Liver function profile in thalassemic children receiving multiple blood transfusions

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ABSTRACT

Background: Hepatic dysfunction is a frequent manifestation in thalassemic patients receiving multiple blood transfusions (BTs) as a part of treatment. **Objective:** The objective of the study was to study the liver function profile in thalassemic children and its correlation with the age of initiation of transfusion therapy. **Materials and Methods:** This cross-sectional study was done among 32 thalassemic patients in the age group of 1–18 years visiting a tertiary care hospital regularly for BTs at the Department of Pediatrics at the tertiary hospital of North India. Liver function tests (LFTs) were done in all thalassemic patients included total bilirubin, liver enzymes (serum glutamic oxaloacetic transaminase [SGOT], serum glutamic pyruvic transaminase [SGPT], and alkaline phosphatase [ALP]), total protein, serum albumin, serum ferritin, hepatitis B surface antigen (HBsAg), and anti-hepatitis C virus. The age of initiation of BT was also recorded. Derangement in LFTs and correlation between the age of initiation of transfusion therapy and derangement of liver function were studied. **Results:** Out of 32 patients, only 7 (21.87%) had normal LFT values. A total of 17 (53.12%) had increased SGOT, 15 (46.87%) had increased SGPT, and 25 (78.12%) had increased bilirubin levels. Total protein and serum albumin were below normal in 5 (15.65%) and 3 (9.3%) patients, respectively. ALP was increased in 24 (75%) patients. Majority of the patients (43.75%) had serum ferritin between 2000 and 2999 ng/ml. Only two patients had significantly deranged LFTs. No patient was positive for HBsAg. However, we did not find a significant correlation between age of initiation of transfusion therapy and derangement of liver enzymes in these patients. **Conclusion:** If thalassemic patients are given properly tested blood and regular chelation therapy, liver function remains normal. Immunization against hepatitis B and testing of blood bags is recommended. It is also recommended that LFT should be done regularly at 3 months interval to detect any abnormality.

Key words: *Chelation, Ferritin, Hepatitis, Thalassemia*

Thalassemias are a group of congenital anemias associated with defective synthesis of one or more of the globin subunits of the normal human hemoglobin. This results in excess production of the other chain which damages the red cell membrane and causes hemolytic anemia [1]. Hepatic dysfunction is a frequent manifestation in thalassemic patients receiving multiple blood transfusions (BTs) as a part of treatment. The liver plays a central role in iron homeostasis. Iron is released from hemolyzed and transfused red cells. This excess iron is initially confined to the Kupffer cells, but when multiple transfusions cause massive iron overload, spillover to hepatic parenchyma cells quickly occurs, with the risk of late development of fibrosis and cirrhosis [2].

Liver dysfunction resulting from ongoing hemolysis, excess iron deposition, and/or chronic viral infections is a major cause of morbidity and mortality among thalassemic children on BT therapy. Excess iron is toxic to all body tissues, including liver, where it causes irreversible damage, such as fibrosis and liver cirrhosis [3]. Regular BT improves the overall survival of thalassemic patients, but it carries a risk of infection with blood-borne viruses such as hepatitis B virus (HBV) and hepatitis C virus (HCV) which can cause hepatic dysfunction [4].

When serum ferritin level exceeds 1000 ng/ml and the numbers of transfusions are >30, derangement in liver enzymes starts occurring in the thalassemia patients [5]. Although with regular BTs and iron chelation therapy, these patients can survive beyond the fifth decade of life [6], liver disease still remains an important cause of morbidity and mortality among these patients. The aim of this study was to study the liver function profile in thalassemic children and its correlation with the age of initiation of transfusion therapy.

MATERIALS AND METHODS

This cross-sectional study was done among thalassemic patients in the age group of 1–18 years visiting a tertiary care hospital of

North India for BTs at the department of pediatrics. The study was approved by the Institutional Ethics Committee. All patients were enrolled for this study after informed consent from their parents and assent from children above the age of 7 years.

A thorough history and clinical examination were done and findings were recorded in predesigned pro forma. Liver function tests (LFTs) were done which included total bilirubin, liver enzymes (serum glutamic oxaloacetic transaminase [SGOT], serum glutamic pyruvic transaminase [SGPT], and alkaline phosphatase [ALP]), total protein, serum albumin, viral markers including hepatitis B surface antigen (HBsAg), and anti-HCV and serum ferritin level. The age of initiation of BT was also recorded. Derangement in LFTs and correlation between the age of initiation of transfusion therapy and derangement of liver function were studied.

Data were analyzed using statistical software MS Excel and SPSS for Windows. Data were reported as mean (SD) and proportions as deemed appropriate for quantitative and qualitative variables, respectively. Correlation between the age of initiation of transfusion therapy and derangement in LFTs was evaluated using Pearson correlation coefficient (r). Frequency and percentages were presented for qualitative variable.

RESULTS

The age-wise distribution of thalassemia patients is discussed in Table 1. The median age was 11.5 years.

In this study, majority of patients (75%) started receiving BT before the age of 1 year and 8 (25%) patients started after 1 year of age. However, we did not find any significant correlation between the age of initiation of BT and derangement of liver enzymes. In this study, males (18, 56.25%) were more in number than females (14, 43.75%).

The values of the LFTs in thalassemic patients are given in Table 2. The mean SGOT, SGPT, and serum bilirubin levels were 70.9±23.4 U/L, 60.8±18.1 U/L, and 1.91±0.08 mg/dL, respectively. The mean total protein and serum albumin were 6.28±0.72 and 3.27±0.35 g/dL, respectively. Significant derangement in liver enzymes was taken as twice the upper limit of reference range.

Table 1: Age-wise distribution of thalassemia patients

Age group (years)	Number of patients	Percentage
1–5	8	25
6–10	7	21.87
11–15	15	46.87
>15	2	6.25
Total	32	100

Only two patients had significantly deranged LFT and one of these patients was anti-HCV positive and another had chronic anemia due to irregular BT therapy. There was no HBV-positive patient in our study. All the patients had received hepatitis B vaccine before the start of transfusion therapy.

The serum ferritin levels of thalassemic patients are discussed in Table 3. Majority of the patients (43.75%) had serum ferritin level between 2000 and 2999 ng/ml and the mean was 2176±868 ng/ml (range: 268–4368 ng/ml). Out of 32 patients, 29 patients (90.62%) were on regular chelation therapy.

DISCUSSION

Derangement in liver function is common in thalassemic patients receiving multiple BTs which are mainly due to iron deposition in liver and hepatitis. With regular iron chelation treatment, the degree of iron overload is reduced in most of our patients as also seen in other studies. In this study, 25 patients (78.12%) had deranged liver function. Significant increase in enzymes levels was seen in only 2 (6.25%) patients. Majority (43.75%) of the patients had ferritin value between 2000 and 2999 ng/ml and most of the patients (90.62%) were on chelation therapy.

In a study conducted by Singh *et al*., SGOT, SGPT, and ALP were found to be increased in 80%, 45%, and 87% of the patients, respectively [7]. Significant derangements of these enzymes were seen in 34%, 19%, and 9% patients, respectively. HBV and HCV were positive in 1% and 12% and serum total protein and albumin were low in 22% and 23% of patients, respectively. Serum bilirubin was increased in 53% of the patients. Majority (28%) of the patients had ferritin value between 2001 and 3000 ng/ml.

The results in our study were in accordance with another study conducted by Ayyash and Sirdah, where liver function was significantly deranged in thalassemic patients [8]. However, the mean serum ferritin levels were higher than that of our study. In another study conducted by Williams *et al*., the prevalence of HCV among thalassemic patients was 11.1% and 66.6% of patients showed evidence of HBV infection [9]. In another study conducted by Salama *et al*., none of the patient tested positive for HBV, but 50% of patients was anti-HCV positive [10]. Similarly, 24% of patients were tested positive for anti-HCV in a study conducted by Agrawal *et al.* [11]. This is in contrast to this study, in which no patient was HBsAg positive and only one patient was anti-HCV positive.

If thalassemic patients are given properly tested blood and regular chelation therapy, their liver function remains normal. Although mild derangement in liver function can be present due to multiple BTs, significant damage to liver can be controlled. In hepatitis seronegative thalassemic patients, regular BT along

Table 2: Liver function tests in thalassemic patients

Liver function tests	Serum bilirubin (%)	Serum glutamic oxaloacetic transaminase (%)	Serum glutamic pyruvic transaminase (%)	Alkaline phosphatase (%)	Total protein (%)	Serum albumin (%)
Normal value	7 (21.87)	15 (46.87)	17 (53.12)	8 (25)	27 (84.37)	29 (90.62)
Abnormal value	25 (78.12)	17 (53.12)	15 (46.87)	24 (75)	5 (15.62)	3 (9.37)

Table 3: Serum ferritin level of thalassemia patients

Serum ferritin (ng/ml)	Number	Percentage
<1000	5	15.62
1000–1999	8	25
2000–2999	14	43.75
3000–3999	4	12.5
4000–4999	1	3.12
Total	32	100

with iron chelation therapy helps in maintaining liver function and decreasing iron overload in liver. It is recommended that immunization against hepatitis B and strict testing of blood bags at blood banks for hepatitis C must be done. It is also recommended that LFT should be repeated regularly at 3 months interval to detect any hepatic dysfunction.

CONCLUSION

In hepatitis seronegative thalassemic patients, regular BT along with iron chelation therapy helps in maintaining liver function and decreasing iron overload in liver. It is also recommended that LFT should be done regularly at 3 months interval to detect any hepatic dysfunction.

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