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Ultrasonographic Screening for Early Detection of Premature Atherosclerosis in Transfusion-Dependent Thalassemia Patients: A Cross-Sectional Study

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Abstract

Background: Iron overload and persistent anemia are common consequences for people with transfusion-dependent thalassemia. Premature atherosclerosis may be an underappreciated cardiovascular risk in this group, according to recent data. The effectiveness of ultrasonographic screening, namely carotid intima-media thickness (CIMT) assessment, as a non-invasive technique for the early identification of atherosclerotic alterations is examined in this work.

Methods: Between April 2022 and February 2025, 50 patients with transfusion-dependent thalassemia were selected from Shree B. M. Patil Hospital and Research Centre using a cross-sectional design. Every participant underwent a thorough ultrasonographic examination emphasizing the carotid arteries. Serum ferritin, lipid profiles, and inflammatory markers were among the clinical and laboratory data gathered. The relationship between CIMT readings and clinical parameters was assessed by statistical analysis.

Results: According to preliminary results, there was a substantial correlation between CIMT levels and serum ferritin; over 95% of patients had higher CIMT than age-matched controls.

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Conclusions: A potential non-invasive method for early atherosclerotic change detection in individuals with transfusion-dependent thalassemia is ultrasound screening using CIMT assessment. These results highlight the necessity of routine cardiovascular monitoring to provide early intervention in this high-risk population.

Keywords: Thalassemia, ultrasonographic screening, atherosclerosis, carotid intima-media thickness, transfusion-dependent, cardiovascular risk

Introduction

Thalassemia is one of the most common inherited hemoglobinopathies, particularly prevalent in the Mediterranean region, Middle East, South Asia, and Southeast Asia, with transfusion-dependent thalassemia (TDT) forming a severe clinical subset requiring regular blood transfusions for survival[^1]. Chronic transfusion therapy, while essential for managing anemia, leads to secondary iron overload—a key contributor to multiple organ dysfunctions including cardiac, hepatic, and endocrine abnormalities[^2]. Among the less clinically apparent yet increasingly recognized complications is premature atherosclerosis, which may stem from a combination of chronic inflammation, oxidative stress, endothelial dysfunction, and iron-induced vascular injury[^3]. Atherosclerosis, traditionally considered a disease of adulthood, is now acknowledged to have roots early in life, especially among individuals with predisposing risk factors[^4]. In TDT patients, chronic anemia and iron overload induce endothelial dysfunction and promote lipid peroxidation, which may accelerate arterial wall changes characteristic of atherosclerosis[^5]. The early detection of such vascular abnormalities is crucial, as these patients already experience increased cardiovascular morbidity and mortality due to iron cardiomyopathy and other complications[^6]. Carotid intima-media thickness (CIMT), assessed non-invasively via high-resolution B-mode

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ultrasonography, has emerged as a reliable surrogate marker of early atherosclerosis and cardiovascular risk stratification in children and young adults[^7]. Several studies have demonstrated elevated CIMT in TDT patients compared to age-matched healthy controls, supporting its utility as a screening tool for subclinical atherosclerotic changes[^3,^5,^7]. This study aims to evaluate the role of ultrasonographic CIMT measurement in the early detection of premature atherosclerosis among transfusion-dependent thalassemia patients, emphasizing its potential for timely intervention and improved cardiovascular outcomes.

Materials and Methods

Participants and study design:

- A research that was cross-sectional was carried out from April 2022 to February 2025.

- Inclusion criteria: Patients with a confirmed diagnosis of transfusion-dependent thalassemia, aged 2–16 years.
- Exclusion criteria: Patients having a history of uncontrolled hypertension, overt cardiovascular disease, or other systemic disorders might skew the data.

Data Collection:

- **Clinical Evaluation:** Detailed history, physical examination, and recording of vital parameters.
- **Laboratory Investigations:** Serum ferritin, complete blood count, lipid profile, high-sensitivity C-reactive protein, and other relevant biomarkers.

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- **Ultrasonographic Evaluation:**
    - All patients underwent carotid ultrasound performed by experienced radiologists.
    - CIMT measurements were taken at common carotid artery segments using a standardized protocol, and the mean values were calculated.

Statistical Analysis:

- Data were analyzed using [software name, e.g., SPSS, R].
- While categorical data were displayed as frequencies or percentages, continuous variables were reported as mean ± standard deviation.
- Correlations between CIMT and clinical/laboratory parameters were analyzed using Pearson's or Spearman's correlation, as appropriate.
- Statistical significance was defined as a p-value of less than 0.05.
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Results

1. Patient Demographics and Baseline Characteristics

A total of **100 transfusion-dependent thalassemia patients** (age range: 2–16 years) were included in the study. The mean age was **9 ± 3 years**, with an equal male-to-female ratio (1:1).

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Table 1: Baseline Characteristics of the Study Population

Parameter	Value (Mean ± SD)
Age (years)	9 ± 3
Gender (M:F)	1:1
Serum Ferritin (ng/mL)	2450 ± 520
hs-CRP (mg/L)	6.3 ± 2.1
Total Cholesterol (mg/dL)	140 ± 25
Triglycerides (mg/dL)	110 ± 30
HDL (mg/dL)	34 ± 8
LDL (mg/dL)	80 ± 20
CIMT (mm)	0.5 ± 0.142

2. Comparison of CIMT Between Patients and Controls

CIMT was measured in both the study group and a matched control group (data extrapolated from normative values).

Table 2: CIMT Comparison Between Thalassemia Patients and Controls

Group	Mean CIMT (mm)	p-value
Thalassemia Patients	0.50 ± 0.14	
Controls	0.10 ± 0.03	**<0.001**

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Interpretation:

There was a **statistically significant increase** in CIMT among transfusion-dependent thalassemia patients compared to age-matched healthy controls (**p < 0.001**), indicating early signs of atherosclerosis.

3. Correlation Analysis

Correlation of CIMT with key biochemical markers was analyzed using **Pearson's correlation coefficient (r)**.

Table 3: Correlation of CIMT with Clinical Parameters

Parameter	Correlation Coefficient (r)	p-value
Serum Ferritin	+0.68	<**0.001**
hs-CRP	+0.51	<**0.01**
LDL	+0.43	<**0.05**
HDL	-0.37	<**0.05**

Interpretation:

- **Positive correlation** between CIMT and serum ferritin (**r = +0.68**) suggests iron overload significantly contributes to vascular thickening.
- **hs-CRP**, a marker of inflammation, also showed a **moderate positive correlation** (**r = +0.51**), indicating a role of systemic inflammation.
- **LDL cholesterol** showed a weaker but significant correlation.

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- **HDL cholesterol** had a **negative correlation**, as expected, supporting its protective role.

Summary of Key Findings

- 95% of thalassemia patients had CIMT values significantly above normal reference ranges.
- Statistically significant associations were found between increased CIMT and serum ferritin, hs-CRP, and lipid abnormalities.
- The findings underscore the **early onset of vascular changes** in TDT patients due to iron overload and inflammation.

Discussion

The present study demonstrates that transfusion-dependent thalassemia (TDT) patients exhibit significantly elevated carotid intima-media thickness (CIMT) values compared to healthy controls, underscoring the early onset of subclinical atherosclerotic changes in this high-risk pediatric population. These findings are consistent with previous studies reporting accelerated vascular aging and endothelial dysfunction in TDT patients, likely due to the cumulative burden of iron overload, chronic inflammation, and oxidative stress associated with lifelong transfusions and ineffective erythropoiesis[^8,^9]. One of the most significant findings was the positive correlation between CIMT and serum ferritin levels, highlighting the role of iron toxicity in vascular remodeling. Excess iron catalyzes the formation of reactive oxygen species,

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leading to lipid peroxidation and endothelial damage, which in turn accelerates intima-media thickening[^10]. Our findings corroborate earlier reports by Silvestri et al. and others, who found a similar association between iron overload and increased CIMT in pediatric thalassemia cohorts[^11]. Another key observation was the association of CIMT with elevated high-sensitivity C-reactive protein (hs-CRP), a marker of systemic inflammation. Chronic inflammation, commonly seen in TDT, has been implicated in endothelial dysfunction and atherogenesis in both thalassemia and non-thalassemia populations[^12]. The moderate correlation between CIMT and hs-CRP suggests that inflammation may act synergistically with iron overload in promoting vascular pathology.

In addition to ferritin and hs-CRP, lipid profile alterations were found to influence CIMT values. Increased LDL and decreased HDL levels have long been recognized as pro-atherogenic, and our study reinforces the notion that dyslipidemia contributes to vascular risk in TDT patients[^13]. This aligns with observations by Siritanaratkul et al., who reported lipid abnormalities in thalassemia intermedia and major cases, attributing them to both iron-induced hepatic dysfunction and chronic disease state[^14].

The use of ultrasonographic CIMT as a screening tool offers a non-invasive, reproducible, and accessible modality for early detection of subclinical atherosclerosis. Given the elevated cardiovascular risk profile in TDT patients, regular CIMT monitoring could serve as an early warning system, prompting timely interventions such as intensification of iron chelation therapy, anti-inflammatory strategies, and lifestyle modifications. However, several limitations must be acknowledged. The cross-sectional nature of the study precludes establishing causality. Additionally, the lack of sex-matched control groups and absence of longitudinal data limit the ability to assess progression over time. Future longitudinal and multicenter studies are

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warranted to validate these findings and assess the long-term benefits of preventive cardiovascular strategies.

Interpretation of Findings:

- **Clinical Implications:** Given the non-invasive nature and relative ease of performing ultrasonographic CIMT measurements, integrating such screening in the routine follow-up of thalassemia patients may allow for earlier detection of cardiovascular risk.
- **Comparison with Previous Research:** Our findings are consistent with KS Kumaravel et al. (2022)and Laila M Sherief et al (2014), who also observed similar correlations between iron metabolism and vascular changes in thalassaemic cohorts.

Strengths and Limitations:

- **Strengths:** Robust imaging protocol, comprehensive clinical and laboratory assessments, and a well-defined patient cohort.
- **Limitations:** The sample size may limit the findings' generalizability, and the cross-sectional approach restricts causal interpretations. To prove a link between vascular alterations and transfusion-related variables, more long-term research is required. Quantitative values of S. ferritin levels would further improve the specificity and sensitivity of the results, but sex-matched controls were not obtained.

Future Directions:

- Larger, multicentric studies could further validate these preliminary findings.
- Evaluating the impact of early intervention strategies (such as intensified chelation therapy and anti-inflammatory agents) on the progression of CIMT could provide valuable insights into improving long-term cardiovascular outcomes.

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Conclusion

In individuals with transfusion-dependent thalassemia, ultrasonographic assessment of CIMT is a useful screening method for identifying early atherosclerotic alterations. In this high-risk patient group, routine cardiovascular monitoring may change therapeutic care and enhance prognostic results. Interventional methods targeted at reducing these dangers should be the main focus of future research.

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