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Clinical profile of Nigerian children with sickle cell anaemia.

BA Animasahun[1], F Bode-Thomas[2], EO Temiye[3], Njokanma OF[4]

[1]Department of Paediatrics and Child Health, Lagos State University College of Medicine, Ikeja. Lagos.Nigeria.
[2]Department of Paediatrics, Jos University Teaching Hospital, Jos, Plateau State. Nigeria
[3]Department of Paediatrics, University of Lagos College of Medicine, Idi-Araba, Lagos. Nigeria.
[4]Department of Paediatrics and Child Health, Lagos State University College of Medicine, Ikeja. Lagos. Nigeria.

Abstract

This study aimed to document the cardiovascular features of children with sickle cell anaemia (SCA), in steady state at the Lagos University Teaching Hospital (LUTH) using clinical evaluation. A prospective and cross-sectional study involving 100 children with SCA and 100 age and sex matched controls aged one to fifteen years. Their cardiovascular statuses were evaluated by clinical examination. About 80% of the subject were diagnosed after one years of age, twenty two [36.7%] of the 60 sixty subjects had received at least one blood transfusion. The commonest signs in subjects were hepatomegaly, pallor and laterally displaced apex beat. They had significantly lower systolic blood pressure and diastolic blood pressure but higher respiratory rates and pulse rates compared to controls. (p< 0.01). Sickle cell anaemia is diagnosed late among Nigerian children. Blood transfusion is common among children with SCA, Increased Respiratory rate and heart rate but lower systolic and diastolic blood pressure. The commonest clinical signs were hepatomegaly, pallor and laterally displaced apex beat, due to chronic anaemic state.

Keywords: Sickle cell anaemia, Clinical evaluation**.**

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Introduction

Sickle cell anaemia (SCA) affects practically every system in the body and may sometimes present as crisis situations. Anaemia causes a reduction in the oxygen carrying capacity of the blood resulting in tissue hypoxia [1]. Cardiac output at rest is not usually increased in most chronic anaemia until haemoglobin levels fall below 7g/dl but abnormal rise in output with exercise may occur with levels as high as 10g/dl [2]. Increased cardiac output tends to increase the work load on the heart, but this is somewhat counteracted by the decreased blood viscosity and reduced peripheral vascular resistance. The increase in cardiac output has been observed to correlate well with the degree of anaemia [2,3] such that there is a tendency for the cardiac output to increase with decreasing haemoglobin concentration. Other compensatory mechanisms to chronic anaemia available to the body include decreased circulation time and increased tissue oxygen uptake. The latter is facilitated by a shift to the right of the oxygen-haemoglobin dissociation curve. [1-2, 4-5]. Redistribution of blood flow away from "less important" organs such as the skin may also be important in maintaining the cardiac output to the more vital ones such as the brain and liver [5]. Through these mechanisms, the chronically anaemic patients like sickle cell anaemia patients are able to tolerate low levels of haemoglobin concentration for a long time.

It is believed that apart from the anaemia, there is additional strain on the heart as a result of sickling which takes place in small vessels. This sickling occurs both in the systemic and pulmonary circulations, further burdening the left and right ventricles respectively [5, 6]

Another factor that may increase the workload on the heart in these patients is the fact that the blood viscosity is not reduced, as it is in other chronic anaemia. It may, in fact, be increased. [1, 6] This is thought to be consequent upon the abnormal shape of the erythrocytes and tends to increase the work of the heart even more than it does for the same degree of anaemia of another type. [7] In addition, due to increased plasma volume in association with increased work load consequent upon the increased cardiac output, the heart undergoes dilatation and hypertrophy which eventually leads to cardiomegaly. [1, 7]

Signs of hyperdynamic circulation found in sickle cell anaemia patients on physical examination include widened pulse pressure, active precordial impulses and a lat-

erally displaced prominent apex beat. The jugular venous pressure is rarely raised except in cardiac failure. The heart sounds are often loud with a frequently split second heart sound and accentuation of the pulmonary component due to increased blood flow across pulmonary valves rather than pulmonary hypertension. [8] They commonly have systolic murmurs which may either be pan-systolic or ejection in type. A third heart sound is commonly heard which is due to the hyper dynamic state and there may be diastolic flow murmurs due to increased flow across a normal valve especially mitral. [8] Blood pressures are typically low in them except during crisis situations. [9] Intermittent hypertension has been described during crisis situations but the frequency or mechanism of this finding is unknown. Also, hypertension with convulsion has occasionally followed blood transfusion [10, 11] Peripheral oedema, crepitations in the lungs and hepatomegaly may be present as complications of sickle cell anaemia which may confuse the clinical picture by mimicking cardiac failure. [9]

Although all the above have been documented in the literature, these has been from studies carried out among the Caucasians and the few studies done among Africans have mostly been in adults. It will be ideal to document what the spectrum is among African children hence the need for this study which aimed to document the clinical and cardiovascular features of children with sickle cell anaemia in steady state.

Material and Methods

This was a prospective, cross sectional carried out as part of a large study at the Lagos University Teaching Hospital (LUTH) in Idi-Araba between March and October 2005. The subjects included 100 paediatric patients attending the LUTH sickle cell anaemia outpatient clinic and were consecutively recruited. They had haemoglobin genotype 'SS' confirmed with haemoglobin electrophoresis and were aged 12 months to 15 years. They were in steady state at the time of recruitment. [12] Informed consent was sought from parents or caregivers of potential subjects and the controls before enrolment into the study. Ethical clearance for the study was obtained from the Ethical Committee of the Lagos University Teaching Hospital.

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. 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.

Each subject and control was examined clinically. Pulse was taken from the right radial artery at the wrist, counted over 60 seconds. Blood pressure measurements were done using a standard mercury sphygmomanometer (Accosson) ® with the child seated and rested for at least five minutes and the right arm supported on a horizontal surface at the level of the heart. The cuff size selected for each child covered at least two-third of the length of the upper arm while allowing clearance of 2-3cm from the ante-cubital space. Three readings were taken at one-minute interval deflating the cuff completely between readings; the mean of the three readings was regarded as the subject's blood pressure. Reading was recorded to the nearest 2mmhg, the first Korotkoff sound (K1) was the systolic blood pressure while the fifth Korotkoff sound (K5) was taken as diastolic blood pressure [13].

2mls of blood was collected into an heparinised bottle after the clinical evaluation and haemoglobin estimation was by oxy-haemoglobin method.

Data was analyzed using Microsoft Excel program supplemented by Megastat statistical package. Mean, standard deviations 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 coefficients of correlation and associated p-values were derived. Statistical significance was set at p-value < 0.05.

Results

A total of 200 children were recruited into the study. Out of this number, 100 were test subjects in the 12 month to 15 year age bracket confirmed to have haemoglobin genotype SS. They were all in steady state and receiving routine drugs consisting of folic acid, paludrine and multivitamins. The control group consisted of 100 children within the same age, sex and socioeconomic status who had haemoglobin genotype AA. The male: female ratio in each group was 1.9:1.

The age at diagnosis of sickle cell anaemia patients is illustrated in table 1. Twenty-one (21%) of the 100 subjects were first diagnosed in infancy, more than 70% were diagnosed between one year and five years while 8% were diagnosed after 5 years of age. In terms of the frequency of blood transfusion among the sixty subjects; twenty two [36.7%] out of sixty subjects had received at least one blood transfusion. Table II shows the clinical signs elicited in subjects and controls. The commonest clinical signs were hepatomegaly, pallor and laterally displaced apex beat.

Table 1. *Ages of the subjects at first diagnosis of sickle cell anaemia*

Age at diagnosis in months	No of cases (%)
6 to <12	21 [21.0]
12 to < 60	71 [71.0]
60 and above	8 [8.0]

Haemoglobin level

The mean [SD] haemoglobin level in the subjects was significantly lower than in the controls [76.9 ± 19.5g/L Vs 118 ± 2.0g/L, p< 0.0001].

Table II. *Clinical signs in subjects and controls at recruitment into the study*

Features	Subjects [% n = 100	Controls [%] n =100	p
Hepatomegaly	90 [90.0]	14[14.0]	0.000
Pallor	69 [69.0]	31[31.0]	0.000
Displaced apex beat	47 [47.0]	0 [0.0]	0.000
Bossing of skull bones	18 [18.0]	2 [2.0]	0.000
Jaundice	14 [14.0]	0 [0.0]	0.000
Splenomegaly	15[15.0]	0 [0.0]	0.000
Cardiac murmur	14[14.0]	1 [1.0]	0.002
Left Parasternal heave	5[5.0]	0 [0.0]	0.024

Some children had more than one clinical sign

Table III. *Comparison of selected continuous variables between test subjects and controls*

Variables	Subject n = 100	Controls n = 100	p
Temperature	36.6± 0.4	36.5 ± 0.4	0.25
Respiratory rate/min	24.3± 5.1	22.6±5.6	0.003
Pulse rate/min	97.4±16.3	93.8±13.6	0.01
Systolic BP (mm/Hg)	84.8±11.2	90.6±9.6	0.0004
Diastolic BP (mmHg)	44.9±9.6	50.8±7.6	0.001

Figures shown are mean ± one standard deviation of the mean.
BP = Blood Pressure
mm/Hg = millimetres of mercury

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Discussion

The present study documents the clinical and cardiovascular features of SCA patients aged one year to fifteen years at the LUTH. It was partly based on the fact the chronic anaemia have effects on the cardiovascular system. The study indicated that sickle cell anaemia was diagnosed after infancy in about 80% of subjects. This figure is rather high but inevitable considering that there is no neonatal screening programme for the condition in Nigeria. Thus diagnosis usually depends on appearance of symptoms and the degree of enlightenment of parents.

Another prominent finding is the fact that up to 40% of the subject has had at least one episode of blood transfusion. In the presence of late diagnosis, subjects do not benefit from preventive measures against repeated infections like malaria which may haemolyse their blood leading to the possibility of blood transfusion. The high frequency of blood transfusion may also predispose the sub-

jects to infectious diseases like HIV and hepatitis among others.

The commonest observed signs in subjects were hepatomegaly, pallor and displaced apex beat. The occurrence of each of these signs has a basis in significant and chronic anaemia. Hepatomegaly and splenomegaly result from the involvement of extramedullary sites in erythropoiesis as a homeostatic response to meet the needs of oxygen carriage. Displaced apex beat signifies cardiomegaly and is due to increased cardiac output which occurs in chronic anaemia. Cardiomegaly may also be as a result of the increased workload on the heart from the increased viscosity of blood in SCA patients. [1, 6] The increase in viscosity of the blood is thought to be consequent upon the abnormal shape of the erythrocytes and tends to increase the work of the heart even more than it does for the same degree of anaemia of another type. [7] In addition, due to increased plasma volume in association with increased work load consequent upon the increased cardiac output, the heart undergoes dilatation and hypertrophy which eventually leads to cardiomegaly.

Sickle cell anaemia patients had significantly higher respiratory rate compared with controls, A similar finding was documented by Blumgart et al [7], Duke et al [2] and Chinawa et al.[14] Increased respiratory rate in the subjects may be an effect of hypoxic drive secondary to the chronic hypoxia which results from the chronic anaemic state. It may also be due to reduced pliability of the lungs in these patients which may be due to repeated episodes of vaso-occlusion in the lungs leading to infarction of the lungs which in turn reduce the pliability of the lungs. Reduced pliability of the lungs in this patient may also be due micro-thrombotic phenomenon in the lungs leading to infarction. It may also occur secondary to repeated chest infections in these patients. In addition, a significantly higher pulse rate was also found among the subjects compared with controls. This is in conformity with findings of Covitz et al [15], Ogunkunle and her colleague [16] and Chinawa et al [14]. It is a compensatory response to the chronic anaemia which serves to increase cardiac output and thereby increasing blood supply to the organs and ultimately improving oxygenation to the tissues. However the study found a similar range of temperature among the subjects and controls. This is contrary to the report of Chinawa. [14] The reason for this is not immediately clear as SCA is documented to be an inflammatory disease which causes release of cytokine and tumor necrosis factors (TNF) which may alter the body's temperature. [17] Furthermore, Alexandra and colleagues [18] also noted that in SCA, there are endothelial activation and subclinical microvascular occlusions which trigger the release of interleukin 6 (1L-6), alpha-2-microglobullin, and acute phase proteins which can cause a rise in body temperature.

Furthermore, this study documented a significantly lower mean blood pressure among subjects compared with controls. This is similar to the documentation of Sergeant et al [19] and Pegelow et al [20] .This is due to the chronic hypoxia secondary to the chronic anaemic state in these subjects, the hypoxia causes vasodilatation leading to lower peripheral resistance and hence lower systemic blood pressure in the subjects. Reduced peripheral resistance in subjects is also explained by relatively larger plasma volume resulting from lower packed cell volume. There is therefore reduced blood viscosity and hence lower peripheral resistance. Another prominent contributory factor to vasodilatation and hence reduced peripheral resistance in sickle cell anaemia is higher level of plasma prostacyclin (a potent platelet aggregation inhibitor). Renal tubular damage with concentration defects and sodium loss, alterations in circulating aldosterone, rennin, vasopressin levels and stimulation of production of renal prostanglandins are other mechanisms for reduced blood pressure documented in adults with SCA [21-23]. Elebute [24] has shown that Nigerian children with SCD do have reduced concentrating ability in the kidney, the defect increasing with age. This also explains the reason for lower BP in SCA patients

In conclusion, SCA is diagnosed late among Nigeria Children despite the high prevalence of the disease in the country. Blood transfusion rate is high, lower systolic and diastolic blood pressure but higher respiratory and pulse rate has been documented in SCA patient. These are due to hemodynamic changes as a result of chronic anaemia. There is a need to encourage neonatal screening for sickle cell anaemia.

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Authors' contributions

Animasahun B.A was the project leader. Bode-Thomas F participated in the design, supervision and writing. Temiye E.O participated in the conceptualization, design and supervision of the study and Njokanma O.F participated in conceptualization and critical review of the manuscript. All authors read and approved the final manuscript.

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Correspondence to:.

BA Animasahun
Department of Paediatrics and Child Health
Lagos State University College of Medicine
Ikeja. Lagos, Nigeria.

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