Original article:

The electrocardiographic profile in non-sickle cell anaemia children and sickle cell anaemia children

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ABSTRACT

Introduction: Anaemia is a major cause of morbidity and mortality in African children. It affects all the systems of the body including the heart. The effects of anaemia on the heart of children was investigated in this study using an electrocardiogram.

Method: Eighty three consecutive patients aged 6 months to 16 years with anaemia (packed cell volume (PCV) <33%) and 94 age and sex- matched controls without anaemia (PCV >33%) were recruited from the Paediatric Unit of a tertiary institution in Edo state, Nigeria. The cases were classified into sickle cell anaemia (SCA) cases and non-SCA cases. They were assessed clinically and cardiovascular function was evaluated using electrocardiography. Data was analysed using the appropriate statistical test.

Results: Overall, 66.7% of the non-SCA cases had abnormal ECG, 82.9% of the SCA had abnormal ECG and 40.4% of the controls had abnormal ECG. A significantly higher number of the non-SCA cases than the controls had tachycardia ($X^2=6.1$, $p=0.014$). Only the SCA cases had BVH and deep Q waves in V5 and they also had statistically higher long QTc than the controls ($p=0.012$).

Conclusions: Anaemia is associated with an increased prevalence of ECG abnormalities particularly those of sinus tachycardia. The main additional effects of SCA were biventricular hypertrophy, deep Q waves in V5 and long QTc interval.

Keywords: Anaemia, Children, Tachycardia, Electrocardiogram

INTRODUCTION

Anaemia is the reduction in haemoglobin concentration below the determined normal ranges for age and gender. It is the most common haematological disorder in children. It is an important contributor to the high childhood morbidity and mortality in Africa. According to the WHO about 1.620 billion people (24.8% of the world population) worldwide suffer from anaemia. Anaemia can occur as a result of acute or chronic blood loss, impaired red blood cell production or increased red blood cell destruction. In developing countries anaemia is usually caused by iron deficiency and deficiency of other micronutrients, malaria, hookworm infestation and haemoglobinopathies. The clinically significant haemoglobinopathies result from mutation of the β-globin gene. This is seen in Sickle cell anaemia (SCA) and results from substitution of a valine residue for a glutamic acid residue at the sixth position of the β-globin chain. In haemoglobin SC (HbSC) there is substitution of lysine for glutamic acid at the same position. Under conditions of decreased oxygenation there is...
molecular polymerization which results in the formation of spiny and brittle sickle erythrocytes. This disorder is characterized by severe chronic haemolytic disease resulting from premature destruction of brittle and poorly deformable RBCs.

In anaemia, there is decreased oxygen carrying capacity of the blood which results in tissue hypoxia. This can lead to secondary organ dysfunction including cardiac arrhythmias and failure. Some of the well established findings on the effect of anaemia on the heart include tachycardia, heart murmurs, bounding pulses, increased cardiac output, left ventricular hypertrophy, isolated premature ventricular beats, complex ventricular arrhythmias, interventricular conduction delay, congestive cardiac failure and ischaemic heart disease. This can occur either as a result of physiologic adjustment to hypoxia or as a direct effect of anaemia on the myocardium. The maintenance of tissue oxygen delivery in acute reduction of red blood cell concentration depends on both an increase in cardiac output and an increase in blood oxygen extraction, and these require the preservation of an ample circulating blood volume. There is a shift of the oxyhaemoglobin dissociation curve to the right and increase in the concentration of 2,3 diphosphoglycerate (2,3 DPG) and a decreased affinity of oxygen for Hb. The initial increase in cardiac output is believed to be due to an increase in stroke volume and increased myocardial contractility. Later, an increase in heart rate comes into play as the Hb concentration continues to fall. There is also decreased blood viscosity in anaemia, which also plays a fundamental role in the rise in stroke volume. This results in increase in venous return and a decrease in peripheral resistance which is attributed to the decreased scavenging ability of the blood to inactive nitric oxide with its accumulation leading to peripheral vasodilation.

In anaemia there is redistribution of blood flow to areas of high demand e.g. the heart and the brain. The heart is a flow dependent organ, which means that coronary blood flow must be increased to increase oxygen delivery to the heart. There is vasodilatation and increased sympathetic activity in anaemia and these cause an increase in cardiac output, heart rate and contractility. These lead to volume mediated left ventricular dilatation, which accounts for the cardiomegaly seen in anaemia. In children with sickle cell anaemia (SCA), the cardiovascular problems of the chronic anaemic state develops from around the 4th or 5th year of life. The plasma viscosity is not decreased in sickle cell anaemia unlike in other anaemias, but may in fact be increased. This increases the workload of the heart. These patients also have a higher cardiac output than other anaemic patients, a feature believed to be secondary to arterial oxygen desaturation from pulmonary compromise. Studies have shown that in sickle cell haemoglobinopathy, anaemia causes the initial changes of chamber dilatation, while the microvascular effects of sickled cells results in left ventricular mass increase and dysfunction.

Anaemia is a common problem in Nigerian children but few studies have been done to determine its effect on the heart of children. Electrocardiography was used in this study to investigate the prevalence and pattern of ECG abnormalities in children with sickle cell anaemia and anaemia from other causes.

**METHOD**

The study was a prospective cross sectional study of the ECG changes in 177 children between the ages
of 6 months and 16 years seen in the Paediatric Department of a tertiary institution. The cases were 83 in number and had PCV of less than 33% and the controls were 94 and had PCV of 33% and above. The subjects were categorized into 5 groups in line with standard practice: 6-<12 months, 12-<36 months, 36-<96 months, 96-<144 months and 144-<192 months. The anaemic cases were further classified into sickle cell anaemia cases (SCA) or non-SCA cases based on their genotype.

Children with diagnosed or suspected congenital or acquired heart disease, renal impairment, diarrhoeal disease and children on cardiovascular acting drugs like antihypertensives and β-agonists were disqualified from the study.

The weight, height, pulse rate, and blood pressure of each child was taken using standard equipments. Blood samples were collected for genotype and PCV check. A resting period of not less than 30 minutes was given to calm each child before an ECG was performed. This was to ensure that the values obtained are truly representative of their resting state.

The ECG was recorded with a portable commercially available BTL-08 SD ,3 channel machine with a sampling frequency of 1000 Hz. The ECG parameters were read from the ECG tracing and the normal references were from Myung Park’s “How to read Paediatric ECGs” unless otherwise stated. The parameters checked were rhythm, rate, frontal plane axis of the QRS and T waves, QRS-T angle, PR, QRS complex duration, QT interval, QTc, P wave duration and amplitude, ST elevation or depression and T wave amplitude and duration.

The data was analysed using Microsoft Excel programme 2002 and Statistical Package for Social Sciences (SPSS) version 16. Means and standard deviations of various ECG variables were determined. Independent Student’s t test was used to compare the means of ECG variables between cases and controls. Analysis of variance was used to analyse more than two sample means and chi-square test was used for the analysis of discrete data. P-value <0.05 was considered to be statistically significant.

RESULTS

A total of 177 children were recruited for the study comprising 83 cases who were anaemic and 94 controls who were not anaemic. The ages of the children ranged from 6 months to 16 years. Among the cases 35 were SCA (sickle cell anaemia) cases. Thirteen (37.1%) were males and 22 (62.9%) were females with a male/female ratio of 1:1.7. Forty eight cases were non-SCA children, 23 were males and 25 were females giving a male/female ratio of 1:1.1.

The mean PCV of the SCA cases was 23.8 ± 4.1%, for the non-SCA cases 28.3 ±5.6% and for the controls 36.03 ± 2.4%. The differences in the mean PCV in the three groups was statistically significant (F = 221.8, p =0.000 respectively).

The only significant difference in the ECG of the 6-<12 months age group was in the mean QT interval in the females (p = 0.02) which was lowest in the non-SCA cases and highest in the SCA cases.

Analysis of the ECG parameters with sex distribution in SCA and non-SCA cases in the 36-< 96 months age group showed that the
The highest mean RV6 was among the male (22.9± 12.5) and female (24.4 ±13.04) SCA cases and the lowest among the male(13.9 ± 5.5) and female (13.9 ± 4.2) controls. The differences among the three groups were statistical significant (p = 0.01 for male and p = 0.002 for female). The mean RV6 in the SCA male cases was statistically higher than the mean RV6 in the non-SCA male cases( t = 2.1, p = 0.039) and the male controls ( t = 3.36, p = 0.003) but there was no statistically significant difference in the mean RV6 between the male non-SCA cases and the controls. Among the females the statistically significant difference was only between the SCA cases and the controls. The SCA cases had a statistically higher mean RV6 than the controls ( t = 3.4, p = 0.001).

Table I shows the mean of the ECG parameters with sex distribution in SCA and non-SCA cases and controls in the 96 < 144 months age group.

In the 144- < 192 months age group, the mean R/SV6 in the male SCA and non-SCA cases were statistically higher than the mean value in the controls ( t = 4.6, p = 0.002 and t = 4.4, p = 0.003 respectively), but there was no statistically significant difference between the values in the SCA and non-SCA cases.

The mean P duration was significantly higher in the non-SCA cases and the control than in the SCA cases ( t = 3.03, p = 0.023 and t = 2.9, p = 0.02 respectively), there was no statistically significant difference between the mean P duration in the non-SCA and the controls.

Among the females the statistically significant difference was only between the SCA cases and the controls . The SCA cases had a statistically higher mean RV6 than the controls ( t = 3.4, p = 0.001).

### Table I: Sex distribution of the ECG parameters in the SCA and non-SCA cases without heart failure and controls in the 96-< 144 months age group

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Sex</th>
<th>Non-SCA M=1, F=5 Mean ± SD (range)</th>
<th>SCA M=3, F=5 Mean ± SD (range)</th>
<th>Controls M=12, F=9 Mean ± SD (range)</th>
<th>F-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>M</td>
<td>68</td>
<td>96 ±17.9(88-100)</td>
<td>78.7 ±12.1 (62-103)</td>
<td>3.5</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>104 ±12.8(88-120)</td>
<td>80.2 ±20.1(62-115)</td>
<td>92.6 ±11.4(75-107)</td>
<td>1.8</td>
<td>0.20</td>
</tr>
<tr>
<td>QRS axis (degrees)</td>
<td>M</td>
<td>30</td>
<td>20 ± 37.7(-30-60)</td>
<td>37.5 ± 28.9 (-30-60)</td>
<td>0.4</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>42 ± 34.2(0-90)</td>
<td>42 ± 16.4(30-60)</td>
<td>43.3 ± 21.8(0-60)</td>
<td>0.007</td>
<td>0.99</td>
</tr>
<tr>
<td>T axis (degrees)</td>
<td>M</td>
<td>30</td>
<td>30.0± 0.0(30)</td>
<td>45 ± 15.7 (30-60)</td>
<td>1.6</td>
<td>0.23</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>54 ± 13.2(30-60)</td>
<td>24 ± 32.9(-30-60)</td>
<td>36.7 ± 20.0(0-60)</td>
<td>2.2</td>
<td>0.14</td>
</tr>
<tr>
<td>QRS-T angle (degrees)</td>
<td>M</td>
<td>0</td>
<td>30 ± 28.7(0-60)</td>
<td>22.5 ± 25.9 (0-90)</td>
<td>0.4</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>24 ± 25.09(0-60)</td>
<td>30 ± 36.7(0-90)</td>
<td>13.3 ± 15.8 (0-30)</td>
<td>0.8</td>
<td>0.47</td>
</tr>
<tr>
<td>P amplitude (mm)</td>
<td>M</td>
<td>1</td>
<td>1.1± 0.1(1-1.2)</td>
<td>1.5 ± 0.5 (0.8-2)</td>
<td>1.4</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>2 ±0.0(2)</td>
<td>1.4 ± 0.6(0.7-2.0)</td>
<td>1.7 ± 0.5 (0.8-2.2)</td>
<td>2.2</td>
<td>0.14</td>
</tr>
</tbody>
</table>

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Overall 32/48 (66.7%) of the non-SCA cases had abnormal ECG, 29/35 (82.9%) of the SCA cases had abnormal ECGs and 38/94 (40.4%) of the controls had abnormal ECGs. The frequency of ECG abnormalities was statistically higher in the SCA cases \( (X^2 = 18.4, p < 0.0001) \) and the non-SCA cases \( (X^2 = 8.8, p = 0.003) \) than in the controls. Though the frequency of abnormalities was higher in the SCA cases than in the non-SCA cases the difference was not statistically significant \( (X^2 = 2.7, p =0.09) \).

The frequency of the individual abnormalities in the SCA and non-SCA cases is shown on Table II. The statistically significant differences were in the frequency of sinus tachycardia \( (p = 0.029) \) and Prolonged QTc \( (p = \) \)
A significantly higher number of non-SCA cases than controls had tachycardia, while a significantly higher number of SCA cases than controls had long QTc. Only the SCA cases had BVH and deep Q waves in V5.

Table II: The abnormalities in SCA cases, non-SCA cases and controls

<table>
<thead>
<tr>
<th>ECG abnormalities</th>
<th>SCA cases n=35 (%)</th>
<th>Non-SCA cases n=48 (%)</th>
<th>Controls n=94 (%)</th>
<th>X²</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low atrial ectopic rhythm</td>
<td>1 (2.9)</td>
<td>0 (0)</td>
<td>1(1.1)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Sinus tachycardia</td>
<td>10 (28.6)</td>
<td>15 (31.3)</td>
<td>13(13.8)</td>
<td>7.02</td>
<td>0.029</td>
</tr>
<tr>
<td>Prolonged PR interval</td>
<td>1 (2.9)</td>
<td>2 (4.2)</td>
<td>3(3.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>LVH</td>
<td>12 (34.3)</td>
<td>11 (22.9)</td>
<td>21(22.3)</td>
<td>2.1</td>
<td>0.35</td>
</tr>
<tr>
<td>RVH</td>
<td>4 (11.4)</td>
<td>4 (8.3)</td>
<td>4(4.3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>BVH</td>
<td>6 (17.1)</td>
<td>0 (0)</td>
<td>0(0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Long QTc</td>
<td>9 (25.7)</td>
<td>8 (16.7)</td>
<td>7(7.4)</td>
<td>7.8</td>
<td>0.02</td>
</tr>
<tr>
<td>RAH</td>
<td>0 (0)</td>
<td>1 (2.1)</td>
<td>0 (0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Inverted T wave</td>
<td>1 (2.9)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Notched T wave</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1(1.1)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>ST segment elevation</td>
<td>2 (5.7)</td>
<td>6 (12.5)</td>
<td>5(5.3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>ST segment depression</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0(0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>rSR pattern</td>
<td>4 (11.4)</td>
<td>5 (10.4)</td>
<td>3(3.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Deep Q wave in V5</td>
<td>2 (5.7)</td>
<td>0 (0)</td>
<td>0(0)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>52</td>
<td>58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Frequencies with similar letters are significantly different with $X^2/p$ values as follow: $^6 6.1/0.014$, $^6 6.2/0.012$.

BVH = Biventricular hypertrophy, LVH = Left ventricular hypertrophy, RVH = Right ventricular hypertrophy, RAH = right atrial hypertrophy, NA = Not applicable, n= number of subjects.

**DISCUSSION**

The effects of anaemia on the heart of Nigerian children using the ECG were documented in this study. The prevalence of ECG abnormalities in the non-SCA cases was 66.7% . The reported prevalence of ECG abnormalities in anaemia ranges from 10-80% which is inclusive of the prevalence of 66.7% found in this study. This is significantly higher than the prevalence in the controls ($X^2 = 8.8$, $p= 0.003$). However, none of the abnormalities had a prevalence that was significantly different from that of the controls except sinus tachycardia ($t= 6.1$, $p = 0.014$). These observations (significant difference in overall prevalence of ECG abnormalities without accompanying significant difference in the pattern of abnormalities) could be interpreted to mean that anaemia has a non-specific effect on ECG abnormalities, increasing the overall prevalence but not altering the pattern of abnormalities.

The higher prevalence of sinus tachycardia in the cases is similar to the finding by authors including Feiner et al. The female cases were noted to have a higher mean heart rate than the male cases. Increased heart rate in anaemia is one of the compensatory mechanisms to increase oxygen supply to the vital organs like the brain and the heart. Myocardial ischemia resulting from imbalance between myocardial oxygen supply and demand may also be a contributory factor to the observed increased heart rate.

SCA is a multisystemic disease associated with chronic tissue hypoxia and ischaemia. The prevalence of ECG abnormalities in SCA cases (82.9%) although higher it was not significantly different from that in the non-SCA subjects (66.7%) ($X^2 = 2.7$, $p =0.09$). This could mean that the anaemia, rather than the SCA, was the principal factor in the pathogenesis of ECG changes in children with SCA.

Unlike the overall prevalence of abnormalities, however, there was a significant difference between SCA and non-SCA cases in the pattern of abnormalities. The differences were in the significantly higher prevalence of biventricular hypertrophy (17.1% versus 0%, $p = 0.01$) in the SCA cases and deep Q waves in V5.

Chamber enlargement in SCA has been reported by several workers. The enlargement may be multifactorial in origin. First, anaemia causes the initial changes in cardiac dilatation while the microvascular effects of sickled cells results in increased ventricular mass. Second, ventricular hypertrophy is a compensatory mechanism in chronic anaemia. Third, the increases in blood viscosity as a result of the sickling process results in further increases in ventricular workload and therefore ventricular hypertrophy. The deep Q wave in V5, noted in 5.7% of the SCA cases but in none of the non-SCA cases and controls, is evidence of the increased ventricular workload and left ventricular strain in SCA. Rijnbeek reported that deep Q wave in V5 is suggestive of LVH in his study of normal children. Fourth, children with SCA also have a higher cardiac output due to secondary arterial oxygen desaturation from pulmonary compromise.
Among the SCA cases, 25.7% had prolonged QTc compared to 16.7% of the non-SCA cases and 7.4% of the controls. This is similar to the findings reported by Bode -Thomas et al. Long QTc interval in the SCA cases in their study. Myocardial ischaemia, a recognized feature of sickle cell anaemia, is a cause of QTc prolongation. Long QTc indicates abnormal repolarization, which may predispose to ventricular arrhythmia and sudden death. QTc interval prolongation is a valuable tool for detecting and quantifying the risk of arrhythmia.

It has been associated with sudden infant death syndrome or apparently life threatening events in children.

**Conclusion**

From this study it can be concluded that anaemia is associated with an increased prevalence of ECG abnormalities particularly those of sinus tachycardia. Increased prevalence of biventricular hypertrophy, deep Q wave in V5 and QTc prolongation are the additional effects of sickle cell anaemia.

References:


