

## AN OBSERVATIONAL STUDY OF LIVER FUNCTIONS IN MULTIPLE TRANSFUSED THALASSEMIA PATIENTS ON REGULAR CHELATION THERAPY VERSUS IRREGULAR CHELATION THERAPY IN A TERTIARY CARE CENTER OF JAIPUR, RAJASTHAN

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Received: 14 January 2024, Revised and Accepted: 05 March 2024

### ABSTRACT

**Objectives:** The aim of our study was to determine liver functions in thalassemia patients on regular versus irregular chelation therapy.

**Methods:** 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.

**Results:** A total of 50 patients were enrolled in this study. Ninety percent of patients were under 15 years of age and the male-to-female ratio was 2.85:1. In 82.35% regular chelation therapy, patients have normal liver functions as compared to 49.5% in irregular chelation therapy patients.

**Conclusion:** Patients having abnormal liver functions in thalassemia patients due to iron overload. As a result of chelation therapy, serum glutamic oxalocetic transaminase and serum glutamic pyruvic transaminase levels were significantly reduced. In the study, regular chelation therapy should be started as early as indicated in thalassemia patients.

**Keywords:** Thalassemia, Chelation therapy, Multiple transfusion, Liver function.

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### INTRODUCTION

In 1925, Cooley and Lee described anemia, hepatosplenomegaly, pigmentation of the skin, thickening of long bones and skull, decreased osmolar fragility, and leukocytosis in 5 children. They gave the general term "Von Jaksch's Anemia." Later, the eponym Cooley's anemia was given. The term "Thalassemia" is derived from the Greek word "θαλάσσιον" and the sea was first used in 1936 by Whipple and Wradford [1].

The thalassemia syndrome is the most common genetic disorder in the world. The selective pressures that have made thalassemia so common are not known but are assumed to relate to the geographic distribution of malaria. Although there are more than 200 mutations for beta-thalassemia, most are rare. About 20 common alleles constitute 80% of the known thalassemia worldwide [2]. Thalassemia is characterized by a lack of or decreased synthesis of either the alpha or the beta globin chain of hemoglobin.  $\beta$ -thalassemia is characterized by a deficient synthesis of the beta-globin chain and in  $\alpha$ -thalassemia is alpha globin chain. The hematological consequences of diminished synthesis of one globin chain lead to low intracellular hemoglobin (hypochromia) and relative excess of the other chains [3]. As a result of an excess of the other globin chain, they aggregate into insoluble inclusions within erythrocytes 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) [3]. The quantitative defect in globin chain synthesis is defined as thalassemia [4].

As per the World Health Organization estimate, 4.5% of the world's population are carriers of hemoglobinopathies [5]. The frequency of the thalassemia gene in the Indian population varies between 0% and 17%

in different ethnic groups, with an average of over 3%. Its prevalence is high among Gujaratis, Punjabis, Sindhis, Lohans, etc. [5].

Thalassemia itself and the complications of iron overload can damage multiple organs such as the liver, heart, and endocrine system due to iron overload, chronic and severe hemolytic anemia, long-term effect of hypoxia, and the consequence of therapy [6].

The role of chelation therapy in thalassemia is by reducing iron overload in the body. Iron chelation therapy causes a reduction in liver iron concentration, improvement in laboratory abnormalities of liver function, and arrest of hepatic fibrosis [7]. The guidelines for starting iron chelation therapy are serum ferritin concentration >1000  $\mu$ g/L and hepatic iron concentration >3.2 mg/g/dry weight. Two iron chelators are commonly used: Subcutaneous deferoxamine and oral deferasiprone [2].

### Aims and objectives

The aims and objectives are to determine the liver functions in multiple transfused thalassemia patients on regular and irregular chelation therapy.

### MATERIALS AND METHODS

#### Materials

This observational study was done among thalassemia patients in the age group of 1-year visiting a tertiary care hospital in Jaipur, Rajasthan. After taking approval from the Ethical Committee of the Institute, we enrolled 50 already diagnosed thalassemia patients. The enrolled patients were admitted to the thalassemia ward of Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, for blood transfusion from January 2018 to January 2020. The patients who had received >50 blood transfusions considered "multiple transfused."

**Inclusion criteria**

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

**Exclusion criteria**

- Patients who are receiving hepatotoxic drugs
- Any chronic liver disease in thalassemia patients
- 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 pre-designed pro forma. Liver function tests were done which included liver enzymes serum glutamic pyruvic transaminase and serum glutamic oxalocetic transaminase (SGPT and SGOT) and total bilirubin. The age of initiation of blood transfusion was also recorded.

Following laboratory parameters are taken into consideration: SGPT>150 U/L, SGOT>88 U/L, serum bilirubin >2 mg/dL. The serum transaminase levels are regarded best indicators of liver damage. If either transaminase level is higher than 2.5 times of upper limit of normal range, it is considered a significant derangement [8].

**Study design**

Hospital-based observational study.

**Setting**

Thalassemia ward, Department of Pediatrics, M.G. Medical College and Hospital, Jaipur, Rajasthan.

Data were analyzed using statistical software.

**RESULTS**

Table 1 shows that 37 (74%) were male and 13 (26%) were female (male: female ratio=2.85:1) in the present study. Ninety percent of patients were under the age of 15 years in the study.

The most common religion was Sindhi 26%, followed by Punjabis 22%, and then Muslim 16% and 36% others including Agrawal, Sikh, Rajput, Saini, Mathur, and Brahmin.

Table 2 shows that out of 50 patients on chelation therapies, 17 (34%) were on regular therapy and 33 (66%) were on irregular therapy.

Table 3 shows that out of 17 patients on regular chelation therapy, serum bilirubin levels were increased in 5 patients (29.4%) as compared to 33 patients on irregular chelation therapy, Serum bilirubin levels were increased in 15 (45.45%).

Table 4 shows that out of 17 patients on regular chelation therapy, serum transaminase levels were increased in 3 (17.65%) as compared to 33 patients on irregular chelation therapy, serum transaminase level was increased in 17 (51.50%).

**DISCUSSION**

In thalassemia patients, there is a need to perform regular blood transfusions to maintain hemoglobin levels at 10–12 g/dL. They are more prone to iron overload and blood-borne infections.

In thalassemia, the liver is affected in non-transfused patients due to extramedullary hematopoiesis in the form of hepatomegaly, whereas in transfused patients, the liver is a primary organ for deposition of excess iron and the liver becomes fibrotic and eventually cirrhotic, due to iron overload. The most important abnormalities of liver functions are hyper-gammaglobulinemia, hypoalbuminemia, a moderate decrease in

**Table 1: Demographic profile distribution of pediatric thalassemia patients according to age, sex, and caste**

Demographic Profile	Number	Percentage
Age (%)		
1–5 years	13	26
6–10 years	15	30
11–15 years	17	17
>15 years	5	10
Gender		
Male	37	74
Female	13	26
Caste		
Sindhi	13	26
Panjabi	11	22
Muslim	8	16
Others	18	36

**Table 2: Patients on chelation therapy**

Route	Regular	Irregular	Total (n=50) (%)
Oral	7	18	25 (50)
Parenteral	3	3	6 (12)
Oral+parenteral	7	12	19 (38)
Total (%)	17 (34)	33 (66)	50 (100)

**Table 3: Serum bilirubin levels, regular versus irregular chelation therapy**

Serum bilirubin levels	Regular chelation (n=17) (%)	Irregular chelation (n=33) (%)
Increased	5 (29.4)	15 (45.45)
Normal	12 (70.6)	18 (54.55)
Total	17 (100)	33 (100)

**Table 4: Serum transaminase levels, regular versus irregular chelation therapy**

Transaminases levels	Regular chelation (n=17) (%)	Irregular chelation (n=33) (%)
Increased	3 (17.65)	17 (51.50)
Normal	14 (82.35)	16 (49.50)
Total	17 (100)	33 (100)

coagulation factors, increased serum transaminase levels, and moderately elevated serum bilirubin levels.

If proper chelation therapy is started at serum ferritin levels >1000 nL/mL, liver dysfunction due to iron overload may be prevented to some extent. Chelation therapy is mostly started at the age of 5–6 years.

**Age, sex, and caste distribution****Age**

In the present study, we found that 90% of patients are under 15 years of age. A similar study was conducted by Logothetis *et al.* [9] (1972), where 88% of patients were under 15 years of age.

**Sex**

We found male-to-female ratio was 2.85:1 in our study. Singh *et al.* did a similar study that reported male-to-female ratio was 2.33:1 in their study [10].

**Caste**

In the current study, the most common cast affected by the disease was found to be Sindhis (26%), followed by Punjabis (22%), Muslims (16%),

and others (36%). A similar study was conducted by Manglani *et al.* in which the Lohana community (29.7%) was most common followed by Sindhis (22.2%), Punjabis (17%), and others (30.1%) [11].

#### Liver functions in regular versus irregular chelation therapy

In the present study, serum transaminase levels were normal in 82.35% of patients on regular chelation therapy as compared to 49.50% in patients on irregular chelation therapy.

A similar study done by Al-Kaltaan *et al.* showed that serum transaminase levels were significantly raised in patients on irregular chelation therapy [12]. Another study was conducted by Hoffbrand *et al.*, where they found that 50% of patients on regular chelation therapy had normal serum transaminase levels [13]. Beatrix *et al.* also found that 50% of patients on regular chelation therapy had normal liver function in their study [14].

#### CONCLUSION

The present study was conducted in 50 multiple transfused thalassemia patients. In this study, serum transaminase levels and serum bilirubin levels were taken as parameters of liver function.

1. 90% of patients were under 15 years of age
2. Sex ratio (male: female) was 2.85:1
3. Thalassemia is common in the Sindhis and Punjabi population
4. 82.35% of patients on regular chelation therapy had normal serum transaminase levels as compared to 49.50% of patients on irregular chelation therapy
5. 70.6% of patients on regular chelation therapy had normal serum bilirubin levels whereas only 54.55% of patients on irregular chelation therapy had normal serum bilirubin levels.

#### Recommendations

Routinely all thalassemia patients should be screened for liver functions (at 3-month intervals), serum iron, serum ferritin (6 monthly), magnetic resonance imaging study of liver, and liver biopsies at regular intervals. Thalassemia patients should be screened for transfusion-acquired infections. The chelation therapy should be started as early as indicated and should be regular. The adequacy of chelation therapy should be checked by serum ferritin levels done at regular intervals.

#### ETHICAL APPROVAL

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

#### ACKNOWLEDGMENTS

We are thankful to the department faculty and our patients; without their support, this study would not have been possible.

#### AUTHORSHIP CONTRIBUTION

Dr Abhishek Kumar Sharma: Design, manuscript writing, analysis, interpretation of data, and critical review. Dr Rajveer Singh Yadav:

Conception, Design, manuscript writing, analysis, and interpretation of data. Dr Nikita Pal: Design, manuscript writing, analysis, and interpretation of data. Dr Sandip Ray: Design, analysis, interpretation of data, and critical review. Dr Trapta Goyal: Conception, design, manuscript writing, interpretation of data, and critical review. Dr Sweta Yadav: Design, manuscript writing, analysis of data, and critical review.

#### CONFLICT OF INTEREST

None declared.

#### FUNDING

None.

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