

## Hypertriglyceridemia Thalassemia Syndrome: A Report of 4 Cases

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**Abstract** Hypertriglyceridemia in children can be familial or acquired. Acquired forms of hypertriglyceridemia in children may be associated with several other diseases obesity, diabetes mellitus, uremia/dialysis, hypothyroidism, nephrotic syndrome, drugs etc. Hypertriglyceridemia with  $\beta$ -thalassemia major is an association of unknown pathogenesis which is rarely described in the literature but is important to recognize, for the prevention of complications and proper management of thalassemic children.

**Keywords** Thalassemia · Hypertriglyceridemia · HPLC

### Introduction

Hypertriglyceridemias are traditionally defined as conditions in which the concentration of triglyceride carrying lipoproteins in plasma exceeds the normal limits ( $>150$  mg/dl). Hypertriglyceridemia may be familial or acquired and reflect increased hepatic synthesis or

decreased catabolism [1]. We report a rare association of  $\beta$ -thalassaemia major and hypertriglyceridemia in four cases.

### Materials and Methods

All four cases were referred to hematology clinic, MAMC for chronic anemia and hepatosplenomegaly. The age ranged from 11 months to 2 years (average 1.5 years) with male: female ratio of 1:3. Complete hemogram with red cell indices (MCV:MCH ratio), peripheral smear and reticulocyte count were carried out in all the cases. This was followed by high performance liquid chromatography (HPLC) Variant II  $\beta$  thal short programme. Incidentally it was noticed that plasma turned diffusely milky on standing (Fig. 1) so serum lipid profile was obtained.

### Results

On HPLC all four cases were diagnosed as thalassemia major (Fig. 2a–d). Family studies were carried out which showed both the parents to be thalassemia trait in all four cases. Serum LDL-C, HDL-C and total cholesterol were within normal limits while the triglycerides were found to be markedly raised in all four cases. The values ranged from 800 to 1,400 mg/dl (average 1,050 mg/dl;  $N = 46$ –236 mg/dl). Suspecting hyperlipidemia, children were re-examined for xanthomas, corneal arcus or tonsillar hypertrophy which was absent in all of them. Other causes of secondary hypertriglyceridemia, including hypothyroidism and diabetes mellitus, were ruled out with appropriate testing. Neither the mother nor father had laboratory

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**Fig. 1** Blood sample showing milky white colour of plasma in a patient of Thalassemia major indicating high lipid content

evidence of hyperlipidemia in any of the cases. Results are tabulated in Table 1.

## Discussion

In  $\beta$ -Thalassemia major, level of HbF is variable depending upon the presence of  $\beta^0$  or  $\beta^+$  mutation. In  $\beta^0$  thalassemia major, almost all the hemoglobin is comprised of HbF and there is no detectable HbA while in  $\beta^+$  thalassemia major, level of HbF varies from 30 to 90 % but in both the instances patient usually presents within first year of life with failure to thrive, poor feeding, intermittent bouts of infection and general malaise, pallor and splenomegaly similar to our first case

who presented with pallor, hepatosplenomegaly and poor growth at 11 months of age with microcytic hypochromic indices and marked degree of anisoipoikilocytosis on peripheral blood smear while HbF levels on HPLC were only 31 %.

There are five groups of Primary lipid disorders according to Frederickson Classification of Dyslipidemias-Type I, IIA, IIB, III, IV, V. The most common dyslipidemias associated with markedly elevated triglyceride levels are types I, III, IV and V. Type I, type III and V are rare in pediatric patients. Our patients had markedly elevated levels of triglycerides (mean 1,050 mg/dl), while rest of the lipid profile (Total cholesterol, HDL-C, and LDL-C) was normal. Possibility of primary hypertriglyceridemia was ruled out by the presence of absolutely normal lipid profile in parents of all the four children and absence of associated findings of primary hyperlipidemias like tendon and tuberous xanthomas.

A variety of diseases have been linked to secondary hypertriglyceridemia, including infection, renal insufficiency, and diabetic ketoacidosis which were ruled out proper history and clinical examinations along with relevant investigations.

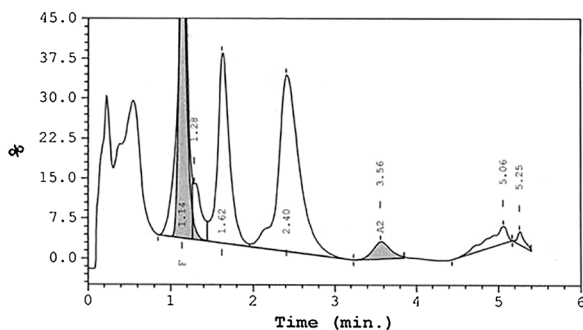
Hypertriglyceridemia may accompany acute, massive hemolysis [2]. The association of thalassemia major with hypertriglyceridemia termed as Hypertriglyceridemia-thalassemia syndrome has been described by some authors in India [3, 4, 5]. Most of these children had presented in the age group of 4 months to 2.5 years. In our study the patients' age ranged from 11 months to 2 years (average 1.5 years). Though pathogenesis of such association has remained unclear but when present might put the thalassemic children at high risk for developing atherosclerosis and acute pancreatitis at a very early age which can further increase morbidity and mortality in such cases.

**a**

F Concentration = 31.0\* %  
 A2 Concentration = 3.2 %

\*Values outside of expected ranges

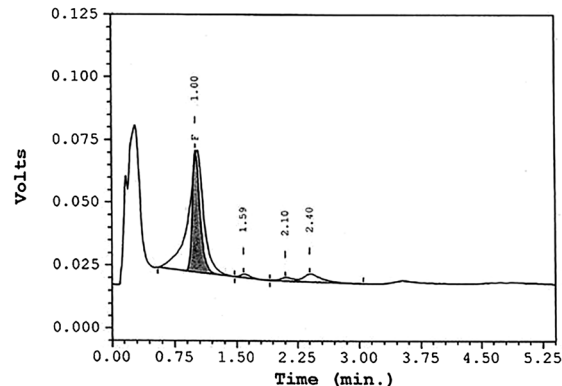
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**b** F Concentration = 94.9\* %  
 A2 Concentration = %

\*Values outside of expected ranges

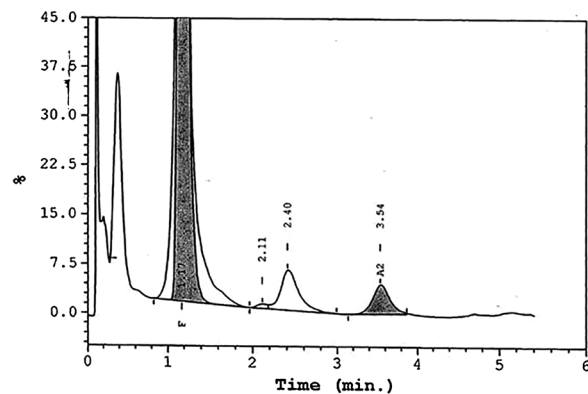
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**c**

F Concentration = 97.6\* %  
 A2 Concentration = 4.5\* %

\*Values outside of expected ranges

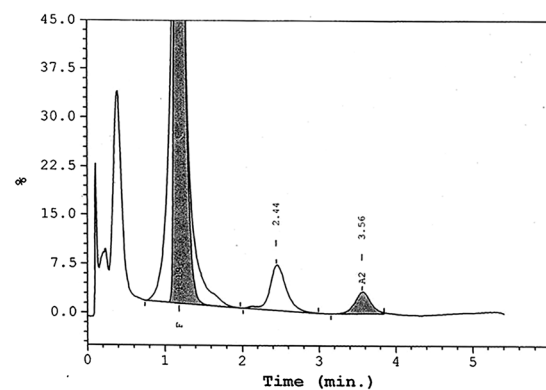
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**d**

F Concentration = 112.0\* %  
 A2 Concentration = 3.3 %

\*Values outside of expected ranges

Analysis comments:



**Fig. 2** HPLC chromatograms in cases of Thalassemia major showing HbF a) 31% b) 94.9% c) 97.6% and d) 112%

**Table 1** Clinical details, hematological parameters and Triglyceride levels in all the four cases

Parameter	C/C	Age/sex	Hb	MCV/MCH	HbF (%)	HbA (%)	HbA2 (%)	TG levels (mg/dl)
Patient 1	Chronic anemia Hepatosplenomegaly Poor growth	11 month/F	5.9	66.9 fL 26.2 pg	31	60.7	3.2	800
Patient 2	Pallor Jaundice Hepatosplenomegaly	2 year/F	4.2	56.7 fL 18.3 pg	94.9	12.2	–	1,100
Patient 3	Severe anemia Failure to thrive	1.5 year/M	1.6	79.7 fL 19.0 pg	97.6	5.6	4.5	900
Patient 4	Anemia Poor growth Splenomegaly	1.8 year/F	5.5	63 fL 21.4 pg	112.6	6.6	3.3	1,400

## Conclusion

We propose that all children suffering from thalassemia major or other conditions associated with massive hemolysis should be screened for abnormal lipid profile especially triglyceride levels, and this entity must be considered in thalasseemics as its early detection and appropriate management could help prevent risk of atherosclerosis, myocardial infarction and acute pancreatitis in such children.

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