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IRON PROFILE IN PATIENTS OF SICKLE CELL ANAEMIA

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ABSTRACT The inherited disorders of blood include hemoglobinopathies which are one of the major public health problems in India.1Sickle cell disease is the second most common hemoglobinopathy next to thalassemia in India.3General incidence of Sickle cell disease in India is 1-44%.5, 6, 7 The average frequency of hemoglobin S (Sickle cell anaemia) is 4.3 % in India.5In this study we aim to evaluate the iron status in patients of sickle cell anemia, to determine the percentage of patients with sickle cell anemia having iron deficiency anemia and to determine iron overload if any in patients of sickle cell anemia. After clearance from Institutional Ethics Committee, patients of diagnosed sickle cell anemia (SS Pattern) were enrolled in the study with their due consent. They were then investigated for complete iron profile i.e. Complete blood count, peripheral blood smear, reticulocyte count with Index, Serum Ferritin, serum Iron, total iron binding capacity, Percentage transferrin saturation. This study was for2 years, from November 2013 to October 2015. Results: Four patients out of 56 had Iron Deficiency Anemia (7.1%).Three patient had not received blood transfusion, One had received transfusion once. In the study majority of subjects i.e.37 (66.7%) where iron overloaded, which was found more common than iron deficiency. We found 3(5.4%) subjects in whom chelation therapy should be considered.

KEYWORDS : Anaemia, sickle cell disease, iron deficiency anaemia, iron overload

INTRODUCTION:

The inherited disorders of blood include hemoglobinopathies which are one of the major public health problems in India.1 In India, there are several hemoglobin variants causing much suffering to afflicted individuals and impose considerable financial, genetic and psycho-social burden on family, society and nation at large.2 Sickle cell disease is the second most common hemoglobinopathy next to thalassemia in India.3 It is the major erythrocytic genetic disorder prevalent in certain parts of the world including India. 4 General incidence of sickle cell dis 5'8 Sickle cell ease in India is 1-44%.5, 6, 7 The gene frequency for sickle cell anaemia in India is 4.3 %. anaemia refers to a group of genetic disorders characterized by presence of sickle hemoglobin (HbS) anaemia and acute and chronic tissue injury secondary to blockage of blood flow by abnormally shaped red cells. Herrick first described a case of sickle cell disease in 1910.9 It is one of the variants of disorders of hemoglobin inherited from both the parents in an autosomal recessive pattern. In this disease, there is single nucleotide substitution in codon 6 of beta globin chain of hemoglobinmolecule. There is polymerization of HbS molecules inside the red cells which is responsible for sickling of red cells.10Iron is a vitally important element in human metabolism. It has central role in erythropoiesis in addition to other intra cellular processes in all the tissues of the body.11 It is commonly said that patients with chronic haemolytic anaemia are iron overloaded because of excessive breakdown of red blood cells and an increased frequency of transfusions. Hence they are prone to the development of iron overload.12 For this reason iron salts are rarely employed in the treatment of sickle cell anaemia. Contrary to this belief widespread prevalence of iron deficiency and relatively small number of transfusions in India makes it likely that children with sickle cell anaemia are not often iron overloaded as is believed and may in some cases be actually iron deficient. This study is conducted to confirm the same fact. In this study we have studied -Hemoglobin (Hb), Mean Corpuscular Volume (MCV), and complete iron profile13,14– serum iron, serum total iron binding capacity,serum ferritin and percentage transferrin saturation in the subjects.

Aim:

- To evaluate the iron status in patients of sickle cell anemia

Objectives:

1) To determine the percentage of patients with sickle cell anemia having iron deficiency anemia.
2) To determine iron overload if any in patients of sickle cell anemia

Material and Method

Children with sickle cell anaemia who were diagnosed by hemoglobin electrophoresis in stable state between the age group 1 to 18 years and who came to the hospital for pediatric outpatient care or hospitalized during the period of November 2013 to July 2015 were enrolled. The study was cross sectional. The sample size of the study during the above mentioned study period was 56. They were then investigated for complete iron profile i.e. haemoglobin, MCV, Serum Ferritin, serum Iron, total iron binding capacity, Percentage transferrin saturation.

Inclusion Criteria -

- Patients who are confirmed SS pattern on Hemoglobin electrophoresis in stable state.

Exclusion Criteria -

1. Participants other than 'SS' pattern on Hemoglobin Electrophoresis
2. Patients presenting in crisis or acute febrile illnesses.
3. Patients not giving consent for study.

RESULTS:

There was a strong positive (Correlation Coefficient=0.71, p=0.00012) correlation between Serum Ferritin and PRC transfusion. We found 4 subjects i.e. 7.1% were iron deficient. Majority of them i.e.3 subjects had not received transfusion.

In the study majority of subjects i.e.37 (66.7%) where iron overloaded, which was found more common than iron deficiency in our study. We found 3(5.4%) subjects in whom chelation therapy should be considered.

In the study, serum iron and % transferrin saturation was significantly higher in PRC transfused subjects as compared to non transfused subjects (p=0.001). This suggests that iron overload was more in PRC transfused subjects. While serum TIBC does not have significant difference in PRC transfused and non-transfused group(p=0.104) but the values in PRC

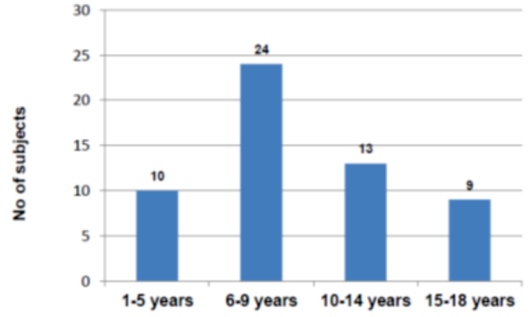
transfused(310.38 ± 79.01) group where lower than non-transfused (354.63 ± 119.04).

Demographic Details:

A total of 56 cases had fulfilled the inclusion criteria during the study period who were included in the study.

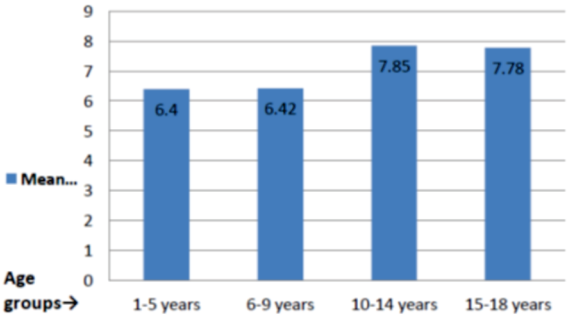
The mean age of the study population is 9.21 years with a standard deviation of 4.13 years. The range of the age is 16 i.e. the minimum 2 years and the maximum of 18 years.

Figure 1: The bar chart showing age distribution of study subjects



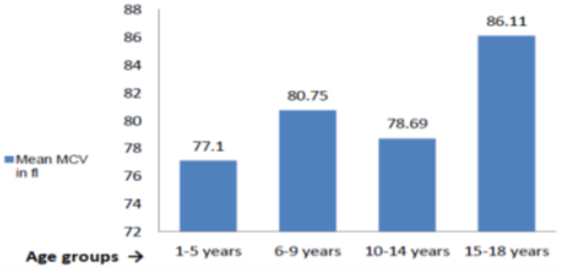
Mean Hemoglobin of the study population was 7.03 g/dl with a standard deviation of ± 1.8 g/dl. One way ANOVA Applied showed p=0.028 but multiple comparison Boneferroni in all Age groups shows no significant changes in mean Hb in g/dl.

Figure 2: Bar chart showing distribution of mean Hemoglobin (Hb) in g/dl according to age.



The mean MCV of the study population was calculated to be 80.5 fl with a standard deviation of 10.9 fl. The age group with the least mean MCV was 1-5 years and the maximum mean MCV was 15-18 years but the difference in mean MCV in fl was not significant.

Figure 3: Bar chart showing distribution of mean Mean corpuscular hemoglobin (MCV) in femtolitres (fl) according to age.



There was a strong positive (Correlation Coefficient=0.71, p=0.00012) correlation between Serum Ferritin and PRC transfusion.

Of the 56 study subjects, 29 received transfusion (51.8%) whereas 27 i.e. 48.2% did not. The mean transfusion was 38.97 ml/kg/year with a standard deviation of ±32.33ml/kg/year. Majority (79.3%) of the subjects received less than 50 ml/kg/year of transfusion. See table no.1

Table 1 shows correlation of serum ferritin with PRC transfusion

Categories of PRC transfusion ml/kg/year	Study subject	Mean serum ferritin (ng/dl)	
Not Transfused	27	203.6 ± 158.6	Pearson's Correlation Coefficient=0.71
1-50	23	255.76 ± 193.6	
51-100	4	864.25 ± 355.3	p=0.00012
>100	2	962 ± 336.6	
Total	56	299.3 ± 283.4	

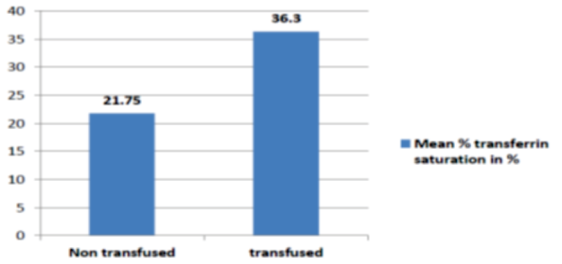
	Number of subjects	Mean % transferrin Saturation	
Not transfused	27	21.75 ± 11.6	Mann Whitney U Test P=0.001
transfused	29	36.30 ± 14.3	
Total	n=56	29.29 ± 14.9	

The mean Percentage (%) Transferrin Saturation was found to be 29.29 with a standard deviation of 14.9%.

Figure no.4 shows the mean Percentage (%) Transferrin Saturation among the transfused subjects was found to be higher than that of the Non-Transfused subjects i.e. 36.30% & 21.75% respectively.

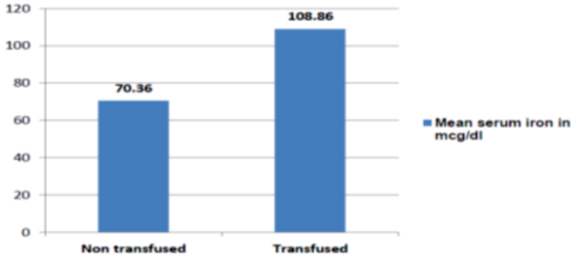
Mann Whitney U Test shows that the difference in the means was Statistically significant with a p-value of 0.001.

Figure 4: Distribution of mean % transferrin saturation in % according PRC transfusion



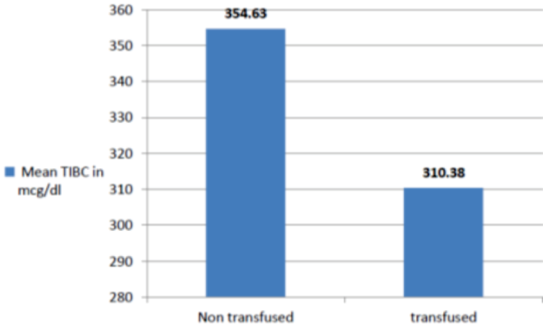
The mean serum Iron among the transfused subjects (108.86±48.3mcg/dl) was found to be higher than that of the Non-Transfused subjects (70.36±40.8mcg/dl). Mann Whitney U Test shows that the difference in the means was statistically significant with a p-value of 0.001

Figure 5: Distribution of mean serum iron in mcg/dl with PRC Transfusion



The mean TIBC was found to be 331.72 mcg/dl with a standard deviation of ± 101.9 mcg/dl figure no.6 shows that the mean TIBC among the nontransfused subjects was found to be higher than that of the Transfused subjects i.e. 354.62 & 310.39 mcg/dl respectively but Mann Whitney U tast shows that the difference in the means was not statistically significant with a p-value of 0.104

Figure 6: Distribution of mean TIBC in mcg/dl according PRC Transfusion



Out of 56 cases studied, 4(7.1%) had iron deficiency anaemia.

Table 2: Iron deficiency anaemia and PRC transfusion

Age in years	PRC transfusion in ml/kg/year	Hb in g/dl	MCV in fl	Sr. ferritin in ng/dl	TIBC in mcg/dl	% transferrin saturation
8	10	6.7	67	12	469.51	6.47
13	0	7.5	69	13	545	7.3
14	0	8.6	68	11	566.99	6.17
18	0	5.3	69	13.2	456	9.18

n=56	Subjects with iron deficiency anaemia	Fisher exact test
Transfused (29)	1	P=0.55
Non transfused(27)	3	

Out of 56 cases studied, 4(n=56 7.1%) had iron deficiency anaemia. 3(n= 27 10.3%) of non-transfused subjects had iron deficiency anaemia while 1(n=29 3.4%) of transfused subjects had iron deficiency anaemia but this difference was statistically not significant. See table no. 2

Table 3 - Iron overload and PRC transfusion

PRC Transfusion	Iron Overload		
	Present	Absent	
Transfused (29)	21	8	Chi square=1.07 P=0.30
Non transfused(27)	16	11	
Total=56	37	19	

Out of 56 cases studied, 37(66.1%) had iron overload. In transfused subjects 21(n=29 72.4%) had iron overload while in non-transfused subjects 16 (n=27 59.3%) had iron overload but this difference statistically not significant. See table no. 3

Table 4: Patients of Iron overload to be considered for chelation Therapy

Age in years	PRC transfusion in ml/kg/year	Sr. ferritin in ng/dl
7	80	1200
8	160	1200
15	60	1100

Table 4 shows patients of sickle cell anaemia with serum ferritin value >1000ng/dl and in whom chelation therapy should be considered. Total 3(5.4%) subjects from study population should be considered for chelation therapy.

CONCLUSION

In our study, a risk of iron overload was found more than iron deficiency in patients of sickle cell anaemia. Being a chronic hemolytic anaemia, these patients always need blood transfusions to their rescue which pose them at a risk of iron overload which is transfusion related in addition to ongoing microhemolysis. Iron deficiency anaemia being symptomatic is easily recognizable and treated but there are no specific symptoms related to iron overload unless and until the patient reaches to a level of iron toxicity which then becomes too late for chelation therapy and the hepatotoxicity and ardiotoxicity secondary to iron overload may then become irreversible.

We are well aware of chelation therapy in thalassemics but no such protocol has ever been laid down for patients of sickle cell anaemia. As in Conclusion our study, we find iron profile going high from the transfusions of 50ml/kg/year, one should be on a look out when the transfusion reaches this level by doing repeatedly serum ferritin levels which is a sensitive marker for iron overload.

In our study, we found 3 patients with iron overload at the level of serum ferritin > 1000 ng/dl; in whom the protocol is to start chelation therapy

Limitation of the research

- Limited sample size
- Areas based research

Annexure-I

LIST OF ABBREVIATIONS

%TS - Percentage Transferrin Saturation
EDTA - Ethylenediaminetetraacetic acid
fl - femtolitre
g/dl - gram/decilitre
Hb - Hemoglobin
HbA - Adult hemoglobin
HbA2 - Hemoglobin A2
HBB gene - Hemoglobin subunit Beta gene
HbF - Fetal hemoglobin
HbS - Sickle Hemoglobin
HbSS - Sickle Cell Anaemia
HPLC - High-Performance Liquid Chromatography
IDA - Iron Deficiency Anaemia
mcg/dl - microgram/decilitre
mcg/l - microgram/litre
MCH - Mean Corpuscular Hemoglobin
MCV - Mean Corpuscular Volume
ng/dl - nanogram/decilitre
ng/ml - nanogram/ millilitre
no. - Number
PRC - Packed Red blood Cells
SCD - Sickle Cell Disease

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