

## Original Research Article

# Study of lipid profile in $\beta$ thalassemia major pediatric patients with multiple blood transfusion and its correlation with serum ferritin level in tertiary care hospital in Kolkata

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## ABSTRACT

**Background:**  $\beta$ -Thalassemia major is associated with iron overload toxicity. This study was done to investigate lipid profile abnormality in  $\beta$ -Thalassemia major patients and to establish their correlation with serum ferritin. Another motto of this study was to signify deleterious effect of multiple blood transfusion and facilitate to understand how it will affect the lipid profile parameters changes so that we can also prevent early dyslipidemia induced complications like atherogenesis by early detection of lipid profile abnormality and also to establish derangement of lipid profile as an indirect evidence of iron overload.

**Methods:** 102 nos.  $\beta$ -Thalassemia major paediatric patients with multiple blood transfusion ( $\geq 10$ ) in age group of 6 to 12 years admitted in pediatric ward of tertiary care hospital (NRSMCH) were enrolled. Serum ferritin level and lipid profile were investigated and their correlation were assessed.

**Results:** Among 102  $\beta$ -Thalassemia major pediatric (6 to 12 years) patients 55.88% were male and 66.67% were Hindu by religion and 69.61% children came from lower socio-economic class. The average value of number of previous blood transfusion was  $42.79 \pm 7.510$ . The mean value of serum ferritin was  $2263.53 \pm 833.904$  ng/ml. The average value of serum total cholesterol, LDL and HDL were  $153.84 \pm 5.428$  mg/dl and  $97.16 \pm 3.982$  mg/dl and  $29.45 \pm 4.445$  mg/dl respectively and their correlation with serum ferritin were negative ( $r = -0.941$  and  $r = -0.964$  and  $r = -0.751$  respectively). Average value of serum triglyceride and VLDL were  $206.22 \pm 67.407$  mg/dl and  $36.16 \pm 3.385$  mg/dl respectively and their correlation with serum ferritin were positive ( $r = +0.606$  and  $r = +0.973$  respectively).

**Conclusions:** There was significant lipid profile derangement. As the serum ferritin level increases, serum total cholesterol, HDL, LDL decreases and serum triglyceride, VLDL level increases.

**Keywords:** Lipid profile, Multiple transfusion, Thalassemia, Serum ferritin

## INTRODUCTION

$\beta$ -thalassemia major is associated with ineffective erythropoiesis, bone marrow expansion and rapid destruction of erythrocytes. Children with  $\beta$ -thalassemia major become symptomatic from progressive anemia with profound weakness and demands frequent blood transfusion. Regular blood transfusion and chelation therapy increases the survival time in patients because  $\beta$ -

thalassemia major patient unable to make enough healthy haemoglobin. So they are dependent on frequent blood transfusion that leads to iron overload manifested by increased serum ferritin levels. This secondary iron overload also due to increase absorption of iron from gut. Transfusion-induced hemosiderosis becomes the major clinical complication of transfusion-dependent thalassemia. Each ml of packed red cells contains approximately 1 mg of iron.<sup>1</sup> Physiologically, there is no

such important mechanism to eliminate excess body iron. The accumulation of iron results in progressive dysfunction of the liver, heart and endocrine glands<sup>1</sup>. Besides liver dysfunction and lipid profile abnormality iron overload also leads to hypothyroidism, hypogonadotrophic gonadism, growth hormone deficiency, hypoparathyroidism and diabetes mellitus, heart failure, arrhythmia and heart disease that may leads to death in inadequately iron chelated patient.

Liver is the earliest site of the iron deposition in transfusion dependent  $\beta$ -Thalassemia major patient causing injury to both hepatocyte and reticulo-endothelial cell that may leads to fibrosis of liver. It is manifested by increased liver enzymes and low serum levels of total cholesterol, low high-density lipo-protein and low-density lipo-protein and high triglycerides levels.<sup>2-5</sup>

A high incidence of thromboembolic event and vascular stiffness and atherogenesis and endothelial dysfunction has been found in  $\beta$ -thalassemia major patient probably due to lipid abnormality, which is mainly due to iron overload in liver. Lipid profile abnormality increases risk of cardiovascular complications due to increased atherogenesis and increases risk of pancreatitis in child due to very high triglyceride.

To prevent these in earlier phase this study helps a lot. There are many studies on lipid profile abnormality and ferritin level indicating iron toxicity in many countries around the world. But in India only few studies done particularly in West Bengal. So this is a new topic to study in west Bengal among school going transfusion dependent thalassemic child.

## METHODS

It was an observational cross sectional study done over a study period of one year between January 2019 to December 2019 among  $\beta$ -Thalassemia major patients of age group 6-12 years who got multiple blood transfusion (minimum 10 blood transfusion).

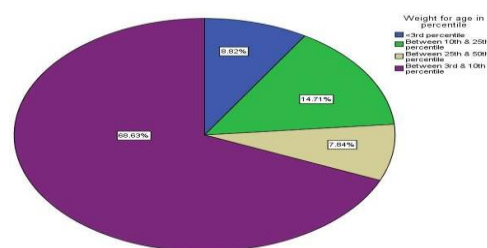
Children who were splenectomised or associated with other hemolytic anemia or receiving any medicine that altering lipid profile or having fever, acute and chronic inflammatory or infectious diseases were excluded. All subjects of study population were studied in a methodical manner in a predesigned structural proforma with detailed history and clinical examination. Thalassemic children, who come for blood transfusion, are asked to come empty stomach next time visit at morning. On next visit 5ml venous blood was taken aseptically in plain vial for serum serum ferritin and serum lipid profile estimation. The lipid profile measured from serum by fully automated clinical chemistry autoanalyzer system with 'Cobas Integra 400 Plus' machine and ferritin is measured from serum by enzyme linked immunosorbent assay technique with 'Beckman Coulter Machine' in our hospital. Anthropometry done with Stadiometer with calibration of

1 mm and Electronic Platform based weighing machine with calibration of 100 gm and plotted on 'Indian Academy of Pediatric (IAP) Growth Chart' (2015). The collected and obtained data was verified using various statistical tests like student t test, unpaired test, chi-square test etc. The SPSS software was used to do statistical analysis. The P value was determined and p value <0.05 was considered significant.

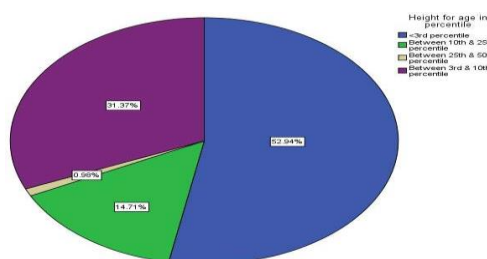
## RESULTS

In our study mean age of presentation was (mean $\pm$ SD) 88.76 $\pm$ 21.67 months. Male outnumbered female by a factor of 1.3 with a Hindu and Muslim ratio of 2:1. Maximum cases presented from urban area (89.22%) of lower socio-economic class (69.61%) as per modified kuppaswamy scale.

Weight for age of 68.63% children were between 3rd-10th percentile followed by 14.71% between 10th-25th percentile and height for age of 52.94% children were less than 3rd percentile followed by 31.37% between 3rd and 10th percentile (Figure 1 and 2).



**Figure 1: Distribution of 'weight for age' (in kg) in percentile.**



**Figure 2: Distribution of 'height for age' (in cm) in percentile.**

All cases had hemolytic facies. Maximum frequency (mode) of number of blood transfusion was 37 with an average value of (mean $\pm$ SD) 42.79 $\pm$ 7.510. Mean value of hepatomegaly and splenomegaly under right and left costal margin were 5.01 $\pm$ 0.605 cm and 4.13 $\pm$ 0.67 cm respectively.

Mean value of Total cholesterol and VLDL were 153.84 $\pm$ 5.428 mg/dl (median value 154 mg/dl and mode 151 mg/dl) and 36.16 $\pm$ 3.385 mg/dl (median 36, mode 35) respectively. Serum Triglyceride value of thalassemia

patient were above the 'high reference value' (>130 mg/dl).

The average value of Ferritin (ng/ml) was (mean±SD) 2263.53±833.904 ng/ml which was much higher than normal reference value of that age (>140 ng/ml) with a median value 1990.50 ng/ml. These frequency distributions are presented by Table 1.

## DISCUSSION

Thalassemia is a huge burden to the health and society in a developing country like India. But increasing awareness regarding the disease among general population, early detection, the increasing availability of blood for transfusion, modern treatment in iron chelation, proper follow up makes easier this disease to handle. But still thalassemia having lots of complication regarding its treatment and disease itself. Due to iron overload thalassemia patients faces lipid profile abnormality along with other complication. Pathogenesis of lipid abnormality in  $\beta$ -Thalassemia may be suggested by accelerated erythropoiesis resulting in increased cholesterol uptake by activated monocytes, macrophages and histiocytes of the reticulo-endothelial system, defective liver functioning due to iron overload, macrophage system activation with cytokine release and hormonal disturbance.<sup>7-10</sup>

In our study, average value of Total cholesterol (mg/dl) of thalassemia patient was (mean±SD) 153.84±5.428 mg/dl. This study reveals serum 'Total cholesterol' was negatively correlated with 'Number of previous blood transfusion', 'Hepatomegaly under RCM', 'Splenomegaly under LCM', 'Triglyceride', 'VLDL', 'Ferritin' (Pearson's correlation coefficient - 0.290, - 0.626, - 0.653, -0.589, -0.922, -0.941 respectively) and positively correlated with 'HDL' and 'LDL' cholesterol (Pearson's correlation coefficient +0.734, +0.960 respectively) which were statistically significant (Table 2). Similar findings were also seen in Suman et al and Arica et al study and Mansi et al.<sup>2,4,12</sup>

The mean value of HDL cholesterol (mg/dl) of thalassemia patient was (mean±SD) 29.45±4.445 mg/dl. Serum 'HDL' cholesterol negatively correlated with 'Age in months', 'Number of previous blood transfusion', 'Hepatomegaly under RCM', 'Splenomegaly under LCM', 'Triglyceride', 'VLDL', 'Ferritin' (Pearson's correlation coefficient - 0.230, -0.405, - 0.565, -0.578, 0.382, -0.706, -0.751 respectively) which were statistically significant. 'HDL' cholesterol positively correlated with 'Total cholesterol' and 'LDL' cholesterol (Pearson's correlation coefficient +0.734, +0.757 respectively) which were statistically significant. (Table 2) These inverse correlation between high ferritin and low HDL-C levels is corroborative with Dey et al, Arica et al, Obed et al and Suman et al. High density lipoprotein (HDL) was on lower side of the range with values of 36.58±12.22 mg/dl.<sup>13,14,2</sup>

This study reveals average value of LDL cholesterol (mg/dl) of thalassemia patient was (mean±SD) 97.16±3.982 mg/dl. Serum 'LDL' cholesterol negatively correlated with 'Number of previous blood transfusion', 'Hepatomegaly under RCM', 'Splenomegaly under LCM', 'Triglyceride', 'VLDL', 'Ferritin' (Pearson's correlation coefficient - 0.284, - 0.633, - 0.672, -0.572, - 0.942, -0.964 respectively) which were statistically significant. 'LDL' cholesterol positively correlated with 'Total cholesterol' and 'HDL' cholesterol (Pearson's correlation coefficient +0.960, +0.757 respectively) which were significant (Table 2) just like Arica et al, Suman et al and Mansi et al.<sup>4,2,12</sup>

The mean value of Triglyceride (mg/dl) of thalassemia patients in our study was (mean±SD) 206.22±67.407 mg/dl. Serum 'Triglyceride' negatively correlated with 'Total cholesterol', 'HDL' and 'LDL' cholesterol (Pearson's correlation coefficient -0.589, -0.382, -0.572 respectively) which were statistically significant. Serum 'Triglyceride' positively correlated with 'Hepatomegaly under RCM', 'Splenomegaly under LCM', 'VLDL', 'Ferritin' (Pearson's correlation coefficient +0.281, +0.356, +0.638, +0.606 respectively) which were statistically significant. (Table 2) In Papanastasiou et al, Hassanin et al and Suman et al studies.<sup>6,2</sup> TG was also significantly increased and showed positive correlation with serum ferritin with coefficient of correlation ( $r=+0.85$ ) just like our study.

Mean value of VLDL (mg/dl) of thalassemia patient was (mean±SD) 36.16±3.385 mg/dl. Serum 'VLDL' negatively correlated with 'Total cholesterol', 'HDL' and 'LDL' cholesterol (Pearson's correlation coefficient - 0.922, -0.706, - 0.942 respectively) which were significant. Serum VLDL positively correlated with 'Number of previous blood transfusion', 'Hepatomegaly under RCM', 'Splenomegaly under LCM', 'Triglyceride', 'Ferritin' (Pearson's correlation coefficient +0.231, +0.579, +0.633, +0.638, +0.973 respectively (Table 2). Similar findings seen in Babu et al and Papanastasiou et al study.<sup>15,6</sup>

As per our study, average value of Ferritin (ng/ml) of thalassemia patient was (mean±SD) 2263.53±833.904 ng/ml. Serum Ferritin positively correlated with 'Number of previous blood transfusion', 'Hepatomegaly under RCM', 'Splenomegaly under LCM', 'Triglyceride', 'VLDL' (Pearson's correlation coefficient +0.291, +0.607, +0.660, +0.606, +0.973 respectively) which were statistically significant (Table 2). Arica V et al stated that Ferritin values in the group with Beta-Thalassemia major were found to be significantly higher than in the control group ( $p<0.005$ ).<sup>4</sup> Balci et al was comparing the correlation between ferritin and lipid parameters, while a significantly negative relationship was detected between ferritin and high-density lipoprotein cholesterol (HDL-C) ( $p=0.000$ ,  $r=-0.602$ ), a significantly positive relationship was detected between ferritin and triglyceride (TG) levels ( $p=0.02$ ) in TM patients.<sup>5</sup>

Table 1: Results of various parameter.

	Age in months	Numbers of previous blood transfusion history	Hepatomegaly under RCM (cm)	Splenomegaly under LCM (cm)	Total cholesterol (mg/dl)	Hdl cholesterol (mg/dl)	Ldl cholesterol (mg/dl)	Triglyceride (mg/dl)	VLDL (mg/dl)	Ferritin (ng/ml)
N	Valid	102	102	102	102	102	102	102	102	102
	Missing	0	0	0	0	0	0	0	0	0
Mean	88.76	42.79	5.01	4.13	153.84	29.45	97.16	206.22	36.16	2263.53
Std. error of mean	2.146	0.744	0.060	0.066	0.537	0.440	0.394	6.674	0.335	82.569
Median	76.00	39.00	5.00	4.00	154.00	30.00	97.50	187.50	36.00	1990.50
Mode	72	37	5	4	151	30	99	155	35	930
Std. deviation	21.677	7.510	0.605	0.670	5.428	4.445	3.982	67.407	3.385	833.904
Variance	469.904	56.403	0.366	0.449	29.460	19.755	15.856	4543.735	11.460	695396.331
Range	72	26	2	3	28	19	20	298	19	5003

Table 2: Correlation among various parameter.

		Age in Months	Number of previous Blood transfusion History	Hepatomegaly under RCM (cm)	Splenomegaly under LCM (cm)	Total Cholesterol (mg/dl)	HDL Cholesterol (mg/dl)	LDL Cholesterol (mg/dl)	Triglyceride (mg/dl)	VLDL (mg/dl)	Ferritin Level (ng/ml)
Age in Months	Pearson Correlation	1.000	0.906**	0.445**	0.451**	-0.039	-0.230*	-0.042	-0.005	-0.007	0.048
	sig. (2-tailed)		0.000	0.000	0.000	0.700	0.020	0.678	0.960	0.946	0.629
	N	102	102	102	102	102	102	102	102	102	102
Number of previous Blood transfusion History	Pearson Correlation	0.906**	1.000	0.562**	0.570**	-0.290**	-0.405**	-0.284**	0.116	0.231*	0.291**
	Sig. (2-tailed)	0.000		0.000	0.000	0.003	0.000	0.004	0.244	0.019	0.003
	N	102	102	102	102	102	102	102	102	102	102
Hepatomegaly under RCM (cm)	Pearson Correlation	0.445**	0.562**	1.000	0.876**	-0.626**	-0.565**	-0.633**	0.281**	0.579**	0.607**
	Sig. (2-tailed)	0.000	0.000		0.000	0.000	0.000	0.000	0.004	0.000	0.000
	N	102	102	102	102	102	102	102	102	102	102

Continued.

		Age in Months	Number of previous Blood transfusion History	Hepatomegaly under RCM (cm)	Splenomegaly under LCM (cm)	Total Cholesterol (mg/dl)	HDL Cholesterol (mg/dl)	LDL Cholesterol (mg/dl)	Triglyceride (mg/dl)	VLDL (mg/dl)	Ferritin Level (ng/ml)
Splenomegaly under LCM(cm)	Pearson Correlation	0.451**	0.570**	0.876**		-0.653**	-0.578**	-0.672**	0.356**	0.633**	0.660**
	Sig. (2-tailed)	0.000	0.000	0.000	1.000	0.000	0.000	0.000	0.000	0.000	0.000
	N	102	102	102	102	102	102	102	102	102	102
Total Cholesterol (mg/dl)	Pearson Correlation	-0.039**	-0.290**	-0.626**	-0.653**	1.000	0.734**	0.960**	-0.589**	-0.922**	-0.941**
	Sig. (2-tailed)	0.700	0.003	0.000	0.000		0.000	0.000	0.000	0.000	0.000
	N	102	102	102	102	102	102	102	102	102	102
HDL Cholesterol (mg/dl)	Pearson Correlation	-0.230*	-0.405**	-0.565**	-0.578**	0.734**	1.000	0.757**	-0.382**	-0.706**	-0.751**
	Sig. (2-tailed)	0.020	0.000	0.000	0.000	0.000		0.000	0.000	0.000	0.000
	N	102	102	102	102	102	102	102	102	102	102
LDL Cholesterol (mg/dl)	Pearson Correlation	0.042	-0.284**	-0.633**	-0.672**	0.960**	0.757**		-0.572**	-0.942**	-0.964**
	Sig. (2-tailed)	0.678	0.004	0.000	0.000	0.000	0.000	1.000	0.000	0.000	0.000
	N	102	102	102	102	102	102	102	102	102	102
Triglyceride (mg/dl)	Pearson Correlation	-0.005	0.116	0.281**	0.356**	-0.589**	-0.382**	-0.572**	1.000	0.638**	0.606**
	sig. (2-tailed)	0.960	0.244	0.004	0.000	0.000	0.000	0.000		0.000	0.000
	N	102	102	102	102	102	102	102	102	102	102
VLDL (mg/dl)	Pearson Correlation	-0.007	0.231*	0.579**	0.633**	-0.922**	-0.706**	-0.942**	0.638**	1.000	0.973**
	Sig. (2-tailed)	0.946	0.019	0.000	0.000	0.000	0.000	0.000	0.000		0.000
	N	102	102	102	102	102	102	102	102	102	102
Ferritin level (ng/ml)	Pearson Correlation	0.048	0.291**	0.607**	0.660**	-0.941**	-0.751**	-0.964**	0.606**	0.973**	1.000
	Sig. (2-tailed)	0.629	0.003	0.000	0.000	0.000	0.000	0.000	0.000	0.000	
	N	102	102	102	102	102	102	102	102	102	102



## CONCLUSION

There is significant lipid profile abnormality which is significantly correlated with increased ferritin level due to iron overload complication in  $\beta$ -thalassemia major patient with multiple blood transfusion.

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