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Relationship of age, anthropometry and haemoglobin concentration with echocardiographic findings in Nigerian children with sickle cell anaemia.

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Abstract *Background:* Assessment of the structural and functional effects of sickle cell anaemia (SCA) on the heart can be done using echocardiography. There has been no agreement on which indicator of body size (weight, height, and body surface area (BSA)) or age in children should be used to relate to and correct echocardiographic measurements.
Aim: To correlate the echocardiographic findings of children with SCA aged one to fifteen years in steady state with their age, anthropometry and haemoglobin concentration.
Methods: A prospective study carried out at the Lagos University Teaching Hospital (LUTH), between May and October 2005. The subjects were 60 paediatric patients attending the LUTH SCA outpatient clinic and 60 age, sex and socio-economic matched controls. Their height, weight, and echocardiographic parameters were measured and their BSA and haemoglobin level were determined.
Results: The direct echocardiographic measurement (AO, LA, LVPW, EDD, ESD, IVS) and LVM each increased progressively with body weight, height, body surface area and age in both subjects and controls ($r > 0.3$, $p < 0.001$ in each case). Multivariate analysis showed that height correlated significantly with AO, ESD, EDD and LVPW in the subjects. All the parameters except age were significantly correlated with LVM both in univariate and multivariate analysis.
Conclusion: Echocardiographic parameters in SCA patients are significantly correlated with anthropometric indices and age. Our data suggest best correlation with height in these subjects.

Keywords: Sickle cell anaemia, Echocardiographic parameters, Anthropometry, Steady state

Introduction

Sickle cell anaemia affects practically every system in the body and may sometimes present as crisis situations. Some of the chronic manifestations involve the cardiovascular system as a result of chronic anaemia and recurrent crisis. [1-6] Different studies in normal children have shown the fact that cardiac dimensions increase with age, weight, height and body surface area [7-8]

Oberhansli, Brandon, Lacourt *et al*[8] studied a cohort of 21 normal babies sequentially by M-mode echocardiography during the first year of life and correlated their results with age, weight and length and found that the end diastolic and end systolic diameters of the left ventricle, the diameters of the left atrium (LA), the aorta (AO) as well as septal and left ventricular posterior wall thickness (IVS and LVPW) followed a linear correlation with age and weight.

In conformity with the previous studies, Sutton, Pickard, Oldershaw *et al*[9] also documented increased cardiac dimensions with age in a group of 78 normal children aged one to 12 years.

Oladokun [10] in her study of 183 normal children aged 1 to 12 years in Ibadan noted that all the direct echocardiographic measurements in her study correlated strongly with age, weight and body surface area (BSA). Among the derived parameters, Left ventricular mass (LVM) was also highly correlated with these parameters but Fractional Shortening (FS), Ejection Fraction (EF) and LA/AO ratio showed a weak negative correlation. The BSA correlated best with the echocardiographic parameters studied, followed by height, weight and then age. These findings were consistent with the observations made by Sollinger *et al*[11] Henry *et al* [12] and Roge, Silverman, Hart. [13]

There have also been reports of cardiac dimensions in sickle cell anaemia patients. [5-6, 14-15] The findings are similar to reports from normal patients. Balfour, Covitz, Doris *et al*[5] in a study comparing 124 patients with HbSS referred to a tertiary centre in the USA with 78 healthy controls noted that the left ventricular and left atrial dimensions in the patient group increased with age. This study also found a linear relationship between the cardiac dimensions namely the left atrial dimension, left ventricular EDD, left ventricular wall dimension and the left ventricular mass and the BSA.

Similarly, Lester *et al*[6] in 1990 evaluated 44 children with HbSS aged 2 months to 18 years using M-mode echocardiography and reported the relationship between cardiac dimensions, weight and BSA. The study found a direct linear relationship between the left ventricular EDD, left ventricular mass, aortic root dimensions, left atrial dimensions and the weight of the patients. The dimensions obtained in the study were also observed to increase with age. Similar findings have also been documented by Covitz *et al* [14] who found that the right and left ventricular diastolic dimensions, left ventricular free wall and septal thickness, left atrial dimension, and aortic root dimensions were significantly and directly correlated with BSA.

In all the above studies, a multivariate analysis using these parameters were never carried out hence the need for this study which is aimed at documenting the parameter which best correlate with echocardiographic parameters.

Subjects and methods

This was a prospective, cross sectional and analytical study carried out at the Lagos University Teaching Hospital (LUTH), Idi-Araba, Nigeria as part of a large study between May 2005 and October 2005. The subjects included 60 paediatric patients attending the LUTH sickle cell anaemia outpatient clinic and were consecutively recruited. They had haemoglobin genotype 'SS' confirmed with haemoglobin electrophoresis (as documented in the file) and were aged 12 months to 15 years. They were in steady state at the time of recruitment.

Inclusion criteria for the controls included: Haemoglobin AA, absence of congenital or acquired heart defects, absence of respiratory or renal disease, and absence of protein energy malnutrition and haemoglobin concentration of 10g/l or higher.

Patients with congenital or acquired heart disease, renal disease and hypertension were excluded from the study. Healthy controls were from the Community Health Outpatient and Well baby clinics and healthy children attending other clinics at the Paediatric outpatient department (POD) and were matched for age and sex and socioeconomic class.

The Transthoracic echocardiographic studies were performed on each using a Hewlett-Packard SONOS 500 machine and transducer with a frequency of 5MHz. A baseline two-dimensional echocardiographic examination was carried out on each subject to ascertain normal intracardiac segmental anatomy. The M-mode recording was derived with the simultaneous recording of a 2D – mapping to ensure precision in location and direction of the M-mode cursor. Cardiac measurements were obtained according to the recommendations of the committee on m-mode standardization of the America Society of Echocardiography.[16] These include aortic root dimension (AO), left atrial dimension (LA), left ventricular end diastolic diameter [LVEDD], left ventricular end systolic diameter [LVESD], interventricular septal thickness [IVS], left ventricular posterior wall thickness [LVPW] . The left ventricular ejection fraction (EF), fractional shortening (FS) and left ventricular mass were derived from the m-mode measurements. Haemoglobin concentration was determined using oxy-haemoglobin method.

Height was measured to the nearest 0.5cm with the child barefoot, standing erect with the heels together against the wall, and looking straight ahead with the back against the graduated wall [17]. The height was read with a wooden ruler resting on the scalp and against the wall. Length was measured using an infantiometer. [17] Subjects were weighed standing barefoot, wearing only their underware using a Seca® scale. Weight was read to the nearest 0.1kg. The scale was calibrated with a standard weight after every 10th measurement or whenever it was moved from place to place. [17] All the participants could walk.

BSA was estimated using a body surface area normogram based on weight and height.[17] Each subject and control also had venous blood sample taken for estimation of haemoglobin level.

Data was analyzed using Microsoft Excel program supplemented by Megastat statistical package. Mean, standard deviation and other parameters were generated as necessary for continuous data. The subjects and controls included were compared using student t-test for continuous data, and chi-square test for discrete data. The Pearson correlation coefficient r was calculated to determine the relationship between the cardiac measurements, age, weight, height, body surface area, as well as haemoglobin concentration. Univariate and multivariate correlation analysis was used to study the relationships between selected continuous sets of data. The coefficients of correlation and associated p-values were derived. Statistical significance was set at p-value < 0.05.

Ethical clearance for the study was obtained from the ethical committee of the Lagos University Teaching Hospital and informed consent was sought from parent or care givers of subjects and controls before enrolment into the study.

Results

A total of 120 children were recruited into the study. Of this number, 60 were test subjects in the 12 months to 15 years age bracket *(Mean = 95.41 ± 49.06 months)* confirmed to have genotype SS by haemoglobin electrophoresis. They were all in steady state. The control group consisted of 60 children within the same age bracket *(mean = 95.4 ± 50.92 months) (t = 0.04, p = 0. 96)* who had haemoglobin genotype AA. The mean (SD) haemoglobin level in the subjects was significantly lower than in the controls (77.23 ± 12.88g/L Vs 121 ± 16.09g/L, p< 0.001)

Correlation of echocardiographic measurements with weight, height, body surface area and age

The Univariate correlation of echocardiographic measurements with weight, height and body surface and age, each shows that the echocardiographic measurements namely the AO, LA, EDD, ESD, LVPW,IVS and the LVM each increased progressively with body weight, height, age and BSA in the study population ($r > 0.3$ and $p < 0.001$). There was no significant association between weight and FS, EF, and LA/AO in the study population ($p > 0.1$).

Haemoglobin concentration

In the correlation between the echocardiographic measurements and haemoglobin concentration in the subjects, there was significant linear relationship between haemoglobin level (Hb) and the following echocardiographic parameters namely; AO, EDD, ESD, in the controls.
In addition, IVS, FS, EF, and LA/AO were inversely related to haemoglobin level in the controls but the strength of the relationship was not statistically significant. Similarly a weak and non-significant inverse relationship was observed between most of the echocardiographic measurements (LA, LA/AO, EDD, ESD, LVPW, FS, EF, and LVM) and the haemoglobin level in the subjects ($r < - 0.1$, $p > 0.3$).

Multiple regression

The results show that height correlated significantly with AO and ESD in subjects and controls. It also remained significantly correlated to EDD and LVPW in the subjects. While weight remained significantly correlated to LA and LA/AO in the subjects and surprisingly was significantly correlated to FS and EF in the controls. However HB which did not achieve any significant correlation with any of the echo parameters on univariate analysis was found to be significantly correlated with LVM. All the parameters (Height, Weight, BSA, HB) except age were significantly correlated with LVM both in univariate and multivariate analysis. Age that showed significant correlation on univariate analysis to all the direct echo parameters and LVM was only significantly correlated with LVPW in subjects in the multiple regression models.(Table1 and 2).

Table 1: Multiple regression models with age, height, weight and haemoglobin level as independent variable and the direct echo parameters as dependent variables in subjects.

Echo parameter		Age	HB	HT	WT	R^2	p	
AO	t	0.12	0.07	2.40	-0.41	0.53	0.000000003	
	p	0.91	0.94	0.02	0.68			
LA	t	-0.83	-1.01	0.98	3.28	0.58	0.0000000132	
p	0.41	0.32	0.33	0.02				
EDD	t	-0.64	-1.00	2.34	1.33	0.61	0.00000000118	
p	0.53	0.32	0.02	0.19				
ESD	t	0.84	-0.24	2.47	-0.04	0.40	0.0000151	
	p	0.40	0.82		0.02	0.97		
LVPW	t -2.01	0.20	2.34	0.49	0.20	0.003		
	p	0.04	0.84		0.02	0.63		
IVS	t	-1.00	0.06		0.69	1.61	0.14	0.01
	p	0.32	0.95		0.49	0.11		

Table 2: Multiple regression models with age, height, weight and haemoglobin level as independent variable and the derived echo parameters as dependent variables in subjects.

Echo parameter		Age	Hb	HT	WT	R^2	p
LA/AO	t	-0.67	-0.81	-0.80	2.25	0.03	0.24
	P	0.51	0.42	0.43	0.03		
FS	t	0.73	-0.57	-1.28	1.19	0.12	0.03
	P	0.47	0.57	0.21	0.24		
EF	t	0.59	-0.81	-1.19	1.28	0.02	0.57
	P	0.56	0.42	0.24	0.21		

BSA correlated significantly with LA, EDD and LVPW in subjects. However Hb which did not achieve any significant correlation with any of the echo parameters on univariate analysis was found to be significantly correlated with LVM. All the parameters (height, weight, BSA, HB) except age were significantly correlated with LVM both in univariate and multivariate analysis. (table 3)

Table 3: Multiple regression models with age in months, body surface area (BSA) and haemoglobin level (HB) as independent variable and the direct echo parameters as dependent variables in subjects.

Echo parameter	Age t p	BSA t p	Hb t p	R	p value
AO	1.49	1.87	0.24	0.51	0.00001
	0.14	0.07	0.81		
LA	-0.63	4.22	-0.81	0.56	0.00001
	0.53	0.0001	0.42		
EDD	0.64	3.32	-0.74	0.66	0.00001
	0.52	0.002	0.46		
ESD	0.75	1.76	0.00	0.36	0.00001
	0.46	0.08	0.99		
LVPW	-0.89	2.27	0.43	0.15	0.0065
	0.38	0.03	0.67		
IVS	-0.50	-1.84	1.91	0.16	0.0048

Discussion

This study aimed to correlate the echocardiographic measurements with the weight, height, age, body surface area and haemoglobin level of study subjects and to compare this with those of healthy age, sex and socio-economic class matched controls using univariate and multivariate analysis to be able to document which of the anthropometric parameters best correlate with echocardiographic parameters.

In this study, most of the direct echocardiographic parameters and the LVM increased progressively with anthropometric indices i.e. body weight, height and BSA in both subjects and controls. This finding is similar to those of earlier studies [5,6] .The functional parameters (FS and EF) were independent of the anthropometric indices in both groups. This implies that irrespective of body dimensions, the percentage of blood ejected by the ventricles and the degree of the myocardial contractility with each heart best remains constant in order to maintain the normal body physiology.

Similarly, most of the echocardiographic parameters showed a direct linear relationship with the age in both groups. The correlation between age and echocardiographic findings was also noted by Balfour et al[5] and Cipolotti et al[15]. This linear increase of the cardiac dimensions with increasing age is in keeping with the normal age-dependent effect of growth and development on the heart [11]. However, the functional parameters (FS and EF) in this study did not show a significant relationship with age. Pombo et al[18] and Covarrubias et al[19] here also demonstrated that these parameters remain constant irrespective of age. This also follows same explanation as above.

There has been no agreement on which indicator of body size (height, weight and BSA) or age should be used to relate to and correct echocardiographic measurements. An observation of a linear relationship of echocardiographic measurements with height, weight, body surface area and age has been found in this study using univariate analysis. With multivariate analysis this study found that the height corrsubjects. However, studies in normal children have found elates best with the dimensions followed by BSA in that the BSA correlates best with the dimensions and also shows a linear relationship with the measurements compared to the other anthropometric indices and the age[9, 10,]. This difference may be explained by the fact that a multivariate analysis was carried out in this study which was not done in the earlier studies.

Conclusion

Direct echocardiographic parameters in sickle cell anaemia patients are significantly correlated with anthropometric indices (Height, weight, BSA) and age. Our data suggest best correlation with height in these subjects and significant correlation of haemoglobin level with left ventricular mass in subjects and controls.

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