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SICKLE CELL ANAEMIA AND IRON LEVELS IN SOUTH INDIA

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ABSTRACT

Sickle cell disease (SCD) is the most common genetic hemoglobin disorder in which there is an inheritance of mutant hemoglobin genes from both parents.Iron status in patients with sickle cell anaemia is a matter of continuing investigation. In this study, children with sickle cell anemia were evaluated for iron deficiency. Iron deciency anaemia being symptomatic is easily recognizable and treated but there are no specic 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.

INTRODUCTION:

The iron status of sickle cell anemia patients has previously been reported as indicating either sufficiency or iron overload.[1-4] Some authors have also reported iron deficiency among children with sickle cell anemia.[5,6] Evaluating for iron deficiency in SCA is important, as it could contribute to worsening anemia and impairment in growth and neurocognitive development. Iron is an important component of hemoglobin in the red blood cells. Iron is needed for oxygen transport. While the human body tightly regulates iron absorption and recycling,[7] there is no physiological regulatory mechanism for iron excretion. Iron overload is prevented only by regulating iron absorption.

The common causes of iron deficiency in children, including dietary deficiency, infections, malabsorption and blood loss through hookworm infestation, are prevalent in Nigeria.5 Iron deficiency is mainly prevented by maintaining a balance between iron intake, iron absorption and excretion. Individuals with sickle cell disease have an adequate iron source, potentially from increased red cell turnover and from repeated blood transfusions.[8] An increase in gut iron absorption also contributes significantly to the iron pool in subjects with SCA. However, children with SCA may have a similar predisposition to nutritional inadequacies, similar to others without SCA, and excessive urinary iron loss could additionally result in iron deficiency [9].

Sickle cell anaemia contributes significantly to morbidity and mortality among children. Much is known about the disease presentation and end organ manifestation but the iron status in children with Sickle cell anaemia is still a matter of controversy [10]. In children with sickle cell anaemia, chronic haemolysis results in increased availability of iron directly from lysed red cells and also from increased absorption of iron from the gastrointestinal tract [11]. Additionally, the high load of iron provided by multiple blood transfusions [12,13] would suggest that iron deficiency is unlikely in sickle cell anaemia. However, in some parts of the world, the frequency of blood transfusion among patients is now less as a result of improved management in recent years [14].

Our aim is to evaluate the iron status in patients of sickle cell anemiaand objectives are to determine the percentage of patients with sickle cell anemia having iron deciency anemia. And to determine iron overload if any in patients of sickle cell anemia.

MATERIAL AND METHODS:

Children with sickle cell anaemia who were diagnosed by hemoglobin electrophoresis in stable state between the age group 1 to 16 years and who came to the hospital for pediatric outpatient care or hospitalized The study was cross sectional. The sample size of the study during the above mentioned study period was 28. They were then investigated for complete iron prole i.e. haemoglobin, MCV, Serum Ferritin, serum Iron, total iron binding capacity, Percentage transferrin saturation. Inclusion Criteria - Patients who are conrmed 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 :

Table 1 Shows Correlation Of Serum Ferritin With PRC Transfusion

Categories of PRC transfusion ml/kg/year	Study Subject	Mean Serum Ferritin (ng/dl)	Pearson's Correlation Coefficient = 0.71 P=0.00011
Not Transfused	14	202.81 ± 156.3	
1-50	11	253.81 ± 192.8	
51-100	02	862.32 ± 354.1	
>100	01	961.24 ± 335.3	
Total	28	298.64 ± 282.6	
	Number of Subjects	**Mean % Transferrin Saturation**	Mann Whitney U Test p=0.001
Not Transfused	14	21.72 ± 11.1	
Transfused	14	36.21 ± 14.1	
Total	28	29.26 ± 14.3	

Table 2: Iron Deciency 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	5	6.6	66	11	468.40	6.35
13	0	7.4	68	12	542	7.2
14	0	8.5	67	10	560.21	6.10
18	0	5.2	68	12.2	453	9.11
N=56	Subjects with	Fisher Exact Test p=0.52				

	iron deficiency anaemia	
Transfused (14)	1	
Non-Transfused (14)	2	

Table 3 - Iron Overload And PRC Transfusion

PRC Transfusion	Iron Overload		Chi square = 1.05 P=0.29
	Present	Absent	
Transfused (14)	10	4	
Non-Transfused (14)	8	6	
Total = 28	18	10	

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

DISCUSSION:

There was a strong positive (Correlation Coefficient=0.74, p=0.00012) correlation between Serum Ferritin and PRC transfusion. We found 2 subjects i.e. 7.3% were iron decient. Majority of them i.e.2 subjects had not received transfusion. In the study majority of subjects i.e.10 (70 %) where iron overloaded, which was found more common than iron deciency in our study. We found 2(5.4%) subjects in whom chelation therapy should be considered. In the study, serum iron and % transferrin saturation was signicantly 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 signicant difference in PRC transfused and nontransfused group but the values in PRC transfused group where lower than non-transfused . Mean Hemoglobin of the study population was 7.02 g/dl with a standard deviation of ± 1.7 g/dl. One way ANOVA Applied showed p=0.026 but multiple comparison Boneferroni in all Age groups shows no signicant changes in mean Hb in g/dl. The mean MCV of the study population was calculated to be 80.5 with a standard deviation of 10.6 .The age group with the least mean MCV was 1-5 years and the maximum mean MCV was 15-16 years but the difference in mean MCV in was not significant.

There was a strong positive (Correlation Coefficient=0.69, p=0.00010) correlation between Serum Ferritin and PRC transfusion. The mean Percentage (%) Transferrin Saturation among the transfused subjects was found to be higher than that of the Non-Transfused subjects i.e. 36.86 & 21.54% respectively. Mann Whitney U Test shows that the difference in the means was Statistically signicant with a p-value of 0.001. The mean serum Iron among the transfused subjects (108.78±48.6 mcg/dl) was found to be higher than that of the NonTransfused subjects (70.16±40.2 mcg/dl). Mann Whitney U Test shows that the difference in the means was statistically signicant with a p-value of 0.001.

The mean TIBC was found to be 331.68 mcg/dl with a standard deviation of ± 101.2 mcg/dl gure 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 that shows that the difference in the means was not statistically signicant with a p-value of 0.100. The TIBC measures the availability of iron binding sites [15]. Extracellular iron is transported in the body bound to transferrin, which is the primary iron-transport protein [15]. Hence, TIBC indirectly measures transferrin levels, which increase as stored iron decreases .The possible explanation may be the presence of high body iron stores among subjects with sickle cell anaemia revealed by higher serum ferritin values. The explanation for the higher mean transferrin saturation among HbAA controls is not farfetched. The transferrin saturation is a measure of amount of iron bound to the protein transferrin and reflects iron transport. As the body iron stores are depleted, the transferrin saturation rises. It has been revealed in the current study that children with sickle cell anaemia have higher body iron stores potentially from increased red cell turnover and from blood transfusions. Blood transfusion is offered as needed when anaemia is severe. In consequence, the number of patients who had ever received transfusions was relatively small. Even then, very few of them had received enough units of blood transfusion to potentially affect their iron status. The ability of the study to test the influence of blood transfusion was therefore highly restricted. Serum ferritin is known to reflect mainly reticuloendothelial iron stores [16]. It is considered to be a sensitive indicator of body iron stores and thus elevated serum ferritin concentrations may reflect possible high body iron stores. A higher value of serum ferritin in children with sickle cell anaemia may be due to presence of increased iron in the reticuloendothelial cells resulting from the excessive breakdown of haemoglobin. It is however known that high iron stores as implied from high serum ferritin are associated with increased release of hepcidin which in turn leads to reduced serum iron [17].

CONCLUSION:

The risk of iron overload was found more than iron deciency 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. In sickle cell disease transfusions improve blood flow by reducing the proportion of red cells capable of forming sickle hemoglobin polymer. This limits hemolysis and the endothelial damage that result from high proportions of sickle polymer-containing red cells. Additionally, transfusions are used to increase blood oxygen carrying capacity in sickle cell patients with severe chronic anemia or with severe anemic episodes. Transfusion is well-defined as prophylaxis (stroke) and as therapy (acute chest syndrome and stroke) for major complications of sickle cell disease and has been instituted, based on less conclusive data, for a range of additional complications, such as priapism, vaso-occlusive crises, leg ulcers, pulmonary hypertension, and during complicated pregnancies.

Iron deciency anaemia being symptomatic is easily recognizable and treated but there are no specic 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. Chelation therapy aims to balance the rate of iron accumulation from blood transfusion by increasing iron excretion in urine and or faces with chelators. If chelation has been delayed or has been inadequate, it will be necessary to excrete iron at a rate which exceeds this. Because iron is also required for essential physiological purposes, a key challenge of chelation therapy is to balance the benefits of chelation therapy with the unwanted effects of excessive chelation. In our study, we found 2 patients with iron overload at the level of serum ferritin > 1000 ng/dl; in whom the protocol is to start chelation therapy.Age had poor linear relationship with the transferrin saturation and serum ferritin. Further studies are needed to further explore the additional factors such as body composition that may influence iron status in children with sickle cell anaemia.

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