



Original Research Article

Haematological parameters among sickle cell anaemia patients in steady state and haemoglobin genotype AA individuals at Michael Okpara, University of Agriculture, Umudike, Abia State, Nigeria

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A B S T R A C T

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A great percentage of sickle cell anaemic patients in this University are in steady state because of increased level of fetal haemoglobin (HbF) in most of them but very few have minimal level of HbF which easily undergo crisis. Most of the patients were detected in the course of medical examination. Because of the delicate nature of these patients, the researchers of this study saw the necessity to carry out the study. 20 confirmed sickle cell patients were used as the patients aged 4-34 year, 14 males and 6 females and 40 subjects with haemoglobin genotypes AA were used as the controls. The study showed significant increase in WBC, Neutrophil and Lymphocytes ($P<0.05$), significant decrease in PCV ($P<0.05$) and no significant change in monocyte ($P>0.05$) when the mean values of the SCA patients were compared relative to HbAA subjects. SCA patients should be monitored closely and prevented from triggering factors to crisis.

Introduction

Sickle-cell disease (SCD), or sickle-cell anaemia (SCA), is a hereditary blood disorder, characterized by red blood cells that assume an abnormal, rigid, sickle shape. Sickling decreases the cells' flexibility and results in a risk of various complications. The sickling occurs

because of a mutation in the haemoglobin gene. Individuals with one copy of the defunct gene display both normal and abnormal haemoglobin.

Life expectancy is shortened. In 1994, in the US, the average life expectancy of

persons with this condition was estimated to be 42 years in males and 48 years in females^(Platt et al., 1994), but today, thanks to better management of the disease, patients can live into their 70s or beyond.

Sickle-cell disease occurs more commonly among people whose ancestors lived in tropical and sub-tropical sub-saharan regions where malaria is or was common. Where malaria is common, carrying a single sickle-cell gene confers a fitness. Specifically, humans with one of the two alleles of sickle-cell disease show less severe symptoms when infected with malaria (Wellems et al., 2009).

Sickle-cell anaemia is a form of sickle-cell disease in which there is homozygosity for the mutation that causes HbS. Sickle-cell anaemia is also referred to as "HbSS", "SS disease", "haemoglobin S" or permutations of those names. In heterozygous people, that is, those who have only one sickle gene and one normal adult haemoglobin gene, the condition is referred to as "HbAS" or "sickle cell trait".

Sickle cells in human blood: both normal red blood cells and sickle-shaped cells are present. Sickle-cell disease may lead to various acute and chronic complications, several of which have a high mortality rate (Malowany and Butany et al., 2012).

Sickle cell disease results in anemia and crises that could be of many types including the vaso-occlusive crisis, aplastic crisis, sequestration crisis, haemolytic crisis and others. Most episodes of sickle cell crises last between five and seven days "Although infection, dehydration, and acidosis can act as triggers, in most instances no predisposing cause is identified (Kumar et al., 2009).

Sickle-cell anaemia is caused by a point mutation in the β -globin chain of haemoglobin, causing the hydrophilic amino acid glutamic acid to be replaced with the hydrophobic amino acid valine at the sixth position. The β -globin gene is found on chromosome 11(Lazrus et al., 2011). The association of two wild-type α -globin subunits with two mutant β -globin subunits forms haemoglobin S (HbS). Under low-oxygen conditions, the absence of a polar amino acid at position six of the β -globin chain promotes the non-covalent polymerisation of haemoglobin, which distorts red blood cells into a sickle shape and decreases their elasticity.

The loss of red blood cell elasticity is central to the pathophysiology of sickle-cell disease. Normal red blood cells are quite elastic, which allows the cells to deform to pass through capillaries. In sickle-cell disease, low-oxygen tension promotes red blood cell sickling and repeated episodes of sickling damage the cell membrane and decrease the cell's elasticity. These cells fail to return to normal shape when normal oxygen tension is restored. As a consequence, these rigid blood cells are unable to deform as they pass through narrow capillaries, leading to vessel occlusion and ischaemia.

The actual anaemia of the illness is caused by haemolysis, the destruction of the red cells, because of their misshape. Although the bone marrow attempts to compensate by creating new red cells, it does not match the rate of destruction. Healthy red blood cells typically live 90–120 days, but sickle cells only survive 10–20 days.

About 90% of patients survive to age 20, and close to 50% survive beyond the fifth decade (Kumar et al., 2009). In 2001, according to one study, the estimated

mean survival for sickle cell patients was 53 years old for men and 58 years old for women with homozygous SCD(Wierenga et al.,2001).

The highest frequency of sickle cell disease is found in tropical regions, particularly sub-Saharan Africa, India and the Middle-East(Weatherall and Clegg,2001). Migration of substantial populations from these high prevalence areas to low prevalence countries in Europe has dramatically increased in recent decades and in some European countries sickle cell disease has now overtaken more familiar genetic conditions such as haemophilia and cystic fibrosis. In 2010 it resulted in about 29,000 deaths globally(Lozano,2012).

Three quarters of sickle-cell cases occur in Africa. A recent WHO report estimated that around 2% of newborns in Nigeria were affected by sickle cell anaemia, giving a total of 150,000 affected children born every year in Nigeria alone. The carrier frequency ranges between 10% and 40% across equatorial Africa, decreasing to 1–2% on the north African coast and <1% in South Africa(WHO,2012).

Sickle Cell Anaemia a major cause of morbidity and mortality in Africa where there is no readily effective treatment (Omoti,2005).Patients with sickle cell disease have varying amounts of abnormal haemoglobin called the sickle cell in their erythrocytes. Sickle cell anaemia is due to the substitution of adenine with thymine in the glutamic DNA codon, which results in turn, in substitution of valine for glutamic acid in position of beta globin chain (Pauling et al., 1949).

The disease amounts for over 60% of the world's major haemoglobinopathies with

an estimated 2-3 million Nigerians affected by the S gene(Olatunji,2002).The extent of the problems of sickle cell disease in Nigeria cannot therefore be overemphasized because of the S gene said to be between 25-30%(Omoti,2005).The majority of patients born to rural dwellers do not usually survive childhood (Ukpong,1992). Furthermore, there is no widely acceptable and readily available cure for patients with sickle cell anaemia at present.Curable methods such as gene therapy and bone marrow transplantation,which may be associated with several complications are not readily available in developing nations(Omoti, 2005).

Many patients with sickle cell anaemia are in reasonably good health most of the time and achieving a steady state level of fitness.The importance of early recognition and subsequent clinical and haematological assessment of the disease are greatly facilitated by familiarity with the patient's steady state.A patient with sickle cell anaemia is said to be in steady state when there is absence of infection,acute complicating factors or acute clinical symptoms or crisis for at least three months (Bookchin and Law, 1996).

Materials and Methods

Study Area

The study was conducted in Diagnostic Laboratory Unit, University Health Services Department,Michael Okpara University of Agriculture,Umudike,Abia State,Nigeria.

Subjects

20 Confirmed sickle cell patients in steady

state and subjects with haemoglobin AA were recruited for the study.

Sample Collection

Venous blood samples were collected from the subjects into EDTA anticoagulated containers for haematological parameters analysis.

Statistical Analysis

The results were analysed using t-test and level of significance set at $P<0.05$.

Ethics

Oral consents were made to the subjects prior to sample collection.

Results and Discussion

There is so much disparity in the haematological status of sickle cell anaemic patients and haemoglobin AA genotyped persons. Table 1,3 & 4 showed significant increase($P<0.05$) in WBC, Neutrophil, and Lymphocyte and significant decrease ($P<0.05$) in the mean values of PCV but no significant change($P>0.05$) in the mean values of Monocyte when compared between sickle cell anaemic patients and Hb AA subjects.

The WBC is close to the reports of Ahmed et al (2006) which was $12.3 \times 10^9/L$, Akinbami et al (2012) which was $10.27 \times 10^9/L$ and $11.6 \times 10^9/L$ by Rao et al (2012). This increase could be because of some oxidative stress. The significant decrease in PCV could be as a result of its effect on the bone marrow and on the kidney because of its multisystemic nature. The PCV was lower than what was reported by Ahmed et al (2006) which was 24%, Akinbami et al (2012) which was

24.44%. This could be as a result of changes in diet and management of the patients. Patients with sickle cell disease(SCD) generally have a background rate of red cell sickling, which drastically shortens the life span of red cells leading to a chronic haemolytic anaemia and jaundice even in steady state(Kaul et al,1996).

The moderate leucocytosis in this finding is in line with earlier studies which is a common feature of SCD and was thought to be due to redistribution of granulocytes from marginal pool to the circulating pool(Ahmed et al,2006). The WBC and differential count in steady state were higher than in control.

This is expected because an increase concentration of neutrophils in venous blood of SCA patients which include demargination of intravascular neutrophils, accelerated release from the bone marrow and reduction in the rate at which neutrophils leave the blood. Patients with SCA are known to have significantly higher mean total WBC and differentials than people with AA genotype (Omoti,2005). This could be as a result of generation of a covert inflammatory response leading to the release of cytokine mediators, one of whose main function is increased neutrophils production by the bone marrow (Omoti,2005).

Those involved with the management of SCA patients particularly the physicians should be aware of this variability to avoid confusing the disease with infection as seen in the leucocytosis. The parents should equally be educated on the triggering factors to crisis to maintain steady state of the patients.

Table.1 Mean values of wbc of the sickle cell patients and haemoglobin aa subjects

Subjects	Mean(*10 ⁹ /L)	+/-SD(*10 ⁹ /L)	P-Value
Sickle Cell Patients(20)	12.6	2.3	
Haemoglobin AA Subjects(40)	5.4	1.2	P<0.05

Table.2 Mean value of pcv of wbc of the sickle cell patients and haemoglobin aa subjects

Subjects	Mean (%)	+/-SD (%)	P-Value
Sickle Cell Patients(20)	20.0	1.7	
Haemoglobin AA Subjects(40)	38.0	4.3	P<0.05

Table.3 Mean values of neutrophil of the sickle cell patients and haemoglobin aa subjects

Subjects	Mean(%)	+/-SD(%)	P-Value
Sickle Cell Patients(20)	70.0	7.2	
Haemoglobin AA Subjects(40)	63.0	5.2	P<0.05

Table.4 Mean values of lymphocytes of the sickle cell patients and haemoglobin aa subjects

Subjects	Mean(%)	+/-SD(%)	P-Value
Sickle Cell Patients(20)	29.0	2.5	
Haemoglobin AA Subjects(40)	35.0	5.0	P<0.05

Table.5 Mean value of monocytes of the sickle cell patients and haemoglobin aa subjects

Subjects	Mean(%)	+/-SD(%)	P-Value
Sickle Cell Patients(20)	1.0	0.8	
Haemoglobin AA Subjects(40)	2.0	0.6	P>0.05

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