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Ventricular hypertrophy and ischaemic changes in Children with Sickle Cell Anaemia and its relationship with the Haemoglobin Concentration in Steady State

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ABSTRACT

Objective: The prevalence and burden of Sickle Cell Anaemia (SCA) in Nigeria are high and they contribute to childhood morbidity and mortality. Chronic anaemia and vaso-occlusion usually involve different organs. The involvement of the heart is a common complication of SCA, thus the need for early detection of cardiac abnormalities in children with SCA. To assess cardiac structure using ECG in children with SCA in steady-state and to determine the relationship between abnormal ECG findings and the participants' haemoglobin concentration.

Material and Method: It was a cross-sectional study done in one of the tertiary hospitals in southeast Nigeria. The study participants were 164 children with SCA in steady state within the ages of 2 -17 years. A 12-lead ECG was carried out on the participants and their haemoglobin concentrations determined. The relationship between the presence of cardiac abnormality and independent variables like haemoglobin concentration, age and gender were analyzed.

Result: The prevalence of cardiac abnormality was 59.1%. The commonest cardiac structure abnormality was Left ventricular hypertrophy (LVH) (39.6%). Abnormality in the P-R interval was seen in 14.6%, while ST segment abnormality was seen in 18.3%. The mean Hb of those with abnormal ECG was lower than that of those without abnormal ECG, across each age group. Severe anaemia was a significant ($p< 0.01$) predictor of LVH. However, there was no significant association between the degree of anaemia and the occurrence of ST-segment (p: 0.26) and PR interval abnormalities (p: 0.52).

Conclusion: Cardiac anomalies are common findings in SCA children.

Keywords: SCA, ECG, Ischaemia, LVH, Infarction

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INTRODUCTION

Sickle cell anaemia (SCA) is an inherited condition that results from abnormalities of haemoglobin synthesis (1). In Africa, SCA is a common cause of morbidity and mortality (2) In Nigeria, SCA is found in about 3% of the population,1 and the country has the highest burden of SCA worldwide (3)

In SCA, there is sickling of the red blood cells with consequent occlusion of blood vessels and chronic haemolytic anaemia, leading to chronic hypoxia and ischeamia with or without infarction (4, 5). A common cause of morbidity and mortality is the involvement of the heart (6) as sudden death from cardiac causes has been demonstrated in patients with SCA, contributing to about 25.6% of mortality among those with SCA (7)

A study in Tanzania showed that among patients with SCA who died between 1979 to 2005, 9% of deaths were due to cardiovascular causes, including ischaemic and non-ischaemic heart diseases (8). The chronic anaemia and vaso-occlusion from sludged sickled cells results in chronic tissue hypoxia, which can lead to ischaemia and infarction of cardiac tissues (5, 9). These may involve the myocardium and the conducting system of the heart, resulting in abnormality in cardiac conduction and heart block (10).

The chronic anaemia and occlusion of the coronary artery by the sickled red blood cell causes progressive changes in cardiac structure; proliferation of myocytes, focal degeneration and fibrosis, thus, the chronicity of the effect of SCA on the heart (5). The heart has few collateral blood vessels that will oxygenate the cardiac tissues if the primary arterial conduits are narrowed or blocked (11).

Thus, it is vulnerable to ischaemia and infarction, causing a delay or abnormal electrical activities during the repolarization phase of the myocardial cells (11) This is seen as changes in ST segment and T wave on an electrocardiogram (ECG) (11). Aside the myocardium, ischaemia also affects the conducting systems, affecting the cardiac rhythm and may result in different degrees of heart block (12). This is seen as abnormalities in PR interval (12).

This could signal the effect of ischaemia at a number of sites (sino-atrial node, atrial myocardium and atrio-ventricular node) of the conduction system, since it measures the time depolarization spreads from the atria to the ventricles (12). Consequent upon the chronic anaemia in SCA, there is an increase in the left ventricular stroke volume with some increase in heart rate due to a compensatory attempt to increase the cardiac output (6).

The most common ECG abnormality seen in patients with SCA is left ventricular hypertrophy (LVH) (13, 14, 15) and results from this compensatory increase in the left ventricular stroke volume, resulting to a significant dilatation of the left ventricle over time (16).

This later adapts to the increased wall stress by developing eccentric hypertrophy over time (17). This ventricular hypertrophy is dependent on the degree of anemia (18). Cardiovascular morbidities, such as heart failure, have been associated with left ventricular hypertrophy (19). However, if detected early and with proper management, regression may be achieved, with consequent decrease in the attendant cardiac pathology (19).

MATERIALS AND METHODS

Study Area: The study was carried out in the Alex Ekwueme Federal University Teaching Hospital Abakaliki (AE-FUTHA), Ebonyi State.

Study Population: The participants were children with SCA aged 2- 17 years in steady state who presented in the sickle cell clinic of AE-FUTHA.

Inclusion and Exclusion Criteria: Children with SCA within the ages of 2–17 years who were in steady state. The steady state was defined as absence of crisis or blood transfusion in the preceding four weeks before recruitment (19, 20). Those with history of co-morbidities like congenital heart disease, rheumatic heart disease or other chronic diseases were excluded from the study.

Ethical Consideration and Consent: Before the commencement of the study, an ethical approval (REC Approval No: 05/05/2017-9/3/2018) was obtained from the Research and Ethical committee of the AE-FUTHA, and an informed consent and assent obtained from the parents and their children who were 7 years of age and above, respectively. Results of the investigations were made available and explained to the participants and caregivers.

Study Design: This was a cross-sectional study

Sampling Method: The study participants (164 children with SCA) were consecutively recruited from the SCA out-patient clinic until the minimum sample was achieved. The patients' folders were coded in order to avoid double recruitment.

Data Collection: Socio-demographic data such as age and gender were obtained. Twelve lead ECG was done using a portable ASPEL AsCARD Mint 12 Lead and 3-channel (ASPEL Company, June 2016, Poland) Electrocardiograph.

The electrodes were positioned as recommended by American Heart Association (21) Any evidence of PR interval anomaly and ST segment anomaly were recorded and the QRS complex was analysed for any evidence of ventricular hypertrophy (22, 23, 24, 25)

Data Analysis: The data collected were entered and analysed using the Statistical Package for Social Science (SPSS) version 23 for Microsoft windows 8. Descriptive statistics such as frequency and percentages were used to describe characteristics of the subjects such as gender and number of participants within each age group.

Continuous variables such as SV1, SV2, RV5 and RV6 amplitudes within each age and also, age distribution of each ECG anomaly were not normally distributed, using Shapiro-Wilks test for normality ($p > 0.05$) (26) hence, they were analysed using median and inter-quartile range.

Other continuous variables such as Hb concentration and PR interval duration were normally distributed, hence, they were analysed using mean and standard deviation. The prevalence of ECG abnormality was expressed in frequencies and percentages.

The Spearman's correlation test was used to evaluate for relationship between the Hb concentration and presence of cardiac anomaly. The strength of the relationship was said to be weak (rs= < 0 to > -0.3 or > 0 to < +0.3), moderate (rs= -0.3 to > -0.7 or +0.3 to < +0.7), strong (rs= -0.7 to -1 or +0.7 to +1) or no linear relationship (rs = 0), depending on the value of the correlation coefficient (rs) (27).

The chi-square test or fishers exact test was also used to assess for significant difference within each independent variable such as the gender and age of participants, with regards to each cardiac abnormality.

At confidence level of 95%, any difference observed was said to be significant if the p value was <0.05.

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RESULTS

A total of 164 children (96 males and 68 females) with SCA were recruited for this study. They were within the ages of 2-17 years, with a mean age of 9.7 years (SD, 4.56) and a male: female ratio of 1.4:1. This is illustrated in Table I

Anaemia was observed in the entire participants. Mild anaemia was seen in 11 persons (6.7%), 92 (56.1%) persons had moderate anaemia and 61 persons (37.2%) had severe anaemia. Severe anaemia was observed more in children between the ages of 9- 14 years (59%), moderate anaemia was observed more in children between the ages of 2–7 years (50%), while mild anaemia was observed more in children 15–17 years (54.5%). These are illustrated in Tables II and III

Table I: Gender and age distribution of children with SCA

	Characteristics	n (%)
Gender	Male	96(58.5)
	Female	68(41.5)
	Total	**164(100)**
Age (years)	2	9(5.5)
	3	7(4.3)
	4	12(7.3)
	5	10(6.1)
	6	6(3.7)
	7	18(11)
	8	8(4.9)
	9	8(4.9)
	10	10(6.1)
	11	12(7.3)
	12	12(7.3)
	13	12(7.3)
	14	8(4.9)
	15	14(8.5)
	16	8(4.9)
	17	10(6.1)
	TOTAL	**164(100)**

Table II: Mean haemoglobin of the different ages of children with SCA

Age (years)	Mean Haemoglobin, g/dl (SD)
2	7.69 (0.88)
3	6.63(1.10)
4	7.43(0.41)
5	7.56(1.42)
6	7.13(1.54)
7	7.38(1.11)
8	6.98(0.69)
9	6.53(1.11)
10	7.98(1.72)
11	7.55(1.64)
12	7.83(1.35)
13	7.20(1.61)
14	8.30(1.59)
15	8.25(1.20)
16	6.50(1.60)
17	7.42(1.30)

Abnormal ECG was detected in 97 (59.1%) of the children. It was observed more in males than in female participants, but the difference was not significant ($p = 0.40$, Z-score = -0.25).

Worthy of note was that no ECG abnormality was seen in children aged 2 years. The abnormal ECG results were observed more in older children, as the median age of children with abnormal ECG was 10 years, with an inter-quartile range of 9. This is shown in Table IV.

LVH was the most prevalent cardiac abnormality observed in the participants. This was seen in 65 (39.6%) participants, while none of the participants had right ventricular hypertrophy.

Abnormality in ST segment was seen in 30 (18.3%) participants; ST depression (80%) and ST elevation (20%). Abnormality in PR interval was seen in 24 (14.6%) participants; PR interval prolongation (20) and PR interval shortening (4).

The gender and age distribution of the ECG abnormalities are illustrated in Table VI. There was no significant relationship between gender and development of LVH and PR interval abnormality unlike ST segment abnormality seen more in females.

There was a significant relationship between the age and development of LVH, as 60% of children with LVH were above 10 years of age. Such was not seen with ST segment and PR interval abnormality, as these were fairly distributed among older and younger children.

The mean Hb of those with LVH was lower than the mean Hb of those without LVH, across all ages, difference being significant across almost all ages. This is shown in Table VII. There was a significant negative relationship between the Hb concentration and development of LVH ($rs = -0.71$, $p < 0.01$).

Though the mean Hb of those with ST anomaly in each age was lower than that of their counterpart age without ST anomaly across all ages, the difference was significant only in children that were 10 years and above. There was no significant relationship between the Hb concentration and development of ST anomaly ($rs = -0.14$, $p = 0.06$).

The mean Hb of those with abnormal PR interval was not significantly lower than that of those with normal PR interval across all ages. Also, there was no significant relationship between the Hb concentration and development of PR interval anomaly ($rs = -0.09$, $p = 0.24$).

There was a significant relationship between the degrees of anaemia and the development of LVH ($p < 0.01$), as 70.8% of children with LVH had severe anaemia. This was not seen between degree of anaemia and development of ST segment and PR interval anomalies. This is shown in Table VIII

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Table III: Frequency of anaemia among the different ages of children with SCA

Age (years)	Mild n (%)	Moderate n (%)	Severe n (%)
2	-	8 (4.88%)	1 (0.61%)
3	-	3 (1.83%)	4 (2.44%)
4	-	12(7.32%)	-
5	2 (1.22%)	5 (3.05%)	3 (1.83%)
6	-	4 (2.44%)	2 (1.22%)
7	-	14 (8.34%)	4 (2.44%)
8	-	4 (2.44%)	4 (2.44%)
9	-	2 (1.22%)	6 (3.70%)
10	1 (0.61%)	6 (3.70%)	3 (1.83%)
11	1 (0.61%)	5 (3.05%)	6 (3.70%)
12	-	6 (3.70%)	6 (3.70%)
13	-	3 (1.83%)	9 (5.49%)
14	1 (0.61%)	1 (0.61%)	6 (3.70%)
15	4 (2.44%)	7 (4.27%)	3 (1.83%)
16	-	6 (3.70%)	2 (1.22%)
17	2 (1.22%)	6 (3.70%)	2 (1.22%)
TOTAL	11(6.7%)	92 (56.1)	61 (37.2%)

Table IV: Abnormal electrocardiogram among different ages and genders of children with SCA

Age (years)	n	Gender	n	p-value	z-score
2	-	Male	56	0.4	-0.25
3	8	Female	41		
4	12				
5	6				
6	4				
7	8				
8	6				
9	4				
10	5				
11	6				
12	7				
13	6				
14	8				
15	6				
16	4				
17	7				
TOTAL	97		97		

Table V: Median amplitudes of SV1, SV2, RV5, RV6 waves and mean PR interval among different ages of children with sickle cell anaemia.

AGE (years)	SV1 mv (IQR)	SV2 mv (IQR)	RV5 mv (IQR)	RV6 mv (IQR)	PR interval ms
2	1.46(0.94)	2.02(1.09)	1.62(0.85)	1.19(0.36)	132.33(31.2)
3	2.43(1.37)	2.74(1.79)	3.41(3.26)	1.88(1.35)	161.43(17.5)
4	1.06(1.01)	1.55(1.02)	2.71(2.06)	1.65(0.29)	154.25(23.1)
5	1.74(1.06)	2.12(1.51)	3.13(3.01)	1.57(1.40)	141.20(23.2)
6	1.77(1.16)	2.23(2.19)	2.78(2.17)	1.83(1.02)	143.67(14.3)
7	2.05(1.42)	2.89(1.67)	4.01(1.44)	2.55(1.40)	161.89(34.2)
8	1.95(1.25)	3.13(2.16)	3.93(1.27)	2.33(1.31)	130.75(12.8)
9	2.81(0.92)	3.71(0.24)	3.85(1.20)	2.41(0.98)	139.00(10.8)
10	2.07(1.14)	2.79(2.07)	3.34(2.53)	2.07(1.47)	129.00(15.9)
11	2.71(1.18)	2.69(2.25)	3.50(1.68)	2.08(0.99)	152.50(27.6)
12	2.09(1.48)	2.01(1.45)	2.88(1.98)	1.76(0.84)	176.08(23.1)
13	2.18(1.40)	2.94(1.40)	3.42(2.01)	2.13(0.92)	162.50(32.4)
14	1.90(1.31)	2.41(1.91)	2.52(2.11)	2.36(1.20)	154.31(16.6)
15	1.83(1.10)	2.54(2.08)	3.02(2.65)	2.12(1.28)	166.28(30.1)
16	1.81(1.00)	1.55(1.07)	2.67(2.19)	1.97(0.61)	155.25(6.7)
17	1.85(0.73)	1.79(1.55)	2.64(0.75)	2.05(0.46)	179.10(37.7)

IQR- Inter-Quartile Range mv- millivolt ms- milliseconds

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Table VI. Gender and age distributions of the cardiac abnormalities

			LVH				ST segment anomaly				PR interval anomaly	
Gender	**Present**	**Absent**	χ^2	**P-value**	**Present**	**Absent**	χ^2	**P-value**	**Present**	**Absent**	χ^2	**P-value**
Male	35	61	0.98	0.32	12	84	5.2	**0.02**	13	83	0.22	0.64
Female	30	38			18	50			11	57		
Age (years)	**Present**	**Absent**	**F-exact**	**P-value**	**Present**	**Absent**	**F-exact**	**P-value**	**Present**	**Absent**	**F-exact**	**P-value**
2	0	9	27.1	**0.04**	0	9	19.5	0.07	0	9	33.2	0.11
3	1	6			4	3			3	4		
4	4	8			5	7			3	9		
5	3	7			2	8			1	9		
6	3	3			1	5			0	6		
7	6	12			1	17			5	13		
8	5	3			1	7			0	8		
9	4	4			2	6			0	8		
10	3	7			4	6			0	10		
11	6	6			2	10			1	11		
12	5	7			2	10			2	10		
13	6	6			2	10			2	10		
14	8	0			0	8			1	7		
15	6	8			0	14			1	13		
16	3	5			2	6			0	8		
17	2	8			2	8			5	5		
TOTAL	**65**	**99**			**30**	**134**			**24**	**140**		

Table VII: Mean haemoglobin of participants with and without ECG abnormalities

Age (years)	LVH present	LVH absent	p-value	ST-anomaly present	ST-anomaly absent	p- value	PR-anomaly present	PR-anomaly absent	p-value
2	-	7.69(0.88)	-	-	7.89(0.9)	-	-	7.69(0.9)	-
3	5.90(0.00)	7.60(0.01)	**<0.01**	6.47(1.2)	6.75(1.1)	0.66	7.00(0.8)	7.60(1.2)	0.26
4	7.40(0.41)	7.80(0.05)	**<0.01**	7.43(0.4)	7.45(0.4)	0.90	7.51(0.4)	7.80(0.2)	0.10
5	6.50(0.35)	8.27(1.43)	**<0.01**	7.20(0.1)	7.65(1.6)	0.40	6.90(0.0)	7.71(1.4)	0.15
6	5.20(0.03)	8.10(0.48)	**<0.01**	7.02(0.0)	7.70(1.7)	0.37	-	7.13(1.5)	-
7	7.33(1.37)	7.43(0.86)	0.57	7.50(0.0)	7.68(0.7)	0.44	7.46(1.6)	7.74(0.6)	0.65
8	6.83(0.76)	7.40(0.26)	**<0.01**	6.92(0.0)	6.98(0.7)	0.92	-	6.98(0.7)	-
9	5.90(0.01)	7.61(1.17)	**<0.01**	6.20(0.2)	6.63(1.3)	0.38	-	6.53(1.1)	-
10	6.57(0.64)	8.59(1.69)	**<0.01**	6.75(0.6)	8.80(1.7)	**<0.01**	-	7.98(1.7)	-
11	6.40(1.08)	8.70(1.26)	**<0.01**	5.30(0.2)	8.00(1.4)	**<0.01**	7.44(0.0)	8.00(1.0)	0.13
12	6.67(2.02)	8.22(1.26)	**<0.01**	6.80(0.1)	8.04(1.4)	**0.01**	7.66(1.4)	8.70(1.1)	0.06
13	6.14(0.94)	8.68(1.04)	**<0.01**	6.10(0.4)	7.42(1.7)	**0.02**	7.00(1.7)	8.20(1.3)	0.07
14	6.70(0.35)	8.83(1.47)	**<0.01**	-	8.30(1.6)	-	8.20(0.0)	8.31(1.7)	0.86
15	6.23(1.10)	8.49(1.71)	**<0.01**	-	8.25(1.2)	-	6.80(0.0)	7.48(1.8)	0.32
16	6.30(0.28)	8.50(1.56)	**<0.01**	5.30(0.1)	6.83(1.3)	**0.01**	-	6.45(1.6)	-
17	6.70(0.15)	8.03(1.13)	**<0.01**	6.50(0.0)	7.80(1.4)	**0.02**	6.34(1.1)	7.18(1.1)	0.11

Table VIII: Relationship between degree of anaemia and the ECG abnormalities.

			LVH				ST segment anomaly				PR interval anomaly	
Degree of anaemia	**Present**	**Absent**	χ^2	**P-value**	**Present**	**Absent**	χ^2	**P-value**	**Present**	**Absent**	χ^2	**P-value**
Mild	1	10	52.41	**<0.01**	2	9	2.69	0.26	1	10	1.32	0.52
Moderate	18	74			13	79			16	76		
Severe	46	15			15	46			7	54		

DISCUSSION

All the children were found to be anaemic. The high prevalence of severe anaemia at 9-14 years may be due to the combined effect of the chronic anaemia of SCA and the effect of puberty. This is because, it has been observed that puberty induces a state of anaemia, resulting from a relative deficiency of iron needed for red blood cell production in both male and female, due to its consumption during the exaggerated growth of lean body mass and menstruation; for the females (28). Similar observation was made in a study by Hall et al, (29) where they observed that children within the ages of 12 – 14 years were 1.35 times more likely to be anaemic than children aged 7 – 11 years.

The cardiac abnormality detected in children with SCA portrays that the presence of SCA is a risk factor for the development of cardiac abnormality and has been attributed to the chronic anaemia and vaso-occlusion, with consequent hypoxia and ischaemia of cardiac tissues.16,18 Similar20 and different (13, 21, 30, 31) prevalence have been reported by different authors. The difference in prevalence among several studies may be due to some factors such as the ECG parameters used to define abnormal ECG, differences in diagnostic criteria or cut-off value used, the steady state status of the recruited children with SCA, the age range of the participants and differences in sample size.

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The lower prevalence observed in the 2 studies by Bode-Thomas et al (31, 32) may be due to the ECG parameters used to define abnormal ECG, as their focus was only on presence of arrhythmia (32) and myocardial ischaemic changes (31) The high prevalence observed by Adegoke et al (30) and Odike et al (13) may be due to difference in the diagnostic criteria used; Sokolow and Lyon criteria (33) and centile chart by Davignon et al34 respectively.

Also, the steady state status of children with SCA was not an inclusion criterion in the study by Odike et al, (13) as children that were not in steady state may also have been studied. There was no significant difference in the prevalence of abnormal ECG between males and females in this study, though the prevalence was higher in the former than in the later.

This is similar to previous reports that there is little or no difference in ECG between males and females among children with SCA (20, 30) and also in non-SCA children (30, 35). Abnormal ECG was not seen in any 2-year-old child, rather in older children, with a median age of 10 years. This shows that it may take some years for the cardiac complications of SCA to develop in a child, reflecting the chronicity of the condition. This is similar to that observed in other studies (14, 20)

This finding may also be explained by the observation that 59% of children with SCA who had severe anaemia were older children (9- 14 years), showing that the degree of anaemia may also determine the occurrence of cardiac anomaly, as a result of the cardiac response to the chronic anaemia (16)

LVH was the commonest abnormality detected. It has also been shown to be the commonest ECG abnormality in children with SCA.15 It is as a result of the chronic anaemia with consequent decrease in cardiac output, which then leads to a compensatory cardiac dilatation in an attempt to increase the cardiac output (17, 18)

Overtime, the ventricle adapts to the increased wall stress by developing eccentric hypertrophy (17) LVH has also been observed to be the commonest abnormality by other authors (13, 14, 30, 36) The lower prevalence reported by Naburi et al20 and Ali et al14 may be due to difference in diagnostic criteria, which was not stated. Also, they included infants, whom at that age, may not have developed the compensatory hypertrophy due to the presence of foetal Hb.1,37 LVH was seen more in males than in females, though not significant.

This is similar to that reported in a previous study (20). Regarding the R wave and S wave amplitudes, the median amplitudes were higher in older children with SCA, but without pattern, unlike the RS progression with age that occurs in non-SCA children (35)

There was a significant relationship between the age and development of LVH, as LVH occurred more in older children; 60% of children with SCA were $\geqslant$ 10 years. This may suggest that it may take some years before the heart develops compensatory hypertrophy, consequent to the chronic anaemic. Other studies (14, 20) have reported similar finding.

This finding may also be explained by the fact that severe anaemia was more in older children, as worsening severity of anaemia has been shown to correlate positively with LVH in SCA (14, 18) 70.8% of those with LVH also had severe anaemia, mean Hb of those with LVH was lower than that of those without LVH across all ages and a negative correlation between Hb concentration and development of LVH. This has been corroborated by other studies (13, 14, 20, 38)

The PR interval anomaly observed may be attributed to the effect of ischaemia and infarction on the conducting tissues of the heart (12). It has also been reported to result from increased vagal tone, which is a compensatory mechanism for the hypoxia resulting from the chronic anaemia of SCA (20). This is similar to that observed by Adegoke et al,30 with a smaller prevalence observed in other studies (13, 31, 36).

The similarity with Adegoke et al (30) may be due to similar centile chart used to analyse PR interval. Other studies (13, 31) observed that PR anomaly was commoner in non-SCA with acute anaemia than in children with SCA. The lower prevalence may be attributed to a better adjustment of the conducting system of the heart to chronic anaemia of SCA than to anaemia of acute onset non-SCA children in their studies. In addition, their finding is similar to the finding of a higher mean PR interval in non-SCA children than in SCA children by Odia et al (36). Other studies have also observed PR interval anomaly among children with SCA (14, 20)

In contrast to the present study, Anjan et al (38) did not observe PR interval anomaly among children with SCA. A smaller sample size may explain this and also, the Hb concentration of the participants may be higher, because they also recruited children who were on chronic transfusion. Males had PR interval anomaly than females, though the difference was not significant. This is similar to other studies (13, 20)

There was no significant difference in the prevalence of PR interval anomaly among the ages of the participants, as it was fairly distributed among younger and older children. Thus, it can be inferred that PR anomaly starts early in childhood. A similar finding was observed by Naburi et al. (20) There was no significant relationship between the Hb concentration and PR interval anomaly, though there was a relatively lower Hb concentration among children with SCA who had PR interval anomaly than those without the anomaly in all ages. Also, there was no significant difference among the degrees of anaemia, with regards to development of PR interval anomaly.

Unlike in LVH where majority of children had severe anaemia, majority of children with PR interval anomaly had moderate anaemia. This observation may be inferred to mean that the conducting system of the heart is affected by lesser degree of anaemia, unlike the compensatory hypertrophy that occurs with worsening severity of anaemia. This is similar to the finding by Naburi et al, (20) as they observed that all the children with SCA who had prolonged PR interval had Hb concentration <8g/dl. This is in contrast to the finding by Bode-Thomas et al, (32) where it was observed that the mean Hb of children with SCA who had arrhythmia (including PR anomaly) was higher than that of those without arrhythmia, thus suggesting the possible role of other risk factors in the

occurrence of PR interval anomaly, aside from anaemia and ischaemia.

The ST segment anomaly has been reported to be due to myocardial injury resulting from ischaemia with or without myocardial infarction and impaired myocardial function, due to patchy micro-vascular occlusion and hypo-perfusion that resulted from sickling of red blood cells in SCA (39) The finding of ST segment anomaly in children with SCA had been observed by several authors (13, 20, 30, 31, 36)

However, this was different from the study by Anjan et al,38 as they did not observe ST segment anomaly in children with SCA, possibly because some of the participants involved in the study were on chronic transfusion. The higher prevalence observed by Naburi et al (20) and Odia et al (36) might be as a result of inclusion of participants who were not in steady state; therefore, children who may have had a recent crisis may have been recruited, thus, increasing the chance of detecting ST anomaly.

This is because, Bode-Thomas et al (31) has shown that ST anomaly was significantly higher in children with SCA crisis than in those in steady state. The lower prevalence observed by Bode-Thomas et al (31) and Odike et al (13) may be due to the pattern of ST anomaly observed in their study, as they noted either ST segment elevation (13) or depression (31) in children with SCA, and not both. This pattern is unlike that, observed in the present study, which is also corroborated in other studies (20, 30). Bode-Thomas et al (31) noted that those in steady state had only ST segment depression.

Rather, ST segment elevation was observed in non-SCA children who had acute anaemia. Likewise, Odike et al (13) observed ST elevation more among non-SCA that had anaemia than in SCA children. These two findings may suggest that ST segment depression is seen more in chronic anaemia while ST elevation may be seen more in acute anaemia.

The finding of more ST segment depression (80%) in this study also supports this observation. Also, considering myocardial infarction, the observation of more ST segment depression may suggest that SCA may be associated with non-ST elevation myocardial infarction (NSTEMI) than ST elevation myocardial infarction (STEMI).

In contrast, though Odia et al (36) detected both anomalies, ST elevation was more prevalent than ST depression in children with SCA. This may be due to the fact that some of the subjects may have had acute anaemic crisis recently before recruitment, since the steady status was not an inclusion criterion in their study. The ST segment anomaly was significantly higher in female, unlike the previous ECG anomalies. The reason for this, is not clear, but it was in contrast to the observation made by Naburi et al, (20) where it was seen more males, though the difference was not significant. There was no significant difference among the ages of children with SCA, with regards to occurrence of ST anomaly, showing that the prevalence of the ischaemic changes is fairly distributed in both younger and older children.

In contrast, Naburi et al (20) observed that ST segment anomaly was seen more in older children; above 6 years of age. The mean Hb of those with ST anomaly was lower than that of those without ST anomaly across all ages, portraying the effect of the chronic anaemia of SCA on the myocardium.39 However, there was no significant difference among the different degrees of anaemia, with regards to ST anomaly, as moderate and severe anaemia were fairly distributed among the participants with ST anomaly. This is similar to the observation by Bode-Thomas et al, (31) and may be due to a possible adaptation of the child to the chronic anaemia.

Though Naburi et al (20) observed a significant relationship between degree of anaemia and ST anomaly (they observed that 83.3% of children with SCA who had ST anomaly had Hb concentration below 8g/dl), it may also be likened to the observation made in this study, as the mean Hb of those with ST anomaly for each age was also below 8g/dl.

CONCLUSION

Children with SCA have commonly demonstrated cardiac abnormality on an ECG. The haemoglobin concentration of those with cardiac abnormality was lower than the haemoglobin concentration of those without cardiac abnormality across all ages. Severe anaemia was a significant predictor of LVH, but there was no significant association between the degree of anaemia and the development of PR interval and ST segment anomalies.

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