ORIGINAL ARTICLE

Risk of Premature Atherosclerosis in Patients with Transfusion Dependent Beta-Thalassemia Major

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ABSTRACT

Objective: To assess the risk of premature atherosclerosis in transfusion-dependent beta thalassemia major patients using Atherogenic Index of plasma.

Study Design: Comparative Cross-sectional study.

Place and Duration of the Study: Pathology Department, Fauji Foundation Hospital Rawalpindi, from 1st March 2024 to 31st August 2024.

Materials and Methods: Total 120 participants were included in our study comprising of 64 β-Thalassemia major patients and 56 healthy subjects. Patients with poor compliance for blood transfusions or iron-chelating therapy; individuals with age <3 years, having history of familial hyperlipidaemia, diabetes mellitus, hypothyroidism, liver or renal disease were excluded. Consent was obtained and anthropometric along with clinical details were recorded. Fasting blood samples were analyzed for serum lipid profile, serum Ferritin and plasma hemoglobin. Atherogenic index of plasma was calculated by the formula: log TG/HDL-C. Data was analyzed on SPSS 23.

Results: Sixty-four β-Thalassemia major patients with mean age 13.2±4 years and 56 healthy subjects with mean age 12.6±5 years participated in our study. Elevated serum triglyceride level while reduced serum total cholesterol, low density lipoprotein and high-density lipoprotein cholesterol levels were found among β-Thalassemia major patients than healthy individuals (p <0.001). Atherogenic Index of Plasma was markedly elevated among β-Thalassemia patients than their healthy counterparts; 0.27(0.08-0.38) vs. 0.06(0.03-0.08) (p <0.001), indicating high propensity of premature atherosclerosis in them. Plasma Atherogenic Index exhibited positive correlation with serum Ferritin (r= 0.41, p = 0.001) and negative correlation with plasma Hemoglobin (r= -0.65, p < 0.001).

Conclusion: β-Thalassemia major patients have elevated Plasma Atherogenic Index value than age-matched healthy subjects, implying high risk of premature atherosclerosis and future cardiovascular events in this vulnerable group.

Keywords: *Beta-Thalassemia, Lipid Profile, Premature Atherosclerosis.*

Introduction

Beta-Thalassemia major (βTM) is among the most common genetic disorders characterized by abnormal or decreased production of β-globin chains of hemoglobin leading to hemolysis, chronic anemia in these patients and the need for repeated blood transfusions for their entire life.[1] High prevalence of βTM has been documented in the Indian subcontinent, with the estimated carrier rate of 5-7% in Pakistan.[2]

Cardiovascular complications, particularly those secondary to chronic iron overload, are recognized as the leading cause of mortality in patients with βTM.[3] There is strong evidence that these patients are prone to develop premature atherosclerosis[4]; a condition that is subclinical and has been attributed to iron overload, oxidative stress, chronic hemolysis, dyslipidemia and several other factors.[5] Metabolic lipid derangements commonly observed among βTM patients include reduced levels of total cholesterol (TC), low density lipoprotein cholesterol

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(LDL-C), high density lipoprotein cholesterol (HDL-C) while elevated levels of serum triglyceride (TG).[6, 7] Exact pathogenesis of dyslipidemia is not clear but iron overload and oxidative stress have been mainly attributed for these changes.[8]

Owing to ineffective erythropoiesis, ongoing hemolysis and frequent transfusions, iron overload that is commonly seen in these patients causes oxidative stress and poses the risk of various complications including dyslipidemia.[3] Other factors contributing towards dyslipidemia in βTM patients include plasma dilution secondary to hemolysis and anaemia altering the distribution of the lipids, increased cholesterol uptake by reticulo-endothelial system due to increased erythropoiesis triggered by ongoing hemolysis, altered liver function secondary to iron deposition, and endocrine disorders like hypothyroidism and diabetes mellitus.[9]

These lipid derangements and vascular changes if not detected early can lead to atherosclerotic cardiovascular disease (ASCVD) and even cerebrovascular disease in these patients. To evaluate the risk of atherogenicity in patients with βTM, various investigative tools have been utilized including carotid artery intima media thickness (CAIMT), serum Osteoprotegerin, fasting lipid levels and atherogenic index of plasma (AIP).[10] AIP is an emerging biomarker that has been considered useful for atherosclerosis risk assessment in obese, diabetic, hypertensive, hypothyroid, vitamin D-deficient and other high-risk groups,[11, 12,13] however, its use for risk assessment and stratification in βTM patients has not been studied much. AIP is a lipid-derived index calculated from logarithmic transformation of ratio of serum triglyceride and HDL-c, both of which have strong association with atherogenesis.[14] AIP has been suggested as a better predictor of ASCVD than the standard lipid testing and other atherogenic indices[15,16,17] since AIP is less cumbersome, inexpensive and outperforms than the predictive ability of the individual lipid values.[17,18] High risk of atherogenicity reported in βTM patients by previous studies prompts close monitoring of lipid derangements for early detection and timely management of potential contributors of atherogenesis in order to avoid progression towards cardiovascular complications. Data regarding biochemical assessment of atherosclerosis risk in βTM patients are scarce in our region; therefore, we designed this study to evaluate the risk of premature atherosclerosis in transfusion dependent βTM patients by using Atherogenic Index of Plasma.

Materials and Methods

This was a cross-sectional study executed at Department of Pathology, Fauji Foundation Hospital Rawalpindi from 1st March 2024 to 31st August 2024 after getting permission from the Institutional Ethical Review Board (No. 702/RC/FFH/RWP). Sample size of the study was determined through WHO sample size calculator with the prevalence of βTM in Pakistan 7%, [2] confidence level 95% and margin of error 5%.

Our study comprised of total 120 participants selected through non-probability consecutive sampling. Sixty-four Beta thalassemia major patients > 3 years age, diagnosed on the basis of hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) and registered in the Hospital Blood Bank for receiving regular blood transfusions were included in the study. Fifty-six apparently healthy, age and gender-matched individuals were included for comparison. βTM patients having poor compliance for blood transfusions or iron-chelating therapy, participants with age <3 years, history of other hemoglobinopathies, hereditary hyperlipidemia, diabetes mellitus, hypertension, hypothyroidism, liver disease, renal disease, cardiac disease, acute inflammation, smoking and those taking lipid lowering medication or steroids were excluded.

After getting informed consent, demographic information including gender, age of the subjects, age of βTM diagnosis, frequency of blood transfusions, medical history, drug history, dietary history and family history were recorded on a questionnaire. Anthropometric parameters including weight and height were measured by using calibrated digital weighing scale and stadiometer (Kern MPE, Germany). Fasting blood specimens were collected and analyzed for blood complete picture on fully automated hematology analyzer (Beckman Coulter, USA), serum lipid profile on fully automated chemistry analyzer (Atellica CH by Siemens, Germany) and serum Ferritin on Chemiluminescence immunoassay (Atellica IM by Siemens, Germany).

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Body Mass Index (BMI) and BMI percentile scores were determined by using CDC BMI calculator and BMI-for-Age growth charts respectively. Subjects were categorized into underweight (BMI <5th percentile), healthy weight (BMI between 5th and 84th percentile), overweight (BMI between 85th and 94th percentile) and obese (≥95th percentile) according to CDC guidelines. Serum Ferritin in the range of 15-150 ng/ml for females and 15-200 ng/ml for males was used for reference according to WHO recommendations. For comparison of Hemoglobin level between healthy and βTM subjects, WHO recommended age-specific cutoff values were used. Plasma Atherogenic index was derived by calculating logarithm of ratio of TG (mmol/L) and HDL (mmol/L), as explained by Dobiasova and Frohlich.[14] Based on AIP results, subjects were stratified into three categories of atherosclerosis risk: low-risk (AIP <0.1), moderate risk (AIP 0.1-0.24) and high risk (AIP >0.24).[15] Cutoff value applied for serum TC, TG, LDL-C and HDL-C was according to National Cholesterol Education Program (NCEP) guidelines.[19]

Data were analyzed on SPSS version 23. After analyzing the distribution of data by Kolmogorov-Smirnov test, mean and standard deviation were derived for the parametric continuous data while median and inter-quartile range was calculated for non-parametric data. Mean values of the variables with parametric distribution were compared between βTM patients and healthy subjects by independent sample t-test while Mann Whitney U Test was applied to compare variables with non-parametric distribution. For categorical parameters, frequency was determined and comparison was performed by Chi-Square Test between the two study groups. Association of AIP with serum Ferritin, plasma hemoglobin and BMI was determined by Spearman Correlation test. The probability value (p) was considered significant if it was ≤ 0.05. Association was considered strong with correlation coefficient (r) ≥ 0.60, moderate with r: 0.40-0.59, weak with r: 0.20-0.39, very weak with r: 0.00 to 0.19.

Results

Our study included a total of 120 participants comprising 64 βTM patients and 56 healthy subjects. Mean age of βTM patients was 13.2 ± 4 years while healthy subjects were of average 12.6 ± 5 years age (p = 0.489). Among the βTM patients, 34(53.1%) were from female gender while 30(46.9%) were male and among healthy subjects, 31(55.4%) were female and 25(44.6%) were male (p =0.807). Diagnosis of βTM was confirmed at an average age of 1 ± 0.9 years. Consanguinity was positive in 55(86%), family history of thalassemia was positive in 20(31%) βTM patients. Subjects included in both study groups belonged to the families of ex-service men and were from the same socioeconomic background. Dietary history based on 24-hour recall did not reveal any difference in dietary patterns between the two groups.

Anthropometric parameters including weight, height and BMI were significantly lower in the βTM patients than the healthy individuals. Median values of weight, height and BMI in the βTM and healthy subjects were 25(23-29) kg vs. 35(29-53) kg (p <0.001), 129(124-132) cm vs. 147(131-171) cm (p <0.001) and 15.6(14.4-16.5) kg/m^2 vs. 16.9(15.6-17.8) kg/m^2 (p = 0.001) respectively. Among βTM patients, 36(56.2%) were found underweight with BMI <5th percentile and remaining 28(43.8%) had healthy weight with BMI between 5th and 84th percentile while in the healthy group, only 4(7.1%) subjects were underweight (BMI <5th percentile), 50(89.3%) were in the healthy weight category (BMI between 5th and 84th percentile) and 2(3.6%) were overweight with BMI between 85th and 94th percentile (p <0.001). Low BMI noted in most of the βTM patients can be attributed to persistent anemia due to chronic hemolysis and iron overload following repeated blood transfusions, both of which are commonly observed in this disease group. Majority of the βTM patients in our study, 32(50%) received transfusions every two weeks with average 24 transfusions annually (Table I). Most of the βTM patients in our study, 59(92.2%), were on oral Deferasirox treatment and only 5 (7.8%) were receiving both oral Deferasirox and Inj. Deferoxamine (Table I). Markedly elevated serum Ferritin levels were noted among βTM patients compared to healthy individuals; 1945(1356-2460) ng/ml vs. 56(36-88) ng/ml (p <0.001) (Table II). Among the βTM patients, 8 (12.5%) had serum Feritin <1000 ng/ml, 31(48.4%) had Ferritin level in range of 1000-2000 ng/ml, 14(21.9%) had between 2000-3000 ng/ml, 4(6.3%) between 3000-4000 ng/ml and 7(10.9%) had Ferritin level above 4000

ng/ml. On the other hand, all healthy participants had serum Ferritin level within normal limits. Low pre-transfusion hemoglobin level was seen in βTM patients compared to healthy individuals with median Hb level of 8.3(7.5-9.0) g/dl vs. 12.4(11.9-12.8) g/dl (p <0.001) (Table II). Low hemoglobin and elevated serum Ferritin levels noted in βTM patients reflected anemia secondary to chronic hemolysis and transfusion-associated iron overload among them.

Lipid parameter analysis revealed significantly decreased serum TC, serum HDL, serum LDL while elevated serum TG levels among βTM patients compared to their healthy counterparts; 3.6 (3.1-4.0) mmol/l vs. 4.3 (3.9-4.7) mmol/l (p <0.001), 1.0 (0.9-1.1) mmol/l vs. 1.3 (1.2-1.4) mmol/l (p <0.001), 2.5 (2.0-2.8) mmol/l vs. 2.8 (2.5-3.0) mmol/l (p = 0.002) and 1.8 (1.0-2.2) mmol/l vs. 1.0 (0.9-1.2) mmol/l (p <0.001) respectively (Table II). Low serum total cholesterol level in βTM patients indicated its increased utilization owing to ineffective erythropoiesis while low HDL and elevated triglyceride levels seemed to contribute towards higher plasma atherogenic index among them.

We assessed premature atherosclerosis risk via plasma Atherogenic Index by calculating logarithm of triglyceride to HDL ratio. Markedly elevated AIP results were observed in βTM patients than their healthy counterparts signaling greater predisposition to atherogenic alterations; AIP 0.27 (0.08-0.38) vs. 0.06 (0.03-0.08) (p <0.001) (Table II). Atherosclerosis risk categorization of AIP was carried out, 25(39.1%) βTM patients had high atherosclerosis risk (AIP > 0.24), 15(23.4%) were having moderate risk (AIP 0.1-0.24) and 24(37.5%) patients had low risk of atherogenicity (AIP < 0.1). In comparison, majority of the healthy subjects, 52(92.8%), exhibited low-risk (AIP < 0.1), 3(5.4%) had moderate risk (AIP 0.1-0.24) and 1(1.8%) had high risk of atherogenicity (AIP > 0.24) (p <0.001) (Figure 1). These findings highlight the elevated risk of premature atherosclerotic complications in βTM patients.

Association of AIP with other variables including serum Ferritin, Hb level and BMI was evaluated among βTM patients by Spearman Correlation analysis. AIP exhibited moderate positive correlation with serum Ferritin (r = 0.41, p = 0.001). A negative correlation was observed between AIP and plasma Hb level (r= -0.65, p <0.001). This indicates a possible link of anemia and iron overload with atherogenic lipid alterations. No correlation was noted between AIP and BMI (r = 0.046, p = 0.721) indicating no significant contribution of anthropometric measures in promoting atherogenic derangements among these patients.

Table I: Frequency of demographic and clinical variables among βTM patients (n = 64).

Variables	Categories	Frequency (n)	Percentage (%)
Age (years)	<10	16	25
	10-20	41	64
	>20	7	11
Gender	Male	30	46.9
	Female	34	53.1
Transfusion Frequency	Every 2 weeks	32	50
	Every 3 weeks	4	6.2
	Every 4 weeks	28	43.8
Iron-Chelating Therapy	Deferasirox	59	92.2
	Deferasirox+ Deferoxamine	5	7.8

Table-II: Comparison of Biochemical and Anthropometric Parameters between βTM patients and healthy subjects (n=120)

Biochemical Parameters	βTM patients (n=64) Median(IQR)	Healthy subjects (n=56) Median(IQR)	*P* value (Man-Whitney U test)
Serum Total Cholesterol (mmol/l)	3.6 (3.2-4.0)	4.3 (3.9-4.7)	<0.001*
Serum Triglyceride (mmol/l)	1.9 (1.0-2.2)	1.0 (0.9-1.2)	<0.001*
Serum HDL-c (mmol/l)	1.0 (0.9-1.2)	1.3 (1.2-1.4)	<0.001*
Serum LDL-c (mmol/l)	2.5 (2.1-2.8)	2.8 (2.5-2.9)	0.002*
Atherogenic Index of Plasma (AIP)	0.27 (0.08-0.38)	0.06 (0.03-0.08)	<0.001*
Plasma Hemoglobin (g/dl)	8.3(7.5-9.0)	12.4(11.9-12.8)	<0.001*
Serum Ferritin (ng/ml)	1945(1356-2460)	56(36-88)	< 0.001*
BMI (kg/m^2)	15.6(14.4-16.5)	16.9(15.6-17.8)	0.001*

*Significant p value < 0.05

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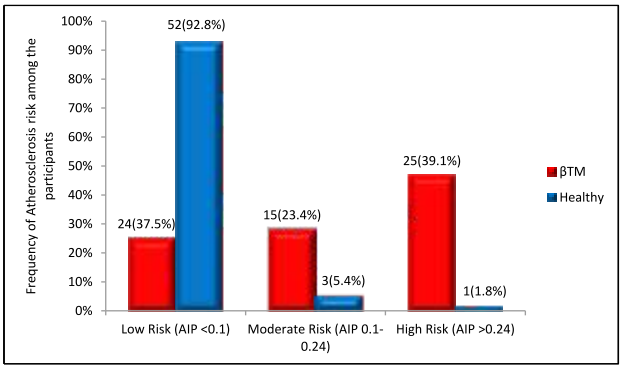

Figure 1: Frequency of Atherosclerosis risk among the study subjects.

Table III: Correlation of serum Ferritin, pre-transfusion Hb level and BMI with Atherogenic Index of Plasma in βTM patients (n = 64)

Variables	Atherogenic Index of Plasma	
	r	*p* value
Serum Ferritin (ng/ml)	0.41	0.001*
Pre-transfusion Hemoglobin (g/dl)	-0.65	<0.001*
Body Mass Index (kg/m^2)	0.046	0.721

*Significant *p* value < 0.05; r = correlation coefficient (≤ 0.19 very weak, 0.2-0.39 weak, 0.40-0.59 moderate, 0.6-0.79 strong, 0.8-1 very strong).

Discussion

Beta thalassemia major is associated with various metabolic derangements notably lipid abnormalities that can subsequently lead to premature atherosclerosis. Dyslipidemia in these patients can not only increase the propensity for cardiovascular events due to increased atherogenesis, but it can also pose a high risk of cerebro-vascular complications in them.[17] AIP has been suggested as a better predictor of ASCVD than the standard lipid testing and other atherogenic indices in different disease groups, since AIP has been reported to be less cumbersome, inexpensive and outperforms than the predictive ability of the individual lipid values.[15, 16, 18] In the current study, we aimed to assess the risk of premature atherosclerosis in βTM patients by using Atherogenic Index of Plasma.

In our study, 46.9% of βTM patients were male while 53.1% were female with slight female predominance. Similar findings have been reported by a previous study from Pakistan with 52.8% female and 47.2% male βTM patients as well as by other international studies.[1, 7, 9] Significantly low BMI was noted among βTM patients with 56.2% being underweight (BMI <5th percentile) compared to only 7.1% underweight among the healthy subjects (*p* < 0.001). Similar findings have been reported by the studies executed in Iraq and India documenting markedly low BMI in βTM patients.[1, 11] We also observed low plasma hemoglobin and elevated serum Ferritin levels in beta-thalassemia patients than the healthy subjects; 8.3(7.5-9.0) g/dl vs. 12.4(11.9-12.8) g/dl (*p* <0.001) and 1945(1356-2460) ng/ml vs. 56(36-88) ng/ml (*p* <0.001) respectively. Other local and international studies from Pakistan, Egypt and India also supported our results and documented similar decline in hemoglobin level and marked elevation of serum Ferritin level in patients with βTM than their healthy counterparts.[1, 8, 9, 10, 20] Low hemoglobin, low BMI and high serum Ferritin identified in βTM patients appear to be inter-linked. Ineffective erythropoiesis and chronic hemolysis cause low Hb and chronic tissue hypoxia in these patients. This can lead to increased basal metabolic rate demand and energy utilization contributing towards low BMI. Sub-optimal growth in these patients can also be attributed to increased utilization of nutrients in erythropoietic activities.[5, 21] Ongoing hemolysis along with frequent transfusions results in a state of iron overload in these patients. Excess iron gets deposited in important organs such as pituitary gland, thyroid gland and liver, further contributing in growth impairment. Iron overload also produces oxidative stress with resultant metabolic disturbances notably affecting lipid metabolism.[20]

Lipid analysis revealed derangements among βTM patients than the healthy subjects characterized by significant decrement in serum TC, LDL-C, HDL-C and a significant increment in TG levels (*p* <0.001). Low cholesterol level has been suggested to result from decreased hepatic cholesterol synthesis due to hepatocyte oxidative injury from iron overload, increased cholesterol consumption for erythropoiesis, and an accelerated cholesterol uptake by histiocytes.[1] Reduced hepatic and extra-hepatic lipase activity in these patients has been speculated to cause hyper-triglyceridemia.[4] Low HDL-C is considered an independent risk factor for cardiovascular disease and high TG levels are also known for their atherogenic potential;[13] however,

role of low total cholesterol and LDL in atherogenicity is not clear. It is proposed that LDL despite of being low in these patients can still contribute in atherogenesis since oxidized LDL is formed in these patients as a result of lipid peroxidation and it is reported to be more atherogenic than the regular LDL.[10] Ashar and colleagues in their study noted lipid derangements among βTM patients similar to our study with low serum total cholesterol, HDL and LDL while elevated triglyceride levels.[7] Sherief and colleagues measured lipid levels and serum Osteoprotegerin levels while Ibrahim and colleagues assessed lipid levels and CAIMT in βTM patients as indicators of atherogenesis. Both of these studies documented decreased serum TC, HDL-C, LDL-C levels and increased TG levels along with increased CAIMT and Osteoprotegerin level, indicating high atherosclerosis risk in these patients.[10, 17] In contrast, a study from Iran conducted by Haghpanah and colleagues didn't find any difference in lipid levels across the two groups.[6] Another study by Shekar and colleagues reported elevated TC and LDL-C levels in these patients, unlike our results.[20] These discrepancies can be attributed to variable dietary preferences and lifestyle across different ethnic regions.

We evaluated the risk of premature atherosclerosis in our subjects via Plasma Atherogenic Index and found considerably elevated levels among βTM patients than their healthy counterparts with median levels 0.27 (0.08-0.38) vs. 0.06 (0.03-0.08) respectively (p <0.001), highlighting the propensity of increased atherosclerosis in βTM patients. There are only few available studies who evaluated atherosclerosis risk in βTM patients by using AIP and most of them have reported higher AIP results among βTM patients than in healthy individuals suggesting high risk of atherogenicity in them.[11, 17, 20] Sanghamitra and colleagues executed a research in India to determine atherosclerosis risk in children with beta thalassemia major and reported elevated lipid indexes including plasma atherogenic index, Castelli's risk index I & II and Atherogenic coefficient in these patients compared to healthy children; AIP 4.43 ± 2.25 vs. 1.78 ± 0.92 respectively.[11] Another study conducted in Egypt compared AIP levels between βTM patients with CAIMT <0.5mm and those with CAIMT >0.5mm. They documented elevated AIP in both βTM groups irrespective of CAIMT size; AIP 0.29±0.04 and 0.52±0.08.[17] Shekar and colleagues evaluated atherogenic lipid derangements in βTM children and compared them with healthy subjects. They also reported significant increase in atherogenic risk in βTM children than the healthy comparators as reflected by AIP 0.87±0.45 vs.0.48±0.21.[20] Further prospective studies are however needed to validate the use of AIP as an early atherogenic marker in βTM patients.

Association of plasma atherogenic index was assessed with Ferritin level which revealed moderate positive correlation of AIP with serum Ferritin (r = 0.41, p= 0.001) indicating role of iron overload in premature atherosclerosis. Consistent with our finding; Ibrahim et al, Shekar and colleagues, AlSaadi and Jabbar also documented significant positive correlation of AIP with serum Ferritin in βTM patients.[1, 13, 17, 20] Formation of reactive oxygen species in iron overload by Fenton reaction followed by oxidation of lipids has been suggested to play a vital role in pathogenesis of altered lipid metabolism. This oxidation results in formation of more atherogenic oxidized LDL as well as causes a reduction in functional HDL which otherwise has anti-atherogenic and anti-oxidant effects.[8] Iron accumulation in liver also leads to altered lipid metabolism, decreased synthesis of apolipoproteins and decline in fatty acid oxidation.[21] Net result will be low serum total cholesterol and HDL while increased triglyceride levels leading to high AIP. We also noted a strong negative correlation of AIP with pre-transfusion Hb level (r= - 0.65, p <0.001), implying that patients having low pre-transfusion Hb can have increased risk of atherogenicity. This can be explained by ongoing hemolysis causing low Hb level in these patients which not only alters lipid levels due to dilution effects but also augments ineffective erythropoiesis with increased utilization of cholesterol. In addition, hemolysis as reflected by low Hb also causes synthesis of oxidative stress markers causing lipid per-oxidation and further derangement of AIP. Supporting our findings, AlSaadi and Jabbar concluded that determinants of AIP; TG and HDL-c, were negatively associated with hemoglobin level among βTM patients in their studies (p <0.01).[1, 13] We observed no significant association of AIP with BMI. Likewise, Shekar and

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colleagues also observed no relationship between plasma atherogenic index and anthropometric parameters.[20]

Elevated AIP levels and increased risk of atherogenicity in βTM patients prompts the need for regular assessment of lipid derangements in them in order to identify high-risk cases earlier and mitigate the effects of the cardio-metabolic complications in them. It is also emphasized that more effective strategies should be formulated to manage potential pro-atherogenic factors identified in these patients including iron overload and dyslipidemia. Parents of these patients should also be counseled to ensure timely blood transfusions for maintaining pre-transfusion hemoglobin level above the recommended cutoff. The limitation of our study was inclusion of small sample size from a single centre. Since it was a cross-sectional study, patients were evaluated at one point of time and could not be re-assessed on follow-up for ongoing biochemical deterioration. In addition, only biochemical evaluation was carried out in this study and no radiological assessment was included. Further prospective, multi-centered researches including larger sample size and addressing the deficient areas are needed to validate these findings and explore the underlying pathogenic mechanisms.

Conclusion

Higher risk of premature atherosclerosis is associated with β-Thalassemia Major, as indicated by elevated plasma atherogenic index level in βTM patients compared to age-matched healthy subjects. In addition, AIP exhibited positive correlation with serum Ferritin and negative correlation with pre-transfusion hemoglobin level among βTM patients. No significant correlation was noted between AIP and BMI in these patients. High atherosclerosis risk in these patients necessitates regular monitoring and timely intervention to reduce future cardiovascular events in this vulnerable population.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon request.