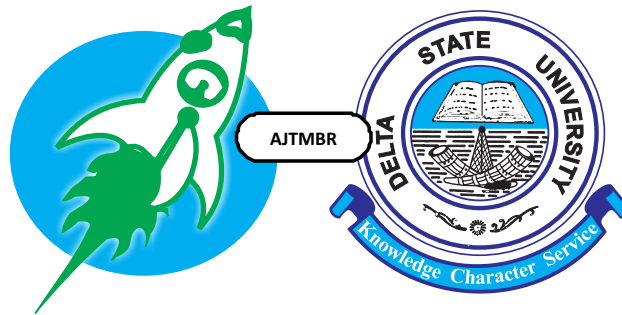


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Table of Contents

Effect of Occupational exposure to Gasoline on Reproductive and Thyroid hormones among male Petrol station attendants in Kwara State <i>Adunmo Godwin O.; Seyi Taiwo; Ibrahim Muniru; Busari, A. O.</i>	6-11
Production of L-lysine under submerged fermentation by <i>Corynebacterium glutamicum</i> using different agricultural plants leaves <i>Theresa Ezedom, Egoamaka Olsieneku Egbune, Solomon Adanoritsewo Atseponu, Mary Ogochukwu Charles, Blessed Achughue Benson, Diana Ebbah, Promise Chika Amechi, Oghenetega Benjamin, Akperweoghene Rejoice Egbodje, Lucky Ebinum, Blessing Ifechi Chukwudozie, Stephen Eboe, Ifeanyi Benedict Alexander, Sophia Fejiro Edijana and Nyerhovwo Tonukari</i>	12-24
Use of Cognitive Enhancers among students of Nigerian Tertiary Institutions <i>Uchendu Adaeze Phina, Uchendu Obiora Jude</i>	25-35
Prevalence of gestational diabetes mellitus, fetal and maternal outcomes of parturients with risk factors versus parturients without risk factors for gestational diabetes mellitus: A preliminary analysis of the comparative study of blood sugar levels at a tertiary hospital in southern Nigeria <i>Omo-Agboja LO, Onobwakpor EA, Adeyinka AT, Asaboro N, Oyeye Lucky</i>	36-47
Comparative assessment of renal volume and doppler velocimetric indices among subjects with sickle cell disease and controls in Benin, Nigeria <i>Jeffrey Imuetinyan Imade, Festus Oghanina Ebigiamusoe, Adenike O. Akhigbe,</i>	48-63

Comparative assessment of renal volume and doppler velocimetric indices among subjects with sickle cell disease and controls in Benin, Nigeria.

¹Jeffrey Imuetinyan Imade, ²Festus Oghanina Ebigiamusoe, ³Adenike O. Akhigbe,

Abstract

Background: Sickle Cell Disease (SCD), a hereditary blood disorder caused by an abnormality in haemoglobin can be complicated by impairment of renal function. Renal Doppler ultrasound has been found to be an effective method of evaluating reno-vascular events prior to abnormal laboratory renal function tests.

Aim and Objectives: This study aimed to evaluate and compare the renal volume (RV), intra-renal resistive and pulsatility indices (RI, PI) among sickle cell patients and controls in UBTH, Benin City using ultrasonography.

Materials and Method: This was a cross-sectional comparative study of renal volume, intra-renal resistive and pulsatility indices among 50 sickle cell disease patients attending sickle cell clinic of the University of Benin Teaching Hospital and equal number of "Age and Sex" matched controls. The study was conducted using a 2-8MHz curvilinear transducer of a SONOACE X6 (Medison Inc., Korea 2010) Doppler ultrasound machine.

Data analysis: Collated data was analysed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp, Armonk. N.Y., USA)

Results: The mean age for the HbSS subjects was 22.4 ± 3.7 years while that of the control group was 23.3 ± 4.5 years. The left RV was higher than the right RV in HbSS and HbAA: $169.3 \pm 40.2 \text{ cm}^3$ versus $162.2 \pm 40.3 \text{ cm}^3$ and $153.9 \pm 30.9 \text{ cm}^3$ versus $134.7 \pm 26.4 \text{ cm}^3$ respectively. The mean RV, RI and PI was significantly higher in HbSS than controls (RV: $165.8 \pm 39.8 \text{ cm}^3$ versus $122.9 \pm 13.4 \text{ cm}^3$; $p = 0.0001$, RI: 0.74 ± 0.02 versus 0.61 ± 0.04 ; $p = 0.0001$, PI: $1.43 \pm 0.06 \text{ cm}^3$ versus 0.90 ± 0.05 ; $p = 0.0001$).

Conclusion: Renal volume, RI and PI were statistically significantly higher in HbSS patients than controls.

Keyword: Sickle cell disease, renal volume, renal Doppler indices, ultrasonography

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INTRODUCTION

Sickle cell disease (SCD) is a genetic disorder in which there is an alteration in the normal globin

chain within the red blood cell (RBC), which causes rigid sickling of the cell, leading to vascular occlusion, and ischemia in multiple organs¹.

Mutation in HbB (haemoglobin subunit beta) gene which encodes for the beta-globin of haemoglobin molecule results in SCD. The normal human haemoglobin molecule is composed of two alpha and two beta globin chains². A single mutation leads to replacement of Glutamic acid with Valine in position 6 of the beta-globin chain resulting in mutant form of Hb known as sickle Hb (HbS), double mutation involving both globin chains results in HbSS also known as sickle cell anemia (SCA)^{2,3}.

Nearly 90% of the world's SCD population live in three countries: Nigeria, India and the Democratic Republic of Congo where the disease affects up to 2% of the population and the carrier prevalence rate (sickle cell trait) is as high as 10 to 30%⁴⁻⁷. In Nigeria, carrier prevalence is about 20 to 30%^{8,9}. Nigeria alone has been estimated to have at least 150,000 newborn with sickle cell annually^{4,10}. The prevalence of SCD in newborn is 3% in Benin City¹¹. A retrospective study in Benin City, Nigeria revealed SCD prevalence of 2.39% and a carrier rate of about 23%¹².

DeoxyHbS polymerizes when its concentration reaches a critical threshold leading to RBC sickling. Sickled RBC is prone to haemolysis and causes vascular stasis¹³. Stasis induces vascular occlusion, which either leads to infarction or resolves and causes ischemia-reperfusion¹³. Recurrent episodes of ischemia-reperfusion in the microcirculatory bed amplify organ injury because they induce inflammation and endothelial dysfunction, both regionally and systemically¹³. Endothelial dysfunction promotes the adhesion of RBCs and WBCs to the endothelium. Adhesion impedes the transit of RBCs through the microcirculation, thereby promoting RBC sickling, vascular stasis and vascular occlusion¹³. Additionally, sickle RBCs

exhibit abnormally high adhesion to the endothelium, owing to acquired membrane changes and to retained adhesion receptors on the reticulocytes^{14,15}.

Renal vasculopathy in SCD include cortical hyper-perfusion, medullary hypo-perfusion and increased stress-induced vaso-constrictive response which manifests by increased pulsatility index (PI) and resistive index (RI) values¹⁶.

Studies in Nigeria have reported a range of intra-renal resistive index (RI) of 0.56 to 0.68 in healthy subjects^{17,18}. An RI value of 0.70 is considered as the upper limit of normal, when increased; it is regarded as a non-invasive marker of renal histological damage in various pathological conditions and an early sign of renal impairment¹⁹.

The study was carried out to sonographically evaluate and compare renal volume, intra-renal RI and PI among sickle cell disease and non-sickle cell disease patients in UBTH, Benin City.

MATERIALS AND METHODS

The study was a prospective cross-sectional study comparing renal volume and Doppler indices amongst 50 sickle cell disease patients and 50 non-sickle cell disease volunteers as control in UBTH, Benin City carried out between February 2020 and August 2020.

Approval for this study was obtained from the Ethics and Research Committee of the University of Benin Teaching Hospital. Subjects were examined after informed consent has been granted following a thorough explanation of the study objectives and method of examination.

Inclusion criteria for subjects were diagnosed HbSS adults attending the sickle cell clinic of the

University of Benin Teaching Hospital and subjects in steady state (no history of painful crisis, inter-current illness in the past 4 weeks, no history of blood transfusion in the previous 4 months, no treatment with medications such as antibiotics in the past 3 weeks²⁰). Inclusion criteria for control included adults of both sexes with no co-morbidity and laboratory confirmation of HbAA.

The subjects were encouraged to fast overnight (12 hours) on the day of the examination. Assurance of confidentiality was given. A detailed history was obtained from both groups of patients and entered into a questionnaire assessing socio-demographic and medical history.

The temperature of the subjects was obtained using an infrared thermometer and recorded. The respiratory rate was recorded by counting the number of breaths per minute with the aid of a stopwatch. The radial pulse was counted for a minute and recorded with the aid of a stopwatch. The blood pressure of the subjects and volunteers was recorded using the mercury sphygmomanometer with the cuff tied and inflated around the mid-arm with the subject in sitting position. The height and weight were measured using a clinic stadiometer and a calibrated scale (Avery Co. Ltd, England 1981). The body mass index BMI was calculated using the formula shown below²¹.

$$\text{BMI (kg/m}^2\text{)} = \text{Weight/Height}^2$$

The blood sample was obtained from the thumb pulp of all subjects following a needle prick and

their fasting blood sugar was determined using calibrated test strips of an ACCU-CHEK glucometer (Roche, Mannheim, Germany). PCV, urine micro-albuminuria was obtained from sickle cell patient case notes if done within the last 4 weeks or samples were obtained for the test. Samples from HbAA volunteers were sent for urine micro-albuminuria and PCV. Those with abnormal test parameters were excluded from the study.

Grey Scale and Doppler Ultrasonography

Subjects were made to lie on the couch in supine position and the abdomen was exposed from the xiphisternum to the symphysis pubis. Acoustic gel was applied on the abdomen. All scans were done using a 3.5- 5.0MHz curvilinear array transducer of a SONOACE X6 ultrasound machine and utilizing colour Doppler.

To obtain renal length and thickness the transducer was placed on the longitudinal axis of the kidney. The length (L) was obtained by determination of the longest distance between the superior and inferior poles of the kidney using electronic calipers and the thickness (T) was taken as the widest distance between the anterior and posterior walls of the kidney (figures 1). Renal width (W) was taken as the maximum transverse distance on a transverse scan at the level of the hilum (fig 2). These measurements (L, T, and W) were taken three times for both sides and the average was taken to reduce intra-observer variation. The ellipsoid formula in built within the machine was used to determine the renal volume ($L \times T \times W \times 0.523$) by obtaining the length, thickness, and width of each kidney.

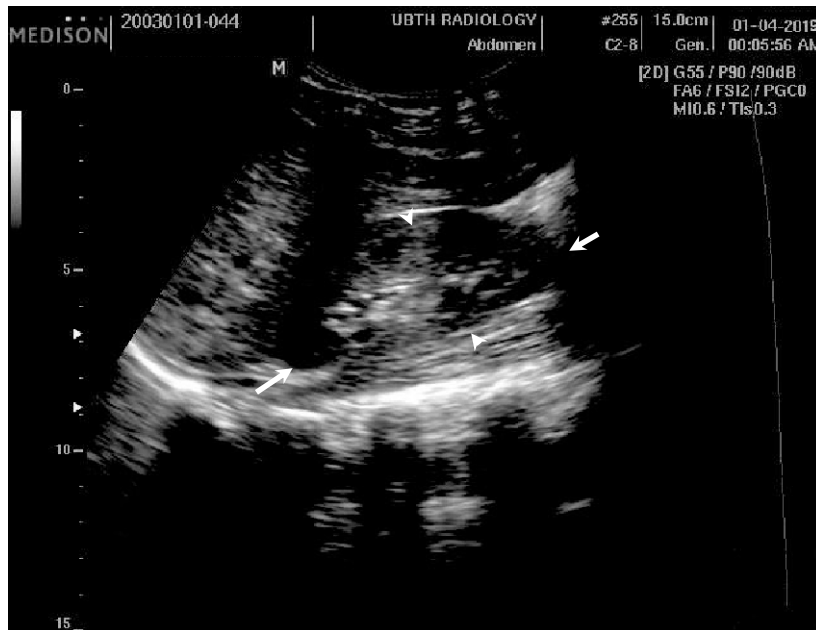


Figure 1: A trans-abdominal B-mode sonogram showing a longitudinal section of the right kidney and the points of measurement of renal length (long arrows) and thickness (arrow heads)

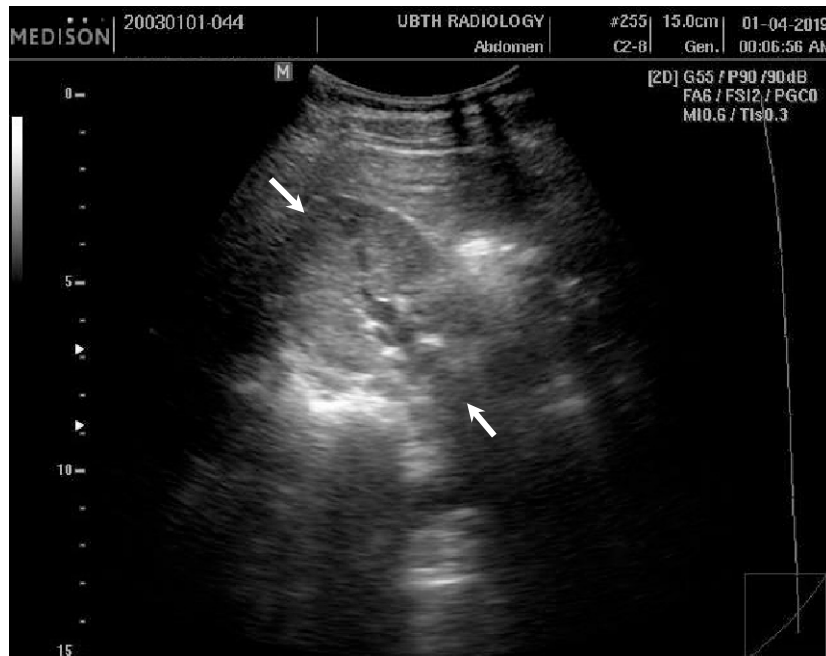


Figure 2: A trans-abdominal B-mode sonogram showing a transverse section of the right kidney at the level of the hilum and points of measurement of the renal width (arrows).

The resistive index (RI) is the ratio of the difference in the peak systolic velocity (PSV) and end diastolic velocity (EDV) to the peak systolic velocity within a vessel while the pulsatility index (PI) is the ratio of the difference in peak systolic velocity and end diastolic velocity to the mean velocity.

The patients were positioned in the right lateral decubitus to visualize the left renal artery and the left lateral decubitus to visualize the right renal artery. Using a 3.5MHz curvilinear array transducer of a SONOACE X6 ultrasound machine and utilizing colour Doppler with a wide colour box, the segmental vessels were located in the renal hilum. They were traced as they branch out to become the inter-lobar arteries which lie between the renal pyramids. The arcuate arteries were traced as they branch off from the inter-lobar arteries at the base of

the renal pyramids.

The colour box size was minimized prior to sampling with a focus on the vessels of interest. Pulse wave Doppler with an incidence angle at 0 degrees, a Doppler gate of 1mm and a minimum pulse repetition frequency that does not produce aliasing was used to acquire the waveform. The patients were asked to hold their breath and spectral tracing for the inter-lobar arteries was obtained with a stable signal and adequate waveform. The following Doppler parameters were obtained for the inter-lobar arteries on each side: PSV, EDV, RI and PI. Three values were obtained for inter-lobar arteries from the upper, middle, lower poles and the mean values of RI and PI were recorded (fig 3). At the completion of the evaluation, the acoustic gel was gently cleaned off the abdomen using a hand towel and the subject was asked to come down from the examination couch.

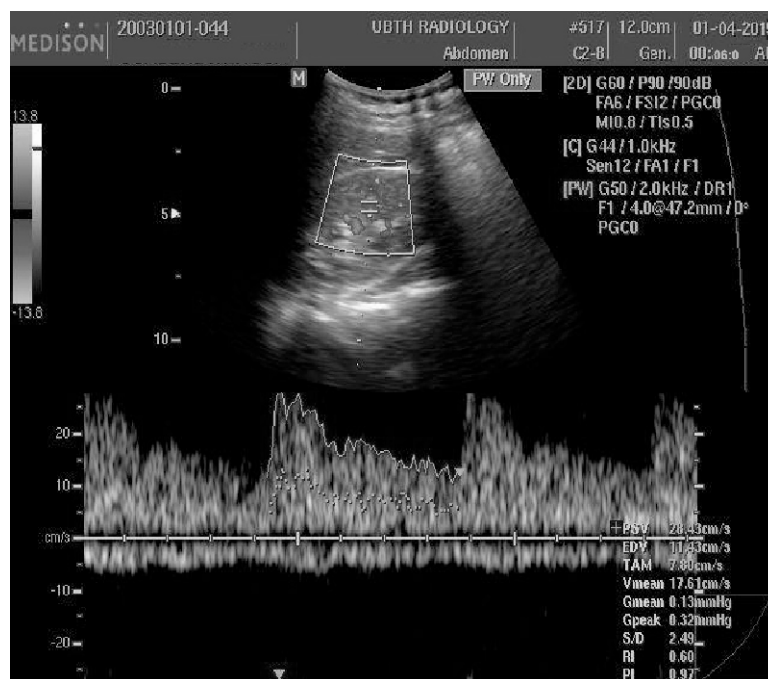


Figure 3: Spectral Doppler tracing of the right middle pole inter-lobar artery.

Data Analysis

The data obtained was entered into excel spread sheet and analysis was done using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp, Armonk. N.Y., USA). Data comparison (statistical test of significance) was done with a t-test and ANOVA (analysis of variance) for continuous variables and a Chi-square test for categorical data. Frequency and contingency tables, charts and graphs as appropriate were used to present the results. A 95% confidence interval was used and statistical significance was considered only for $p \leq 0.05$.

RESULTS

Socio-Demographic Characteristics of Participants

A total of 100 subjects consisting of 50 subjects with HbSS and an equal number of age and sex matched HbAA controls participated in this study.

Table 1 shows the socio-demographic parameters (age, gender, educational status and occupation) of the study participants. The age range for both study groups was 18-35 years. The mean age for the HbSS subjects was 22.4 ± 3.7 years while the mean age for the control

group was 23.3 ± 4.5 years. The difference in the mean age between both groups was not statistically significant ($p=0.258$).

The HbSS group and the HbAA group were aged matched, the difference in age distribution between the HbSS group and the HbAA groups was not statistically significant ($p = 0.476$). This is shown in Table 1.

The distribution according to gender was equally matched between the groups; 24(48.0%) males and 26(52.0%) females for the HbSS group and 30(60.0%) males and 20(40.0%) females in the HbAA group. The difference in the sex distribution between both groups was not statistically significant ($p=0.229$) as shown in Table 1.

The secondary level of education was highest among the SCD patients 32 (64.0%) while most of the control had a tertiary level of education 29 (58.0%).

Majority of the study participants were students [34 (68.0%) and 32 (36.0%) for HbSS and HbAA groups respectively]. The difference in occupation between the study groups was not statistically significant ($p= 0.117$). These findings are shown in Table 1.

Table 1: Socio-demographic Characteristics of Study Subjects.

Parameters	SCD (N = 50) Frequency (%)	Control (N = 50) Frequency (%)	Chi-square (c ²)	p-value
Age group				
18 – 23	31 (62.0)	25 (50.0)	1.468	0.476
24 – 29	15 (30.0)	20 (40.0)		
30 – 35	4 (8.0)	5 (10.0)		
Mean age (years)	22.4±3.7	23.3±4.5	-1.138 [†]	0.258
Gender				
Male	24 (48.0)	30 (60.0)	1.449	0.229
Female	26 (52.0)	20 (40.0)		
Level of Education				
Primary	0 (0.0)	2 (4.0)	7.471 [§]	0.015*
Secondary	32 (64.0)	19 (38.0)		
Tertiary	18 (36.0)	29 (58.0)		
Occupation				
Civil servant	4 (8.0)	11 (22.0)	5.418	0.117
Self employed	10 (20.0)	7 (14.0)		
Student	34 (68.0)	32 (64.0)		
Unemployed	2 (4.0)	0 (0.0)		

[§] Fisher's Exact Test[‡] Yates Continuity Correction[†] Independent t-test***Statistically significant****Anthropometric, Clinical and Biochemical Parameters of Study Subjects.**

The HbAA group had statistically significantly higher mean height, weight and BMI than HbSS group (1.66 ± 0.06 m² against 1.63 ± 0.03 m²; $p=0.001$), (72.1 ± 9.3 kg against 61.9 ± 6.8 kg; $p=0.0001$) and (26.0 ± 2.0 kg/m² against 23.3 ± 1.9 kg/m²; $p=0.0001$).

Temperature, Pulse rate, respiratory rate and fasting blood sugar were statistically significantly

higher in HbSS compared to HbAA: Temperature (36.5 ± 0.8 °C against 36.2 ± 0.4 °C; $p = 0.028$), Pulse rate (80.6 ± 8.6 bmp against 73.8 ± 7.6 bmp; $p = 0.0001$), respiratory rate (18.3 ± 2.6 cpm against 16.8 ± 2.2 cpm; $p = 0.002$) and fasting blood sugar (81.0 ± 7.5 mg/dl versus 75.5 ± 9.2 mg/dl; $p = 0.001$). Haemoglobin was statistically significantly higher in HbAA than HbSS (15.9 ± 1.2 g/dl against 7.2 ± 0.3 g/dl; $p = 0.001$). These are shown in table 2.

Table 3: Comparison of Renal volume, Resistive and Pulsatility indices of the right with the left kidney in HbSS and Control Subjects

Variables	HbSS (N = 50) Mean \pm SD	Control (N = 50) Mean \pm SD
Right kidney mean volume	162.2 \pm 40.3	117.5 \pm 18.3
Left kidney mean volume	169.3 \pm 40.2	128.3 \pm 16.8
t-test	-0.885	-3.079
p value	0.379	0.003*
Right kidney mean RI	0.7 \pm 0.0	0.6 \pm 0.0
Left kidney mean RI	0.7 \pm 0.0	0.6 \pm 0.0
t-test	-1.363	1.232
p value	0.176	0.221
Right kidney mean PI	1.4 \pm 0.1	0.9 \pm 0.1
Left kidney mean PI	1.4 \pm 0.1	0.9 \pm 0.1
t-test	-0.135	-0.320
p value	0.893	0.750

RI: Resistive index,

PI: Pulsatility index

Statistically significant*Comparison of Renal Volume, Resistive and Pulsatility Indices in HbSS and Control Subjects**

The mean RV, RI and PI was significantly higher in HbSS than controls (RV: 165.77 \pm 39.85cm³

versus 122.94 \pm 13.39cm³; $p = 0.0001$, RI: 0.74 \pm 0.02 versus 0.60 \pm 0.03; $p = 0.0001$, PI: 1.43 \pm 0.06 versus 0.90 \pm 0.05; $p = 0.0001$) as shown in Table 4.

Table 2: Comparison of Anthropometric, Clinical and Biochemical Parameters of Study Subjects.

Parameters	HbSS (N = 50) Mean \pm SD	HbAA (N = 50) Mean \pm SD	t-test	df	p-value
Height (m)	1.63 \pm 0.03	1.66 \pm 0.06	-3.599	98	0.001*
Weight (kg)	61.9 \pm 6.8	72.1 \pm 9.3	-6.282	98	0.0001*
Body Mass Index (kg/m ²)	23.3 \pm 1.9	26.0 \pm 2.0	-3.599	98	0.0001*
Temperature (°C)	36.5 \pm 0.8	36.2 \pm 0.4	2.231	98	0.028*
Pulse rate (bpm)	80.6 \pm 8.6	73.8 \pm 7.6	-4.148	98	0.0001*
Respiratory rate (cpm)	18.3 \pm 2.6	16.8 \pm 2.2	-3.188	98	0.002*
Haemoglobin concentration (g/dl)	7.2 \pm 0.3	15.9 \pm 1.2	-49.136	98	0.0001*
Fasting blood sugar (mg/dl)	81.0 \pm 7.5	75.5 \pm 9.2	46.321	98	0.001*

*Statistically significant

Renal Size in HbSS Group

In the HbSS group, a total of 26 (52.0%) patients had normal kidney size, 21 (42.0%) patients had enlarged kidneys and 3 (6.0%) patients had shrunken kidneys.

Comparison of Renal Volume, Resistive and Pulsatility Indices of the Right Kidney with the Left Kidney in HbSS and Control Subjects

The left mean RV was higher than the right mean

RV in both HbSS and HbAA: 169.3 \pm 40.2cm³ versus 162.2 \pm 40.3cm³ and 128.3 \pm 16.8cm³ versus 117.5 \pm 18.3cm³ respectively. These differences were not statistically significant in the HbSS group ($p=0.379$) but was statistically significant in the HbAA group ($p=0.003$). There was no difference between the right and left mean intra-renal RI and PI in both HbSS and HbAA ($p>0.05$) as shown in Table 3.

Table 4: Comparison of Renal Volume, Resistive and Pulsatility Indices in HbSS and Control Subjects

Variables	HbSS (N = 50) Mean \pm SD	Control (N = 50) Mean \pm SD	t-test	p-value
Right renal volume	162.21 \pm 40.37	117.54 \pm 18.28	4.040	0.0001*
Left renal volume	169.33 \pm 40.15	128.34 \pm 16.76	2.157	0.0001*
Average (right and left) renal volume	165.77 \pm 39.85	122.94 \pm 13.39	7.205	0.0001*
Right kidney mean RI	0.74 \pm 0.02	0.61 \pm 0.04	21.939	0.0001*
Left kidney mean RI	0.75 \pm 0.02	0.60 \pm 0.04	24.749	0.0001*
Average (right and left) mean RI	0.74 \pm 0.02	0.60 \pm 0.03	25.729	0.0001*
Right kidney mean PI	1.43 \pm 0.06	0.90 \pm 0.06	45.205	0.0001*
Left kidney mean PI	1.43 \pm 0.07	0.90 \pm 0.05	45.177	0.0001*
Average (right and left) mean PI	1.43 \pm 0.06	0.90 \pm 0.05	47.538	0.0001*

RI: Resistive index,

PI: Pulsatility index,

statistically significant*Correlation of Resistive and Pulsatility Indices with Age, BMI and Hb Among HbSS Subjects**

RI showed a statistically insignificant positive correlation with age in the HbSS group ($r=0.268$; $p=0.060$), a positive but statistically insignificant correlation with BMI ($r=0.215$; $p=0.133$) and a

statistically insignificant negative correlation with Hb ($r= -0.042$; $p=0.770$) as shown in Table 5. PI showed a statistically significant positive correlation with age in the HbSS group ($p=0.022$), a positive but statistically insignificant correlation with BMI ($p=0.244$) and a statistically insignificant negative correlation with Hb ($p=0.159$) as shown in Table 5.

Table 5: Correlation of Resistive and Pulsatility Indices with Age, BMI and Hb among HbSS Subjects.

Parameters	PI		RI	
	Pearson's correlation coefficient	<i>p</i> -value	Pearson's correlation coefficient	<i>p</i> -value
Age	0.322	0.022*	0.268	0.060
Body mass index	0.168	0.244	0.215	0.133
Haemoglobin concentration	-0.202	0.159	-0.042	0.770

*Statistically significant

CORRELATION OF RENAL VOLUME, RESISTIVE AND PULSATILITY INDICES WITH AGE AND BMI AMONG HbAA SUBJECTS

RV showed a statistically insignificant positive correlation with age among the HbAA group ($r = 0.190$; $p = 0.186$) while it was statistically significant and positively correlated with BMI ($r = 0.280$; $p = 0.049$) as shown in Table 6.

RI showed a statistically significant positive correlation with age among the HbAA group ($r = 0.456$; $p = 0.001$) while it was statistically insignificant and positively correlated with BMI ($r = 0.020$; $p = 0.888$) as shown in Table 6.

PI was negatively correlated with age and BMI among the HbAA group but it was not statistically significant ($p = 0.456$ and $p = 0.208$) as shown in table 6.

Table 6: Correlation of Renal Volume with Age and BMI among HbAA Subjects.

Parameters	RI		PI		RV	
	Pearson's correlation coefficient	<i>p</i> -value	Pearson's correlation coefficient	<i>p</i> -value	Pearson's correlation coefficient	<i>p</i> -value
Age	0.456	0.001*	-0.106	0.465	0.190	0.186
Body mass index	0.020	0.888	-0.181	0.208	0.280	0.049*

*Statistically significant

DISCUSSION

This study sets out to compare renal volume and Doppler indices among sickle cell disease patients with age and sex-matched volunteers as controls. In this study, 50 SCD patients and 50 HbAA volunteers were recruited with an age range of 18 to 35 years and a mean age of 22.4 ± 3.7 years and 23.3 ± 4.5 years respectively. Aikimbaev *et al.*,²² worked on spectral pulsed Doppler sonography in sickle cell disease among 40 patients in Turkey and Ibinaiye *et al.*,²³ worked on the incidence of abdominal ultrasound abnormalities in patients with sickle cell anaemia in Zaria, Nigeria among 74 patients. In both studies, the mean ages were 24.2 ± 7.6 years and 23.2 ± 5.3 years respectively which are similar to the present study because both studies were on adult SCD patients.

There were more females in this study which is similar to the findings in other studies done by Shogbesan *et al.*,²⁴ and Hamim²⁵. This has been attributed to higher health-seeking behaviour among females^{26,27}.

The age group with the highest number of SCD patients and HbAA volunteers in this study was 18-23 years. However, a study done by Geofery *et al.*,²⁸ on sonographic evaluation of abdominal organs in SCD among 252 subjects in Nigeria showed the highest number of patients and control in the age group 10-16 years. This difference in the age group with the highest number of patients and controls may be due to a much higher sample size of 252 used in their study.

In this study HbAA group had significantly higher mean height, weight and BMI than HbSS group. During childhood and adolescence, SCD is associated with growth retardation, delayed sexual maturation and being underweight. Growth delay during puberty in adolescence

with SCD is independently associated with decreased Hb concentration and increased total energy expenditure²⁹.

HbSS group had statistically significant higher mean pulse rate of 80.6 ± 8.6 . This finding is similar to that of Aikimbaev *et al.*,²² who reported a mean pulse rate of 86.5 ± 12.3 for HbSS group. This finding may be related to the compensatory mechanisms in SCD patients in response to anemia which is part of the complications of sickle cell disease.

Haemoglobin was significantly higher in HbAA group than HbSS group. Repeated crisis in SCD patients predispose them to lower Hb concentration.

The left mean RV was higher than the right mean RV in HbSS group and HbAA group in this study. These differences were not statistically significant in the HbSS group. Shilan *et al.*,³⁰ in Iraq and Udoaka *et al.*,³¹ in Nigeria found significantly high mean left renal volume in comparison to the right mean renal volume in their study of healthy adult volunteers. This was believed to be due to the location of the liver which may not allow comparable vertical growth of the right kidney to that which is attained by the left kidney³⁰.

The mean RV was higher in the HbSS group than the HbAA group. This finding was statistically significant ($p = 0.0001$). Previous studies reported renal enlargement in SCD patients^{23-25, 28, 32-35}. Glomerular hypertrophy, vascular dilatation, increased renal blood volume, engorgement of vessels and interstitial oedema have been suggested as likely contributors to renal enlargement in SCD patients^{36,37}.

In the HbSS group, 52.0% had normal kidney size, 42.0% had enlarged kidneys and 6.0% had shrunken kidneys. Previous studies done by Mapp

et al.,³⁸ in the United States of America found renal enlargement in 50%, Ibinaie *et al.*,²³ in Nigeria found renal enlargement in 2.7% and renal size reduction in 27.1%, Nosiba *et al.*,³⁵ in Sudan found renal enlargement in 22.3%, Balci *et al.*,³³ in Turkey found renal enlargement in 30.1%, and Bhushita *et al.*,³⁹ in India found renal enlargement in 19% and shrunken kidney in 37%. The differences in the findings may be due to variation in ethnicity or race, methodology and differences in population size. Other factors suggested include; focal scarring, interstitial fibrosis and analgesic abuse as likely contributors to reduced renal size⁴⁰

There was a positive correlation of RV with age among the HbAA group but it was not statistically significant. However, RV was positively correlated with BMI among the HbAA group and this was statistically significant. Studies done by Shilan *et al.*,³⁰ in Iraq and Udoaka *et al.*,³¹ in Nigeria on healthy volunteers showed a statistically significant positive correlation between RV with age and BMI.

The mean RI and PI were significantly higher in HbSS than in HbAA in our study. These findings are in agreement with previous studies^{22,24,41}. The difference in the values of RI was believed to be due to the difference in the haplotype of the HbSS gene in the study population⁴². The Arab-Indian haplotype with high foetal haemoglobin and low severity may account for the lower RI value found by Kishor *et al.*,⁴¹ in India while the Benin haplotype found in Nigeria with intermediate foetal haemoglobin and intermediate severity may account for the higher RI found in this study⁴². The increase in RI and PI among SCD patients has been ascribed to increased renal vascular tone resulting from various vascular occlusive mechanisms (vascular intima hyperplasia, thrombosis, altered vascular

reactivity and frank vasospasm) occurring in sickle affected kidneys¹⁶. High RI among individuals with HbSS compared to those with HbAA has been described as an early predictor of reno-vascular changes in SCD which can guide clinicians in monitoring other laboratory values to expedite early and appropriate treatment⁴¹.

This present study found a positive correlation of RI with age among the HbSS group but it was not statistically significant. A previous study in Sudan⁴³ showed a significant positive correlation of RI with age in SCD patients. Renal RI is a complex interaction between renal interstitial pressure, peripheral vascular compliance and systemic hemo-dynamics, all of which are deranged with increasing age in SCD patients¹⁹.

In this study there was a positive correlation of RI with BMI among HbSS and HbAA group respectively but it was not statistically significant. Mohamed *et al.*,⁴³ in their renal Doppler study of SCD patients and control reported a positive correlation of RI with BMI in SCD patients and control. An increase in BMI is associated with an increase in renal vascular resistance and glomerular filtration fraction⁴⁴.

RI was negatively correlated with Hb concentration among HbSS group but it was not statistically significant. Aikimbaev *et al.*,²² in their study reported RI to be negatively correlated with Hb concentration. Haematological abnormalities are associated with alteration in renal vascular resistance; hypoxaemia is associated with an increase in renal vascular tone in SCD patients⁴⁵.

A thorough literature search showed that apart from one study in Southwest Nigeria,²⁴ this is the second documented study on renal Doppler velocimetry in in Sick cell patients in Nigeria.

In conclusion, renal volume, RI and PI were

found to be significantly higher in the HbSS group than the HbAA group.

RECOMMENDATIONS

We recommend that renal Doppler scan should be an integral part of routine follow up examination of sickle cell disease patients and that further studies using large scale, community-based cohort of sickle cell disease patients in different centres in Nigeria should also be done to validate the accuracy of the findings in this study.

LIMITATION OF STUDY

- Ultrasound is operator dependent and thus may result in intra-observer error. This was minimized by taking the average of three measurements.
- Respiratory movement of the abdomen made it difficult taking Doppler spectral tracing but this was minimized by asking the patient to hold his/her breathe at the time of Doppler insonation of the intra-renal arteries.

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