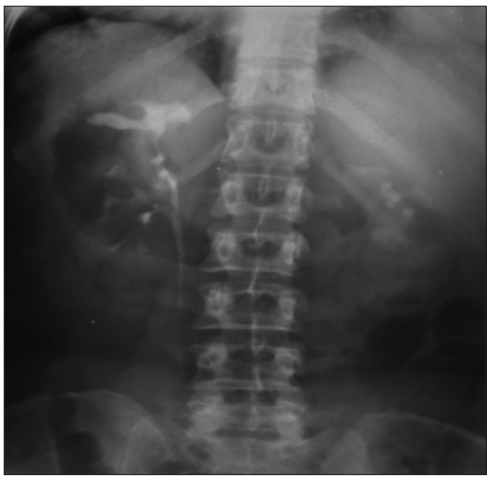

Figure 3: Urogram of the patient described in Figure 2 showing corresponding changes in the upper pole calyces compatible with papillary necrosis

Discussion

An ultrasound scan is a simple, rapid, noninvasive, and nonionizing tool for assessing the renal manifestations of SCA. Chronic sickling underlies several mechanisms for kidney injury. The arterial side of the renal microvasculature has a low oxygen tension. The hypertonicity and low PH of the renal medulla promote the formation of hemoglobin polymers in the red cells with deformation of the sickled cells, resulting in an increase in the blood viscosity, functional venous engorgement, and interstitial edema, predisposing the renal microcirculation to ischemia and infarction.[7] Obliteration of the medullary vasculature produces segmental scarring and interstitial fibrosis (structural papillectomy), resulting in the formation of dilated renal pelvic capillaries and veins. Hematuria may result from rupture of the vessels from early venous engorgement or from dilated vessels that result from scarring. The development of collateral vessels and their abnormal orientation in the medulla interferes with the countercurrent exchange mechanism, culminating through the years in irreversible loss of medullary tonicity.[7] Renal cortical blood flow and glomerular filtration rate (GFR) are increased perhaps by the secretion of medullary vasodilator prostaglandins.[7]

The results in Table 1 suggest that renal size is increased in patients with SCA. This is particularly seen in the left kidney. Results of the statistical analysis suggest that the differences in renal size between the control group and the sickle cell patients were significant. This finding is in agreement with previous studies.[8-11] However, unlike the previous studies that used only the renal length as an index for renal size, the present study considered all the indices of renal size (length, AP diameter, transverse diameter, and renal parenchymal thickness) in both the case and control groups. Enlargement of sickle cell kidneys has been attributed to vascular dilatation, engorgement of vessels, glomerular hypertrophy, increased blood volume, and interstitial edema.[7] The apparent greater enlargement of the

left kidney could be explained by the fact that the longer left renal vein, joined by other veins, causes more venous stasis and consequently sickling.[12] The reduction in renal size in all the patients above 50 years could be attributed to sickle cell nephropathy, a chronic condition that may progress to end-stage renal disease as part of renal complications in SCA.

The poor correlation of renal size with PCV, red blood cell count, urea, and creatinine were in agreement with an earlier study carried out by Walker *et al*.[9] However, there was positive correlation between the renal size and reticulocyte count. Further analysis suggested that the stronger relationship was between renal length and high reticulocyte count. This is due to a high erythropoietic drive which is seen commonly in SCA as a result of chronic anemia. The increase in the value of creatinine in our study group may be due to the high incidence of sickle cell nephropathy.

SCA is associated with many structural and functional complications of the kidney,[13] which may progress to chronic renal failure and end-stage renal disease.[11] Several studies have reported medullary or diffuse increase in reflectivity on renal ultrasonography in patients with SCA.[9,14,15] The cause and significance of this entity is unknown; however, renal papillary necrosis, high concentrations of iron deposits within tubular epithelial cells, focal scaring and interstitial fibrosis in the vasa recta system, glomerular hypertrophy, and renal sclerosis have been suggested as factors that may cause increased renal echogenicity.[9,14,15] Walker *et al*.[9] reported increased medullary echogenicity in 5 of 179 patients with SCA (2.8%) and 17 of 25 patients with S/βthal (68%). In the same study, diffusely increased renal echogenicity was reported in 15 of 179 patients with S/S (8.4%), and none of the 25 patients with S/βthal. In another report,[15] increased renal echogenicity was observed in 26 of 189 patients with sickle cell disease (13.8%). In our study, medullary hyperechogenicity was observed in 14 of 74 patients (18.9%), and the prevalence of diffusely increased renal echogenicity was 9.5%. Medullary hyperechogenicity has been reported in many conditions including hypercalciuria, medullary sponge kidney, hyperparathyroidism, and papillary necrosis.[16] A simple renal cyst was observed in two patients. The left hydronephrosis noted in one patient was due to distal ureteric obstruction from calculus. One patient had typical ultrasonographic findings of renal papillary necrosis, multiple round or triangular cystic spaces communicating with the collecting system in the medullary region without dilated renal pelvis.[17] The intravenous urogram of this patient showed corresponding changes in the upper pole calyces compatible with papillary necrosis.

Conclusion

Renal ultrasound imaging of patients with SCA showed a high incidence of renal complications. Repeated vascular occlusion, chronic hemolysis, anemia, and iron overload contribute to the pathogenesis of multiple renal complications of SCA. However, inadequate clinical care due to lack of good health education, ignorance, poverty, and poor standard of care as well as lack of therapeutic agents may be contributory factors in a developing country like Nigeria.

Acknowledgments

The authors appreciate the contributions of the resident doctors and nursing staff of the Radiology, Hematology and Blood Transfusion, and Chemical Pathology departments of the Ahmadu Bello University Teaching Hospital, Zaria, Nigeria in conducting this study. No grant or sponsorship was received toward the conduct of this study.

References

1. Herrick JB. Peculiar elongated and sickle-shape red blood corpuscles in a case of severe anemia. Arch Int Med 1910;6:517.
2. Sydenstricker VP, Mulherin WA, Houseal RW. Sickle cell anemia, report of 2 cases in children with necropsy in one case. Am J Dis Child 1923;26:132.
3. Konotey-Ahula FI. The sickle cell diseases. Arch Intern Med 1974;133:611.
4. Lonergan GJ, Cline DB, Abbondanzo SI. From the Archives of the AFIP: Sickle cell anemia. Radiographics 2001;21:971-4.
5. Fixer J, Styles L. Sickle cell disease. Pediatr Clin North Am 2002;49:1193-210.
6. Papadaki MG, Kattamis AC, Paapadaki IG. Abdominal ultrasonographic findings in patients with sickle cell anemia and thalassemia intermedia. Pediatr Radiol 2003;33:515-21.
7. Van-Eps LW, de Jong. Sickle cell disease. In: Diseases of the kidney, Schrier RW, Gottschalk CW, editors. Boston: Little, Brown and Co.; 1997. p. 561-90.
8. Karen L, Gardiner RT. The Renal Sonographic Appearance of Sickle Cell Disease. Med J of Ultra. 1987;3:14-9.
9. Walker TM, Beardsall K, Thomas PW, Serjeant GR. Renal length in sickle cell disease: Observations from a cohort study. Clin Nephrol 1996;46:384-8.
10. Balci A, Karazincir S, Sangün O, Gali E, Daplan T, Cingiz C, *et al*. Prevalence of abdominal ultrasonographic abnormalities in patients with sickle cell disease. Diagn Interv Radiol 2008;14:133-7.
11. Mapp E, Karasick S, Pollack H, Wechsler RJ, Karasick D. Uroradiological manifestations of S-hemoglobinopathy. Semin Roentgenol 1987;22:186-94.
12. Goodman MS, Jacobs JA. Sickle cell Hematuria controlled by intrarenal oxychlorosene irrigation. J Urol 1983;130:326-7.
13. Ataga KI, Orringer EP. Renal abnormalities in sickle cell disease. Am J Hematol 2000;63:205-11.
14. Zinn D, Haller JO, Cohen HL. Focal and diffuse increased echogenicity in the renal parenchyma in patient with sickle hemoglobinopathies: An observation. J Ultra Med 1993;12:211-4.
15. Namjoshi SP. Punctate echogenic foci in spleen and increased echogenicity in renal cortex in sickle cell anemia. J Clin Ultrasound 1999;27:52.
16. Shultz PK, Strife JL, Strife CF, McDaniel JD. Hyperechoic renal medullary pyramids in infants and children. Radiology 1991;181:163-7.
17. Hoffman JC, Schnur MJ, Koenigsberg M. Demonstration of renal papillary necrosis by sonography. Radiology 1982;145:785-7.

How to cite this article: Ibinaiye PO, Babadoko AA, Yusuf R, Hassan A. Renal complications of sickle cell anemia in Zaria, Nigeria: An ultrasonographic assessment. West Afr J Radiol 2013;20:19-22.

Source of Support: Nil, **Conflict of Interest:** None declared.