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**RENAL ULTRASONOGRAPHIC PATTERNS IN PATIENTS WITH SICKLE CELL
DISEASE**

RENAL ULTRASONOGRAPHIC PATTERNS IN PATIENTS WITH SICKLE CELL DISEASE

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ABSTRACT

Introduction: This study evaluates the pattern of renal ultrasonographic abnormalities in patients with sickle cell disease.

Methods: This was a prospective study where 100 stable (steady state) sickle cell patients aged between 15 and 60 years (mean \pm standard deviation: 24 ± 8.7 years), comprising of 62 females and 38 males had renal ultrasound to assess the renal sizes (volume), blood flow velocity (resistive index) and pattern of renal echogenicity.

Results: The renal size and resistive index were higher in the study group as compared to controls with statistical significance. 33 kidneys (16.5%) had increased length, 111 kidneys (55.5%) had increased resistive index and 4 kidneys (2%) had abnormal echogenicity, with 2 kidneys having diffuse increase in renal parenchymal echogenicity with partial loss of corticomedullary differentiation (Grade 2), whilst another 2 kidneys had increase renal medullary echogenicity. Other findings documented include simple renal cysts in 6 kidneys (3%).

Conclusion: Renal ultrasound imaging of patients with sickle cell disease showed an increase in renal size and resistive index as compared to controls, with other renal abnormalities such as increase parenchymal / medullary echogenicity and cysts.

Keywords: Sickle cell disease, Renal size and resistive index, Renal echogenicity, Ultrasound

INTRODUCTION

Sickle cell disease is a hemolytic anemia characterized by abnormally shaped (sickled) red blood cells (RBCs) which are removed from circulation and destroyed at increased rates, leading to anaemia.¹ The sickled RBCs cause vascular occlusion, which leads to tissue ischemia and infarction. The underlying abnormality in the RBCs of sickle cell disease is the presence of abnormal sickle hemoglobin S which when deoxygenated, becomes relatively insoluble and forms aggregates with other hemoglobin molecules within the RBCs.¹ These aggregates develop into long chains, which distort the RBC into a sickled shape and impair flow through vessels. In addition, the deformed RBCs tend to adhere to endothelium, worsening vascular occlusion, ischemia and the likelihood of tissue infarction.¹ Vascular occlusion of small and large vessels can lead to chronic damage of multiple organs including brain, lung, kidney, bone, liver, spleen and retina.²

Being familiar with the radiological signs of expected complications of sickle cell disease in different systems, helps much to control advance of the disease and protect against early organ damage.³ Renal complications are a well-known cause of morbidity and mortality in sickle cell disease (SCD), and the

incidence of renal failure increases as patient survival improves.⁴ The onset of chronic kidney disease is insidious, and the multifactorial aetiology requires on-going vigilance and monitoring of patients to detect those that are most at risk of developing significant renal complications.^{5,6} Sickle cell nephropathy (SCN) is a debilitating complication of sickle cell disease which develops as a result of RBCs sickling in the renal circulation. This leads to ischemia causing infarction and renal papillary necrosis, as well as renal tubular injury. It may be associated with proteinuria, nephrotic syndrome, azotemia, hyperuricemia and renal failure.³ The clinical manifestations of renal involvement in sickle cell disease include urinary concentrating defects, incomplete urinary acidification, glomerular hyperfiltration, microalbuminuria / proteinuria, hematuria and renal failure.⁷ Glomerular hyperfiltration may play an important role in the pathogenesis of SCN and if treated, may prevent development of proteinuria and eventually renal failure. Hyperfiltration has been described in both children and adults with SCD. The glomerular filtration rate (GFR) usually increases as children get older and may eventually decrease in young adults. However hyperfiltration can persist into adulthood,⁷ and set in place the mechanism whereby the patient is predisposed to end stage renal disease.

Ultrasound is a good imaging modality for nephropathic changes as it shows cortical echogenicity accentuation, loss of corticomedullary differentiation, large renal size, shrunken renal size (late stage) and increased resistive index (RI) on Doppler examination.^{3,8}

The aim of this study is therefore to evaluate the pattern of renal ultrasonographic abnormalities seen in patients with sickle cell disease with the purpose of identifying, managing and ultimately averting renal failure in individuals at risk.

METHODS

Research design

This was a comparative descriptive cross-sectional study of sickle cell patients with controls. One hundred adult sickle cell patients of age range 15 - 60 years were selected at random from the sickle cell unit of the Hematology clinic of the Lagos State University Teaching Hospital, between May 2016 and July 2017. A hundred apparently healthy age and sex matched controls were selected at random for comparisons, however they were not screened for haemoglobinopathies and other renal conditions, as haemoglobin electrophoresis and renal function tests were not done to validate their health status. Renal ultrasound was then performed on each patient using B-mode and Doppler imaging.

Ethical Approval

Ethical approval to carry out the study was obtained from the research and ethics committee of the Lagos State University Teaching Hospital, Ikeja. A written informed consent was obtained from each participant, having filled a data form. Information required in the data form include: age, sex, marital status, occupation, ethnicity history of diabetes/hypertension, weight and height. Confidentiality was maintained by allotment of numbers as codes

Inclusion Criteria

Patients with urinalysis evidence of either protein or hemoglobin in urine detected via urinalysis by dipstick method.

Exclusion Criteria

Patients with hypertension, recent hemolytic crisis, patients less than 15years and greater than 60 years, non- consenting patients were excluded from the study. Patients with recent hemolytic crises were excluded from the study because of ongoing exacerbation of renal complications, as this will invalidate the hypothesis that the study sought out to ascertain, being that persons living with SCD even in their usual state of health are constantly at risk of renal affectation.

Ultrasonographic Technique⁹

Ultrasound of the kidneys was carried out using a GE Ultrasound machine (Logiq C5 premium) with color and pulsed wave Doppler facilities, and a multi-frequency probe at 3.5-5MHz. The examination was performed with the patient in the supine, left and right oblique positions to obtain an optimal view of the kidneys for B-mode evaluation, with left and right lateral decubitus positions and 30 degrees cranial elevation for Doppler assessment of the renal vessels after adjusting for image optimization. Kidneys were defined as having diffusely increased echogenicity if the renal cortex was more echogenic than adjacent liver or spleen, whilst medullary echogenicity was described as increase in the reflectivity of the renal medulla. Measurements of the renal sizes were obtained in the longitudinal, antero-posterior and transverse dimensions in centimeters (cm), with renal volume in milliliters (mls) – (Length x Anteroposterior x Width x 0.523). The main renal vessels were identified using color Doppler and flow velocity was assessed with Spectral pulsed wave to obtain the peak systolic and end diastolic velocities for estimation of the resistive index. The sample volume (SV) was taken from the mid portion of the renal artery, exclusive of the renal hilum and ostium. A total of three readings were recorded and averaged to obtain the final value used for statistical computation.

The kidneys were also assessed for calculi, cysts and other parenchymal abnormalities.

Data analysis

The data collected was entered into a Statistical Package for Social Sciences Software (SPSS) version 20.0 Chicago Illinois, USA, and the results were documented using tables, graphs and charts. Association between variables was explored using Independent Samples t-test and Bivariate Correlations for comparison at 95% confidence interval and associations were considered significant if p value were < 0.05. Fischer's exact test was used to determine the significance level between proportions. Renal measurements were expressed as mean+/- standard deviation (SD). Pearson correlation

coefficient was reported for investigating the relation between renal size and resistive index. Other renal abnormalities were expressed as percentages of SCD patients.

Outcome Measures

These are renal size, renal resistive index and renal parenchymal echogenicity.

RESULTS

The study subjects comprised of 100 patients with SCD, 98 with genotype HbSS and 2 with genotype HbSC as documented by electrophoresis, while the control group was made up of 100 healthy patients without any clinical evidence of renal disease. Out of the 100 subjects evaluated, 62.0% were females whilst 38.0% were males. The controls comprised of 65.0% females and 35.0% males. The mean age of the subjects was 24.4 ± 8.7 years while that of the controls was 26.4 ± 8.4 years (range was 15 – 60 years). Females in the 21 – 35 age group category were most affected (Table 1), whilst the educational level of participants ranged from primary to post-tertiary, with 106 (53.0%) of all participants having attained secondary education. Renal size and resistive index in the study subjects was compared with that of the controls and found to show increase with statistical significance (Table 2). Relationship between the indices of renal size and renal vascular resistance (resistive index) shows a weak positive correlation with the right renal length, width and volume; $r = 0.15, 0.098$ and 0.05 respectively, whilst the left renal width and volume was $r = 0.138$ and 0.11 respectively (Table 3). Correlation between the right renal length and renal vascular resistance is shown in a scatterplot distribution (Figure 1).

Renal length was increased in 33 kidneys, with 20 left kidneys (10%) and 13 right kidneys (6.5%). The resistive index was increased in 64 right kidneys (32%) and 47 left kidneys (23.5%) giving a total of 111 kidneys with elevated resistive index (Figure 2a), whilst 89 kidneys had normal resistive index (Figure 2b).

Table 1: Socio - demographic characteristic of subjects

Variable	Category	Case(100)	Control(100)	Total
Age (Years)	≤ 20	42	38	80
	21 -35	48	47	95
	>35	10	15	25
Gender	Male	38	35	76
	Female	62	65	127
Educational Level	Primary	4	2	6
	Secondary	54	52	106
	Tertiary	31	35	66
	Post-tertiary	11	11	22

Table 2: Mean comparison of right and left renal parameters in cases and controls

Renal Parameters	Right kidney		P - value	Left kidney		P - value
	Case(100)	Control(100)		Case(100)	Control(100)	
Lenght	10.76±1.03	9.87±0.70	0.001	11.10±0.95	10.49±0.73	0.001
Anteroposterior	4.09±0.94	3.85±0.56	0.003	5.56±0.54	4.91±0.76	0.001
Width	5.80±0.80	4.99±0.93	0.001	5.41±0.83	4.96±0.78	0.001
Volume	139.83±4.68	100.53±25.91	0.001	177.10±53.35	131.79±45.84	0.001
Resistive index	0.72±0.07	0.60±0.06	0.001	0.71±0.48	0.60±0.07	0.001

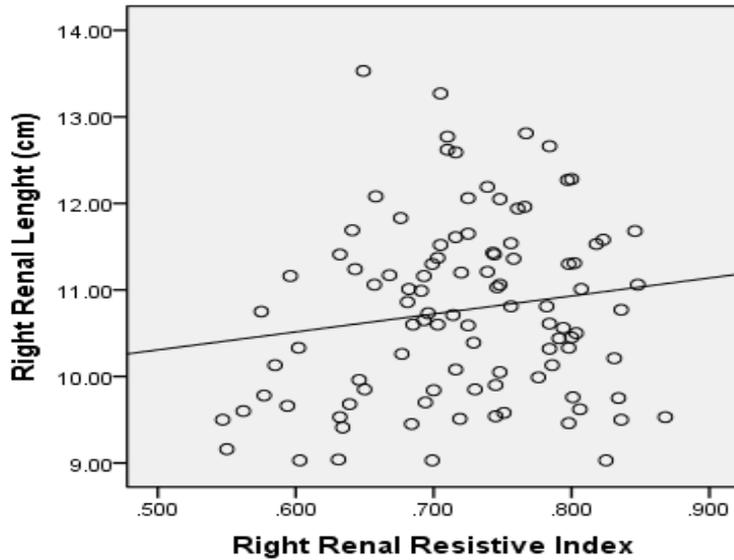
Table 3: Correlation of renal vascular resistance (resistive index) against indices of renal size among cases

Renal size indices	Right kidney		Left kidney	
	r	p- value	r	p- value
Lenght	0.15	0.136	0.03	0.782
Anteroposterior	-0.060	0.556	0.048	0.635
Width	0.098	0.331	0.138	0.192
Volume	0.05	0.595	0.11	0.292

r = Pearson correlation coefficient

Renal parenchymal echogenicity was increased in 4 (2%) kidneys, diffuse bilateral renal parenchymal hyperechogenicity (Figure 3) was observed in 1 patient, while bilateral increased renal medullary echogenicity was also seen in 1 patient (Figure 4). Renal

cortical cysts were observed in 6 kidneys (3%), with 4 unilateral (Figure 5) and 1 bilateral involvement.



$r = 0.15, p = 0.136$

Figure 1: Scatterplot with fitted line. (Trend line as edited by the Chart Editor in SPSS). Correlation of right renal resistive index (X-axis) and right renal length (Y-axis) in cases. It shows a random and fairly clustered arrangement. The trend line in the scatterplot is typical for a correlation with small strength ($r = 0.15$)

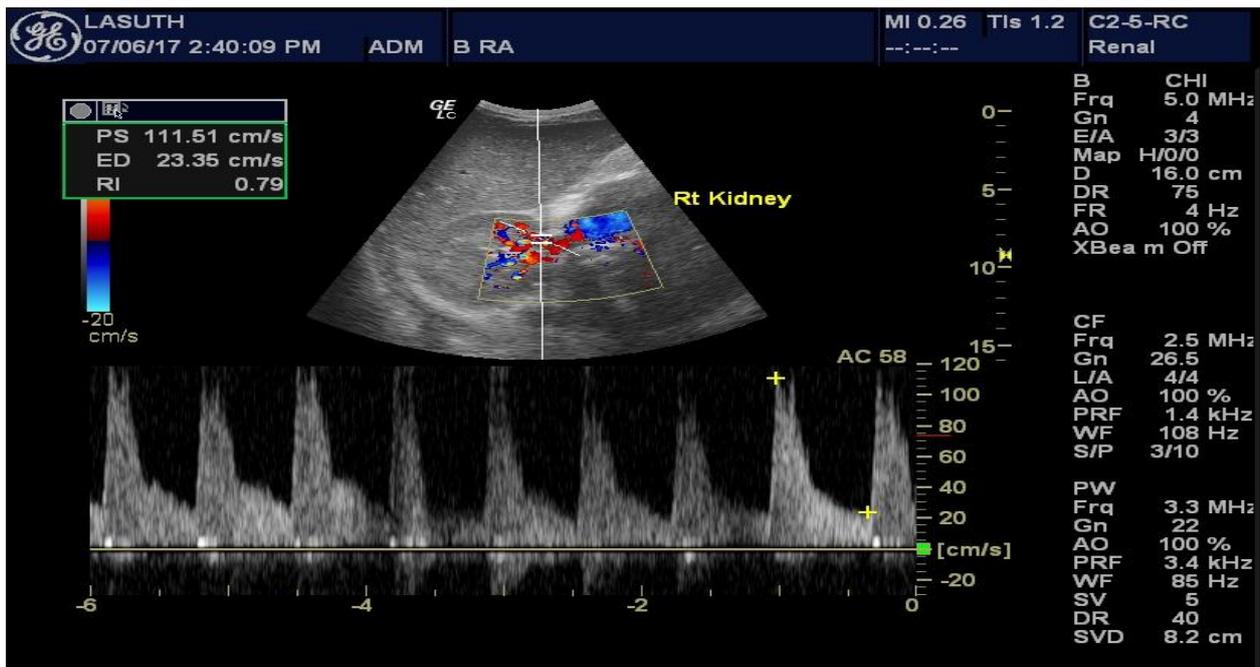


Figure 2a: Duplex ultrasound image with spectral doppler waveform of the right main renal artery showing measurement of the resistive index. The peak systolic velocity (PSV) is 111.51cm and the end diastolic velocity (EDV) is 23.35cm, with an elevated resistive index (RI) of 0.79.

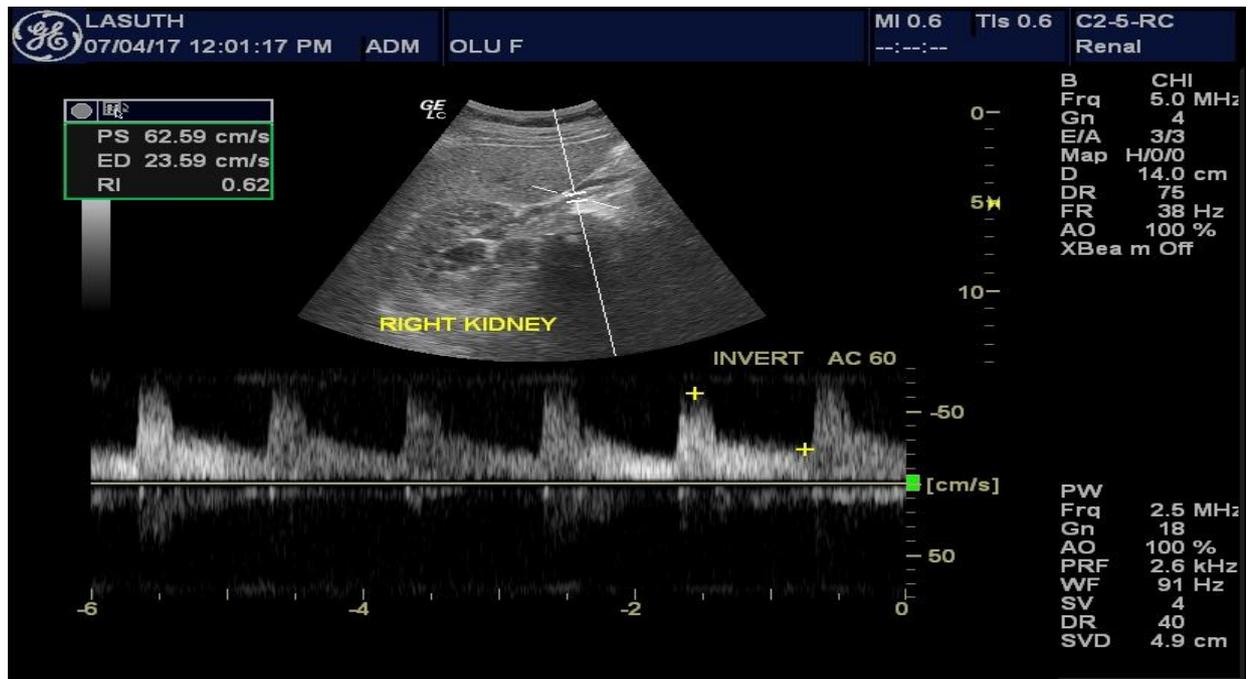


Figure 2b: Duplex ultrasound image with spectral doppler waveform of the right main renal artery showing measurement of the resistive index. The peak systolic velocity (PSV) is 62.59cm and the end diastolic velocity (EDV) is 23.35cm, with a normal resistive index (RI) of 0.62

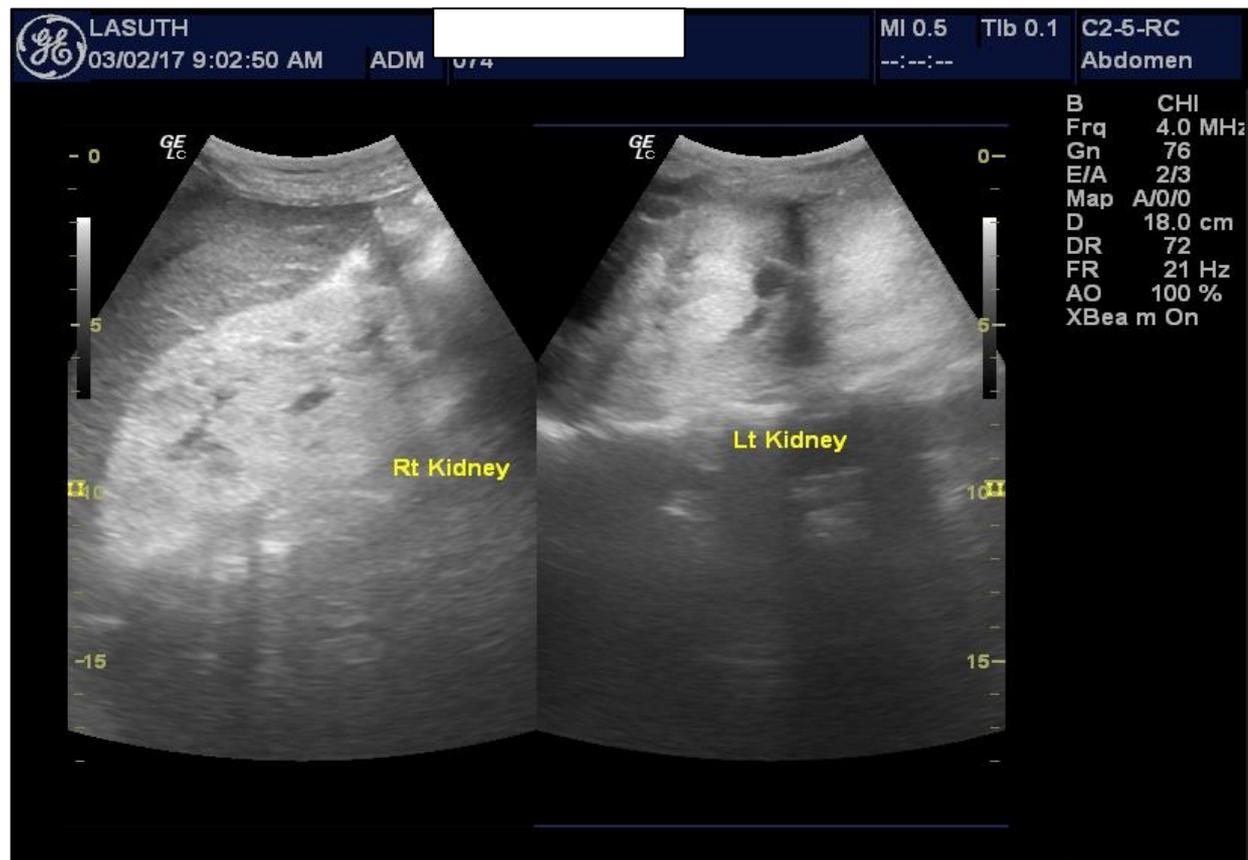


Figure 3: Renal ultrasound image (longitudinal view) of a 43-year-old male HbSS patient with bilateral diffuse increased renal parenchymal echogenicity (grade 3).



Figure 4: Renal ultrasound image (longitudinal view) showing bilateral increased renal medullary echogenicity in a 19 year old male HbSS patient. Note the sparing of the renal cortices (curved arrows)



Figure 5: Renal ultrasound image (longitudinal view) showing unilateral multiple renal cysts (arrows) in the right kidney of a 31-year-old male HbSS patient.

DISCUSSION

Ultrasound is a readily-available, generally affordable and non-invasive diagnostic imaging tool for assessing the renal complications of sickle cell anemia (SCA). Sickling of haemoglobin within the renal vasculature causes the vaso-occlusive events that characterize SCA. Repeated vaso-occlusive episodes in SCA leads to chronic microvascular disease with reduction in renal blood flow and consequent hypoxia within the renal medulla, with its characteristic low pH and hypertonicity. This stimulates the production of prostaglandins and prostacyclin (potent vasodilators) which promote an increase in renal blood flow resulting in a hyperdynamic state with hyperfiltration from increased glomerular filtration rate (GFR).^{5,10,11}

Persistently elevated GFR predisposes the glomerular epithelium to damage and increase permeability to plasma proteins, both of which contribute to focal segmental glomerulosclerosis (FSGS). It has been suggested that FSGS (a renal biopsy and histological diagnosis) is the major cause of renal failure in SCD.¹⁰ FSGS is divided into classic and collapsing varieties. The classic variety is described in SCD and begins with segmental tuft adhesions of the glomerular capillary to the surrounding parietal epithelium that progresses to segmental collapse of the glomerular capillary with eventual sclerosis that can subsequently involve the entire glomerulus.¹⁰ Studies have shown that renal failure occurs in about 4% to 18% of SCD patients.^{1,5,10-13} Features of SCD that may likely contribute synergistically to the development of renal failure include increase oxidative state (increase production of reactive oxygen species), hyperfiltration (increase GFR) and proteinuria (high levels of filtered plasma proteins). However, it has been suggested that genetically determined activity of non-SCD genes acts with these factors to determine the risk of renal failure in an individual with SCD. These non-SCD factors include fetal haemoglobin level, production of immature RBCs, adhesion molecule expression and activity of RBC cation transporters.¹⁰

Renal ultrasound findings in this study include enlarged renal size, increase resistive index, weak positive correlation between renal size and resistive index, as well as parenchymal abnormalities such as increase renal echogenicity and renal cysts. The results obtained in this study suggest that renal size is increased in patients with SCA as compared with controls. A total of 33 kidneys, 13 right and 20 left kidneys had increased renal volume when compared to 5 of controls. This difference in renal size between the subjects and controls was significant, a finding that is in agreement with those of McCarville et al,¹⁴ Agha,³ and Ibinaiye,¹⁵ who found an increase in mean renal size indices of SCD patients as compared to controls. The values of the mean renal parameters obtained in this study were similar to those of Ibinaiye and colleagues,⁴⁵ who reported mean right renal length of 10.65±0.97cm and 9.95±0.80cm in study and control groups (p<0.001) respectively, similar to those obtained in this study of 10.76±1.03cm and 9.87±0.70cm (p<0.001), respectively. Also, they obtained left renal length of 10.70±1.02cm and 10.00±0.66cm (p<0.001) for study and control groups respectively, similar to those obtained in this study of 11.00±0.95cm and 10.49±0.73cm (p<0.001) respectively. Similar values were obtained for the renal width and anteroposterior diameters.

Enlargement of renal size in SCD has been attributed to various causes amongst which are increased blood volume from anemia, engorgement of vessels, glomerular hypertrophy, vascular dilatation and interstitial edema.¹⁵ It may also indicate glomerular hyperfiltration, a process that begins in childhood.⁴ Renal parenchymal thickness as an index of renal size has also been shown to be increased in SCD kidneys as compared to controls, further suggesting that all the indices of renal size are increased in SCD.^{15,16}

Furthermore the increase in size is more evident in the left kidney, a finding that is also in agreement with Emamian and co-workers,¹⁷ who reported greater size of the left kidney as compared to the right in 665 normal healthy adult volunteers. This may be

explained by anatomical variation in the blood supply and location of both kidneys.¹⁷ The left renal artery is shorter and straighter than the right one, hence increased blood flow in the left artery may result in relatively increased volume. Another possible explanation is that because the spleen is smaller than the liver, the left kidney has more space for growth.¹⁷

The results of the renal resistive index (RI) suggest that the renal vascular tone is increased in patients with SCD. A total of 47% and 64% SCD patients had raised values of the left and right renal RI respectively as compared to controls with 4% and 3% for the left and right kidneys respectively. Although the mean RI of both kidneys in the study group was only slightly greater than 0.7, 18 and 46 patients had RI greater than 0.8 and 0.7 respectively, bringing to total of 64 (64%) patients with RI greater than 0.7. This is similar to the findings of Aikimbaev and co-workers who reported increased resistive index of more than 0.7 in 60% of their patients.^{16,18} The values of the mean RI of > 0.7 obtained in this study were also similar to those reported by El Sarraf and colleagues, who reported values greater than 0.7 in their study subjects.¹⁷ A total of 25 patients had RI greater than 0.84 ± 0.05 , while 29 patients had RI greater than 0.73 ± 0.06 . Increased renal vascular tone in SCD may be a sequel of the vasoocclusive events that characterize SCA, with factors in the renal medulla that promote sickle cell haemoglobin polymerization. Other mechanisms that have been described include vascular intimal hyperplasia, thrombosis, altered vascular reactivity and vasospasm. The mechanisms of vascular intimal hyperplasia and thrombosis are related to the abnormal adhesive and procoagulant properties of sickled RBC.^{18,19}

Previous studies done by McCarville et al.¹⁴ have shown strong positive correlations between renal size and biochemical parameters such as GFR, while El Sarraf et al.¹⁸ reported strong correlation between renal resistive index and a high "normal" creatinine level. Aikimbaev, Abolarinwa and Patre found strong correlations between the renal RI and other haematological and biochemical parameters such as reticulocyte

count, mean cell haemoglobin concentration (MCHC), serum creatinine and GFR in SCD patients.^{8,16,20} Correlations with biochemical markers and haemoglobin levels were not carried out as these were outside the scope of this study, which sought to ascertain renal ultrasound abnormalities in persons living with SCD, selected on the basis of protein in urine (qualitative analysis).

The results of statistical relationship in this study shows weak positive correlation of renal size with resistive index (RI) in SCD kidneys. The highest correlation of RI with renal size observed in this study was with the right renal length ($r = 0.15$; $p = 0.136$), followed closely by that of the left renal volume ($r = 0.11$; $p = 0.272$). This observation might suggest the lack of a strong relationship between these variables.

There may be variable and independent underlying mechanisms for the renal enlargement and increased renal vascular tone in SCD, as mentioned earlier. This further suggests that sonographic renal size (volume) enlargement may not predict increased renal vascular resistance (RI) as assessed by pulsed Doppler ultrasound in patients with SCA which this study sought to ascertain. Furthermore, this may imply that the sequence of events that resulted in an increase in renal blood flow and subsequent increase in renal size are predominantly independent of those within the renal vasculature that mediate an increase in renal vascular tone (RI). Clinical implications for patient management may involve building of fetal haemoglobin levels with hydroxyurea. This will reduce to minimum the occurrence of sickling events which may precipitate the onset of renal affection (increase in renal size and resistive index) in patients with hyperfiltration and proteinemia.¹⁰

This study however, sought to ascertain correlation between the renal RI and renal size, an area of research which had not been explored by previous researchers, with the expectation of utilizing both parameters in identifying and monitoring patients with SCN.

Renal parenchymal abnormalities were seen in seven patients in this study as additional sonographic findings. These include diffusely increased renal echogenicity (1 patient), increased medullary echogenicity (1 patient) and renal cysts (5 patients). These findings are also in keeping with documentation by McCarville et al,¹⁴ (diffuse increase in renal echogenicity (6 patients), increased medullary echogenicity (2 patients); Lonergan,¹ (diffuse increase in renal echogenicity (5 patients), increased medullary echogenicity (3 patients); Ibinaiye,¹⁵ (diffuse renal hyperechogeneity (7 patients), medullary echogenicity (14 patients), papillary necrosis (1 patient) ; Maaji,²¹ (medullary echogenicity (1 patient); Attalla,²² (hyperechoic lesion 3 patients), anechoic lesion (1 patient) as part of renal sonographic abnormalities in SCD.

The observation of increased renal echogenicity in 1 patient in this study is at variance with that of Lonergan,¹ McCarville,¹⁴ and Ibinaiye,¹⁵ who reported this abnormality in 5, 6, and 7 patients respectively. The reasons for this difference cannot really be explained, but might be attributed to age differences in the study populations.

The finding of increased medullary echogenicity in 1 patient in this study is in keeping with those of McCarville,¹⁴ Lonergan,¹ and Maaji,²¹ who also found this in 2, 3 and 1 patient respectively. It is however at variance with that of Ibinaiye,¹⁵ who reported this finding in 14 patients.

This may be attributed to the higher incidence of papillary necrosis as a notable cause of medullary echogenicity in that patient population who were slightly younger than those used in this study.²³ There were no recorded cases of renal papillary necrosis and renal artery stenosis in our study population.

One of the patients with bilateral diffuse renal echogenicity in this study who had developed end stage renal disease (ESRD), for which he had been having regular dialysis, passed on after 5 months of follow-up. He had normal sized kidneys, with increased RI (0.80), probably suggesting that changes in renal vascular tone and parenchymal abnormalities

might precede reduction in renal size. Renal parenchymal abnormalities may occur as a result of structural and functional alteration in progressive renal dysfunction.

A major limitation of this study is that it only evaluated SCD patients in their stable state, while excluding those with acute haemolytic crisis, hence precluding the observations and outcomes that might have been noted in this category of patients

CONCLUSION

Renal ultrasonographic evaluation of patients with sickle cell anaemia revealed a range of abnormalities, amongst which were an increase in both renal size and resistive index, as compared to age and sex matched controls. The weak correlation between renal size and resistive index may suggest independent underlying factors as seen in sickle cell nephropathy. Few renal parenchymal abnormalities (increased renal parenchymal echogenicity, increased medullary echogenicity and renal cysts) were also elicited.

RECOMMENDATION

Annual ultrasonographic evaluation of the kidneys should be included as part of the diagnostic workup for sickle cell patients, as this will enable early detection of renal abnormalities and complications. It could also help in the establishment of baseline values that can be used as reference for monitoring and follow up. In conjunction with the clinical correlates (biochemical and haematological) of SCD, timely and appropriate intervention can be instituted to avert renal failure and the need for renal replacement therapy.

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REFERENCES

1. Lonergan GJ, Cline DB, Abbondanzo SL. Sick cell Anemia 1. Radiographics. 2001; 21(4):971-994.
2. Voskaridou E, Christoulas D, Terpos E. Sick cell disease and the heart: review of the current literature. British journal of haematology. 2012; 157(6):664-673.
3. Agha M, Eid AF, Sallam M. Sick cell anemia: Imaging from head to toe. The Egyptian Journal of Radiology and Nuclear Medicine. 2013; 44(3):547-561.
4. Inah GB, Ekanem EE, Obiora CI, Ogbole GI. Systemic complications and imaging challenges of sick cell disease in sub-Saharan Africa. Journal of Radiation Medicine in the Tropics. 2021; 2(2):48-54.
5. Sharpe CC, Thein SL. Sick cell nephropathy—a practical approach. British journal of haematology. 2011; 155(3):287-297.
6. Solomon N, Segaran N, Badawy M, Elsayes KM, Pellerito JS, Katz DS, et al. Manifestations of sick cell disorder at abdominal and pelvic imaging. Radiographics. 2022; 42(4):1103-1122.
7. Aygun B, Mortier NA, Smeltzer MP, Shulkin BL, Hankins JS, Ware RE. Hydroxyurea treatment decreases glomerular hyperfiltration in children with sick cell anemia. American journal of hematology. 2013; 88(2):116-119.
8. Patre V, Chandrakar N. The pattern of renal artery Doppler indices in patients with sick cell disease. Journal of Ultrasonography. 2024; 24(97):1-4.
9. Granata A, Fiorini F, Andrulli S, Logias F, Gallieni M, Romano G, et al. Doppler ultrasound and renal artery stenosis: an overview. Journal of ultrasound. 2009; 12(4):133-143.
10. Wesson DE. The initiation and progression of sick cell nephropathy. Kidney international. 2002; 61(6):2277-2286.
11. Schein A, Enriquez C, Coates TD, Wood JC. Magnetic resonance detection of kidney iron deposition in sick cell disease: a marker of chronic hemolysis. Journal of Magnetic Resonance Imaging. 2008; 28(3):698-704.
12. Scheinman JI. Sick cell nephropathy. Pediatric Nephrology: Springer; 2009. p. 1181-1197.
13. Mancini EA, Culbertson DE, Yang YM, Gardner TM, Powell R, Haynes J, et al. Causes of death in sick cell disease: an autopsy study. British journal of haematology. 2003; 123(2):359-365.
14. McCarville MB, Luo Z, Huang X, Rees RC, Rogers ZR, Miller ST, et al. Abdominal ultrasound with scintigraphic and clinical correlates in infants with sick cell anemia: baseline data from the BABY HUG trial. American Journal of Roentgenology. 2011; 196(6):1399-1404.
15. Ibinaiye PO, Babadoko AA, Yusuf R, Hassan A-A. Renal complications of sick cell anemia in Zaria, Nigeria: An ultrasonographic assessment. West African Journal of Radiology. 2013; 20(1):19.
16. Aikimbaev K, Oğuz M, Güvenç B, Başlamışli F, Kocak R. Spectral pulsed Doppler sonography of renal vascular resistance in sick cell disease: clinical implications. The British journal of radiology. 1996; 69(828):1125-1129.
17. Emamian SA, Nielsen MB, Pedersen JF, Ytte L. Kidney dimensions at sonography: correlation with age, sex, and habitus in 665 adult volunteers. AJR American journal of roentgenology. 1993; 160(1):83-86.
18. El Sarraf NA, Zahra M. Renal Doppler Indices in patients with Sick Cell Disease; is it helpful for early detection of Sick Cell Nephropathy? Kasr El Aini Med J. 2009; 15(4):1-8
19. Eltahir MA, Gar-el-nabi MEM, Omer MAA, Abdelgadir O, Abdallah EA. Impact of sick cell disease in renal arteries blood flow indices using ultrasonography. Int J Med Imaging. 2017; 5:9-13.
20. Bolarinwa RA, Ayoola O, Onakpoya U, Onakpoya O, Adedeji T, Aderibigbe A, et al. Evaluation of Renal Arterial Resistivity Index and Some Biochemical Parameters in Sick Cell Disease: A Preliminary Study for Early Detection of Renal Impairment. Nigerian Journal of Haematology. 2019; 3(1&2):23-30.

21. Ma'aji SM, Jiya NM, Saidu SA, Danfulani M, Yunusa GH, Sani UM, et al. Transabdominal ultrasonographic findings in children with sickle cell anemia in Sokoto, North-Western Nigeria. *Nigerian Journal of Basic and Clinical Sciences*. 2012; 9(1):14.
22. Attalla BI. Sonographic Findings in Sudanese Children with Sickle Cell Anemia. *Journal of diagnostic medical sonography*. 2010; 26(6):276-280.
23. Cozzo D, Pianca S, Ognà VF, D'Arpa S, Cippà PE, Bellasi A. Papillary necrosis, fluid intake, and sickle cell nephropathy: lessons for the clinical nephrologist. *Journal of Nephrology*. 2025; 38(1):271-274.