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Clinical evaluation of hematological profile of children's affected by sickle cell disease

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Abstract
Iron deficiency in sickle cell patients may result in lowering the intracellular haemoglobin concentration and this may ameliorate sickling. The patients with sickle cell disease do not acquire excessive iron burden during the first two decades of life. Hence the study was planned with the foremost purpose to assess the haematological profile of children in special reference to body iron status of patients with sickle cell disease.
All the established cases of children detected with sickle cell disease or sickle β thalassemia were imperilled to comprehensive haematological examination in distinct allusion to body iron store by assessment of serum iron, TIBC, % transferrin saturation and serum ferritin to find out total body iron store.
Thus, based on present and previous studies available, out of various parameters for diagnosis of iron status in SCD-SS patients, low MCV and MCH are more consistently associated with iron deficient state. Such patients need to be further evaluated on long term basis after giving trial of iron therapy.

Keywords: sickle cell disease, serum iron, anemia, haematological profile

Introduction
Sickle-cell disease (SCD) is a group of blood disorders typically inherited from a person's parents. The most common type is known as sickle-cell anaemia (SCA). It results in an abnormality in the oxygen-carrying protein haemoglobin (haemoglobin S) found in red blood cells. This leads to a rigid, sickle-like shape under certain circumstances. Problems in sickle cell disease typically begin around 5 to 6 months of age. A number of health problems may develop, such as attacks of pain ("sickle-cell crisis"), anemia, swelling in the hands and feet, bacterial infections, and stroke. Long term pain may develop as people get older. The average life expectancy in the developed world is 40 to 60 years.
Sickle-cell disease occurs when a person inherits two abnormal copies of the haemoglobin gene, one from each parent. This gene occurs in chromosome 11. Several subtypes exist, depending on the exact mutation in each haemoglobin gene. An attack can be set off by temperature changes, stress, dehydration, and high altitude. A person with a single abnormal copy does not usually have symptoms and is said to have sickle-cell trait. Such people are also referred to as carriers. Diagnosis is by a blood test and some countries test all babies at birth for the disease. Diagnosis is also possible during pregnancy.
Sickle cell anemia (SCA) is a genetic blood disorder caused by abnormal inherited hemoglobin. The abnormal hemoglobin causes distorted or sickle-shaped red blood cells i.e. the red blood cells are shaped like a crescent. It is the most common form of sickle cell disease (SCD). It is also known as Hemoglobin SS disease, Hemoglobin S disease, HbS disease or sickling disorder due to hemoglobin S.
The highest frequency of Sickle Cell Disease is found in tropical regions, particularly Sub-Saharan Africa, India and the Middle-East. Migration of substantial populations from these high prevalence areas to low prevalence countries in Europe has dramatically increased in recent decades. The prevalence of Sickle Cell Anemia is highly common in the tribal belt of Central and Southern India. The public health implications of Sickle Cell Anemia are significant leading to poor quality of life, lower life expectancy and higher rates of infant mortality.
Sickle cell disease (SCD) with an estimated 5,200 live births each year is a major public health problem in India. Although SCD has been described in India in numerous ethnic groups, it is most prevalent. Prevalence of Sickle Cell gene is 5 to 34 % in scheduled tribes, who have a high prevalence of socio-economic disadvantage and are frequently medically underserved.
India has also a very huge populations of tribal community about 18 crore and expected to have 1.80 crore sickle cell trait and 14 lakhs of sickle cell disease. These show the big burden on the public health of India.
SCD is a serious group of conditions which are inherited (genetic). It affects the red blood cells in the blood. Sickle cell anaemia is the name of a specific form of SCD in which there are two sickle cell genes. Sickle cell disease (SCD) is one of the most common monogenic disorders globally with an autosomal recessive inheritance [1]. James Herrick, a physician first described the characteristic sickle shaped red cells in a medical student from Grenada in 1910. Linus Pauling and his colleagues showed that sickle haemoglobin (HbS) had an altered electrophoretic mobility and they were the first to define it as a molecular disease in 1949. A few years later in 1957, Vernon Ingram discovered that sickle haemoglobin resulted from a single amino acid substitution in the haemoglobin molecule [2, 3]. The disease results from a single base A>T mutation in the triplet encoding the sixth residue of the β-globin chain, leading to a substitution of valine for

glutamic acid and the abnormal haemoglobin S (HbS).

The primary pathophysiology is based on the polymerization of deoxyHbS with formation of long fibers within the RBCs causing a distorted sickle shape which eventually leads to increased haemolysis and vaso-occlusion of sickle red cells. However, the clinical presentation of SCD patients is extremely variable and there are several events that may trigger vaso occlusion. Recent work has shown the importance of red cell dehydration, abnormal adhesion of RBCs to the vascular endothelium, imflammatory events, and activation of all the cells in the vessel and abnormalities of nitric oxide metabolism in the pathophysiology of this multi-organ disease [4].

Earlier reports have shown that American Black children with sickle cell disease were shorter with lower weights and generally thinner body build than normal children [5] In India, the βS gene is prevalent especially in the tribal populations and the prevalence rate varies from 0 - 40% in different population groups [6] Several workers have reported the molecular basis of sickle cell disease particularly with reference to its milder clinical manifestations as compared to the Afro-Carribean counterpart [7, 8].

It has been reported that iron deficiency anemia is uncommon in individuals with sickle cell disease because of availability of an adequate iron source potentially from increased red cell turnover and from blood transfusion [6, 7]. It is believed that iron released by hemolysis is available for reutilization and that iron deficiency is uncommon in these conditions. However, contrary to the previous belief few studies reported that iron deficiency was common than expected in un transfused sickle cell anemia cases [8, 9]. Iron deficiency anemia often goes unnoticed because the sickle cell disease patients are already anemic. Iron deficiency in sickle cell patients may result in lowering the intracellular haemoglobin concentration and this may ameliorate sickling [5]. The patients with sickle cell disease do not acquire excessive iron burden during the first two decades of life.

Hence the study was planned with the foremost purpose to assess the hematological profile of children in special reference to body iron status of patients with sickle cell disease.

Methodology [9, 10]

The study was planned into the 40 sickle cell disease children's were evaluated. All the childrens are from Viswabharathi Medical College, The study includes about the 40 male and female children's. visited the Pediatric Out-Patient Department (OPD) and in-patient department (IPD) of Viswabharathi Medical College, were considered in the study. All the patients are informed consents.

Inclusion Criteria

1. Children's of either sex.
2. Age between 6 months to 15 years
3. Patients referred in IPD & OPD both departments.

Exclusion Criteria

1. Children's below 6 months & new-born.
2. Children's having chronic infective diseases
3. Children's having history of blood transfusion

The patients showing the presence of band representing HbS in the Hb electrophoresis were further categorized as Sickle Cell Disease, Sickle cell Disease with thalassemia and sickle cell trait depending upon HbS and HbA2 levels. All the patients having HbS more than 50% were enrolled in the study for further analysis. Patients with sickle cell disease and sickle cell disease with thalassemia were further investigated for Serum Iron, Serum ferritin, Total iron Binding capacity (TIBC) and Percentage Transferrin Saturation (%TFR). All Children were investigated for complete blood picture (Hemoglobin, Total leucocyte count, Platelet Count, RBC Indices).

Results & Discussion

The data from the total 40 sickle cell disease children's were collected and presented as below. The study group was divided in 2 groups as SCD-SS and SCD-B-Thal according to the type of the sickle cell disease. The SCD-SS stands for the Sickle cell syndromes include sickle cell anaemia and SCD-B-Thal represent the Sickle cell disease results from Haemoglobin S beta thalassemia (SCD-β-thal).

Table 1: Haematological profile in selected study group patients

Hematological parameter	SCD-SS (20)	SCD- b– Thal (20)
Hemoglobin (gm%)	8.5±1.5	8.1±1.3
TLC(count/mm3)	10,450±3950	11,620±4120
Platelet count(L/mm3)	2.55±0.7	2.79±0.9
PCV(vf)	23.5±3.5	24.3±4.3
MCV(fl)	68.00±7.1	64.30±6.8
MCH(pg/cell)	24.1±1.9	22.5±2.1
MCHC(g/dl)	33.5±2.0	34.2±2.9
RDW(%)	21.5±2.4	19.8±2.6

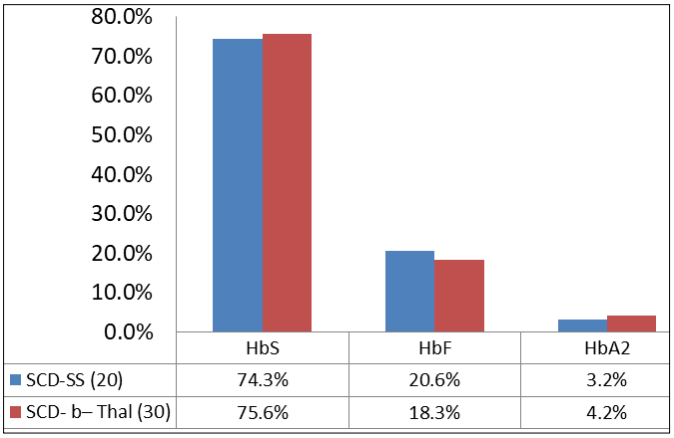

Fig 1: Mean of HbS, HbA2, Hb F

Table 3: Mean body iron stores

	SCD-SS (20)	SCD- b– Thal (20)
Serum Iron (µg/dl)	62.6±30.5	59.3±25.2
TIBC (µg/dl)	271.9±39.2	245±43.8
Serum Ferritin(ng/ml)	201.6±19.5	239.1±21.5
%TFR	27.9±1.9	32.3±2.6

We have included the patients from 6 months to 15 years. Most of the patients were in the age group of 7-12 years as also seen in study by Sahu *et al* [9]. However Kar *et al* found minimum age of presentation to be 6 months. Probable reason

for patients reporting at a later stage in our study might be initial treatment at primary level before reporting to our hospital [10].

In our study, out of total patients screened positive for sickle cell, 52% were heterozygous and 48$ were homozygous. Mandout *et al* in 2009, in a cross section analysis of tribal patients attending hospitals or mobile clinics in south India, showed that the prevalence of sickle cell anemia was 9.2% out of which 0.8% were homozygous and 8.4% were heterozygous [11].

All the patients were found to be anaemic. The mean haemoglobin concentration was 8.5 gm% in patients with SCD-SS and 8.1 gm% in patients with SCD-B-thal. The reticulocyte count was found to be high in majority of patients (81.1%) suggesting chronic response to haemolysis. Similar findings were seen in study done by Khan *et al* [12] and Juwah *et al* [13].

In our study low MCV & MCH and normal MCHC values. Haddy *et al*. [14] Showed low Hb, decreased MCV, MCH and MCHC values in patients with sickle cell disease who showed response to iron supplements. Davis *et al.* [15] found low MCV and MCH in his patients and raised the suspicion of iron deficiency anaemia. Walke *et al.* [16] found low MCV, MCH, MCHC and raised reticulocyte count.

Thus, based on present and previous studies available, out of various parameters for diagnosis of iron status in SCD-SS patients, low MCV and MCH are more consistently associated with iron deficient state. Such patients need to be further evaluated on long term basis after giving trial of iron therapy.

The limitation of the study was the small study group which was not enough regarding the actual status of body iron among patients with sickle cell disease. The confounding effect of underlying illness of serum ferritin used to assess iron stores also added to problems.

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