IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 6 Ver. XI (June 2016), PP 69-72
www.iosrjournals.org

Changes in Some Electrocardiographic Parameters amongst Children with Sickle Cell Anemia in Port Harcourt, Nigeria

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Abstract:*Sickle cell anemia is a genetic blood disorder affecting mostlyAfricans, Hispanics, Indians and people of Middle Easterndescent; involving major organs of which the heart is the mostfatal and commonest cause of morbidity and mortality. Thepresent study aims to determine some electrocardiographicparameters of sickle cell anemia children attending the sicklecell clinic at the University of Port Harcourt Teaching Hospital, Port Harcourt,Nigeria. A total of 118 subjects comprising of 55 sickle cell anemia (HbSS genotype) patients (Group A) and 63 normal controls consisting of 40 subjects (HbAA genotype) Group B and 23 subjects (HbAS genotype) Group C were recruited into the study. Control subjects were matched for weight and sex with sickle cell anemia (HbSS genotype) (Group A) patients. All subjects were aged between 2 and 15years. Height, weight, body mass index, hemoglobin concentration and heart rates were determined and a thorough physical examination conducted to exclude the presence of co-morbidities. Electrocardiographicparameters were subsequently determined usinga standard resting 12-lead electrocardiogram. Results were analyzed using Analysis of Variance; a P value less than 0.05 were considered significant.Results obtained showed no significant differences in age,body mass index and heart rate between patients with sickle cell anemia (HbSS genotype) and the control groups. However, control subjects had significantly higher haemoglobin concentration compared to sickle cell anemia (HbSS genotype) patients ($p<0.05$). Differences were also observed in some electrocardiographic parameters of sickle cell anemia (HbSS genotype) patients as compared to control subjects. For instance, higher percentages of left ventricular hypertrophy, ST segment depression, ischemic changesand axis deviation were observed amongst sickle cell anemia (HbSS genotype) patients compared to control subjects. Further, the QTc interval of Group A sickle cell anemia (HbSS genotype) patients was significantly higher than values for Group C (HbAS genotype) control subjects ($p<0.05$); however, the P-axis of Group A sickle cell anemia (HbSS genotype) patients was significantly lower than values for Group C (HbAS genotype) control subjects ($p<0.05$).Our study is of value and confirms suggestions that routineelectrocardiography amongst children with sickle cell anemia can help detect those prone to arrhythmia, ischaemic changes and sudden cardiac death and therefore enhance mortality and morbidity.*

Keywords:*sickle cell disease, children, Electrocardiographic parameters*

I. Introduction

Sickle cell anemia is a genetic blood disorder affecting mostly Africans, Hispanics, Indians and people of Middle Eastern descent; involving major organs of which the heart is the most fatal and commonest cause of morbidity and mortality.(Oguanobi *et al*., 2010).It is passed from parent to children through a defective hemoglobin gene. The sickle cell disease occurs when the seventh amino acid (if the initial methionine is counted), glutamic acid, is replaced by valine to change its structure and function.

In Africa, the average life expectancy for children with sickle cell disease is less than 20 years (Orin, 2010).Nigeria has the largest number of sickle cell traits and sickle cell disease in the world (WHO, 2012). 24%of Nigerian population are carriers and 150,000 children are born annually with SCD.

Normal and abnormal electrocardiographic presentations of sickle cell disease patients, needs to be clearly investigated and defined. Knowledge of the ECG pattern of sicklers will provide a good cardiovascular assessment of sickle cell disease

The present study is aims to determine some electrocardiographic parameters of sickle cell anemia children attending the sickle cell clinic at the University of Port Harcourt Teaching Hospital, Port Harcourt,Nigeria.

II. Materials and Method

A total of 118 subjects comprising of 55 sickle cell anemia (HbSS genotype, Group A) patients and 63 normal controls consisting of 40 subjects (HbAA genotype, Group B) and 23 subjects (HbAS genotype Group C) were recruited into the study. Control subjects were matched for weight and sex with sickle cell anemia (HbSS genotype) (Group A) patients. All subjects were aged between 2 and 15years. Age, Body mass index, hemoglobin concentration and heart rates were determined and a thorough physical examination conducted to

exclude the presence of co-morbidities. Electrocardiographic parameters were subsequently determinedwith a standard resting 12-lead electrocardiogram, using an approved methodology recommended by the American Heart Association and the Cardiac Society of Great Britain and Ireland, (Standardization of precodial leads, 1938.)

Sample Size Estimation:The minimum sample size of subjects of 110 children (55 per study group) required for the study was calculated using the Kish Method (Kish *et al*., 1965) 95% C.I, p = 3% and q = (1-p) and 10% non response.

Medical / Experimental Ethics

The nature of the study and its objectives were explained to the parents of the subjects before they were enlisted into the study. Ethical clearance was obtained from the University of Port Harcourt Teaching Hospital Ethics Committee and written informed consent was obtained from the parents of the subjects.

Statistical Analysis

Results were analyzed using Chi Square Test and analysis of variance; a P- value less than 0.05was considered significant.

III. Results

Results are as presented in Tables 1-4.And

Table 1: Age and Sex Distribution of Study Population

	HbSS (Group A)	HbAA(Group B)	HbAS (Group C)
	(n=55)	(n=40)	(n=23)
Age Group(years)			
1-5	17(30%)	17(43%)	9(39%)
6-10	19(35%)	14(35%)	11(48%)
11-15	19(35%)	9(22%)	3(13%)
Sex			
Male	34(62%)	18(45%)	9(39%)
Female	21(38%)	22(55%)	14(61%)

Table 2: Antropometric and Electrocardiographic (ECG) Parameters of Subjects and Controls

Electrophoreses **Parameters**	**HbSS** **(Group A)** **n = 55**	**HbAA** **(Group B)** **n = 40**	**HbAS** **(Group C)** **n = 23**	**p-value**
Age(years)	8.09±0.53(2-15)	6.83±0.63(2-14)	6.61±0.64(2-13)	0.163
BMI(kg/m^2)	15.45±0.27(11.2-22.6)	15.96±0.54(10.8-24.2)	16.43±0.53(12.2-22.2)	0.303
Heart rate(bpm)	94.89±2.40(63-140)	102.70±3.46(58-151)	101.22±4.95(55-144)	0.155
Hb conc.(g/dl)	7.45±0.21*(4.30-12.0)	11.19±0.31(6-17)	11.18±0.40(7-16.5)	0.001
P axis(^{o})	50.44±4.41(9-263)	53.45±2.44(9-90)	69.78±12.14*(12-236)	0.028
QRS-axis(^{o})	45.60±3.26(-21-82)	57.35±3.66*(-10-95)	48.00±4.68 (-19-74)	0.053
T-axis(^{o})	46.76±1.58(7-77)	47.43±3.83(-30-90)	37.96±4.74(-10-90)	0.124
QRS-duration(ms)	77.05±1.12(62-94)	77.65±1.46(64-104)	75.91±1.59(60-92)	0.738
PR-interval(ms)	148.35±3.61(90-236)	148.60±5.98(100-342)	152.00±9.06(116-292)	0.906
QT-interval(ms)	346.47±4.70(268-416)	347.88±6.95(268-528)	341.30±8.24(276-412)	0.806
QTc-interval(ms)	414.62±3.01*(353-463)	404.55±4.77(354-525)	393.35±5.15(351-439)	0.004

**significantly different from control at P<0.05) All Values = mean ± SEM range in parenthesis.*

Results obtained showed no significant differences in age, body mass index and heart rate between patients with sickle cell anemia (HbSS genotype; Group A) and the control.

However, control subjects had significantly higher haemoglobin concentration compared to sickle cell anemia (HbSS genotype; group A) patients ($p<0.05$). Further, the QTc interval of Group A sickle cell anemia (HbSS genotype) patients was significantly higher than values for Group C (HbAS genotype) control subjects ($p<0.05$); however, the P- axis and QRS-axis of Group A sickle cell anemia (HbSS genotype) patients was significantly lower than values for HbAS genotype (Group C) and HbAA genotype (Group B) control subjects respectively ($p<0.05$).

Considering ST-segment abnormalities; Group A(HbSS) had a significantly higher proportion of those with ST-segment depression. Group C,(HbAS) however recorded a significantly higher proportion of those with ST-segment elevation (χ^2 =9.693, p-value=0.046).

Ahigher percentage of ischaemic changeswas observed in HbSS subjects; group A, compared to the controls(χ^2 =0.371, p-value=0.831) but wasnot statistically significant. However,abnormalities such as

arrhythmia is found to be more prevalent in group B (HbAA Subjects) than in other groups ($\square^2$=14.683,p=0.001) as shown in table 3 below.

Table 3: Frequency Distribution of ST Segment Changes and Some Abnormalities Among Sampled Subjects

	HbSS (Group A) n = 55	**HbAA (Group B) n = 23**	**HbAS (Group C) n = 55**	$\square^2$	**Df**	**p-value**
ST Segment Changes						
Normal	39(71%)	36(90%)	14(61%)	9.693[a]	4	0.046
Elevation	9(16%)	2(5%)	7(30%)			
Depression	7(13%)	2(5%)	2(9%)			
Some ECG abnormalities						
Ischeamic Changes	10(18%)	6(15%)	3(13%)	0.371	2	0.831
Arrhythmia	1(2%)	10(25%)	1(4%)	14.683	2	0.001
Axis Deviation	2(4%)	1(3%)	0(0%)	2.817	6	0.831

Table 4: Prevalence of Ventricular and AtrialHypertrophy (right and left) among HBSS Subjects and Control.

	Hypertrophy	(LVH)	(RVH)	(LAH)	(RAH)
Genotype					
HbSS (GroupA) n=55	with hypertrophy	31(56%)*	1(2%)	1(2%)	0(0%)
	without hypertrophy	24(44%)	54(98%)	54(98%)	55(100%)
HbAA (Group B n = 40	with hypertrophy (%)	16(40%)	0(0%)	4(10%)	0(0%)
	without hypertrophy	24(60%)	40(100%)	36(90%)	40(100%)
HbAS (Group C) n = 23	with hypertrophy (%)	6 (26%)	0(0%)	0(0%)	2(9%)*
	without hypertrophy	17(74%)	23(100%)	23(100%)	21(91%)
$\square^2$		6.600	1.155	5.085	8.403
Df		2	2	2	2
p-value		0.037	0.561	0.079	0.015

LVH=Left ventricular hypertrophy, RVH=Right ventricular hypertrophy, LAH=Left atrial hypertrophy, RAH=Right auricular hypertrophy.

IV. Discussion

From this study, several changes occurred in the qualitative ECG patterns of HbSS subjects (sicklers) and sampled population. Higher percentages of ischaemic changes, Axis deviation and ST-segment abnormalities, than the control were found.

In this present study, the test group recorded 39(71%) subjects with normal ST-segment, while control group A and B had 35(88%) and 16(70%) respectively. ST segment elevation was found in 9(16%) of the test group; 3(7%) of control group A and 6(26%) of control group B. Why the Percentage of ST-segment elevation is higher in HbAS genotype is unclear.

The work done by Bode-Thomas et al 2003, whose study designed a scoring system that showed that non sickle cell subjects are more likely to have ST-segment elevation than the sickle cell anemic subjects may be considered. However, T-wave and ST-segment abnormalities have long been associated with Sickle Cell Aneamia and other chronic anaemias, (Uzsoy, 1964, Reimer, 1986), ST depression in particular appears to be associated with chronic anaemia. Since the sicklers are mainly anaemic, they are likely to have more ST-segment depression.Our data however, showed that ST segment depression was found in 7(13%) of the test group; 2(5%) of control group A and 1(4%) of control group B as shown in table 2.

The major abnormalities found in this study were Ischeamic changes, Arrhythmias and axis deviation (right and left). In this study, 10(18%), 6 (15%), and 3(13%) of the test group (HbSS), control group A, and control group B respectively, had ischeamic changes. In the long term, recurrent episodes of ischaemia might have detrimental effects on myocardial performance, especially as that organ also has to cope with the stress of chronic anaemia.

In the short-term, patchy micro-vascular occlusion will lead to areas of hypo-perfusion, myocardial injury from ischaemia with or without infarction, and impaired myocardial function, as demonstrated by several authors. (Norris *et al*., 1991, De Montalembert *et al*., 2004). Since severe ischaemia can predispose to sudden death during sickle cell crises, its early detection may be life-saving. The availability of a simple screening tool becomes invaluable, especially in resource-poor settings such as ours.

Arrhythmia was found in 21(38%) of the test group, 10(25%) of control group A, and 17(74%) of control group B.The assessment of the voltages in the chest leads revealed that there are statistically significant increase of LVH mass amongst the SCD patients when compared with control. In this study, Left ventricular hypertrophy (LVH) was found in 31(56%) of the test group (HbSS subjects), 16(40%) of control group A (HbAA subjects) and 6 (26%) of control group B (HbAS subjects). The prevalence in the study group is more than the control This is in keeping with the LVH seen in SCD (Odia,1990).

Right ventricular hypertrophy (RVH) was found in only 1(2%) of the test group (HbSS subjects), but not in any of the control groups. Left Atrial Hypertrophy (LAH) was found in 1(2%) of the test group and 3(8%) of control A (HbAA subjects). but was not found in control group B. Right atrial hypertrophy (RAH) was found in only 2(9%) of control group B (HbAS subjects), but not in the test group and control group A.

V. Conclusion

This study has shown the usefulness of a simple screening tool like the ECG, especially in resource-poor settings like ours. Further studies validating the usefulness of this ECG-based screening tool in children with sickle cell disease, are however necessary because the ECG could detect those who are prone to arrhythmia (prolong QTc syndrome), ischaemic changes and sudden cardiac death.

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Acknowledgement

The authors acknowledge the assistance of Professor OJ Odia in the course of this study.