

The curse of sickle cell disease



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'You know, haemoglobin is a wonderful substance. I like it. It's a red substance that brings color into the cheeks of girls, and in the course of my haemoglobin investigation, I look about a good bit to appreciate it.' As to the degree of abnormality in sickle cell haemoglobin, it is astonishing how small it is...²

Linus Pauling

Sickle cell disease (SCD) is an autosomal recessive condition due to homozygote sickle cell haemoglobin (HbSS), identified in 1949.³

This abnormal Hb variant results from the substitution of a valine for glutamic acid at the sixth amino acid position in the beta-globin chain. Upon deoxygenation, the poorly soluble HbS undergoes polymerisation leading to the characteristic sickle cell.⁴

These damaged cells are then removed by the reticuloendothelial system, hence a grossly reduced red blood cell (RBC) life span of only 17 days compared to the expected 120 days in the unaffected population.⁴

WHO statistics reveal that about five per cent of the world's population carries genes responsible for haemoglobinopathies. SCD is common

to people of African, Mediterranean and Asian descent. Nigeria has the largest burden of SCD in the world, with 24 per cent of the population being carriers of the mutant gene and two per cent prevalence of sickle cell anaemia.⁵

There are different variations of this disease but the three more severe types are:⁶

- Homozygous sickle cell disease (HbSS)
- Sickle cell/haemoglobin C (HbSC)
- Sickle cell thalassaemia.

Diagnosis of haemoglobinopathies is made by haemoglobin electrophoresis for the couple. Genetic counselling/prenatal diagnosis should be offered. The option of cord blood storage should be explained.

Bola was my friend. As a child I often wondered why she looked so tired and I envied her for so many days off from school!

The sickle cell trait (SCT) or the carrier state confers some resistance to falciparum malaria, favouring survival of the host. However, inheritance of two abnormal Hb genes in SCD confers no such protection and malaria is a major cause of ill health and death in children with sickle cell anaemia.⁷

Bola's brother Yomi had sickle cell trait. He never had malaria attacks. She'd got the short straw.

The clinical picture emerges after four months of age with highly phenotypically variable disease:⁸

- Anaemia
- Jaundice
- Hand-foot syndrome
- Frequent infections
- Painful crisis
- Retinopathy
- Splenic sequestration
- Leg ulcers
- Acute chest syndrome
- Bone marrow fat embolism
- Stroke
- Renal medullary infarction, hyposthenuria and papillary necrosis
- Aseptic necrosis of bone¹⁸.

With time I understood that SCD can be a life-long sentence. During childhood Bola had failure to thrive, infective episodes and often repeated crisis attacks requiring hospital admissions.

Management in pregnancy

Pregnancy in sickle cell disease is high-risk and associated with exacerbation of sickle cell disease, with increase obstetric complications including mortality; acute chest syndrome; pneumonia; sepsis; cerebral vein thrombosis; pyelonephritis; urinary tract infection; preeclampsia; thromboembolic events; intrauterine growth restriction; preterm birth; antepartum hospitalisation; increased rate of caesarean sections; blood transfusion; postpartum infections; and systemic inflammatory response syndrome. Despite this, the outcome for pregnancy in the developed world has improved, with a mortality rate of less than one per cent.¹⁰

Folic acid supplementation is recommended. The patient should have pre-conceptual pneumococcal vaccine. Serial ultrasonic assessment of fetal growth is important.

Prophylactic RBC transfusion in SCD pregnancy is controversial. A multicenter, randomised controlled trial of 72 patients with HbSS disease showed no significant difference in overall perinatal or maternal outcome, except for a lower incidence of painful crises in the transfused group.⁹ However, this benefit has associated increased hospitalisation rates, cost and alloimmunisation risk.

Hence, some recommend a selective transfusion policy for patients with previous perinatal mortality, new onset neurologic event, severe anaemia preeclampsia, acute chest syndrome, or in preparation for surgical intervention.²⁴

At 26 years of age and 35 weeks into her first pregnancy, Bola was admitted to hospital. She had features of vaso-occlusive crisis, manifested as severe bone pain of acute onset. Such intense bone pain is considered 'worse than labour pain'.

Pregnant women are at higher risk of developing sickle cell crisis (SCC), which are usually vaso-occlusive (35 per cent of pregnant sicklers¹³) and may be triggered by infection. They may be associated with thrombophlebitis or preeclampsia. SCC can be due to acute severe anaemia, splenic sequestration, aplastic crisis or hyperhemolytic crisis. The typical pattern is sudden recurrent pain attacks involving the extremities, abdomen, chest, or vertebrae.

Fetal complications include the following:

- Spontaneous abortion¹²
- Intrauterine growth restriction¹¹
- Increased rate of fetal death in utero
- Low birthweight¹²
- Preterm delivery.

Antenatal investigations include frequent full blood counts to determine the level of anaemia. A baseline haemoglobin concentration of 6-8g/dL is typical for SCD patients plus a high reticulocyte count or sickle cells on the peripheral smear. An elevated white blood cell count (without a left shift) may be observed in cases of SCC. Elevated lactate dehydrogenase (LDH) levels are found in SCD. Arterial blood gas and group and cross-match of blood is done on admission.

Aims of management¹⁹ are based on a multi-disciplinary team approach:

1. Management of vaso-occlusive crisis (IV fluids);
2. Management of chronic pain syndromes;
3. Management of chronic haemolytic anaemia;
4. Prevention and treatment of infections;
5. Management of complications and organ damage syndromes associated with SCD;
6. Prevention of stroke; and
7. Detection and treatment of pulmonary hypertension.

Despite receiving antibiotics, supplemental oxygen, IV hydration, blood transfusions and liberal analgesia, Bola's life ended tragically as did that of her unborn fetus. Rest in Peace.

Hence, the management strategies in SCD are to avoid tissue hypoxia, and to prevent and rapidly control infections or other stressors that could provoke a crisis.

Prenatal counselling and diagnosis for sickle cell haemoglobin and other haemoglobinopathies are preventive measures for at-risk women. Due to the immigrant population in Australia and New Zealand, there may be an increased presentation of women like Bola, to our maternity units. However, with appropriate management by healthcare providers (obstetrician, physician and haematologist), who are familiar with sickle cell disease, the majority of such women with sickle cell hemoglobinopathies can have successful pregnancy outcomes.

The Cooperative Study of SCD (CSSCD) estimated that the median survival for individuals with sickle cell anaemia (SS) was 48 years of age for women and 42 years of age for men.

Neonatal screening, penicillin prophylaxis for children, pneumococcal immunisation, red cell transfusion for selected patients and chelation therapy, hydroxyurea therapy, parental and patient education and, above all, treatment in tertiary centres have contributed to these improved statistics.

The only current cure for sickle cell anaemia is a bone marrow transplant.

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