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A STUDY OF BLOOD TRANSFUSION RELATED COMPLICATIONS IN BETA-THALASSEMIA PATIENTS WITH SPECIAL REFERENCE TO LIVER FUNCTIONS

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ABSTRACT **Background:** Thalassemia is the most prevalent inherited disease worldwide. This disease is a diverse group of genetic abnormalities associated with reduced synthesis of haemoglobin chains. Accordingly, transfusion transmitted infections (TTIS) continue to be a major public health issue in many parts of the world and multi-transfused patients of Thalassemia (a group of inherited hemoglobinopathies caused by mutations in the beta globin chain of hemoglobin) are at a particularly increased risk of TTIS.(2) The Thalassemia International Federation (TIF) recommended that Transfusion dependent thalassemia (TDT) patients should receive blood transfusions at a rate sufficient to maintain pre-transfusion Hb above 9-10.5 g/dL or higher (11-12 g/dL) for patients with cardiac complications. (3) **Objectives:** 1. To determine various blood transfusion related complications among beta thalassemia patients. 2. To estimate iron overload by estimation of serum ferritin and to determine its correlation with liver functions among beta thalassemia patients. **Materials And Methods:** This was cross sectional study conducted at Paediatric department of tertiary care centre in Western Maharashtra during December 2020 to May 2022. 120 Children fulfilling the criteria were included in the study. Previous medical records were retrieved and analysed. Complete clinical examination was done. Thorough clinical examination with particular emphasis on presence of pallor, jaundice, and signs of thalassaemic features was done. Abdominal examination was done to rule out hepatosplenomegaly. Details regarding iron chelation therapy (dose, age of start, complications and compliance) and laboratory investigations were obtained. Data collected in the study was analysed using SPSS version 26.0 and MS Excel. **Results:** In present study out of total 120 study subjects 34.16 % were females and 65.84% were males. Also, 27.5% were belong to 2 to 5 years of age group and 72.5% belong to 6 to 12 years age group. mean age, mean weight and mean height was 9.23 years, 23.41 kg and 120.57 cm in age group with 6-12 years. In age group 2 to 5 years mean age, mean weight and mean height was 4.09 years, 13.24 kg and 96.30 cm. Total number of transfusions required was significantly more in age group of 6-12 years (106.54) as compared to age group of 2-5 years. More than 50 transfusions were significantly more in age group of 6-12 years as compared to 2-5 years. **Conclusion:** From present study findings it was concluded that there was positive significant correlation between serum ferritin and total bilirubin, direct bilirubin and SGPT. So, as serum ferritin increases there is increase in liver function parameters and enzymes and there will be more derangement in liver function probably because of iron overload condition.

KEYWORDS : Paediatric, thalassemia, Blood transfusions, Transfusion complications.

INTRODUCTION

Thalassemia is the most prevalent inherited disease worldwide. This disease is a diverse group of genetic abnormalities associated with reduced synthesis of haemoglobin chains. If the body is unable to produce sufficient amounts of these chains, an imbalance of haemoglobin chains will result in ineffective erythropoiesis and chronic haemolysis. This anaemia starts in early childhood and continues throughout the whole life. If this chain deficiency presents in □-chain of Hb, this type of thalassemia is called □-thalassemia, but β-thalassemia is the reduced synthesis of haemoglobin β-chain. Homozygous β-thalassemia major (βTM) is an inherited autosomal recessive disease, with a contagion rate involving 23000 babies every year, mostly in low- or middle-income countries. Chelating therapy, besides blood transfusion, has improved the lifespan of thalassaemic patients. [1]

Annually, million units of blood are collected from the donors worldwide as the blood transfusion is integral to management of patients suffering from diverse diseases, particularly haematological disorders. From a record of 2013, it has been seen that there were more than 112 million units of blood donation all over the world that year. Accordingly, transfusion transmitted infections (TTIS) continue to be a major public health issue in many parts of the world and multi-transfused patients of Thalassemia (a group of inherited hemoglobinopathies caused by mutations in the beta globin chain of haemoglobin) are at a particularly increased risk of TTIS.[2] The Thalassemia International Federation (TIF) recommended that Transfusion dependent thalassemia (TDT) patients should receive blood transfusions at a rate sufficient to maintain pre-transfusion Hb above 9-10.5 g/dL or higher (11-12 g/dL) for patients with cardiac complications. In Non transfusion dependent thalassemia (NTDT) patients, more frequent blood transfusions should be considered in some cases including growth failure, frequent haemolytic crisis or poor quality of life. [3]

Endocrine complications such as hypogonadism, hypothyroidism, hypoparathyroidism, and pancreatic and adrenal insufficiency are frequently observed among the thalassemia patients. Delayed puberty, growth retardation, diabetes and hypogonadism are among the most prevalent manifestations of endocrinopathies. [4]. The hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most common transfusion-transmitted infectious agents which became known in 1963 and 1975 respectively [5].

The liver has the maximum capacity to store excess iron in the body but also very susceptible to damage as a result of iron toxicity. In other studies, the correlation between serum ferritin and hepatic iron concentration has been reported in multiple blood-transfused thalassemia patients. However, there is a paucity of data regarding the correlation between iron overload and liver damage in thalassaemic patients. Hence, the objective of this study was to correlate liver function tests with serum ferritin levels in multi-transfused thalassemia patients. This study has been conducted to find out the proportion of transfusion transmitted infections and transfusion-related complications of beta-thalassemia major in paediatric age group patients.

OBJECTIVES

1. To determine various blood transfusion related complications among beta thalassemia patients.
2. To estimate iron overload by estimation of serum ferritin and to determine its correlation with liver functions among beta thalassemia patients.

MATERIALS AND METHODS

This was cross sectional study conducted at Paediatric department of tertiary care centre in Western Maharashtra during December 2020 to May 2022. Known beta thalassaemic children aged between 2 years to 12 years on repeated blood transfusion coming to paediatric outpatient department of tertiary care centre were recruited for study. Children with other hemoglobinopathies such as haemoglobin J variant etc were excluded from the study. 120 study subjects fulfilling the criteria were

included in the study.

Written consent obtained from the parents. Approval from institutional ethics committee was taken. Medical history taken with specific emphasis to family and treatment history. Previous medical records were retrieved and analysed. Complete clinical examination was done. Thorough clinical examination with particular emphasis on presence of pallor, jaundice, and signs of thalassaemic features was done. Abdominal examination was done to rule out hepatosplenomegaly. Details regarding chelation therapy (dose, age of start, complications and compliance) and laboratory investigations were obtained. Blood samples were collected for relevant investigations including blood grouping & typing, complete hemogram, iron studies (Iron status as indicated by serum ferritin level and transferrin saturation.), haemoglobin electrophoresis, liver function tests, viral markers for hepatitis, ELISA for HIV. All findings are recorded in well-structured proforma.

Data collected in the study was analysed using SPSS version 26.0 and MS Excel. 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 was used.

OBSERVATIONS AND RESULTS

Out of total 120 study subjects, 34.16 % were females and 65.84% males. 27.5% were belong to 2 to 5 years of age group and 72.5 % belong to 6 to 12 years age group. it was observed that mean age, mean weight and mean height were 9.23 years, 23.41 kg, 120.57 cm and 4.09 years, 13.24 kg and 96.30 cm. in age group of 6 to 12 years and in age group 2 to 5 years respectively. Total number of transfusions required was significantly more in age group of 6 to 12 years as compared to age group of 2 to 5 years.it was observed that mean age, mean weight and mean height was 7.87 years, 21.22 kg ,114.23 cm and 7.71 years, 19.46 kg ,113.27 cm in males and females respectively. Total number of transfusions required was significantly more in males (90.25) as compared to females (97.98).

Table 1: Distribution of study subjects according to gender and Different Variables

Variables		GENDER		Total	P value
		MALE	FEMALE		
Number of units blood transferred	2 to 50	13	6	19	0.58
	51-100	29	19	48	
	101-150	37	16	53	
Age of first blood transfusion	0-6 months	42	19	61	0.50
	7 to 12 months	37	22	59	
Iron Chelation	No	7	3	10	0.77
	Yes	72	38	110	
Liver Function	Jaundice	71	38	109	0.61
	Ascites	28	16	44	0.69
	Hepatomegaly	79	41	120	
Febrile non-haemolytic reactions	Fever	23	14	37	0.79
	Chills	13	4	17	0.53
	Tachycardia	19	11	30	0.37
Allergic reactions	Rash	19	5	24	0.12
	Urticaria	5	1	6	0.16
	Pruritis	9	1	10	0.06
Infection	Yes	3	1	4	0.57
	No	76	40	116	
Liver function test	Increased SGPT	65	36	101	0.43
	Increased SGOT	58	23	81	0.055
	Increased direct bilirubin	60	32	92	0.79

From above table it was observed that there was no significant difference between male and female study subjects with respect to total number of transfusions require till now (p>0.05)., 92.68% females and 91.13% males were on chelation therapy. 30.83%, 14.16% and 25% study subjects had fever, chills and tachycardia as a non-hemolytic febrile reaction during blood transfusion. Mean SGOT level significantly more in male as compared to female study subjects with beta thalassemia.

Table 2: Distribution of study subjects according to age and different variables

Variables		Age group in years		Total	P value
		2 to 5	6 to 12		
Number of units blood transfused	2 to 50	19	0	19	<0.01
	51-100	14	34	48	
	101-150	0	53	53	
Iron Chelation	No	10	0	10	<0.01
	Yes	23	87	110	
Liver Function	Jaundice	22	87	109	<0.01
	Ascites	0	44	44	<0.01
	Hepatomegaly	33	87	120	<0.01
Febrile nonhemolytic reactions	Fever	13	24	37	0.21
	Chills	6	11	17	0.43
	Tachycardia	10	20	30	0.4
Allergic reactions	Rash	5	19	24	0.21
	Urticaria	2	4	6	0.74
	Pruritis	2	8	10	0.57
Infection	No	33	83	116	0.13
	Yes	0	4	4	
Liver function test	Increased SGPT	19	82	101	<0.01
	Increased SGOT	18	63	81	0.06
	Increased direct bilirubin	21	71	92	0.038

From above table it was observed that more than 50 transfusions were significantly more in age group of 6-12 years as compared to 2-5 years. So, as age progresses number of transfusions required were more. It was observed that study subjects with jaundice and ascites were significantly more in age group of 6-12 years as compared to that of 2-5 years. This indicated that in children with beta thalassemia, hepatic dysfunction is more prevalent as age progresses. There was no significant difference between two age groups with respect to allergic reactions during blood transfusion.

Table 3: Comparison between mean liver function parameters and mean ferritin between two age-groups.

Parameter	Age group in years	N	Mean	Std. Deviation	P value
SGPT	2 to 5	33	58.82	14.07	<0.01
	6 to 12	87	103.93	28.98	
SGOT	2 to 5	33	46.82	16.74	0.055
	6 to 12	87	54.46	20.15	
Total Bilirubin	2 to 5	33	4.30	1.92	<0.01
	6 to 12	87	5.84	2.10	
Direct Bilirubin	2 to 5	33	0.58	0.708	0.48
	6 to 12	87	0.68	0.723	
Ferritin	2 to 5	33	1097.36	369.05	<0.01
	6 to 12	87	1537.06	459.16	

From above table it was observed that mean values of SGPT, total bilirubin and serum ferritin were significantly more in age group of 6-12 years. There was no significant difference between mean values of SGOT and direct bilirubin between two age-groups.

Table 4: Comparison between mean liver function parameters and mean ferritin according to gender

Parameter	Sex	N	Mean	Std. Deviation	P value
SGPT	M	79	90.20	33.61	0.54
	F	41	94.07	31.12	
SGOT	M	79	55.18	19.94	0.027
	F	41	46.93	17.64	
Total Bilirubin	M	79	5.20	2.10	0.13
	F	41	5.83	2.23	
Direct Bilirubin	M	79	.68	.74	0.48
	F	41	.59	.67	
Ferritin	M	79	1405.37	465.63	0.73
	F	41	1436.90	504.40	

In Table no. 4, it was observed that mean SGOT level significantly more in male as compared to female study subjects with beta thalassemia. There was no significant difference between male and female study subjects with beta thalassemia with respect to mean values of SGPT, total bilirubin, direct bilirubin and serum ferritin.

In present study, It was observed that there was positive significant correlation between serum ferritin and total bilirubin, direct bilirubin and SGPT. So, as serum ferritin increases there is increase in liver

function parameters and enzymes and there will be more derangement in liver functions.

DISCUSSION

This was cross sectional study conducted at Pediatric department of tertiary care center in Western Maharashtra from December 2020 to May 2022. In present study,120 Children fulfilling the criteria were included in the study out of which 34.16 %, 65.84% were females and males. May Al-Moshary et al (2020) carried out research on clinical and biochemical assessment of liver function test and its correlation with serum ferritin levels in transfusion-dependent thalassemia patients. A total of 138 patients with thalassemia were included in which 61(44.2%) were male and 77(55.8%) were female. [6]

In present study, total number of transfusions required was significantly more in males (90.25) as compared to females (97.98). More than 50 transfusions were significantly more in age group of 6-12 years as compared to 2-5 years. So, as age progresses number of transfusions required were more. Also, there was no significant difference between male and female study subjects with respect to total number of transfusions require till now (p>0.05). Elliott Vichinsky et al (2015) carried out research on Transfusion Complications in Thalassemia Patients in which they found that the median age of transfusion initiation was 1 year with a mean age of 4.5 ± 8.2 years. The mean estimated years of transfusion exposure was 18.5 ± 12.3. The average number of transfusions in this group during the year prior to enrollment was 15.6 ± 5.8 [7].

Iron Chelation Therapy- In present study, there was no significant difference between two age groups with respect to iron chelation therapy. Also, 92.68% females and 91.13% males were on chelation therapy. There was no significant difference between male and female study subjects with respect to iron chelation therapy. Khaled M. Salama1 ET AL (2015) conducted study on liver enzymes in children with beta-thalassemia major. In their study 75 patients were on regular chelation therapy; 78.7 % of these patients were compliant with chelators, 5 patients only were not on any chelation therapy because of the complication of oral chelators or refusal of injections [8]. Neha A Patel (2016) study, there was a statistically significant association between consumption of chelating therapy and complications owing to iron overload. Those who were on chelation therapy showed only 1.13% complications when compared with those who were not taking chelating therapy (36.16%). [9]

Liver Functions- In present study, jaundice and ascites were significantly more in age group of 6-12 years as compared to that of 2-5 years. All study subjects had hepatic enlargement. Jaundice and Ascites was present in 92.68%, 39.02% in female and 89.87%, 35.44 % in male study subjects respectively. Khaled M. Salama1 ET AL (2015) study, 32 patients (40%) suffered from jaundice and 34 (42.5%) had thalassemic features. [8] In Devarshi et al (2015) study, in thalassemia pediatric patients in tertiary care hospital, 24 patients who had been examined for complications, it was found that 12 patients (33.34%) had hepatosplenomegaly. [10]

Febrile non-hemolytic reaction & Allergic reactions-

In current study, out of total 120 study subjects with beta thalassemia, 30.83%, 14.16% and 25% study subjects had fever, chills and tachycardia as a nonhemolytic febrile reaction. It was observed that 20%, 5% and 8.33% study subjects with beta thalassemia had rash, urticaria and pruritis as allergic reactions during blood transfusion. Neha A Patel (2016) study, two-thirds (63.28%) of the children have experienced any kind of 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 diarrhea. [9] In Shraddha Devarshi et al (2015) study, it was observed that patients complained of fever, rash, cough, coryza, weakness during blood transfusion. [10]

Transfusion Associated Infection-

In present study, 3.33% had transfusion associated infections. Out these 4 study subjects with infections, 3 of them had HCV and one had HBV infection. Golam Bhuyan et al (2021) study, infected cases with HCV, HBV and HIV were 13.51%, 3.37% and 0%, respectively. [2] Neha A Patel (2016), 8.47% were affected from transfusion transmitted infections (TTIs), Among them, HIV contributed 3.95% while 2.26% each of HBV and HCV. [9]

Liver function Test-

In present study, Proportion of study subjects with increased SGPT and direct bilirubin (94.25% & 81.60%) were significantly more in age-group of 6-12 years (57.57% & 63.63%) as compared to that of 2-5 years of age-group. This indicate that as age progresses, there is progression of hepatic dysfunction in children with beta thalassemia and multiple blood transfusions. Mukesh Kumar (2013) study, Serum transaminase elevation was detected in 17.9% of the patients, temporary transaminase elevation was detected in 50.7%, and bile stone was detected in 1.5% of the patients. Transaminase elevation was statistically significant in the patients whose mean ferritin level was >2500 ng/mL (p< 0.05). [11] May Al-Moshary et al study (2020), The Pearson bivariate coefficient correlation was positive (r = + 0.319) with a p-value of <0.01 Correlation between ferritin and ALT by correlating serum ferritin with AST with r = + 0.670) and a pvalue of <0.001. Ferritin vs ALP showed a positive correlation of r = + 0.430 and a p-value of <0.001, with bilirubin r= + 0.294 and a p-value of <0.001. [6]

CONCLUSION

In present study, it was concluded that as age progresses, there is progression of hepatic dysfunction in children with beta thalassemia and multiple blood transfusions. there was positive significant correlation between serum ferritin and total bilirubin, direct bilirubin and SGPT. So, as serum ferritin increases there is increase in liver function parameters and enzymes and there will be more derangement in liver function probably because of iron overload condition.

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