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Effect of Haematocrit on Left Ventricular Dimensions and Systolic Function in Children with Sickle Cell Anaemia: A Comparative Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

This was a comparative cross-sectional study where the left ventricular dimensions and functional parameters of 41 children (aged 1 to 18 years) with sickle cell anaemia were compared with those of 52 age-and-sex matched HbAA controls using transthoracic echocardiography. Majority of the left ventricular dimensions were significantly larger in the study group than the controls ($p<0.05$). The mean indices for left ventricular systolic function were higher in the study group than the controls though not statistically significant ($p>0.05$). Left ventricular dimensions correlated positively with age and body surface area in both groups ($p<0.05$) but inversely with haematocrit in the study group especially the left ventricular internal diameters in diastole and systole and left ventricular mass ($p=0.001$). Although 14.6% - 59.5% of the changes in cardiac dimensions were attributable to age, haematocrit level and body surface area in the study group ($p<0.05$), most of this effect was due to haematocrit.

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Keywords: Left Ventricular dimensions; left ventricular systolic function; sickle cell anaemia; children; echocardiography.

1. INTRODUCTION

Sickle cell anemia is an autosomal recessive disease resulting from a single base pair substitution in the gene encoding the β-globin chain of hemoglobin [1]. It contributes significantly to the burden of chronic illnesses in Nigeria, which bears the highest burden of the disease worldwide, with 25% of the population possessing the sickle cell gene, while 2% –3% live with sickle cell anaemia [2,3]. The presence of this genetic abnormality leads to deformation of the normal concave shape of the red blood cell into a sickle shape which results in chronic anaemia due to its shortened life span [4]. The persistent state of anemia and repeated sickling that occurs in patients with sickle cell anaemia is thought to result in myocardial damage which is an important cause of morbidity and mortality in them [5].

The presence of severe chronic anaemia in patients with sickle cell anaemia triggers the onset of various compensatory mechanisms [6,7]. Cardiovascular manifestations usually occur when the haematocrit falls below 7g/dl of blood, though it is not uncommon to observe them with haematocrits as high as 9g/dl in patients with sickle cell anaemia [7,8]. In a bid to maintain adequate tissue oxygenation, there is a compensatory increase in stroke volume and heart rate [5-8]. This leads to an increase in cardiac output which occurs linearly with increasing severity of anaemia until the haematocrit drops to about 2-3g/dl - when further tissue extraction of oxygen becomes impossible.[7] This increase in cardiac output leads to significant left ventricular wall dilatation as the workload on the heart increases which results in compensatory eccentric hypertrophy of the left ventricle through increased wall thickness and myofiber elongation [5-8,9].

The increased left ventricular dimensions especially the left ventricular hypertrophy initially compensates for the chronic volume overload in patients with sickle cell anaemia which could be at a cost to the systolic function of the left ventricle [9,10]. However, most authors have described significant increases in the size of the left ventricular with preservation of systolic function in children [11-15]. With cardiac chamber dilatation and hypertrophy being common in children with sickle cell anaemia, it is imperative to further study the effect of age, body surface area and haematocrit on these echocardiographic parameters.

2. MATERIALS AND METHODS

2.1 Study Site

This was a comparative cross-sectional study conducted at the Niger Delta University Teaching Hospital Okolobiri, Bayelsa State, South-south Nigeria. The Niger Delta University Teaching Hospital is one of two tertiary health facilities in the state and also serves neighbouring Delta and Rivers States. The study was carried out over a four month period (1st November 2019 to 28th February 2020) at the Paediatric Outpatient clinic.

2.2 Study Population

The subjects were children with sickle cell anaemia aged 10 months to less to 18 years in steady state who were recruited consecutively when they presented at the Paediatric Haematology clinic of the hospital for their routine clinic visits. Exclusion criteria included the presence of underlying congenital or acquired heart diseases, the use of medications with cardiac effects and concomitant chronic illnesses like asthma, severe malnutrition and tuberculosis. Those who had received blood transfusion in the preceding three months or those who had crises in the one month prior to the study were also excluded. Controls were age and sex matched children with Haemoglobin AA phenotype.

2.3 Data Collection

Each subject and control had a thorough physical examination and anthropometry performed. Weight was measured in kilograms using a SECA® weighing scale to the nearest 0.1kg. Height was measured in centimetres with child placed on a fixed stadiometer to the nearest 0.1cm and converted to metres. Body surface area was derived for each participant using the Mosteller formula [16] and their haematocrits were also estimated. Thereafter, a complete transthoracic echocardiogram, was performed on each child using a portable My Lab Gamma Esaote® cardiac ultrasound machine fitted with 1-

4Hz and 3-12Hz frequency probes. Left ventricular dimensions in systole and diastole were measured according to the American Society of Paediatric Echocardiography guidelines [17]. M-mode measurements of the left ventricle were taken in the short axis view of the left ventricle at the level of the papillary muscles using the leading edge to leading edge technique. Percentage fractional shortening and the ejection fraction were derived from these dimensions and calculated automatically by the machine. Left ventricular systolic dysfunction was considered present if the fractional shortening was less than 28% or the ejection fraction was less than 50%.

2.4 Statistical Analyses

Data including participants' ages and gender was imputed into an Excel® spreadsheet and analyzed using SPSS 22.0. A test of normality was conducted and means of all continuous variables were compared using the student t-test. The relationship between left ventricular dimensions, functional parameters and age, body surface area and haematocrit was investigated using Pearson's test of correlation. The predictive value of the explanatory variables (age, body surface area and haematocrit level) was explored using a multivariate linear regression analysis. The predictive model exploring the relationship between the cardiac dimensions/functional parameter and age, body surface area and haematocrit level among children with sickle cell anaemia and the control group is presented with the linear regression equation as shown below:

$$y = b_0 + b_1X_1 + b_2X_2 + b_3X_3$$

Where

y is the predicted cardiac dimension/functional parameter in question
b_0 is the constant, b_1 is the coefficient for explanatory variable X_1 (Age),
b_2 is the coefficient for explanatory variable X_2 (Haematocrit level) and
b_3 the coefficient for explanatory variable X_3 (Body Surface Area).

The adjusted R square (an estimate of total variation in the dependent variables that can be explained by the model), the f-ratio (a reflection of the fitness of the model, and its efficiency in predicting the dependent variables) and the regression coefficients for each component of the model was calculated. A p-value less than 0.05 was considered statistically significant.

3. RESULTS

3.1 Anthropometry and Clinical Characteristics of Children in the Study

A total of 93 children were recruited for the study of which 47.3% were male and 52.7% were female. Their ages ranged from 10 months to 18 years with a mean age of 9.3 ± 4.5 years. The mean weight, height and body surface area of the total children in study was 30.2±14.3kg, 1.29±0.24m and 1.0±0.3m^2 respectively. The children in the study group were similar in age, weight, height, body surface area and systolic blood pressure to the control group ($p > 0.05$). However, mean values of clinical indices like oxygen saturation, diastolic blood pressure and haematocrit level were significantly lower in the study group when compared to the control group ($p=0.001$). Significantly higher values were also reported for pulse ($p=0.001$) and respiratory rates ($p=0.028$) in the study group compared to controls (Table 1).

3.2 Left Ventricular Dimensions and Functional Parameters of the Study Group and Controls

All the mean left ventricular dimensions were larger in the study group than the control group. These differences were statistically significant for all parameters except the left ventricular Interventricular septal thickness in diastole ($p=0.059$) and left ventricular Internal diameter in systole ($p =0.120$). The indices for left ventricular systolic function were also higher in the study group than the controls - ($p=0.069$ and $=0.052$ for Ejection Fraction and Fractional Shortening respectively) but the differences were not statistically significant. (Table 2). Using the cutoff of 28% for Fractional Shortening and 50% for Ejection Fraction, there was no case of LV systolic dysfunction in both groups.

3.3 Relationship between Left Ventricular Dimensions, Functional Parameters and Age and Body Surface Area of the study Group And Controls

As expected, there was a significantly positive correlation noted between age and body surface

area, and the different cardiac dimensions assessed in both the study and control groups ($p<0.05$). This implies that the cardiac dimensions increase as the children grow older and with increasing body surface area. The functional parameters in both groups showed an inverse relationship with age and body surface area which was not statistically significant except for the relationship of the Ejection fraction and the body surface area ($p = 0.044$) in the study group (Tables 3 & 4).

3.4 Relationship between Cardiac Dimensions and Functional Parameters, and Haematocrit of the Study Group and Controls

In the study group, there was an inverse relationship between the cardiac dimensions (except the Interventricular Septal diameter in diastole) and haematocrit level implying that these parameters increase with declining haematocrit levels. However, only the

Table 1. Age, anthropometric measures and vital signs among 41 children with sickle cell anaemia and 52 controls

Characteristics	SCA (n=41)		Controls (n=52)		Statistical test	
	Mean	SD	Mean	SD	t-test	p-Value
Age (years)	8.8	5.0	9.7	4.0	1.00	0.313
Weight (kg)	27.6	13.8	32.3	14.6	1.57	0.121
Height (m)	1.26	0.27	1.32	0.21	1.35	0.181
BSA (m^2)	0.9	0.3	1.1	0.3	1.56	0.123
Oxygen saturation (%)	96.7	2.5	98.5	0.9	4.78	0.001*
Respiratory rate (c/min)	25.8	4.3	23.6	4.4	2.24	0.028*
Pulse Rate (beats/min)	101.8	12.6	90.9	15.4	3.56	0.001*
Systolic BP (mmHg)	92.9	13.1	94.1	10.4	0.47	0.643
Diastolic BP (mmHg)	54.2	10.7	61.2	6.9	3.74	0.001*
Haematocrit (%)	23.2	3.4	37.6	2.5	23.6	0.001*

Note: SCA – sickle cell anaemia; kg – kilograms; c – cycles; m – metre; mmHg - millimetres of mercury; min – minute; % - percent; m^2 - metre squared; SD - standard deviation

Table 2. Left Ventricular dimensions and Functional Parameters among 41 children with sickle cell anaemia and 52 controls

Characteristics	SCA	Control	Statistical test	
	Mean (SD)	Mean (SD)	t-Test	pValue
Cardiac dimensions				
Interventricular septal diameter in systole (mm)	17.1 (4.7)	14.6 (4.3)	2.64	0.010*
Interventricular septal diameter in diastole (mm)	13.0 (3.2)	11.8 (3.1)	1.91	0.059
Left ventricular Internal diameter in systole (mm)	24.7 (5.4)	23.0 (4.3)	1.57	0.120
Left ventricular Internal diameter in diastole (mm)	40.5 (6.6)	36.5 (5.3)	3.22	0.002*
Posterior wall in systole (mm)	14.5 (3.4)	12.9 (2.8)	2.58	0.012*
Posterior wall in diastole (mm)	10.1 (3.2)	9.0 (2.0)	2.02	0.047*
Left ventricular mass (g)	199.8 (97.8)	137.9 (64.8)	3.64	0.001*
Functional parameters				
Ejection fraction (%)	70.2 (7.2)	67.4 (7.3)	1.84	0.069
Fractional shortening (%)	39.3 (5.5)	37.1 (5.7)	1.97	0.052

Note: SCA – sickle cell anaemia; mm – millimetres; % - percent;, g – gram; SD- Standard deviation, statistical significance (p<0.005)

relationship between the Left ventricular internal diameter in diastole and haematocrit (r - -0.36; p – 0.023) showed statistical significance (Table 5).

3.5 Effect of Age, Body Surface Area and Haematocrit on Left Ventricular Structure and Functional Parameters using a Predictive Model

In the model summary results presented in Table 6, the adjusted R square ranged between 0.146 for the interventricular septal diameter in diastole and 0.595 for the left ventricular mass among the study group. This implies that between 14.6% and 59.5% of changes in cardiac dimensions is influenced by the interaction between age, haematocrit level and body surface area among children with sickle cell anaemia. The F-ratio shows that the model is most efficient in predicting the left ventricular mass in children in both the study and control groups. Although the cardiac dimensions in the control group are also influenced by this regression model, the variabilities are not as marked as observed in the study group. Table 6 further reveals that the functional parameters in both groups are not affected by the age, haematocrit level and body surface area ($p > 0.05$).

The regression coefficients as presented in Table 7 show that the variables in the model do not demonstrate enough magnitude to individually impact on most of the cardiac dimensions and functional parameters in the study and control groups. However, haematocrit level (*b* - -0.60; p – 0.013) and body surface area (*b* – 13.41; p – 0.023) demonstrated a statistically significant magnitude in the prediction

Table 3. Correlation of Left ventricular dimensions and functional Parameters with age of 41 children with sickle cell anaemia and 52 controls

Characteristics	SCA		Control	
	r	p-Value	r	p-Value
Cardiac Dimensions				
Interventricular septal diameter in systole (mm)	0.50	0.001*	0.32	0.022*
Interventricular septal diameter in diastole (mm)	0.39	0.012*	0.36	0.008*
Left ventricular Internal diameter in systole (mm)	0.57	<0.001*	0.59	<0.001*
Left ventricular Internal diameter in diastole (mm)	0.65	<0.001*	0.60	<0.001*
Posterior wall in systole (mm)	0.65	<0.001*	0.41	0.003*
Posterior wall in diastole (mm)	0.69	<0.001*	0.36	0.008*
Left ventricular mass (g)	0.76	<0.001*	0.66	<0.001*
Functional Parameter				
Ejection fraction (%)	-0.25	0.118	-0.27	0.053
Fractional shortening (%)	-0.21	0.185	-0.24	0.094

r - Pearson's correlation coefficient; SCA – sickle cell anaemia, mm – millimetres % - percent; g – gram; , statistical significance (p<0.005)

Table 4. Correlation of Left ventricular dimensions and functional Parameters with Body Surface Area of 41 children with sickle cell anemia and 52 controls

Characteristics	SCA		Control	
	r	pValue	r	pValue
Cardiac Dimensions				
Interventricular septal diameter in systole (mm)	0.55	<0.001*	0.33	0.018*
Interventricular septal diameter in diastole (mm)	0.45	0.004*	0.38	0.006*
Left ventricular Internal diameter in systole (mm)	0.58	<0.001*	0.60	<0.001*
Left ventricular Internal diameter in diastole (mm)	0.63	<0.001*	0.64	<0.001*
Posterior wall in systole (mm)	0.57	<0.001*	0.42	0.002*
Posterior wall in diastole (mm)	0.60	<0.001*	0.34	0.013*
Left ventricular mass (g)	0.73	<0.001*	0.69	<0.001*
Functional Parameter				
Ejection fraction (%)	-0.32	0.044*	-0.24	0.093
Fractional shortening (%)	-0.28	0.076	-0.18	0.210

r - Pearson's correlation coefficient; SCA – sickle cell anaemia; mm – millimetres; % - percent; g – gram; , statistical significance (p<0.005)

Table 5. Correlation of Left ventricular dimensions and functional Parameters with haematocrit level of 41 children with sickle cell anaemia and 52 controls

Characteristics	SCD		Control	
	r	p-Value	r	p-Value
Cardiac Parameters				
Interventricular septal diameter in systole (mm)		0.08	-0.07	0.622
Interventricular septal diameter in diastole (mm)	-0.03	0.857	0.06	0.677
Left ventricular Internal diameter in systole (mm)	-0.28	0.074	0.21	0.129
Left ventricular Internal diameter in diastole (mm)	-0.36	0.023*	0.16	0.273
Posterior wall in systole (mm)	-0.23	0.152	0.01	0.956
Posterior wall in diastole (mm)	-0.21	0.199	-0.07	0.620
left ventricular mass (g)	-0.28	0.085	0.08	0.554
Functional Parameter				
Ejection fraction (%)	0.08	0.611	-0.21	0.137
Fractional shortening (%)	0.06	0.723	-0.20	0.149

r - Pearson's correlation coefficient; SCA-sickle cell anaemia; mm-millimetres; %-percent, g-gram, statistical significance (p<0.005)

of left ventricular internal diameter in systole. Table 7 further shows that the haematocrit level also impacts significantly on left ventricular internal diameter in diastole (*b* - - 0.77; p – 0.004) and left ventricular mass (*b* - - 7.23; p – 0.050).

Table 6. Summary statistics of the predictive model for cardiac dimensions and functional parameters among 41 children with sickle cell anaemia and 52 controls

Variable	SCA				Control			
	Adjusted R square	Standard Error	F-ratio	P Value	Adjusted R square	Standard Error	F-ratio	P Value
Cardiac dimensions								
Interventricular septal diameter in systole (mm)	0.243	4.09	5.29	0.004*	0.087	4.19	2.62	0.061
Interventricular septal diameter in diastole (mm)	0.146	2.99	3.28	0.032*	0.096	2.96	2.81	0.049*
Left ventricular Internal diameter in systole (mm)	0.406	4.18	10.10	0.001*	0.334	3.51	9.554	0.001*
Left ventricular Internal diameter in diastole (mm)	0.509	4.60	14.81	0.001*	0.379	4.19	11.39	0.001*
Posterior wall in systole (mm)	0.392	2.69	9.58	0.001*	0.147	2.60	3.94	0.014*
Posterior wall in diastole (mm)	0.441	2.41	11.52	0.001*	0.109	1.90	3.08	0.036*
left ventricular mass (g)	0.595	62.20	20.11	0.001*	0.481	46.67	16.74	0.001*
Functional parameters								
Ejection fraction (%)	0.077	6.91	2.11	0.115	0.045	7.14	2.11	0.161
Fractional shortening (%)	0.048	5.46	1.67	0.191	0.040	5.63	1.71	0.178

SCA – sickle cell anaemia; mm – millimetres; % - percent; g – gram;, statistical significance (p<0.005)

Table 7. The regression coefficients of Age, Haematocrit level and BSA for the different cardiac dimensions among 41 children with sickle cell anaemia and 52 Controls

Variable	SCA					Control				
	Regression Coefficient	95%CI		T test	P Value	Regression Coefficient	95%CI		T test	P Value
		Min	Max				Min	Max		
Interventricular septal diameter in systole (mm)										
Age in months	0.01	-0.06	0.07	0.15	0.881	0.01	-0.05	0.06	0.15	0.881
Haematocrit level	0.08	-0.37	0.53	0.36	0.721	-0.33	-0.83	0.17	-1.32	0.193
Body surface area	6.54	-4.73	17.80	1.18	0.247	4.76	-4.05	13.58	1.08	0.283
Interventricular septal diameter in diastole (mm)										
Age in months	-0.02	-0.06	0.03	-0.64	0.526	0.01	-0.03	0.05	0.32	0.746
Haematocrit level	-0.11	-0.44	0.22	-0.65	0.518	-0.07	-0.43	0.28	-0.41	0.679
Body surface area	6.62	-1.62	14.86	1.63	0.112	3.02	-3.21	9.25	0.97	0.335
Left ventricular Internal diameter in systole (mm)										
Age in months	-0.03	-0.09	0.04	-0.76	0.454	0.02	-0.02	0.07	1.03	0.308
Haematocrit level	-0.60	-1.06	-0.14	-2.62	0.013*	0.08	-0.34	0.50	0.39	0.696
Body surface area	13.41	1.92	24.90	2.37	0.023*	4.61	-2.77	11.99	1.25	0.216
Left ventricular Internal diameter in diastole (mm)										
Age in months	0.01	-0.08	0.07	-0.03	0.978	0.01	-0.05	0.07	0.31	0.761
Haematocrit level	-0.77	-1.27	-0.26	-3.06	0.004*	-0.10	-0.60	0.40	-0.40	0.692
Body surface area	12.40	-0.28	25.07	1.98	0.055	9.84	1.01	18.67	2.24	0.030*
Posterior wall in systole (mm)										
Age in months	0.04	-0.01	0.08	1.74	0.090	0.01	-0.03	0.04	0.28	0.780
Haematocrit level	-0.14	-0.43	0.16	-0.94	0.355	-0.15	-0.46	0.16	-0.96	0.341
Body surface area	-0.22	-7.62	7.19	-0.06	0.953	3.45	-2.02	8.93	1.27	0.211
Posterior wall in diastole (mm)										
Age in months	0.04	0.00	0.08	2.19	0.035	0.01	-0.02	0.03	0.69	0.497
Haematocrit level	-0.08	-0.35	0.18	-0.63	0.532	-0.15	-0.37	0.08	-1.29	0.204
Body surface area	-1.07	-7.72	5.57	-0.33	0.745	1.35	-2.65	5.35	0.68	0.500

Variable	SCA					Control				
	Regression Coefficient	95%CI		T test	P Value	Regression Coefficient	95%CI		T test	P Value
		Min	Max				Min	Max		
left ventricular mass (g)										
Age in months	0.40	-0.64	1.43	0.78	0.443	0.16	-0.47	0.79	0.51	0.614
Haematocrit level	-7.23	-14.45	-0.01	-2.03	0.050*	-3.66	-9.24	1.91	-1.32	0.193
Body surface area	143.35	-30.54	317.23	1.67	0.103	129.83	31.71	227.96	2.66	0.011
Functional Parameter Ejection fraction (%)										
Age in months	0.07	-0.04	0.18	1.26	0.216	-0.06	-0.15	0.04	-1.16	0.252
Haematocrit level	0.46	-0.31	1.22	1.21	0.234	-0.52	-1.37	0.34	-1.22	0.228
Body surface area	-17.77	-36.80	1.26	-1.89	0.066	3.43	-11.58	18.43	0.46	0.648
Fractional shortening (%)										
Age in months	0.05	-0.04	0.14	1.21	0.233	-0.06	-0.13	0.02	-1.48	0.146
Haematocrit level	0.31	-0.30	0.91	1.03	0.310	-0.46	-1.13	0.22	-1.37	0.178
Body surface area	-13.05	-28.09	1.99	-1.76	0.087	5.53	-6.30	17.36	0.94	0.352

SCA – sickle cell anaemia; mm – millimetres; % - percent , g-gram, statistical significance (p<0.005)

4. DISCUSSION

Studies on the left ventricular structural and functional changes of children with sickle cell anaemia have been described by other authors but with slightly varying findings.[11-14] Our study showed significantly increased mean left ventricular chamber dimensions in the study group compared to the control group. These differences were statistically significant for all parameters except the Interventricular septal thickness in diastole and left ventricular internal diameter in systole. Increased chamber dimensions have similarly been described in children with sickle cell anaemia by various authors [8,12-15]. Bamigboye-Taiwo et al.[12] in Ile-Ife and Animashaun et al. [13] in Lagos, both in South West Nigeria similarly described significantly larger left ventricular dimensions of children with sickle cell anaemia than controls, although both studies noted statistically larger Interventricular septal thickness in diastole and left ventricular internal diameter in systole in contrast to our findings. The studies by Omokhodion et al. [14] and Bamigboye-Taiwo et al. [13] also found no significant differences in the left ventricular posterior wall thickness between the study group and controls, unlike the present study which demonstrated a larger dimension of this parameter in the study group. The reason for the differences in the individual chamber enlargements between these studies is not immediately clear but may be due to the older ages of children in the present study compared to those previous studies. There is, however, a converging view that cardiac dimensions are larger among children with sickle cell anaemia compared to their age and sex-matched counterparts.

Increase in cardiac size of children with sickle cell anaemia is not unexpected, as the chamber size dilatation and hypertrophy can be attributed to the chronic state of anaemia which leads to various compensatory mechanisms [5-8]. Arteriolar dilatation and decreased afterload results in an increase in the stroke volume and therefore cardiac output [5-8]. The resulting increase in venous return to the heart causes a chronic volume overload state, which over time leads to cardiac chamber enlargement and left ventricular hypertrophy [5-8]. It was thus not surprising that significantly larger left ventricular dimensions and left ventricular mass in sickle cell anaemia patients was reported in our study, which was similar to previous reports [8,12-14,18,19]. Saidu et al18 who studied sickle cell anaemia patients 13 years and older similarly reported increases in left ventricular dimensions and mass in their study while Gerry et al19 described greater hypertrophy in adults than children with sickle cell anaemia which was attributed to the progressive increase in ventricular wall stress with time.

Left ventricular systolic function was noted to be within normal limits in both the patients with sickle cell anaemia and controls in our study despite changes in left ventricular chamber sizes. Normal systolic function has been widely reported among both children and adults with sickle cell anaemia [12-14,18,20-22] and has been attributed to the increase in blood volume and preload which help to maintain normal ventricular function in chronic anaemic states [7]. Although the left ventricular functional parameters were similar in both of our study groups, they were noted to be higher in the sickle cell anaemia patients compared to the controls. Higher functional indices are to be expected in children with sickle cell anaemia because of the increased preload and reduced afterload which enhances ventricular pump performance in chronic anaemia.10 Our findings correspond to reports from other authors who noted similar functional parameters in sickle cell anaemia patients and controls [8,12-14,23-25]. Using the Doppler myocardial performance index to determine cardiac function, Lamers et al. [24] who studied children between the ages of 3 months and 18 years reported lower percentage fractional shortening in sickle cell anaemia children than controls. Arslankoylu et al. [26] however using similar load independent echocardiographic indices, reported higher functional parameters in sickle cell anaemia children though they were within normal limits.

Our study showed a positive correlation between age and body surface area, and the left ventricular cardiac dimensions and left ventricular mass in both groups which implies that cardiac dimensions increase as the children grow older and with increasing body surface area. Similar relationships have been described by other authors [8,12,14] and have been attributed to the normal age dependent effect of growth and development on the heart in children [27]. However, the functional parameters showed an inverse relationship with age and body surface area in sickle cell anaemia children and controls in the present study implying that systolic function may decrease with increasing age and body surface area. This finding is at

variance with the report from Bamigboye-Taiwo et al. [12] who found no relationship between left ventricular systolic function and body surface area in the study and control groups. Poludasu et al. [25] and San et al. [28] reported similar findings to ours and noted that in children with sickle cell anaemia, left ventricular structural and functional abnormalities were age dependent and were associated with progressive left ventricular dilatation and impairment of systolic function over time. This can be explained by the chronic anaemia which is associated with abnormal loading conditions that eventually lead to chamber dilatation and myocardial remodeling which results in ventricular dysfunction [28].

As to be expected, the mean haematocrit of the children with sickle cell anaemia was significantly lower than that of the controls. The study group also demonstrated a greater increase in cardiac dimensions in relation to decreasing haematocrit compared to the controls. The predictive regression model showed a significant impact of age, body surface area and haematocrit on left ventricular diameters and left ventricular mass, with 14.6% to 59.5% of changes being attributed to these variables. However what was more striking was the significant effect of haematrocrit level in predicting left ventricular internal dimensions and left ventricular mass in the sickle cell children. Oguanobi et al [29] found that haematocrit accounted for 8% of the changes to the left ventricular mass of adult sickle cell patients with severe anaemia and also described an inverse relationship of cardiac mass to haematocrit levels. Ali et al. [22], Lamers et al. [24] and Harrington et al. [30] similarly found that increases in left ventricular dimensions and mass correlated with severity of anaemia in children with sickle cell anaemia. Our report however contrasts with findings of other Nigerian authors [12-14] and of Cipolotti et al. [31] in Spain who found no relationship between the cardiac dimensions and haematocrit levels for subjects and controls in their studies. Different sampling methods in the various studies could account for these differences. The effect of chronic anaemia on cardiac dimensions is to be expected as the anaemia is compensated by high cardiac output with minimal increase in heart rate. The resultant increase in left ventricular stroke volume leads to chamber enlargement and cardiomegaly [5-8]. The lack of effect of haematocrit on the systolic function of sickle cell patients was also noted in our study. Batra et al. [32] who studied 77 sickle cell subjects aged 2-22 years similarly reported normal systolic function in those who had lower haematocrit and larger left ventricular dimensions and mass when load-independent measures of systolic function were used compared to the sickle cell group on chronic transfusion. The hyperdynamic state of children with sickle cell anaemia leads to decreased peripheral resistance thus preserving systolic function even in the presence of chronic anaemia.

Our study is not without its limitations. Despite the fact that we were able to demonstrate a significant effect of haematocrit on the echocardiographic parameters measured, the individual impact of age and body surface area using the predictive model was not clearly demonstrated. This could be attributed to the small sample size of our study population.

5. CONCLUSION

Left ventricular chamber dimensions are larger in children with sickle cell anaemia and tend to increase with age and increasing body surface area though systolic function remains normal. Increases in left ventricular dimensions and mass correlate with increasing age, body surface area and decreasing haematocrit in children with sickle cell anaemia and controls but the effects are greater in the sickle cell group. However, the most significant impact is that of increasing severity of anaemia on left ventricular internal dimensions and mass in children with sickle cell anaemia.

CONSENT AND ETHICAL APPROVAL

Ethical clearance was obtained from the Research and Ethics Committee of the Niger Delta University Teaching Hospital Okolobiri Bayelsa State prior to commencement of the study. Parental informed consent and assent (where applicable) were obtained from all the subjects.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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