International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Assessment of Iron Status in Sickle Cell Patients and its relationship with the Frequency of Blood Transfusion

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Abstract: ***Background: Sickle Cell Disease (SCD) is common in Indian subcontinent. Sickle Cell Disease (SCD) patients can have iron deficiency or transfusional iron overload. It is important to know the pattern of iron parameters in different clinical states of SCD to decide whether these patients require iron supplementation, blood transfusion or chelation therapy. Materials & Methods: The study was conducted in the Department of Pathology, Pt. J.N.M. Medical College and DR. B.R.A.M. Hospital, Raipur, C.G. from January 2015 to august 2016 among patients who attended the OPD and hospitalized in Paediatrics and Medicine Ward. Serum Iron was measured by Ferrozine/Magnesium Carbonate method using fully automated biochemistry I-Lab 650i autoanalyser. Serum Ferritin was measured by ELISA test kit. Results: Out of 100 patients, 58 cases were of Sickle Cell Disease (SCD) and 42 cases were of Sickle Cell Trait (SCT), so the ratio of SCD and SCT patients was 1.38:1. Male: Female ratio was 1.04:1. Maximum number of cases (67 %) belongs to age group between 5-20 years. Out of 100 patients, 40 % had increased serum ferritin, 50 % had normal and 10 % had decreased level while serum iron level was increased in 23 % patients, normal in 38 % patients and decreased in 39 % patients. Serum iron and serum ferritin level was found normal in 52 % patients of Sickle Cell Disease who had transfused < 5 units of blood. Serum ferritin and serum iron level was increased as numbers of blood transfusions were increased. Conclusion: Sickle Cell Trait patients were in iron deficiency state while Sickle Cell Disease patients were in iron overload state. Because of multiple blood transfusions in SCD patients that lead to progressively increase in serum ferritin and serum iron level. This iron overload should be prevented by exchange transfusion rather than conventional transfusion. Thus the correlation between these (serum ferritin, serum iron) parameters can help in iron overload and iron deficiency states in the patients of Sickle Cell Disease and Sickle Cell Trait.***

Keywords: Sickle Cell Patients, Serum Iron, Serum Ferritin, Iron Overload, Iron Deficiency

1. Introduction

Sickle hemoglobin (HbS) is first molecular disease known to man. It is structural variant of Hb in which Glutamic acid, an amino acid at position number six of beta globin chain of Hb, is replaced by valine.[1] In Chhattisgarh the sickle Hb is common in central and southern part of state.[2] Iron deficiency anemia was found to be most common in Sickle Cell Anemia patient as compared to Sickle Cell Trait and this could be due to low dietary intake during vaso-occlusive crisis, infection and malabsorption.[3] In Sickle Cell Disease transfusion improves blood flow by reducing the proportion of red cell capable of forming Sickle Hb polymer. This limit hemolysis and endothelial damage that results from high proportion of Sickle polymer containing red cell. Additionally transfusions are used to increase blood O_2 carrying capacity in Sickle Cell patients which leads to iron overload.[4]

2. Aims and Objectives

(1) To know the difference of iron status in Sickle Cell Disease patients and Sickle Cell Trait patients.

(2) To know the relationship between iron status and frequency of blood transfusion in Sickle Cell Disease patients.

3. Materials and Methods

It was a prospective, observational and descriptive study.

Study area- Department of Pathology, Pt. J.N.M. Medical College and DR. B.R.A.M. Hospital, Raipur; C.G.

Study duration- January 2015 to August 2016

Sample source- Patients who attended the OPD and hospitalized in the Paediatrics and Medicine Ward, who fulfill inclusion and exclusion criteria.

Inclusion Criteria:

1) Patient should be with HbSS or HbAS blood type on Hb electrophoresis.
2) Age group between 0 - 65 years.

Exclusion Criteria:

1) Patients who are taking iron chelation therapy.
2) Patients presented with other haemoglobinopathy like thalassemia.

3) Patients presented with any other bleeding disorders, bleeding piles or bleeding peptic ulcer.

Detail history about blood transfusion and other examination were done to rule out other causes of anaemia. Peripheral venous blood was collected for serum iron and serum ferritin measurement.

Serum Iron was measured by Ferrozine/Magnesium Carbonate method using fully automated biochemistry I-Lab 650i autoanalyser.

Serum Ferritin was measured by ELISA test kit.

4. Results

The study included total 100 Sickle Cell Patients. Out of them 52 patients were of Sickle Cell Disease and 48 patients were of Sickle Cell Trait. Maximum number of cases (67 %) belongs to the age group of 5-20 years. Male: Female ratio was 1.04:1.

Table 01 shows level of Serum Ferritin in Sickle Cell Disease (SCD) and Sickle Cell Trait (SCT) patients. Out of 58 Sickle Cell Disease patients, 51.7% had increased serum ferritin level, 37.9% had normal and 10.4% had decreased serum ferritin level. Out of 42 Sickle Cell Trait patients, 23.8% had increased serum ferritin level, 66.7% had normal and 9.5% had decreased serum ferritin level.

Table 02 shows level of Serum Iron in Sickle Cell Disease (SCD) and Sickle Cell Trait (SCT) patients. Out of 58 Sickle Cell Disease patients, 32.7% had increased serum iron level, 41.4% had normal and 25.9% had decreased serum iron level. Out of 42 Sickle Cell Trait patients, 9.5% had increased serum iron level, 33.4% had normal and 57.1% had decreased serum iron level.

Sickle Cell Disease patients require frequent blood transfusion. We had compared serum ferritin level in these patients according to the number of blood transfusion in ***Table 03***. Out of 58 Sickle Cell Disease patients, 25 patients were transfused with up to 04 units of blood. In which 13 (52%) patients had normal serum ferritin level, 08 (32%) patients had increased and 04 (16%) had decreased level of serum ferritin. 19 patients were transfused with 5-10 units of blood. Out of them 11 (57.9%) patients had increased serum ferritin, 07 (36.8%) patients had normal and 01 (5.3%) patient had decreased level of serum ferritin. 05 patients were transfused with 11-15 units of blood. In which 03 (60%) patients had increased serum ferritin, 01 (20%) patient had normal and 01 (20%) patient had decreased level of serum ferritin. Patients who had transfused > 15 units of blood were having almost 100 % increased serum ferritin.

We also compared the level of serum iron in Sickle Cell Disease patients according to the number of blood transfusion in

Table 04. 25 patients were transfused with up to 04 units of blood, in which 13 (52%) patients had normal serum iron level, 02 (8%) patients had increased and 10 (40%) had decreased level of serum iron. 19 patients were transfused with 5-10 units of blood, in which 04 (21%) patients had increased level of serum iron, 10 (52.6%) patients had normal and 05 (26.4%) patients had decreased level of serum iron. 05 patients were transfused with 11-15 units of blood, in which 04 (80%) patients had increased level of serum iron, 01 (20%) patient had normal level of serum iron. 09 patients were transfused with more than 15 units of blood. Increased serum iron level was found in all 09 (100%) patients.

Table 1: Level of Serum Ferritin
In Sickle Cell Disease (SCD) and Sickle Cell Trait (SCT) patients

	Total cases	Increased Male > 220 ng/ ml Female >124 ng/ml		Normal Male- 16-220 ng/ml Female-10-124 ng/ml		Decreased Male < 16 ng/ml Female<10ng/ml	
		Number of cases	%	Number of cases	%	Number of cases	%
SCD	58	30	51.7%	22	37.9%	06	10.4%
SCT	42	10	23.8%	28	66.7%	04	9.5%
Total	100	40		50		10	

Table 2: Level of Serum Iron
In Sickle Cell Disease (SCD) and Sickle Cell Trait (SCT) patients

	Total cases	Increased Male > 160 µg/ dl Female > 145 µg/dl		Normal Male- 60-160 µg/dl Female-35-145 µg/dl		Decreased Male < 60 µg/dl Female <35 µg/dl	
		Number of cases	%	Number of cases	%	Number of cases	%
SCD	58	19	32.7%	24	41.4%	15	25.9%
SCT	42	04	9.5%	14	33.4%	24	57.1%
Total	100	23		38		39	

Table 3: Level of Serum Ferritin
Comparison according to Number of Blood Transfusion in Sickle Cell Disease (SCD) patients

No. of Blood Trans fusion	Total cases	Increased Male > 220 ng/ ml Female>124ng/ml		Normal Male- 16-220 ng/ml Female-10-124ng/ml		Decreased Male < 16 ng/ml Female <10 ng/ml	
		Number of cases	%	Number of cases	%	Number of cases	%

0-4 Units	25	08	32.0 %	13	52.0 %	04	16.0 %
5-10 Units	19	11	57.9 %	07	36.8 %	01	5.3 %
11-15 Units	05	03	60.0 %	01	20.0 %	01	20.0 %
16-20 Units	02	02	100.0%	00	00 %	00	00 %
21-25 Units	01	01	100.0%	00	00 %	00	00 %
26-30 Units	01	01	100.0%	00	00 %	00	00 %
>30 Units	05	04	80 %	01	20.0 %	00	00 %

Table 4: Level of Serum Iron
Comparison according to Number of Blood Transfusion in Sickle Cell Disease (SCD) patients

No. of blood trans fusion	Total cases	Increased Male > 160 µg/ dl Female > 145µg/dl		Normal Male- 60-160µg/dl Female 35-145µg/dl		Decreased Male < 60 µg/dl Female <35 µg/dl	
		Number of cases	%	Number of cases	%	Number of cases	%
0-4 Units	25	02	8.0 %	13	52.0 %	10	40.0 %
5-10 Units	19	04	21.0 %	10	52.6 %	05	26.4 %
11-15 Units	05	04	80.0 %	01	20.0 %	00	00 %
16-20 Units	02	02	100.0%	00	00 %	00	00 %
21-25 Units	01	01	100.0%	00	00 %	00	00 %
26-30 Units	01	01	100.0%	00	00 %	00	00 %
>30 Units	05	05	100.0%	00	00 %	00	00 %

5. Discussion

Sickle Cell Anaemia is a formidable problem in India and is more prevalent in Chhattisgarh. The present study was undertaken to investigate whether the patients of SCD and SCT had significantly different iron status (serum iron and serum ferritin) and to confirm the suspicion of iron overload or iron deficiency.

In this study we found maximum numbers of Sickle Cell Disease cases (51.7 %) were having increased serum ferritin level, which was similar to the study of **Patra P.K. et al[5]**, **V.N. Mishra et al[6]**, and **D.A. Okoh et al[7].** While maximum number of Sickle Cell Trait cases (66.7 %) was having normal serum ferritin level. The study of **Patra P.K. et al[5]**, **Debkumar Ray et al[8]** and **V.N. Mishra et al[6]** were also having concordance with our study.

We observed that maximum patients of Sickle Cell Disease (41.4 %) were having normal serum iron. Similar findings were noted by **Rodrigues P.C. et al[9], Debkumar Ray et al[9],** and **V.N. Mishra et al[6].**

In Sickle Cell Trait patients we observed 57.1 % cases with decreased serum iron. Other studies had reported the higher serum iron in Sickle Cell Disease patients than Sickle Cell Trait patients.

The probable reason is the excessive intravascular haemolysis as well as increased blood transfusion in Sickle Cell Disease patients. Our study indicated that iron deficiency was more common among Sickle Cell Trait than Sickle Cell Disease cases. Study done by **Debkumar Ray et al[9]** also supported it.

We noticed linear relationship between number of blood transfusion and serum iron level similar to the study of **Debkumar Ray et al.[9]**

Patients who were transfused with more than 15 units of blood had increased serum iron level in all the patients (100%). In another study done on effect of blood transfusion on iron status in Sickle Cell Disease and Trait by **Devis et al[10],** they found that serum ferritin was lower than normal in patients who were not transfused.

Multiple blood transfusions on a chronic basis lead to excessive accumulation of iron, especially in adults with Sickle Cell Disease (SCD) that leads to progressively increase in serum ferritin. The majority of adults with Sickle Cell Anemia, however requires episodic blood transfusions on a chronic basis and, hence are at risk to develop iron overload.

In our study also there was significant increase in serum ferritin level in transfused patients of Sickle Cell Disease because most of the patients were previously transfused.

6. Conclusion

Sickle Cell Trait patients were in iron deficiency state and can be treated with iron supplementation, which is indicated when iron deficiency is proved by laboratory investigation. In patients of Sickle Cell Disease there is iron overload state, because of multiple blood transfusions on a chronic basis lead to excessive accumulation of iron, leads to progressively increase in serum ferritin. This iron overload should be prevented by exchange transfusion rather than conventional transfusion. Medical management for iron overload would be chelation therapy, which is indicated when the serum ferritin level > 1000 ng/dl or when patients require more than 10 blood transfusions per year. Thus the correlation between these (serum ferritin, serum iron) parameters can help in iron overload and iron deficiency states in the patients of Sickle Cell Disease and Sickle Cell Trait.

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