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Original Research Article

An Observational Study of Correlation between Serum Ferritin Levels and Liver Functions in Multiple Transfused Thalassemia Patients in a Tertiary Care Centre at Jaipur, Rajasthan

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Abstract

Background: Thalassemia is a heterogeneous group of mendelian disorders. Thalassemia itself and complications due to iron overload can damage multiple organ systems.

Objective: Aim of our study was to correlate between serum ferritin level & liver functions in multiple blood transfused thalassemia patients.

Materials and Method: This was an observational study conducted in the department of pediatrics in a tertiary care hospital, Jaipur, Rajasthan. All those patients who received more than 50 blood transfusions are considered as multiple transfused patients and were included in this study. The Pearson correlation coefficient was applied to observe the correlation between serum ferritin level and liver function tests. A p- value of < 0.05 was considered statically significant.

Result: A total of 50 patients were enrolled in this study. 92% patients were under 15 years of age and male to female ratio was 2.33:1. There was significant correlation between serum ferritin level > 1000ug/L and serum transaminases levels (p value < 0.001) with strongly positive correlation coefficient was SGPT $r = +0.622$ and SGOT $r = + 0.704$. The correlation between serum bilirubin level with serum ferritin level <1000ug/L was static but further increase when serum ferritin level more than 1000ug/L a p-value <0.001 and $r = +0.784$.

Conclusion: Patients having abnormal liver functions in thalassemia patients due to iron over-load. Iron over-load in the body, which turn to lead to increased serum ferritin levels in multiple transfused thalassemia patients. High serum ferritin levels is associated with liver functions derangement. Serum ferritin levels should be monitoring routinely in multiple transfused thalassemia patients. Chelation therapy should be started as early as indicated to prevent liver functions derangement.

Keywords: Thalassemia, Serum Ferritin, multiple transfusions, SGPT, SGOT, Bilirubin.

Introduction

The term "Thalassemia" is derived from a Greek words, Thalas , which mean sea and Emia, which means blood, signifying that it is more common in the Mediterranean, these was first used in 1936 by Whipple and Wradford. Cooley and Lee described anemia, hepatosplenomegaly, pigmentation of the skin, thickening of long bones and skull, decreased osmolar fragility and leukocytosis. They gave the general term "Von Jaksch's Anemia". Later the eponym Cooley's anemia was given. [1] The thalassemia characterized by lack of or decreased synthesis of either the alpha or the beta globin chain of hemoglobin. β- thalassemia is characterized by deficient synthesis of the beta globin chain & in α- thalassemia is alpha globin chain. The hematological consequences of

diminished synthesis of one globin chain leads to low intracellular hemoglobin (hypochromia) and relative excess of the other chains. [2]

As a result of excess of the other globin chain , they aggregate into insoluble inclusions within erythrocyte and their precursors, causing premature destruction of maturing erythroblasts within the marrow (ineffective erythropoiesis) as well as lysis of mature red cells in the spleen (hemolysis). The quantitative defect in globin chain synthesis are defined as thalassemia. [3] The Thalassemia syndrome is the most common genetic disorder in the world. The selective pressures that have made the thalassemia so common are not known but are assumed to relate to the geographic distribution of malaria. [4] As per WHO estimate 4.5% of world's populations are carriers of hemoglobinopathies. Frequency of thalassemia gene in Indian population varies between 0 - 17% in different ethnic groups, with average of over 3%. Its prevalence is high among Gujaratis, Punjabis, Sindhis, Lohans etc. [5]

In Thalassemia, iron over load can damage multiple organs like liver, heart, endocrine system etc. are due to iron overload, chronic and severe hemolytic anemia, and long term effect of hypoxia & consequence of therapy. [6] In thalassemia patients iron over-load measured by serum iron, total iron binding capacity and serum ferritin. There is a correlation between serum ferritin and liver functions derangements. For liver function the use of transaminases level is a rapid & an inexpensive screening test. [7]

Aims & Objectives

To correlate between serum ferritin levels and liver functions in multiple transfused thalassemia patients.

Materials and Methods

Materials- This observational study was done among thalassemia patients in the age group of 2-18 years visiting a tertiary care hospital in Jaipur, Rajasthan. After taking approval from ethical committee from institute, we enrolled 50 already diagnosed thalassemia patients. The enrolled patients were admitted in thalassemia ward Mahatma Gandhi Medical College & Hospital, Jaipur, Rajasthan for blood transfusion from January 2019 to January 2021. The patients who had received > 50 blood transfusions considered as "multiple transfused.

Inclusion Criteria: -

- Patient who received at least 50 blood transfusions.
- Only Hb electrophoresis (HPLC) diagnosed cases of thalassemia.
- Patients willing to give consent for the study.

Exclusion Criteria: -

- Patients who are receiving hepatotoxic drugs.
- Acute & chronic liver disease (causes other than thalassemia).
- Patients with congenital liver diseases.

Methods: -

All patients were enrolled for this study after informed consent from their parents. A thorough history and clinical examination were done and findings were recorded in predesigned Proforma. Serum Ferritin and liver function tests were done which included liver enzyme (SGPT & SGOT) and total bilirubin. The age of initiation of blood transfusion was also recorded. Following laboratory parameters are taken into consideration: SGPT> 40U/L, SGOT > 50U/L & serum Bilirubin > 2 mg/dl. The serum transaminase levels are regarded best indicators of liver damage. [8] Study Design: Hospital Based Observational study. Setting: Thalassemia ward, Department of Pediatrics, M.G. Medical College & Hospital, Jaipur, Rajasthan. Data was analyzed using statistical software.

Results

Table 1: Demographic profile distribution of pediatric thalassemia patients according to Age & Sex
Age:-

Age		
2 – 5 Years	13	26%
6 – 10 Years	16	32%
11 – 15 Years	17	34%
>15 Years	4	8%
Sex		
Male	35	70%
Female	15	30%

Table 1 depicted that 35 (70%) were male and 15 (30%) were female (Male: Female ratio = 2.33: 1) in present study. 92% patients were under age of 15 years in the study.

Table 2- Serum Ferritin levels among multiple transfused thalassemia patients

Serum Ferritin Levels (<1000ug/l)	Serum Ferritin Levels (>1000ug/l)	Total
25 (50%)	25 (50%)	50 (100%)

Table 2 showed that out of 50 patients, 25 (50%) patients had serum ferritin levels <1000ug/l and 25 (50%) patients had serum ferritin levels > 1000ug/l.

Table 3- Serum ferritin versus serum transaminases levels in multiple transfused thalassemia patients

Serum Ferritin level	SGPT (Mean)	SD	p value	r value	SGOT (Mean)	SD	p value	r value
<1000ug/l (Mean=887.76 ug/l) N = 25	44.12 U/L	6.57	>0.05	+0.376	48.48 U/L	7.31	>0.05	+0.343
>1000ug/l (Mean=1757.32ug/l) N= 25	57.28 U/L	8.49	<0.001	+0.622	60.68 U/L	11.41	<0.001	+0.704

Table 3 Showed that in serum ferritin levels < 1000ug/l, SGPT and SGOT had p value > 0.05 with mean of SGPT was 44.12 U/L (95% CI 41.56 – 46.7) and mean of SGOT was 48.48 U/L (95% CI 45.62-51.35) and correlation coefficient was r = + 0.376 and + 0.343 respectively. The correlation between serum ferritin levels <1000 ug/l with serum transaminases level was poorly statistically significant. In serum ferritin levels >1000ug/L, SGPT and SGOT had p value <0.001 with mean of SGPT was 57.28 U/L (95% CI 53.59 – 60.61) and mean of SGOT was 60.68 U/L (95% CI 56.21 – 65.15) and correlation coefficient was r = +0.622 and + 0.704 respectively. The correlation between serum ferritin levels >1000ug/l with serum transaminases levels was statistically significant.

Table 4 – Serum Ferritin levels versus serum Bilirubin levels in multiple transfused thalassemia patients

Serum ferritin	Serum Bilirubin (Mean)	SD	p value	r value
<1000ug/L (Mean=887.76 ug/l) N=25	1.47 mg/dl	0.583	>0.05	+0.283
>1000ug/L (Mean=1757.32 ug/l) N=25	2.31mg/dl	0.795	<0.001	+0.784

Table 4 showed that in serum ferritin level <1000ug/L, serum bilirubin level had p value >0.05 with mean was 1.47 mg/dl (95% CI 1.24 – 46.7) and correlation coefficient was r =+ 0.283. The correlation between serum ferritin <1000ug/L with serum bilirubin was poorly statistically significant. In serum ferritin level >1000ug/L, serum bilirubin p value <0.001 with mean was 2.31 mg/dl (95% CI 2.0 – 2.62) and correlation coefficient was r =+ 0.784. The correlation between serum ferritin level >1000ug/L with serum bilirubin was statistically significant.

Discussion

In thalassemia, liver is affected in non-transfused patients due to extramedullary hematopoiesis in form of hepatomegaly, where as in transfused patients, the liver is primary organ for deposition of excess iron and liver becomes fibrotic and eventually cirrhotic, due to iron overload. The most important abnormalities of liver functions are hyper-gammaglobulinemia, hypoalbuminemia, moderate decrease in coagulation factors, increased serum transaminases levels and moderately elevated serum bilirubin levels. Iron over-load is measured by serum iron, serum ferritin and total iron binding capacity. Liver iron may also be increased in the post-splenectomy thalassemic patients. If proper chelation therapy is started at serum ferritin levels > 1000ug/L, liver dysfunction due to iron over load may be prevented to some extent.

Age, Sex and Caste distribution-

Age: In the present study, we found 92% patients are under15 years of age. A similar study was conducted by John et al (1972), where 88% patients were less than 15 years of age. [9]

Sex: We found male to female ratio was 2.33:1 in our study. Sing H et al did a similar study that reported male to female ratio was 2.33:1 in their study. [10]

Liver Functions correlation with serum ferritin-

In present study, 25 (50%) patients have serum ferritin levels < l000ug/l and 25 (50%) have > serum ferritin levels > 1000ug/l.

A similar study was done by Tahrindi Supiapperuma et al (2018) showed that 29.6% patients had < 1000ug/l serum ferritin levels and 70.1% patients had > 1000ug/l serum ferritin levels. [11]

In present study showed that serum transaminases levels were increased when serum ferritin levels >1000ug/L and a p-value <0.001 with SGPT r = +0.622 and r = + 0.704.

A similar study was done by Mohmood Asif et al (2014), showed that serum transaminases levels was significantly raised in high serum ferritin levels.12 Another study conducted by Rameshwar L. Suman et al (2016), showed that poorly chelated beta- thalassemia had hepatic dysfunctions in the form of abnormal liver enzymes and this starts occurring as soon as serum ferritin levels >1000ug/l.13 Another study conducted by Harsh G V et al (2019), showed that significant correlation between serum ferritin levels and transaminases levels (P<0.05).14 A similar study was conducted by May Al-Moshary et al (2020), showed that positive correlation with serum ferritin levels and liver enzymes, a p<0.05 with SGPT r = + 0.319 and SGOT r = + 0.670 .15

In present study showed that serum bilirubin level was increased when serum ferritin level >1000ug/L, a p-value <0.001 and r = + 0.784.

A similar study was done by Harsh G.V. et al (2019), showed that a weak correlation was found between serum ferritin levels and serum bilirubin.14 A similar study was done by May Al-Moshary et al (2020), showed that serum ferritin with serum bilirubin r = +0.294 and a p-value of <0.001.15

Conclusion

Present study was conducted in 50 multiple transfused thalassemia patients. In this study, serum transaminases levels and serum bilirubin levels were taken as parameter of liver function.

1.92% patients were under 15 years of age.

2.Sex Ratio (male: female) was 2.33:1.

3.Serum transaminases level significantly increased when serum ferritin level was increased more than 1000ug/L.

4.Serum bilirubin level also increased when serum ferritin level was more than 1000ug/l.

Recommendations

Routinely all thalassemia patients should be screened for liver functions (at 3month interval), serum iron & serum ferritin (6 monthly). Thalassemia patients should be screened for transfusion acquired infections. The chelation therapy should be started as early as indicated and should be regular. Before splenectomy in hyper transfused thalassemia patients, Pneumococcal, Hemophilus influenza type b and Meningococcal vaccine should be given at 14 days ago.

Ethical Approval

This study was approved by the Ethical Committee of Mahatma Gandhi Medical College, Jaipur, and Rajasthan, India.

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