STUDY OF IRON PROFILE IN SICKLE CELL PATIENTS

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ABSTRACT

BACKGROUND
Sickle cell disease is inherited as an autosomal recessive disorder that affects red blood cells. People with sickle cell disease contain abnormal haemoglobin, which is haemoglobin S. The aim of this study is to find out whether sickle cell patients are iron overloaded or iron deficient.

MATERIALS AND METHODS
This is a descriptive study. Concentrations of serum iron, total iron binding capacity and ferritin were analysed and compared between transfused and non-transfused sickle cell anaemia and sickle cell trait patients.

RESULTS
Serum iron was significantly more in sickle cell anaemia patients as compared with sickle cell trait patients. Serum ferritin was elevated more in patients who presented with features suggestive of vaso-occlusive crisis than those in steady state. Iron deficiency state was found more in sickle cell anaemia patients as compared to sickle cell trait patients, but iron overload state was also found only in those sickle cell patients who were hypertransfused.

CONCLUSION
Sickle cell disease, though a chronic haemolytic condition, can also present with iron deficiency and iron status of these patients varies according to their diet, number of transfusions received and number of crisis episodes. Therefore, we recommend that patients with sickle cell disease should be screened for iron deficiency by conventional laboratory tests.

KEY WORDS
Iron, Ferritin, Sickle Cell Disease, Total Iron Binding Capacity, Haemoglobin.

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BACKGROUND

Sickle cell disease is inherited as an autosomal recessive disorder that affects red blood cells. People with sickle cell disease contains abnormal haemoglobin, which is haemoglobin S. Sickle cell disease are hereditary disorders, which primarily affects the beta chain of HbA and forms HbS in the red cells. Sickle cell haemoglobin is produced by substitution of valine for glutamic acid at 6th position of β chain of normal haemoglobin. An individual develops sickle cell anaemia (HbSS) when gene mutation is homozygous and when gene mutation is heterozygous it leads to sickle cell trait (HbAS). Therefore, individuals with heterozygous mutation has about 55 - 60% of HbA and 35 - 40% of HbS.[1] Sickle cell gene is an example of a gene that has persisted and spread in the population. It has its origin in the black population in Africa and it also provides resistance to one type of malaria. This occurs secondary to impaired parasite growth at low oxygen tension. As low oxygen tension that causes sickling of red blood cells and also hampers the growth of the parasite. In addition to this sickle cells then gets sequestered in spleen, so that the malaria parasite could not complete its life cycle and the individual get protected from the infection.[2] Homozygous sickle cell disease (Hb-SS) is genetically inherited disorder and transmitted equally by males and females.[3] Iron plays a vital role in various metabolic activities in humans, such as erythropoiesis.[4] Chronic haemolytic anaemia are usually found to be iron loaded because of excessive breakdown of red blood cells and also due to increased blood transfusion frequency to maintain the required haemoglobin. Hence, due to this such patients are at a risk of developing hemosiderosis.[5] Due to this reason, iron salts are rarely employed in the treatment of sickle cell anaemia.[6] Contrary to this belief, there is widespread prevalence of iron deficiency and relatively small number of transfusion in India makes it likely that children with sickle cell anaemia are not often iron loaded as is believed and may in some cases be actually iron deficient. Also it is found that sickle cell patients have ferritinuria, hemosiderinuria as well as urinary iron excretion (Sears DA et al),[7] (Washington R et al),[8] (Lipschitz DA et al).[9] Therefore, the present study is concerned with evaluation of iron status in cases with sickle cell patients by estimating serum iron, serum ferritin, serum TIBC and % transferrin saturation.

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MATERIALS AND METHODS

The present descriptive study was carried out during the period of November 2014 to November 2016 in the Department of Medicine, Government Medical College, Nagpur. The study protocol was approved by the Institutional Ethical Committee. An informed written consent was obtained from all the study subjects who were enrolled in the study. This study was conducted in sickle cell disease patients

attending the Medicine OPD and those admitted in the Medicine wards included in the study. 100 Sickle cell disease patients obtained from estimation of sample size, who fulfilled inclusion and exclusion criteria as mentioned below were studied. Out of total 100 patients included in the study, 55 were Sickle cell anaemia (SS) patients and 45 were Sickle cell trait (AS) patients. History, general physical examination and systemic examination of the selected patients were taken according to the proforma. The study sample comprised of 100 patients, out of which 55 were Sickle cell disease and 45 were Sickle cell trait patients.

Inclusion Criteria**:** Patients more than 12 years of age, diagnosed cases of Sickle cell anaemia (SS) and Sickle cell trait (AS) patients in steady state or Sickle cell crisis.

Exclusion Criteria**:** History of surgery in last 3 months, history of blood transfusion in last 3 months, patients with acute or chronic blood loss e.g. bleeding piles, bleeding acid peptic ulcer disease, patient unwilling to take part in above study, pregnant females, patients with haemoglobinopathies other than SCD like Sickle thalassemia disorder. Estimation of Sr. ferritin was carried out on the principle of immunoenzymometric assay (IEMA) by Ferritina Kit. Serum Iron and TIBC was estimated by kit provided by Crest Biosystem.

The Sample Size was calculated from the Formula

N= $Z^2 \times P\ (1\text{-}P)/d^2$

N- Minimum sample size

Z- Confidence interval (1.96)

P- Prevalence rate (6% - 7%)

d- Precision or Desired level of significance (0.05)

Thus, the sample size calculated was 100.

Statistical Analysis

All values were reported as mean ± SD. Chi-square test was used to assess the significance of the difference in the values in the sickle cell patients. The differences were considered as statistically significant at a probability value, $p < 0.05$.

RESULTS

(Table 1) Gender specific distribution of Sickle cell patients in the study, (Table 2) Age specific distribution of Sickle cell patients in the study, (Table 3) Level of serum iron (µg/dL) in Sickle cell patients, (Table 4) Level of serum ferritin (ng/mL) in Sickle cell patients, (Table 5) Level of TIBC (µg/dL) in Sickle cell patients, (Table 6) Level of % transferrin saturation in Sickle cell patients, (Table 7) Distribution of number of patients according to units of blood transfusion, (Table 8) Level of serum iron (µg/dL) in transfused and non-transfused Sickle cell patients, (Table 9) Evaluation of iron status among Transfused and Non-transfused Sickle cell patients in the study**.**

	Male		**Female**	
	n	**%**	**n**	**%**
SS (55)	29	52.72	26	47.28
AS (45)	23	51.12	22	48.88
Total	**52**		**48**	

Table 1. Gender specific distribution of Sickle Cell patients in the Study

	Increased Male > 180 µg/dL Female >180 µg/dL		**Normal Male:70-180 µg/dL Female:60-180 µg/dL**		**Decreased Male < 70 µg/dL Female < 60 µg/dL**	
	N	**%**	**n**	**%**	**n**	**%**
SS (55)	06	10.9	27	49.1	22	40
AS (45)	03	6.66	33	73.33	09	20
Total	09		60		31	
p-value= 0.04706						
Chi-square= 6.113						
Df= 2						

Table 2. Level of Serum Iron (µg/dL) in Sickle Cell Patients

	Increased Male > 322 ng/mL Female > 291 ng/mL		**Normal Male: 22-322ng/mL Female: 10-291ng/mL**		**Decreased Male < 22 ng/mL, Female < 10 ng/mL**	
	n	%	N	%	n	%
SS (55)	26	47.27	21	38.18	08	14.54
AS (45)	06	13.34	33	73.33	06	13.34
Total	**32**		**54**		**14**	
p-value= 0.00782						
Chi-square= 9.703						
Df= 2						

Table 3. Level of Serum Ferritin (ng/mL) in Sickle Cell Patients

	Increased Male > 450µg/dL Female > 450µg/dL		**Normal Male: 250-450 µg/dL Female: 250-450 µg/dL**		**Decreased Male < 250 µg/dL Female < 250 µg/dL**	
	N	%	N	%	n	%
SS(55)	21	38.18	25	45.45	09	16.36
AS(45)	07	15.56	34	75.56	04	8.88
Total	28		59		13	
p-value= 0.009						
Chi-square= 9.39						
Df= 2						

Table 4. Level of TIBC (µg/dL) in Sickle Cell Patients

	Increased Male > 45 Female > 45		**Normal Male: 13-45 Female: 13-45**		**Decreased Male < 13 Female < 13**	
	N	%	N	%	n	%
SS (55)	07	12.73	33	60	15	27.27
AS (45)	06	13.33	32	71.11	07	15.56
Total	13		65		22	
p-value= 0.364						
Chi-square= 2.022						
Df= 2						

Table 5. Level of % Transferrin Saturation in Sickle Cell Patients

Units of Blood Transfused	SS (55)	AS (45)	Total Patients (100)
	n (%)	n (%)	N
Nil	31 (56.36)	18 (40)	49
1-4	10 (18.20)	24 (53.34)	34
5-10	03 (5.45)	02 (4.44)	05
11-15	03 (5.45)	01 (2.22)	04
>15	08 (14.54)	00	08
Total	**55**	**45**	**100**

Table 6. Distribution of Number of Patients according to Units of Blood Transfusion

	Increased Male > 180 µg/dL Female >180 µg/dL		Normal Male: 70-180 µg/dL Female: 60-180 µg/dL		Decreased Male < 70 µg/dL Female < 60 µg/dL	
	n	%	n	%	n	%
Transfused (51)	8	15.69	40	78.43	3	5.88
Non-Transfused (49)	1	2.04	20	40.81	28	57.14
Total	**09**		**60**		**31**	
p-value =< 0.0001						
Chi square= 32.25						
Df= 2						

Table 7. Level of Serum Iron (µg/dL) in Transfused and Non-Transfused Sickle Cell Patients

	Iron Deficient		Normal		Iron Overload	
	n	%	n	%	n	%
Non-Transfused (49)	13	26.54	36	73.46	0	0
Transfused (51)	2	3.92	41	80.39	8	15.69
Total	**15**		**77**		**8**	
p-value= 0.009						

Table 8. Evaluation of Iron Status among Transfused and Non-Transfused Sickle Cell Patients in the Study

DISCUSSION

In our study, we found that serum iron was significantly ($p<0.05$) lower in more number of Sickle cell anaemia patients as compared with Sickle cell trait patients. Iron deficiency state was found more in Sickle cell anaemia patients as compared to Sickle cell trait patients. In our study it was also found that iron overload state was found only in those Sickle cell patients who received multiple blood transfusions. Majority of chronic haemolytic anaemia are iron loaded because of enhanced haemolysis and the same was also thought for sickle cell anaemia patients. Similar opinion was given by Reynold et al.[5] But the studies which are recently coming up show that the patients with sickle cell anaemia may be iron deficient. Patel et al[10] found that 4 (2.9%) patients of Sickle cell anaemia (SS) and 3 (17.6%) of Sickle cell trait (AS) patients had decreased serum iron levels. Patra et al found that 35 (58.3%) patients out of 60 Sickle cell anaemia (SS) and 8 (20%) patients out of 40 Sickle cell trait (AS) patients had decreased serum iron levels. In the same study, it was also found that 5 (11.62%) transfused patients and 14 (25%) non-transfused patients had decreased serum iron. Kassim et al[11] found that serum iron values were more in transfused patients as compared to non-transfused patients. The study done by Ikusemoro et al[12] showed a positive correlation between serum ferritin and number of units of blood transfused with a linear increase in serum ferritin levels seen in cumulative transfusions. The study conducted by Das PK and Sarangi A et al[13] also found high serum ferritin levels in 15.4% of Sickle cell anaemia patients, which was well correlated to the number of blood transfusion. The study conducted by Davies et al[14] found that patients who were hypertransfused (≥ 5 units of blood within 6 months to 2 years) had significantly higher serum ferritin concentration than those who have never been transfused or who had received 4 or less than 4 units of blood transfusion in the past 2 years. Vichinsky et al[15] found 6 (16%) non-transfused patients had iron deficiency and none of the transfused patients had iron deficiency. The diet of these individuals is poor in iron content and other essential nutrients, which contribute to the iron deficiency in these individuals.[16],[17],[18] Other reason which results in decrease in serum iron levels in sickle cell patients are due to urinary iron excretion increased in sickle cell anaemia, interference of absorption of iron by Phytates.[19] Serum ferritin was elevated more in patients who presented with features suggestive of vaso-occlusive crisis than those in steady state. Serum ferritin is an acute phase reactant, so its value is usually high in inflammatory states, so it is not a reliable marker of iron deficiency state and vaso-occlusive crises events also leads to inflammation which leads to increased ferritin.

CONCLUSION

In this study, it was found that sickle cell anaemia patients are more at risk of iron deficiency as compared to Sickle cell trait. Although, Sickle cell disease is considered as a chronic haemolytic anaemia, still the iron status of these patients varies according to their diet, number of transfusion received and number of crisis episodes. Thus, in the course of treatment of sickle cell disease, the fact that these individuals are in iron deficiency state should be taken into consideration.

REFERENCES

[1] Benz EJ. 635 Disorders of Hemoglobin. In: Kasper DL, Braunwald E, Fauci AS, et al. eds. Harrison's principles of internal medicine. 17th edn. New York: McGraw-Hill Medical Publishing Division 2008:637-8.

[2] White NJ, Breman JG. Malaria. In: Kasper DL, Braunwald E, Fauci AS, et al. eds. Harrison's principles of internal medicine. 17th edn. New York: McGraw-Hill Medical Publishing Division 2008: p. 1283.

[3] Sickle-cell disease. Wikimedia Foundation Inc. 2009. http://en.wikipedia.org/wiki/Sickle-cell_disease

[4] Aisen P. Current concepts in iron metabolism. Clin Haematol 1982;11(2):241-57.

[5] Reynolds J. An evaluation of some roentgengraphic signs in sickle cell anemia and its variants. South Med J 1962;55:1123-8.

[6] Sergents GR. Quote by Lewis R. Sickle States. Clin Features in West Africa 1969.

[7] Sears DA, Anderson DR, Foy AL, et al. Urinary iron excretion and renal metabolism of hemoglobin in hemolytic diseases. Blood 1966;28(5):708-25.

[8] Washington R, Boggs DR. Urinary iron in patients with sickle cell anemia. J Lab Clin Med 1975;86(1):17-23.
[9] Lipschitz DA, Allegre A, Cook JD. The clinical significance of ferritinuria. Blood 1980;55(2):260-4.
[10] Patel C, Jha BM, Jana S, et al. Iron status in sickle cell disorders. Int J Med Sci Public Health 2016;5:1759-63.
[11] Kassim A, Thabet S, Al-Kabban M, et al**.** Iron deficiency in Yemini patients with sickle cell disease. East Mediterr Health J 2012;18(3):241-5.
[12] Ikusemoro AI, Halim NKD, Awodu OA, et al. Iron status of multiple transfused sickle cell anaemia patients attending a sickle cell clinic in Benin city, Nigeria. Open Journal of Pathology 2014;4(2):25-31.
[13] Das PK, Sarangi A, Satapathy M, et al. Iron in sickle cell disease. J Assoc Physicians India 1990;38(11):847-9.
[14] Davies S, Henthron JS, Win AA, et al. Effect of blood transfusion on iron status in sickle cell anaemia. Clin Lab Haematol 1984;6(1):17-22.
[15] Vichinsky E, Kleman K, Embury S, et al. The diagnosis of iron deficiency anemia in sickle cell disease. Blood 1981;58(5):963-8.
[16] NNMB Technical Report No. 20. National Nutrition Monitoring Bureau (NNMB). Report on the food and nutrient intakes of individuals. Hyderabad, India: National Institute of Nutrition, Indian Council of Medical Research 2000.
[17] Bamji MS, Lakshmi AV. Less recognized micronutrient deficiencies in India. NFI Bull 1998;19:5-8.
[18] Krishnaswamy K, Nair KM. Importance of folate in human nutrition. Br J Nutr 2001;85(Suppl 2):S115-24.
[19] National Institute of Nutrition, Indian Council of Medical Research. Annual Report 2005-2006:18-26.