Doppler Sonographic evaluation of the Splenic artery among Sickle Cell Anemia Patients in a Nigerian Tertiary Health Institution.

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Abstract

Introduction: Doppler sonography has revolutionalized the use of ultrasonography in medicine and its use in the vascular imaging of sickle cell patients is invaluable. The aim of this study was to evaluate the splenic artery Doppler indices in sickle cell anemia and to compare the indices with Hemoglobin AA subjects. **Methods:** This was a case control study carried out at the Alex Ekwueme Federal University Teaching Hospital between July 2017 and March 2018. Participants were scanned using the trans-abdominal route with a 3.5MHz curvilinear transducer of a Medison Accuvix A30 (Samsung Medical Systems, February 2013). The splenic artery Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Pulsatility Index (PI), Resistivity Index (RI) and Systolic/ Diastolic ratio (S/D ratio) were measured. Data analysis was carried out using Statistical Package for Social Sciences version 20.0 (SPSS Inc Chicago, IL, USA). **Results**: One hundred subjects with Sickle Cell Anemia (SCA) and one hundred Hemoglobin AA control participated in the study and were made up 100 males and 100 females with age range 0 to 30 years. The splenic artery PSV, EDV, PI, RI and S/D ratio are all statistically significantly higher in patients with Hb SS compared with Hb AA with p values of 0.00, 0.00, 0.00, 0.00 and 0.00 respectively. There was no correlation between the Doppler parameters and age as well as Doppler parameters and sex in both patients with Hb SS and Hb AA control. **Conclusion**: PSV, EDV, PI, RI and S/D ratio of the splenic artery in patients with Hb SS are significantly higher than that of control which suggests an increased risk of splenic complications in SCA patients.

Keywords: Sickle Cell Anemia, Splenic Artery, Doppler, Ultrasonography.

INTRODUCTION

Among people of the African racial origin, sickle cell disease (SCD) is one of the commonest haemoglobinopathy.[1] SCD is a group of inherited haemoglobin abnormality characterized by chronic haemolysis. The haemolysis which is the hallmark of the disease is usually due to an increased tendency of haemoglobin molecules within the red cells to polymerise and deform the red cell into a sickle shape especially in hypoxic states.[2] The commonest form of SCD especially in West Africa and Nigeria, is Sickle Cell Anemia (SCA).[3] Others include, haemoglobin SC disease, sickle beta plus thalassaemia, sickle beta zero thalassemia (which has similar severity with sickle cell anemia), haemoglobin SD Punjab disease and haemoglobin SO Arab disease.3

SCD includes a spectrum of disorders where patients at one end of the spectrum may present with no symptom (heterozygous patients) while those at the other end may require repeated blood transfusions (homozygous patients) and bone marrow transplantation.[4] The symptoms can present as early as 6 months of life and may linger into adulthood.[5]

The complications of sickle cell anemia are multisystemic with affectation of several major organs simultaneously or at different times with the spleen being a commonly affected organ.[6] Most of the sickle cell deaths occur following one or more complications.

Anatomically, the spleen has a slow, tortuous microcirculation that makes it extremely susceptible to congestion, sludging, and polymerization.[7] Over 77% of patients with sickle cell anemia manifest with various degrees of splenic abnormalities before the age of 2years.[8] These abnormalities can be functional or structural. It can range from simple non functional splenomegaly to splenic infarction and occasionally frank splenic abscess.

Doppler ultrasonography is a non invasive radiologic technique of assessing the vessels and vascular flow. Power and Colour Doppler sonography are currently the method of choice for imaging blood flow.[9]

Currently, there is no cure for SCA and even simple, inexpensive and cost-effective procedures such as the use of penicillins to prevent infections are not readily available to most patients in Nigeria.[10] SCA patients with changes in the splenic artery Doppler indices may therefore benefit from preventive measures to avoid further complications. These measures include the use of prophylactic antibiotics, adequate rest, good nutrition, folic acid supplementation, high fluid intake, parental education and psychological support.[11]

This study therefore aimed at determining the splenic artery Doppler indices in patients with sickle cell anemia and comparing these indices with subjects with AA haemoglobin genotype of the same age group and sex. The findings will go a long way in identifying early splenic changes that may be associated with fatal or irreversible complications in the patients with sickle cell anemia.

Methods:

This was a case control study of the splenic artery Doppler indices of 100 patients with homozygous haemoglobin SS and 100 with normal haemoglobin aged 0 to 30 years conducted in the Ultrasound Unit of Radiology Department of Alex Ekwueme Federal Teaching Hospital Abakaliki (AE-FUTHA) formerly known as Federal Teaching Hospital Abakaliki (FETHA) in Ebonyi State, South East of Nigeria. Homozygous SS subjects and the control group for this study were selected by simple random sampling. Subjects were stratified according to age group and matched with a control group.

All sonograms were done by the researcher alone to eliminate inter observer variability. These sonograms were obtained with a curvi-linear transducer of 3.5MHz of a Medison Accuvix A30 (Samsung Medical Systems, February 2013) with an insonation angle of 60 degrees, a pulse repetition frequency (PRF) of 4kHz and a sample volume of 2mm . The privacy of the subjects was guaranteed. The subjects were positioned in the supine position or the right lateral decubitus position on the examination couch. The left arm was raised away from the abdomen. The abdomen was exposed superiorly to the xiphisternum and inferiorly to the pubic symphysis. Coupling gel was applied in order to exclude the air between the skin and the transducer. The splenic artery was scanned in longitudinal and transverse planes using the left intercostal coronal approach via the 9th intercostal space. The subjects were asked to take a very deep breath and hold it. The Doppler indices were taken 1cm from the splenic hilum and measured three times before an average was taken. The following Doppler parameters were documented in the worksheet: PSV, EDV, PI, RI, S/D ratio. The data obtained from this study was analyzed using Statistical Package for Social Sciences (SPSS) for Windows, Version 20.0. Statistical tests were considered significant at p-value less than or equal to 0.05

Results:

Table 1: Demographic characteristics of the study population

Parameters	**Genotype**							
	AA				SS			
	Range	Min	Max	Mean±SD	Range	Min	Max	Mean±SD
Age (yrs)	27.00	3.00	30.00	17.28±7.61	26.00	3.00	29.00	17.11±7.46
Height(m)	0.96	0.94	1.90	1.56±0.25	0.96	0.98	1.94	1.60±0.25
Weight(Kg)	97.71	17.67	115.38	60.89±21.30	66.68	17.96	84.64	54.03±16.95

BMI(Kg/m^2)	20.50	18.50	39.00	24.14±4.36	11.00	17.00	28.00	20.49±2.42

All the study subjects were Christians and speak Igbo language. The modal age for each group is 14years (6%) and 18years (6%) for AA and SS respectively.

Table 2a: Showing age and Doppler indices in subjects with Hb AA genotype

Age (Yrs)	N	PSV (cm/s) mean ±SD	EDV (cm/s) mean ±SD	RI mean ±SD	PI mean ±SD	S/D RATIO mean ±SD
0-4	8	57.26±2.01	19.67±3.39	0.66±0.05	0.99±0.14	2.96±0.33
5-9	14	60.49±3.61	21.97±2.56	0.64±0.03	1.02±0.13	2.78±0.22
10-14	16	60.40±3.79	20.89±2.47	0.65±0.038	1.03±0.12	2.92±0.29
15-19	19	60.67±2.56	22.47±3.48	0.63±0.05	1.04±0.11	2.75±0.34
20-24	27	60.49±1.37	24.75±2.04	0.59±0.03	1.05±0.10	2.46±0.15
25-29	16	58.07±1.76	21.31±3.49	0.63±0.05	1.01±0.08	2.77±0.31

Table 2b: Showing age and Doppler indices in patients with Hb SS genotype

Age Yrs	N	PSV (cm/s) mean ±SD	EDV (cm/s) mean ±SD	RI mean ±SD	PI mean ±SD	S/D RATIO mean ±SD
0-4	6	72.81±4.88	21.81±0.69	0.70±0.01	1.17±0.13	3.34±0.16
5-9	14	75.03±1.54	27.38±2.57	0.63±0.04	1.12±0.09	2.77±0.33
10-14	12	72.16±3.15	23.87±2.71	0.67±0.03	1.10±0.08	3.05±0.30
15-19	26	72.95±1.92	26.68±2.35	0.63±0.03	1.08±0.11	2.75±0.20
20-24	24	73.73±3.33	25.02±2.73	0.66±0.03	1.07±0.11	2.97±0.28

25-29	18	73.21±3.93	24.24±3.46	0.67±0.04	1.13±0.12	3.06±0.35

Table 2b shows that the modal age group was 15-19years (26%).

Table 2c: Comparison of the splenic artery Doppler indices in patients with Hb SS and those with Hb AA

Splenic artery indices	**AA Mean±SD**	**SCA Mean±SD**	Mean diff	t-test	df	P-value
PSV(cm/s)	60.26±2.92	73.35±2.92	-13.09	-31.727	198	0.000
EDV(cm/s)	22.21±3.02	25.32±3.02	-3.11	-7.272	198	0.000
PI	1.04±0.11	1.10±0.11	-0.06	-3.914	198	0.000
RI	0.63±0.45	0.66±0.04	-0.02	-4.082	198	0.000
S/D	2.76±0.34	2.93±2.93	-0.18	-3.831	198	0.000

* P<0.05 there is significant difference

The Relationship between Doppler indices and age in SCA patients and those with AA haemoglobin genotype are as shown in fig. 1 – 5 below.

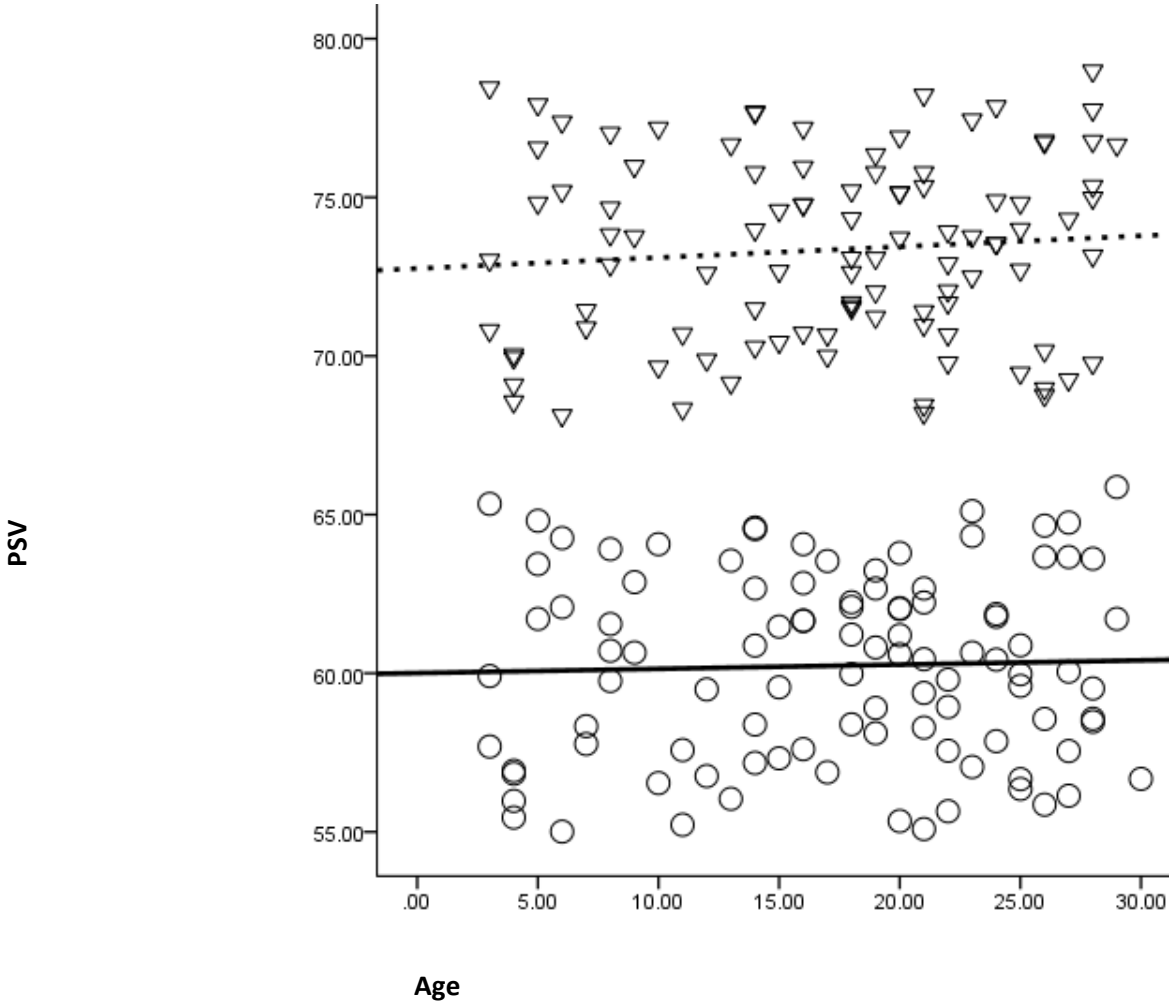

Fig. 7: A scatter plot with trend line of the relationship between PSV and Age of AA and SS haemoglobin

From the fig 7 above, R_{AA}= 0.035, P $value_{AA}$= 0.732, Y_{AA} = 60.006+0.013(Age)

R_{SS}= 0.088, P $value_{SS}$= 0.386, Y_{SS} =72.759+0.034(Age),

Key: O = control group, Δ = patients with Hb SS R= Pearson's correlation coefficient

Y= correlation equation P = the level of significance

Statistically, r>0.3 is significant and p<0.05 is significant

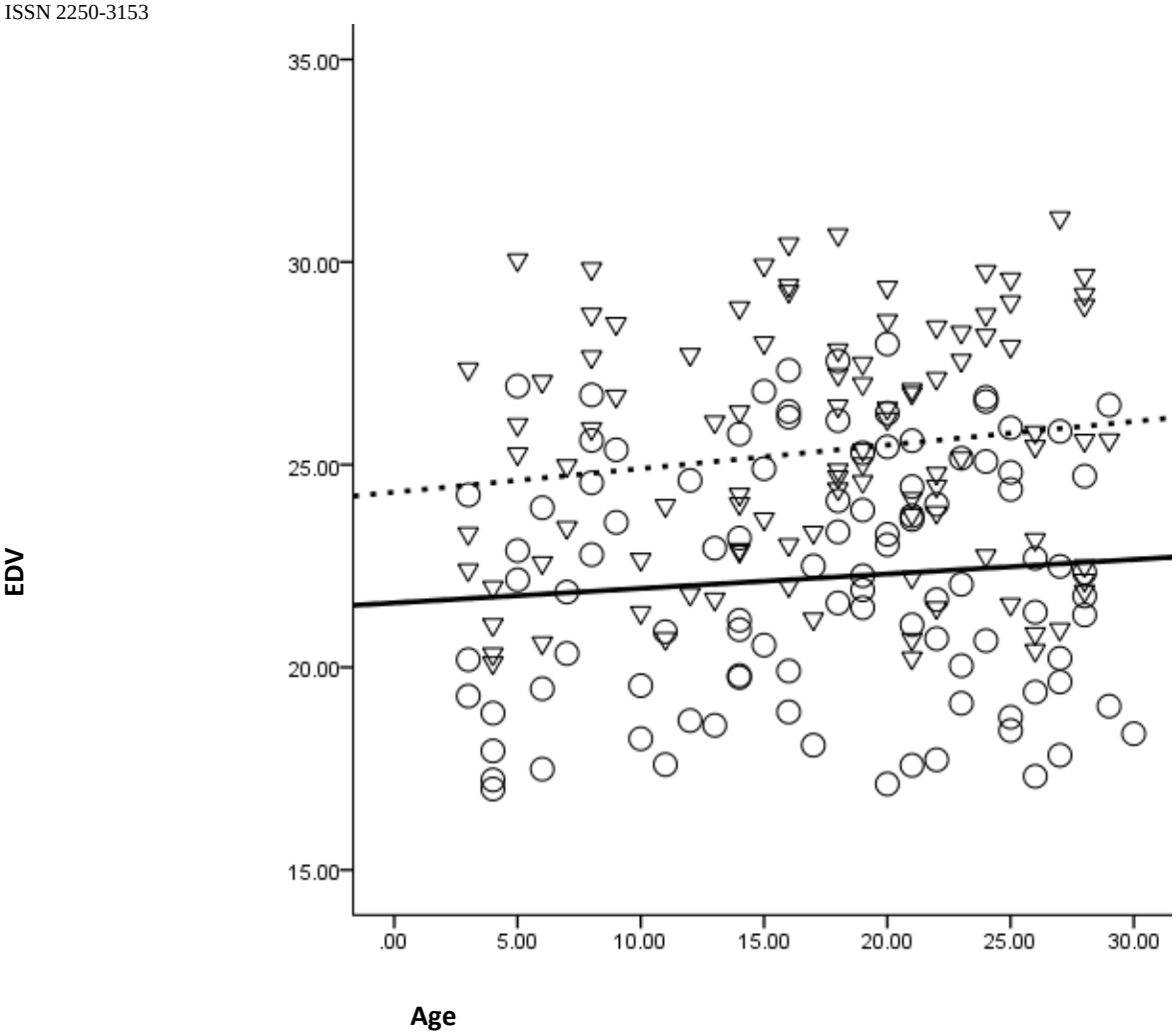

Fig. 8: A scatter plot with trend line of the relationship between EDV and Age of AA and SS haemoglobin

From the fig 8 above, R_{AA}= 0.090, P $value_{AA}$= 0.375, Y_{AA} = 21.591+0.036(Age)

R_{SS}= 0.144, P $value_{SS}$= 0.154, Y_{SS} =24.322+0.058(Age)

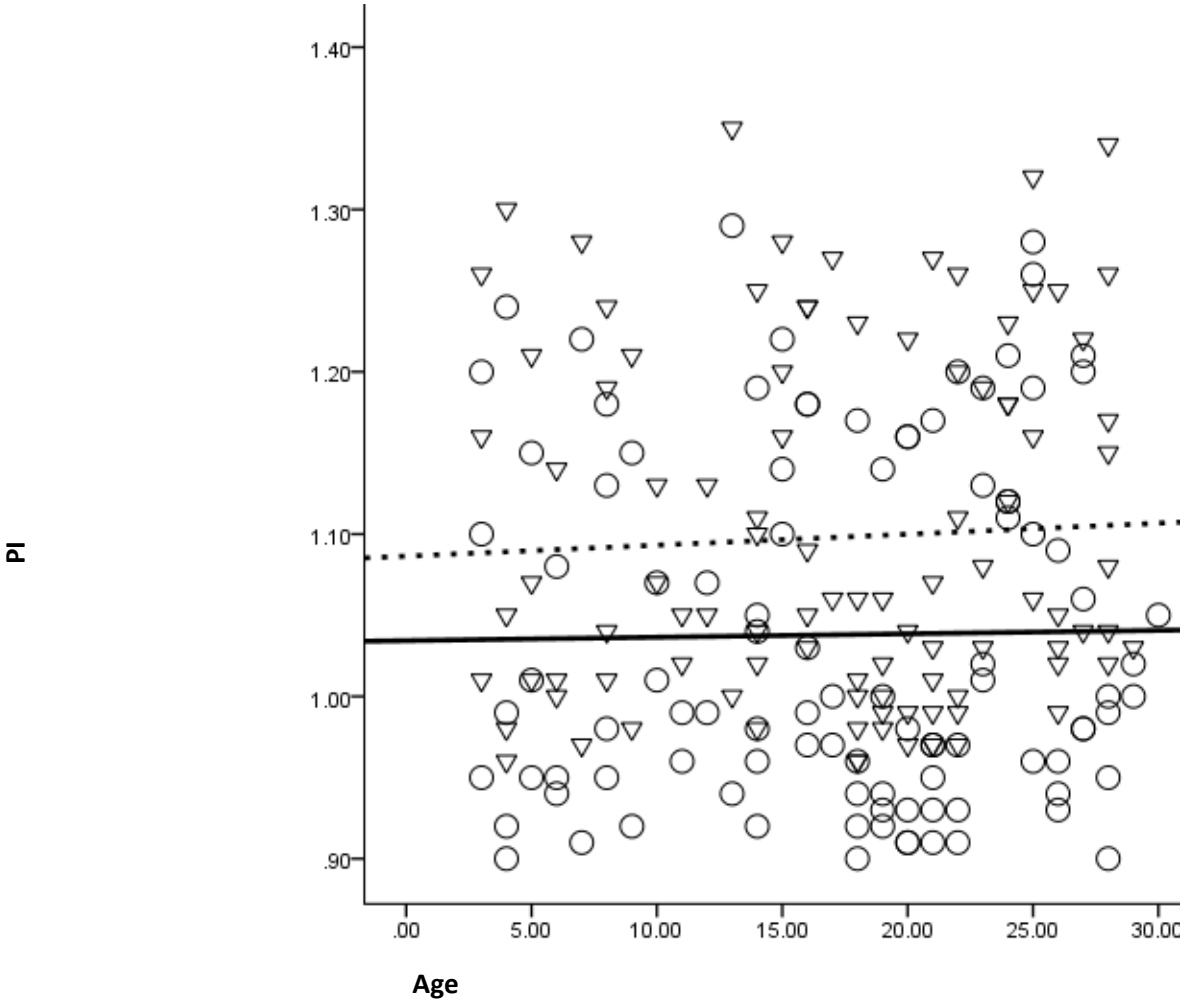

Fig. 9: A scatter plot with trend line of the relationship between PI and Age of AA and SS haemoglobin

From the fig 9 above, R_{AA}= 0.015, P $value_{AA}$=0.884, Y_{AA} = 1.034+0.000(Age)

R_{SS}=0.047, P $value_{SS}$=0.645, Y_{SS} =1.086+0.001(Age)

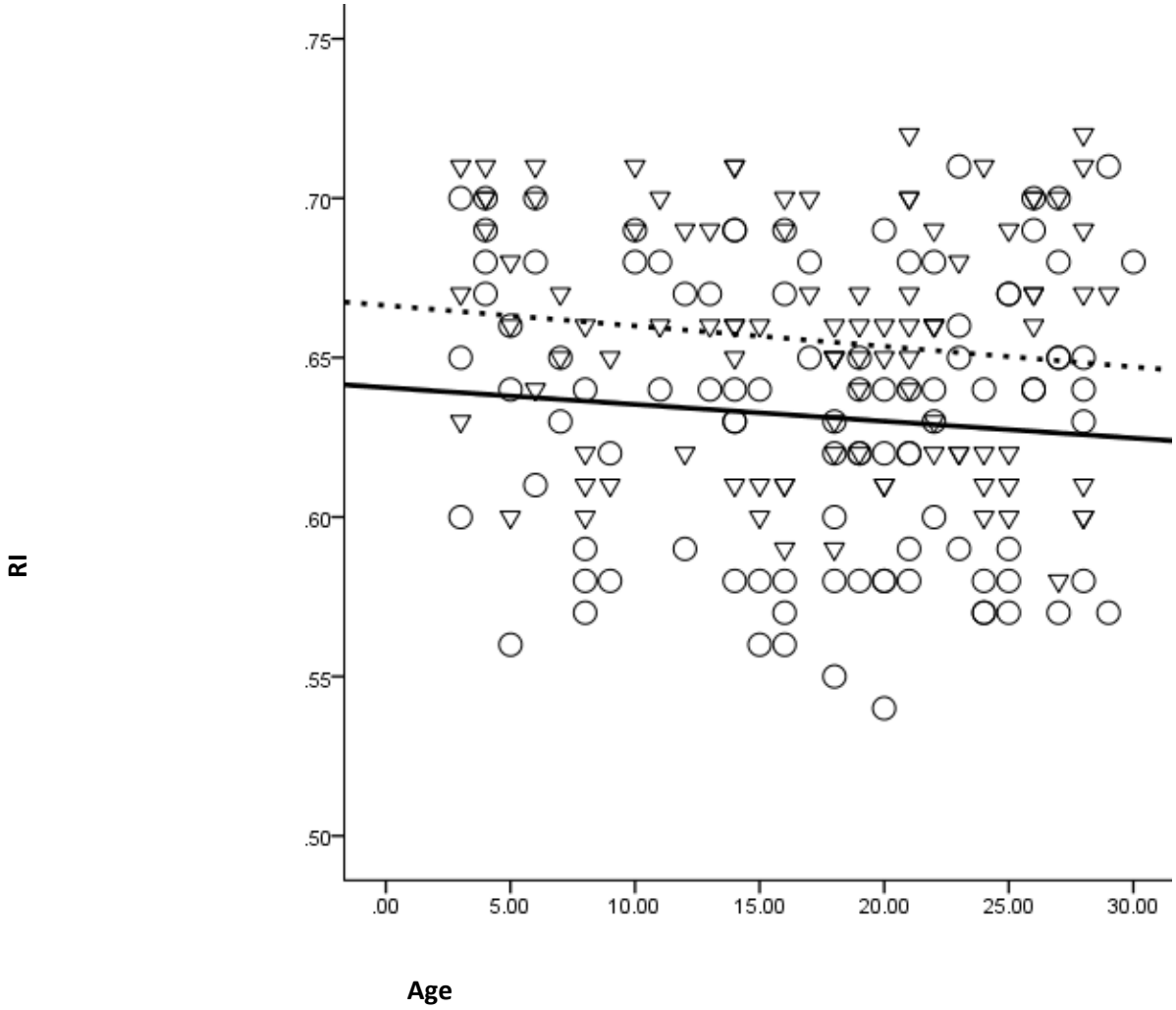

Fig. 10: A scatter plot with trend line of the relationship between RI and Age of AA and SS haemoglobin

From the fig 10 above, R_{AA}= 0.089, P $value_{AA}$=0.376, Y_{AA} = 0.641-0.001(Age)

R_{SS}=0.128, P $value_{SS}$=0.206,Y_{SS} = 0.666-0.001(Age)

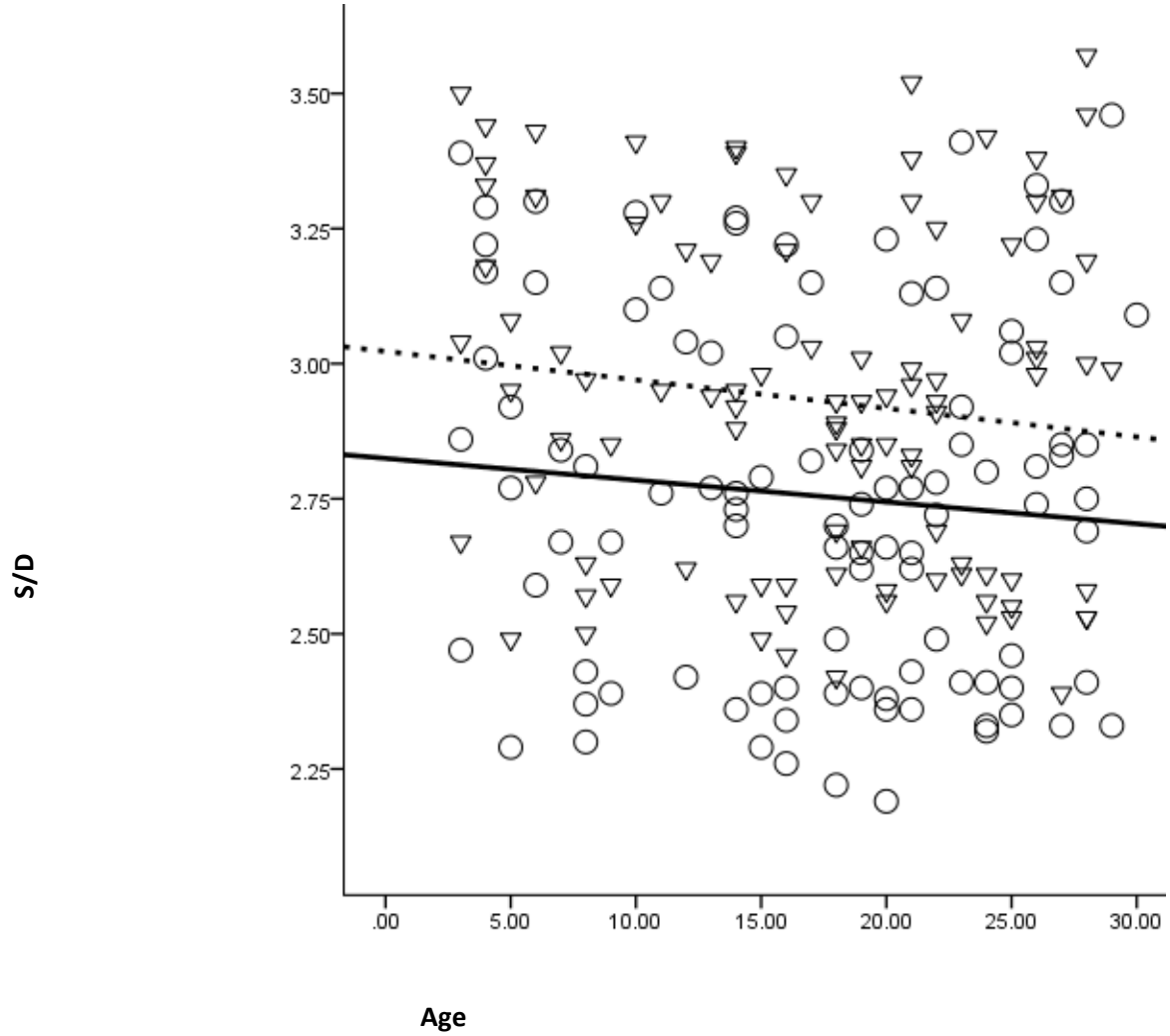

Fig. 11: A scatter plot with trend line of the relationship between S/D and Age of AA and SS haemoglobin.

From the fig 11 above, R_{AA}= 0.091, P $value_{AA}$=0.370, Y_{AA} = 2.825-0.004(Age)

R_{SS}=0.125, P $value_{SS}$=0.217,Y_{SS} =3.023-0.005(Age)

Discussion

In this study, no patient below the age of three years had SS haemoglobin genotype. This is probably due to persistence of fetal haemoglobin (Hb F) in the fetal circulation in the first year of life[12] and also the fact that the index study is a hospital based study. Other reasons for the delayed presentation of children with Hb SS to the hospitals in Abakaliki may be due to the local socio-cultural beliefs, poverty, illiteracy, ignorance and lack of a state or local government health insurance schemes. Sick children with Hb SS are traditionally referred to as *ogbanje (meaning born to die or children who come and go)* and are commonly taken to the native doctors,

herbalist homes, spiritual homes, the churches/ prayer houses and later to the patent medicine shops before they are eventually brought to the hospitals[13].

From the data obtained in this study, the splenic artery Doppler indices of those with Hb SS genotype are higher than those with normal Hb genotype and the difference is statistically significant for PSV, EDV, RI, PI and S/D ratio with p values 0.00, 0.00, 0.00, 0.00 and 0.00 respectively. Studies on splenic artery Doppler indices in patients with Hb SS genotype are not readily available in the literature for comparison. However Doppler studies of other vessels in patients with Hb SS genotype also showed increased Doppler indices which the authors attributed to various degrees of anemia and vasculopathy.

Taori et al[14] found an increase in the PI and RI in the main renal, segmental and interlobar arteries in patients with SCD. RI was found to be a less variable index than PI. The elevated PI was found to be highly significant when comparing those with SS genotype and AA genotype (p values 0.0001, 0.0001, 0.0001, respectively, for main renal, segmental, and interlobar arteries) and also when comparing those with AS genotype and AA genotype (p values 0.0001, 0.0001, 0.0001, respectively). RI was also observed to be significantly elevated in both the SS and AS groups compared with the AA group in the main renal, segmental, and interlobar arteries when comparing SS genotype and AA genotype groups (p values 0.0001, 0.0001, 0.0001, respectively). Also when the RI of subjects with AS genotype and those with AA genotype were compared, it was significantly higher in those with AS (p values 0.0001, 0.0001,0.0001, respectively).

Aaslid R[15] observed that the blood velocity is directly related to the cerebral blood flow and inversely related to the diameter of the vessel.

In Columbia, Brass et al[16] found that children with SCA have 40 to 50% higher mean velocity of flow than those without anemia.

Adams et al[17] also found that in contrast to children without anemia, arterial velocities were higher in children with anemia and vasculopathy.

No correlation was noted between age and the splenic artery Doppler indices in both those with Hb SS genotype and those with normal Hb genotype. For those with normal Hb genotype, the p values are 0.732, 0.375, 0.884, 0.376 and 0.370 for the PSV, EDV, PI, RI and S/D ratio respectively. Their correlation coefficients (r) are 0.035, 0.090, 0.015, 0.089 and 0.091 for the PSV, EDV, PI, RI and S/D ratio respectively.

For those with Hb SS genotype, the p values are 0.386, 0.154, 0.645, 0.206 and 0.217 for the PSV, EDV, PI, RI and S/D ratio respectively. Their correlation coefficients(r) are 0.088, 0.144, 0.047, 0.128 and 0.125 for the PSV, EDV, PI, RI and S/D ratio respectively.

There was no statistically significant difference between the Doppler indices in males and females with Hb SS genotype with the p values of 0.931, 0.986, 0.942, 0.958, and 0.987 for the PSV, EDV, PI, RI and S/D ratio respectively.

Other Doppler studies documented no statistically significant correlation with age.[14,15,16,17] The changes in Doppler parameters are usually associated with vascular occlusions and increased vascular resistance which are age independent.[14]

Splenic artery Doppler sonography can therefore be used to monitor the spleen in sickle cell anemia and pick up early changes before the changes become late or irreversible.

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