Original Article

Associations of ultrasound splenic size and clinico-laboratory values in patients with Sickle Cell Anemia at University College Hospital, Ibadan, Nigeria

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Abstract

Background/Aims: Sickle cell anemia also known as haemoglobin SS (HbSS) is a genetic disease arising from the replacement of glutamic acid with valine at position 6 of the beta hemoglobin chain. This vaso-occlusive disease affects most of the organs in the body with the spleen commonly affected resulting in recurrent infarction. This study aims to assess the relationship between the ultrasound splenic length (LS) with the steady state packed cell volume (PCV), frequency of blood transfusion, and anthropometric parameters (weight and height) among patients with sickle cell anemia.

Materials and Methods: This is an observational cross-sectional study with 128 consenting HbSS patients recruited. Sickle cell anemia (HbSS) patients with no crises/illness within the last 4 weeks prior to the study period were included in the study. Patient's demographics, steady PCV and ultrasound findings of the spleen were documented into the study pro forma. Data were analyzed using the Statistical package for the Social Sciences software version 21. Mean, median, standard deviation, and Chi-square were used. A $P \leq 0.05$ was considered statistically significant and a confidence interval (CI) of 95%.

Results: The median age for all the patients was 19.00 years with a CI of 19.06–23.2 years. For children (2–17 years), the median age was 11.00 years with a CI of 9.35–11.36 years while for the adults was 28.00 years with a CI of 27.40–31.77 years. The median steady-PCV obtained in this study was 25.0%. Adult HbSS patients with normal LS had a significant correlation with the steady PCV.

Conclusion: Normal-sized spleen on sonography may be a pointer to the steady PCV in sickle cell anemia patients. This study, therefore, suggests the need for sonography of the spleen in HbSS patients as part of their routine follow-up investigations.

Keywords: Blood transfusion, packed cell volume, sickle cell anemia, splenic size, ultrasonography

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INTRODUCTION

Sickle cell anemia (HbSS) is an inherited disease condition that was first described by Herrick in 1904 when Ernest Edward his intern discovered some particular elongated and sickle-shaped blood cells in a peripheral blood smear of a dental student admitted to the hospital on account of anemia.[1] The molecular basis is that of a point mutation in both beta chains (β) of hemoglobin with the replacement of glutamic acid with valine at position 6 of the beta chain (β) leading to sickling of the red blood cell.[1-5] Homozygous sickle cell anemia (HbSS) is common among people who have ancestors from sub-Saharan Africa, India, Saudi-Arabia and Mediterranean countries although through migration its frequency has increased in the American continent.[5] The global prevalence of homozygous sickle cell disease is estimated at around 20–25 million individuals worldwide of which 12–15 million are in sub-Saharan Africa.[6] In the West African country of Nigeria, more than 150,000 children are born with the disease annually and over 4 million people are afflicted.[6-8] Fifty percent of those with SCA usually die by the age of 5 years in sub-Saharan Africa from infections such as malaria, pneumococcal sepsis, and anemia.[5]

The spleen is the most common and earliest organ affected in sickle cell anemia patients.[9] This is a sequela of the insults from the pathology earlier than in the other vulnerable organs. The liver, kidneys, and gall bladder are some of the other organs affected in sickle cell anemia.[10,11]

The spleen is an ovoid organ and weighs between 150 g and 200 g in adults however in children it weighs 13 g at birth, and doubles and triples its weight in the first and third postnatal years respectively.[12,13] The spleen increases in weight as an individual grow up till it reaches that of the adult (an increase in organ size is related to growth). It is usually purple in color and located in the left hypochondrium where it is protected by the 9th to 11th ribs.[14] It is the largest lymphatic organ that is involved in the body defensive mechanism.[15]

The spleen usually enlarges towards the end of the 1st year of life in children with sickle cell anemia.[16] However, occasionally the spleen can undergo a sudden very painful enlargement due to the pooling of large numbers of deformed sickled cells.[16] This phenomenon is known as the splenic sequestration crisis. The spleen can also undergo repeated infarction which is aided by low pH and low oxygen tension in the sinusoids and splenic cords and over time, this recurrent infarction leads to fibrosis with shrinking of the spleen and eventually becoming nonvisualized (autosplenectomy).[16] One of the objective and reproducible ways of assessing the size of the Spleen is through the radiological method of ultrasonography.

Ultrasonography is a cross-sectional imaging modality that is readily available, affordable, and accessible to measure the size of the spleen. The splenic length (LS) varies with age, however, in adults, the sonographic length of the spleen ranges between 6 cm and 12.9 cm. Splenomegaly (in adults) is defined as a sonographic length of ≥13 cm while shrunken spleen refers to a visualized spleen on ultrasound with a length <6 cm and autosplenectomy is nonvisualization of the spleen on ultrasound.[9,17] A nomogram is usually used to determine the LS in children <12 years of age.

The packed cell volume (PCV) in sickle cell anemia patients is believed to vary with age and sex in such that it is lower in males than females up to the age of 18 years after which that of the males becomes consistently higher until 40 years when their PCV falls in them.[18,19] This low PCV in them can necessitate the need for a blood transfusion which had played a vital role in their management and had ultimately reduced morbidity and mortality.[20]

Anthropometric measurement (weight and height) of patients had been shown to have an association with the individuals' splenic size with taller patients having larger organ size.[21,22]

This study aims to assess the relationship between the ultrasound splenic length (LS) with the steady state PCV, frequency of blood transfusion, and anthropometric parameters(weight and height) among patients with sickle cell anemia.

MATERIALS AND METHODS

This is an observational cross-sectional study conducted for 17 months (June 2019–November 2020) at the Radiology Department of a tertiary teaching hospital in the Southwestern part of Nigeria. A total number of 128 HbSS registered patients at the Haematology clinics aged 2–60 years were recruited for this study.

Ethical approval was obtained from the hospital's Ethical review committee. Patients with genotype HbSC, HbAS, and HbAC as well as patients with prior history of surgical removal of their spleen, in any crises such as vaso-occlusive, visceral sequestration, hyper-hemolytic and aplastic crises in the 4 weeks before the study, pregnant and those with

known co-infections like HIV and Hepatitis were excluded from the study. Informed consent was obtained from the adult and the caregivers of the children. The study abided by the tenants of the declaration of Helsinki for studies on human subjects. Information about their age, sex, education status, marital status, PCV, and frequency of blood transfusions was sought directly from the adult patients and from the parents/caregivers of the children.

Ultrasound technique

All participants were examined in the supine position using a B-mode real-time transabdominal ultrasound scan using a 3–5 MHz, curvilinear array transducer of Mindray Diagnostic Ultrasound System, model DC-30, 2019® (China). The LS which is the maximum distance from the dome of the spleen to the splenic tip was measured at the splenic hilum in the region of the ninth to eleventh intercostal spaces at the anterior axillary, mid-axillary, and posterior axillary lines[21,23] These measurements were added together and averaged as the LS to minimize intra-observer error.

Data collected were entered and analyzed using the Statistical package for social sciences (SPSS) software version 21 (SPSS Inc. Chicago, IL, USA.) spreadsheet.

The categorical variables such as the demographic data were presented in standardized formats such as frequency tables and percentages for qualitative variables. The correlation between ultrasound LS measurements with the patient's mean PCV and anthropometric measurements were tested using Chi-square. A $P \leq 0.05$ was considered to be statistically significant. The confidence interval (CI) used was 95%.

RESULTS

One hundred and twenty-eight HbSS were recruited for this study with an age range between 2 and 53 years comprising 50 (39.1%) males and 78 (60.9%) females. The median age for all the patients was 19.00 years with a CI of 19.06–23.2 years. There were 56 HbSS children (2–17 years) and 72 HbSS adults (above 17 years). The median age for the children was 11.00 years with a CI of 9.35–11.36 years while the median age for the adults was 28.00 years with a CI of 27.40–31.77 years. Majority (78.1%) were single, 21.1% married and 0.8% were divorced/separated. All the study participants were educated, 25 (19.5%) had primary education, 62 (48.4%) had secondary education while 41 (32.0%) had tertiary education.

The median LS in children and adult groups of HbSS patients in this study were 7.40 cm and 4.95 cm, respectively [Table 1]. The median PCV of patients with the HbSS genotype obtained in this study was 25.0% with a CI of 24.48%–26.06%.

In the adult HbSS group, there was a significant relationship between patients with normal LS and their steady PCV. On the contrary, no significant relationship exists between the LS and the PCV in the children [Table 2].

Eight one (81) out of 128 patients had a previous history of blood transfusion however only 26 of these ones had a transfusion in the last 1 year before the study. The frequency of blood transfusion in both the adult and children with genotype HbSS showed no significant correlation with their LS [Table 3].

Table 1: Comparison between the median splenic length and packed cell volume of different age groups

Ages (years)	*n* (%)	LS			PCV		
		Median (cm)	CI (cm)	SD	Median PCV (%)	CI (%)	SD
2–17	56 (43.7)	7.40	5.74–7.57	3.42	26.00	24.50–26.60	3.55
>17	72 (56.3)	4.95	3.38–5.58	4.67	25.00	23.71–26.16	4.94
Total					128		

PCV – Packed cell volume, CI – Confidence interval, SD – Standard deviation, LS – Splenic length

Table 2: Correlation between the splenic length and steady-packed cell volume

Variable	*n*	Mean LS (cm)	Mean PCV	Pearson correlation (*r*)	*P*
Splenic size (years)					
Normal spleen (2–17)	25	7.64±1.82	24.88±3.79	0.232	0.263
Normal spleen (>17)	32	8.44±1.74	25.34±4.36	0.461	0.008*
Autosplenectomy (2–17)	9	0.00±0.00	26.11±3.72	-	-
Autosplenectomy (>17)	35	0.00±0.00	24.86±5.16	-	-
Shrunken spleen (2–17)	1	5.33	26.00	-	-
Shrunken spleen (>17)	2	4.97±1.08	21.50±3.54	1.000	-
Splenomegaly (2–17)	21	8.42±1.94	26.43±3.15	-0.181	0.432
Splenomegaly (>17)	3	13.08±0.79	22.00±6.08	0.936	0.229

*$P<0.05$ (significant). PCV – Packed cell volume, LS – Splenic length

Table 3: Correlation between splenic length and frequency of blood transfusion

Variable	Mean LS (cm)	Mean no of blood transfusion	Pearson correlation (*r*)	*P*
Splenic size (years)				
Normal spleen (2–17)	7.91±1.69	0.60±1.26	−0.021	0.953
Normal spleen (>17)	8.64±1.86	0.37±0.71	0.283	0.180
Autosplenectomy (2–17)	0.00±0.00	0.60±0.89	-	-
Autosplenectomy (>17)	0.00±0.00	0.62±1.17	-	-
Shrunken spleen (2–17)	5.33	0.00	-	-
Shrunken spleen (>17)	5.73	1.00	-	-
Splenomegaly (2–17)	7.78±0.80	0.55±0.59	−0.348	0.324
Splenomegaly (>17)	13.08±0.79	2.00±1.73	−0.243	0.843

*50 of the 128 patients had no history of blood transfusion. $P<0.05$ (significant). LS – Splenic length

There was a negative association between the LS and the age of the patients, their height as well as their weight.

DISCUSSION

Sickle cell anemia (HbSS) patients are known to be prone to some crises which may decrease their PCV and these crises should be adequately managed to prevent morbidity and mortality hence they require regular and routine follow-up. The spleen is one of the organs affected early by this disease in its size either being small or reduced to a nodule (autosplenectomy), thereby increasing their susceptibility to infections. Likewise it can be enlarged (splenomegaly) with increased accumulation of deformed red blood cells within the spleen causing its breakdown and leading to a reduction in the PCV.[24] The spleen can be objectively assessed using nonionizing ultrasonography which is easily accessible, affordable, and safe for routine follow-up.

The mean PCV of 25.2% observed in this study among the HbSS patients was similar to values obtained from previous studies in Zaria and Ibadan with 25.1% and 25.6% respectively.[6,25] This was however just slightly higher than what was observed in an earlier study in Ibadan where a mean PCV of 23%–24% was reported in the sickle cell patients studied.[26-28] This slight increase may be due to improved awareness and better recent modalities of managing the condition. The index study showed a significant correlation between the mean steady-state PCV of HbSS patients with normal splenic size. This may suggest that HbSS patients with normal splenic size have their PCV within the mean value. Although studies carried out by Brown *et al.* and Adeodu and Adekile indicated a negative correlation between the mean PCV and splenic size, this may likely be due to their subjective way of assessing the splenic size which was by palpation and not objectively by ultrasonography.[26,29]

The frequency of blood transfusion in patients with sickle cell anemia in this study showed no significance with the splenic size. This was corroborated by a study carried out by Durosinmi *et al.*[30] and may suggest that splenic size cannot be used to determine the frequency of blood transfusion in sickle cell anemia patients. The mean frequency of blood transfusion was highest in `patients with splenomegaly. This may likely be due to lower steady-state PCV from hypersplenism with recurrent sequestration crises which require frequent blood transfusion in them. This however disagrees with a study carried out in Ibadan where a higher mean frequency of blood transfusion was demonstrated among the autosplenectomy cases in the adult group.[25] This difference may be accounted for by the lower number of patients used and only adult patients were studied.

Anthropometric measurement of patients had shown to have an association with the individuals' splenic size.[21] This study observed that there was a negative correlation between the splenic dimensions of patients with sickle cell anemia (HbSS) and their anthropometric measurements (height and weight). This may be accounted for by many of the HbSS patients having short stature as a result of premature closure of their growth plate from repeated bone infarctions due to vascular occlusion by the sickled red blood cells. This was corroborated by Ehimwenma and Tagbo[21] in a study carried out on 200 adult subjects and observed that the weight and height of the subjects affected their splenic sizes, as the taller the subject, the more the increase in their splenic size with a significant linear correlation between them. Another study by Rosenberg *et al.*[31] observed that both the height and body weight of subjects had a correlation with the LS however the body weight showed a better correlation when compared to height. Konuş *et al.*[32] also observed that the height of subjects was an important determining factor of their organ size.

CONCLUSION

Normal-sized spleen on ultrasonography in sickle cell anemia patients (HbSS) may be a pointer to their steady PCV. This study, therefore, suggests the need for

ultrasonography of the spleen as part of routine follow-up investigations in HbSS patients.

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Conflicts of interest

There are no conflicts of interest.

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