Contributors: AJ, SK, SS: conceived and designed the study; AJ, SS: were involved in patient care, collected the data; AJ, SK: analysis and interpretation of data, drafting the manuscript. All authors approved the final version of manuscript.
Funding: None; *Competing interests*: None stated.

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Lipid Profile in Children With Thalassemia: A Prospective Observational Study From Eastern India

This was a prospective observational study to evaluate abnormalities in lipid profile in 50 children with transfusion dependent thalassemia. Dyslipidemia characterized by high triglycerides, low high density lipoprotein (HDL), and high total cholesterol: HDL ratio was noted. These pro atherogenic risk factors may be lead to significant cardiovascular morbidity in these patients.

Keywords: *Atherosclerosis, Co-morbidity, E beta thalassemia, Outcome*.

Life expectancy and quality of life of beta-thalassemia patients have improved in recent years. However, non-siderotic complications are known to cause significant morbidity in these patients with beta-thalassemia. In recent years, many studies have shown risk of developing subclinical atherosclerosis in beta-thalassemia patients. Strong association of abnormal serum lipid levels [low total cholesterol (TC) and (high density lipoprotein) HDL-cholesterol, high triglycerides (TG) and TC: HDL ratio) with premature atherosclerosis have been noted in children with beta thalassemia [2-5]. Low HDL - cholesterol and high TC:HDL ratio are pro-atherogenic factors, which help in cardiac risk stratification and prognostication [6,7]. Pediatric data regarding lipid profile in thalassemia is limited. Our primary objective was to evaluate abnormalities in lipid profile in children with thalassemia.

A prospective observational study was performed at Institute of Child Health, Kolkata between July, 2016 and June, 2017. Children with transfusion- dependent thalassemia, under regular follow up in our thalassemia clinic, were included for this study. The patients had been diagnosed following appropriate clinical history, physical examination, complete blood count and high performance liquid chromatography (HPLC) and were on regular transfusion and chelation therapy. Children having family history of dyslipidemia were excluded. None of the patients had previous history of cardiovascular illness. Fifty age- and sex-matched healthy children were taken as control. Ethical clearance was obtained from the institution ethics committee and written consent was obtained from care givers.

Blood samples for serum fasting lipid profile and ferritin were taken after a 12 hour overnight fast. Spectrophotometry was used for assessing fasting lipid profile. Statistical analyses were carried out using GraphPad Prism, version 5.0. Continuous, non-parametric data were compared using the Mann-Whitney U test, while categorical data were compared by chi square test. $P<0.05$ was considered as statistically significant.

Out of a total of 53 eligible children, 3 were excluded for having family history of hyperlipidemia. Thus, 50 children

Table I Comparison of Fasting Lipid Profile between Children with Beta Thalassemia Patients and Control Group

Parameters	*Children with thalassemia (n=50)*	*Control group (n=50)*
Total cholesterol	95.5 (78.75, 111.3)	156.5 (143.5, 184.8)
HDL-cholesterol	23 (19, 32)	48.5 (39.8, 54.3)
Triglycerides	258 (142, 415)	118 (78, 199.3)
*TC:HDL ratio	4.79 (3.79, 6.94)	3.00 (2.73, 4.08)

All values in median (IQR) except total:high density lipoprotein cholesterol ratio (TC:HDL). All P<0.001.

(62% males) with a median age of 2 years 5 month (range 0-18 years) were enrolled. All patients had low HDL-Cholesterol, 74% had high TG levels, 84% had a high TC: HDL ratio and 60% had low total cholesterol (***Table* I**). Out of the 37 patients with elevated triglyceride levels, 28 had hyperferritinemia. Low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were in normal range. Patients with thalassemia had lower HDL cholesterol and higher triglycerides and elevated TC: HDL ratio compared to the controls (***Table* I**). Children with E beta thalassemia had lower TC than children with beta thalassemia major (***Table* II**). TC: HDL ratio was increased and HDL-cholesterol was decreased irrespective of age and gender.

Iron overload and oxidative stress are postulated mechanisms for causing dyslipidemia in patients with thalassemia [4,8,9]. Similar to our results, hypocholesterolemia in patients with thalassemia has been demonstrated in earlier studies [8]. Iron overload contributes to liver injury contributing to decrease in production of cholesterol. Increased consumption of cholesterol due to enhanced erythropoiesis and increased uptake by the histiocytes are other factors [9]. Elevated triglyceride levels, possibly because of decreased lipolytic enzyme activity, have also been reported previously [2,4,9,10]. Unlike our study, females were found to have elevated TG in previous studies. The low HDL-cholesterol levels in our patients weres presumably due to excessive clearing of HDL by the activated macrophages [4].

Table II Comparison of Fasting Lipid Profile between Children with Beta Thalassemia Major and E-beta thalassemia

Parameters	*β-thalassemia major (n=29)*	*E β-thalassemia (n=21)*
Total cholesterol[#]	109 (96,147)	76 (69, 86.5)
HDL cholesterol	23.5 (19.75, 29.75)	23 (17.25, 33)
Triglycerides^	176.5 (137.8, 352.5)	334.5 (254.3 -457)
*TC:HDL ratio	4.32 (3.79 – 6.29)	4.9 (3.86 – 7.13)

*All values in median (IQR). Units for all values in mg/dL; *TC: Total cholesterol. [#]P<0.0001; ^P=0.02*

The limitation of our study was a small sample size. Larger studies with follow up echocardiography and cardiac MRI will provide further insight and information regarding the cardiovascular complications in children with thalassemia having deranged lipid profile. This may also help in framing guidelines for monitoring lipid profile in these children, in order to reduce long term morbidity and mortality.

***Acknowledgements*:** Dr Prabal Niyogi, Deputy Director, Institute of Child Health was involved in planning of the research.

Ethics clearance: Institution ethics committee of Institute of Child Health, Kolkata; No. ICH/13/2016, dated 29 July, 2016.
Contributors: TK, SB: were involved in processing data and statistical analysis; TK, DM: were involved in writing the manuscript which was subsequently approved by all the authors. All the authors were involved in planning of the research and collection of data.
Funding; None; *Competing interest*: None stated.

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