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Assessing Liver Function in Beta-Thalassemia Patients: Exploring Blood Transfusion-Related Complications

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Abstract: ***Aim and objective**: To find out the proportion of transfusion reaction symptoms of beta-thalassemia in paediatric age group patients and to estimate the biochemical parameters of liver functions and correlate them with serum ferritin levels. **Material and method**: The present cross-sectional study was conducted on 120 children with known beta thalassemia aged between 2-12 years on repeated blood transfusion. A thorough clinical examination with particular importance on the presence of pallor, jaundice, and signs of thalassemic features was done. An abdominal examination was done to rule out hepatosplenomegaly. Blood samples were collected for appropriate investigations including serum ferritin level, transferrin saturation, and liver function test. **Results**: In this study, 27.5% and 72.5% of children belonged to the 2-5 years and 6-12 years age category respectively. The majority of study subjects were male (65.33%). The incidence of jaundice, ascites, and hepatomegaly was found to be 90.83%, 36.67%, and 100% respectively. The incidence of jaundice, ascites, and hepatomegaly are more common in older age children. A significant positive correlation was found between serum ferritin and total bilirubin, direct bilirubin, and SGPT (P<0.05). **Conclusion**: In the present study, there was a positive significant correlation between serum ferritin and total bilirubin, direct bilirubin, and SGPT. Thus, as serum ferritin increases there is an increase in liver function parameters and enzymes and there will be more derangement in liver function probably because of an iron overload condition.***

Keywords: β-thalassemia major, Iron overload, Organ dysfunction, viral hepatitis, Liver enzymes

1. Introduction

Thalassemia is the most common hereditary illness in the world. A wide range of genetic defects associated with a decreased synthesis of haemoglobin chains results in the development of thalassemia. [1] an imbalance of haemoglobin chains will lead to inefficient erythropoiesis and prolonged haemolysis if the body is unable to create enough of these chains. Every year, more than 60, 000 babies are born with severe types of thalassemia. Thalassemia is regarded as a significant health burden by the world health organization (WHO). [2, 3]

Millions of units of blood are collected each year from donors throughout the world because blood transfusions are essential to treating patients with a variety of illnesses, including haematological disorders. More than 112 million units of blood were donated globally in 2013 according to records. As a result, transfusion-transmitted infections (TTIS) are still a significant public health concern in many areas of the world, and thalassemia patients who have several transfusions are at an especially high risk of developing TTIS. [4] A thalassemia is a group of inherited hemoglobinopathies brought on by mutations in the beta-globin chain of haemoglobin. According to the recommendations of the thalassemia international federation (TIF), individuals with transfusion-dependent thalassemia (TDT) should have blood transfusions frequently enough to keep their pre-transfusion haemoglobin levels above 9 to 10.5 g/dl or above (11 to 12 g/dl for patients with cardiac problems). In specific situations, such as growth failure, recurrent haemolytic crises, or low quality of life, more frequent blood transfusions in thalassemia patients who are not transfusion dependent (NTDT) may be taken into consideration. [5]

Patients with thalassemia typically experience endocrine difficulties including hypogonadism, hypothyroidism, hypoparathyroidism, and pancreatic and adrenal insufficiency. The most common endocrinopathies appear as hypogonadism, growth retardation, hyperglycaemia, and delayed puberty. The most prevalent infectious agents transmitted by blood transfusions are the hepatitis b virus (HBV) and hepatitis c virus (HCV), which were first identified in 1963 and 1975, respectively. [6]

Traditional therapy approaches in TDT include ongoing iron-chelator medication and routine blood transfusions. [7] despite current developments in the creation of numerous iron-scavenging medications, iron excess in these individuals is still seen to be a difficult issue. In the past, organ dysfunctions brought on by free iron's harmful effects have been the main causes of morbidity and death in TDT patients. Any organ might potentially be negatively impacted by extra iron, but the endocrine system, liver, heart, and kidneys are the main targets. [8]

The liver can retain the most extra iron in the body, but it is also particularly vulnerable to injury from iron poisoning. Several blood-transfused thalassemia patients have observed a link between serum ferritin and hepatic iron content in previous research. [1] However, there is a lack of information on the relationship between liver injury in thalassaemic individuals and iron excess. Therefore, the present study was undertaken to find out the proportion of

transfusion reaction symptoms of beta-thalassemia in paediatric age group patients and to estimate the biochemical parameters of liver functions and correlate them with serum ferritin levels.

2. Materials and Method

The present cross-sectional study was conducted at the Paediatric Department of the tertiary care center in western Maharashtra from December 2020 to May 2022 after institutional ethical committee approval. A total of 120 children with known beta thalassemia aged between 2 years to 12 years on repeated blood transfusion were included in the study. Whereas children with other hemoglobinopathies such as the heamoglobin J variant etc were excluded from the study.

Written informed consent was obtained from the parents before the initiation of the study. Medical history was taken with specific emphasis on family and treatment history. Previous medical records were recovered and evaluated. A complete clinical examination was done. A thorough clinical examination with particular importance on the presence of pallor, jaundice, and signs of thalassemic features was done. An abdominal examination was done to rule out hepatosplenomegaly. Details regarding chelation therapy (dose, age of start, complications, and compliance) and laboratory investigations were performed.

Blood samples were collected for appropriate investigations including blood grouping and typing, complete hemogram, iron studies (iron status as indicated by serum ferritin level and transferrin saturation.), heamoglobin electrophoresis, liver function tests, viral markers for hepatitis, and ELIZA for HIV. All findings were recorded in well-structured proforma.

3. Statistical Analysis

Data collected in the study was analyzed using SPSS version 26.0 and MS Excel sheet. Univariate analysis was done to check the quality of data entry. For the quantitative variables, (mean ± SD) or median was used for data presentation. For categorical variables, frequencies along with their respective percentages were used. Student's t-test for quantitative variables and 'chi-square test' for categorical variables were used for statistical significance. P-value <0.05 was considered statistically significant.

4. Results

In this study, 27.5% and 72.5% of children belonged to the 2-5 years and 6-12 years age category respectively. The majority of study subjects were male (65.33%). In 50.83% of children, the age at first blood transfusion used was 0-6 months whereas in 49.17% of children, it was at 7-12 months of age. The blood transfusion-related complications are shown in table 1.

Table 1: Blood transfusion-related complications

Transfusion-related complications	Subcategories	Frequency (n)	Percentage (%)
Febrile non-haemolytic reaction	Fever	37	30.83
	Chills	17	14.17
	Tachycardia	30	25
Allergic reaction	Rash	24	20
	Urticaria	6	5
	Pruritis	10	8.33
Infection	No	116	96.67
	Yes	4	3.33
Liver function test	Increased SGPT	101	84.17
	Increased SGOT	81	67.5
	Increased DB	92	76.77

The incidence of jaundice, ascites, and hepatomegaly was found to be 90.83%, 36.67%, and 100% respectively. The incidence of jaundice, ascites, and hepatomegaly are more common in older age children (table 2).

Table 2: Distribution of subjects according to liver-related complications and age categories

Liver related complications	2-5 years		6-12 years	
	Frequency (n)	Percentage (%)	Frequency (n)	Percentage (%)
Jaundice	22	66.67	87	100
Ascites	0	0	44	50.57
Hepatomegaly	33	100	87	100

A significant positive correlation was found between serum ferritin and total bilirubin, direct bilirubin, and SGPT ($P<0.05$).

5. Discussion

As the life span of thalassemia patients has dramatically increased, their cumulative exposure to red cell transfusions has resulted in this disease being the most heavily red-cell-transfused syndrome worldwide. [3] The study aimed to find out the proportion of transfusion reaction symptoms of beta-thalassemia in paediatric age group patients and to estimate the biochemical parameters of liver functions and correlate them with serum ferritin levels.

In the current study, out of a total of 120 study subjects with beta-thalassemia, 30.83%, 14.16%, and 25% of study subjects had fever, chills, and tachycardia as a non-haemolytic febrile reaction. Whereas, it was observed that 20%, 5%, and 8.33% of study subjects with betathalassemia had rash, urticaria, and pruritis respectively as allergic reactions during blood transfusion. The study by Patel NA et al. suggested that 63.28% of children had f blood transfusion reaction during the treatment period. Among the patients who experienced reactions, 67% presented fever with rigors, 55% urticaria, and others presented swelling, vomiting, or diarrhoea. [9]

Furthermore, out of 120 study subjects with beta-thalassemia, 3.33% (n=4) had transfusion-associated infections. Among these subjects, 3 had HCV and 1 had HBV infection. All the cases belonged to 6 to 12 years of age-group suggesting incidence of infection is more common in older children. Similarly, Golam SB et al. showed the incidence of HCV, and HBV infection in

13.51%, and 3.37% of children respectively. [10] In the study of Patel NA et al., the incidence of HIV, HBV, and HCV infection in thalassemia children was reported to be 3.95%, 2.26%, and 2.26% respectively. [9] The multi-transfused patients with thalassemia may face increased immune dysfunction in the presence of iron overload following splenectomy, which makes them more susceptible to infections. Although, nowadays, an effective awareness of safe blood transfusions and iron chelation therapy has made the morbidity rate of patients with transfusion-dependent Beta thalassemia lower, new complications like hepatocellular carcinoma are taking hold in patients with thalassemia, which may be due to carcinogenicity of iron overload and chronic infections. Especially, the thalassemia patients who become co-infected with both HBV and HCV are at a greater risk of cirrhosis and hepatocellular carcinoma compared to the mono-infected patients. [10]

Some analysts have depicted the proposed component of activity, however, the correct process is not clear as yet. Seng Suk et al. found liver functions to be three-to four-fold increased in β-thalassemia patients than in normal individuals. [11] The iron deposition is associated with increased oxidative stress, lipid peroxidation, and liver cell damage in transfusion-dependent β-thalassemia major. Jensen et al. also observed that serum transaminases and hepatic fibrosis increases as liver iron concentration increases. [12] The liver is the earliest site of iron deposition in regularly transfused thalassemia patients and a common cause of morbidity. Iron overload occurs both in hepatocytes and reticuloendothelial cells. Free radical production is increased in patients with iron overload through the Fenton reaction. These free radicals accumulate in the liver, heart, and other organs causing extensive tissue damage and play havoc. [13] In this study the incidence of jaundice, ascites, and hepatomegaly was found to be 90.83%, 36.67%, and 100% respectively. The incidence of jaundice, ascites, and hepatomegaly are more common in older age children. Furthermore, a significant positive correlation was found between serum ferritin and total bilirubin, direct bilirubin, and SGPT ($P<0.05$). Similarly, various studies showed a significant positive correlation between serum ferritin and liver function tests. [14-16]

6. Conclusion

In the present study, there was a positive significant correlation between serum ferritin and total bilirubin, direct bilirubin, and SGPT. Thus, as serum ferritin increases there is an increase in liver function parameters and enzymes and there will be more derangement in liver function probably because of an iron overload condition. Further studies are warranted to confirm the present study findings.

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