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Original Research Article

Evaluation of Thyroid Function in Children with Transfusion-Dependent Thalassemia

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Abstract:

Background: Thyroid dysfunction is a common endocrine complication in children with transfusion-dependent beta-thalassemia major, primarily due to iron overload affecting the hypothalamic-pituitary-thyroid axis. Early detection is essential to prevent growth delays and other metabolic consequences.

Aim: This study aims to assess the thyroid function status in transfusion-dependent thalassemic children and examine its association with serum ferritin levels.

Methods: A cross-sectional observational study was conducted on 100 children (aged 6–18 years) diagnosed with beta-thalassemia major at the Department of Pediatrics, Daffodils by Artemis Hospitals, New Delhi,India. Data collected included transfusion history, chelation therapy, anthropometric measurements, and laboratory parameters. Serum levels of FT3, FT4, TSH, and ferritin were measured using ELFA and CLIA methods. Thyroid status was classified as euthyroid, subclinical, or overt hypothyroidism.

Results: Thyroid dysfunction was observed in 26% of participants, with 18% having subclinical hypothyroidism and 8% overt hypothyroidism. Children with thyroid dysfunction had significantly higher serum ferritin levels (mean: 2835.4 ± 885.2 ng/mL) compared to euthyroid counterparts (mean: 1980.6 ± 620.3 ng/mL, $p < 0.01$). A significant proportion of affected children were also underweighted, indicating nutritional vulnerability.

Conclusion: Thyroid dysfunction is prevalent in transfusion-dependent thalassemic children and is strongly associated with iron overload. Routine thyroid screening and aggressive iron chelation are essential to reduce endocrine morbidity and improve long-term outcomes.

Keywords: Beta-Thalassemia Major, Iron Overload, Serum Ferritin, Subclinical Hypothyroidism, Thyroid Dysfunction.

Introduction

Beta-thalassemia major is a severe, inherited hemoglobin disorder characterized by reduced or absent synthesis of the beta-globin chains of hemoglobin. This autosomal recessive disease results in ineffective erythropoiesis and chronic anemia, necessitating regular lifelong blood transfusions for survival. Globally, beta-thalassemia represents one of the most common monogenic diseases, with particularly high prevalence in the Mediterranean, Middle Eastern, South Asian, and Southeast Asian regions [1]. In India alone, the carrier rate ranges from 3–4%, with some ethnic populations showing rates as high as 17% [2]. While blood transfusions improve survival and quality of life, they also contribute to systemic iron overload. Iron progressively accumulates in vital organs such as the heart, liver, and various endocrine glands, leading to a spectrum of complications despite the use of iron chelation therapy [3]. Among the endocrine complications, hypothyroidism is increasingly recognized as a common morbidity, second only to hypogonadism [2].

The pathophysiology of thyroid dysfunction in thalassemic children is complex. Iron deposition in the thyroid gland and hypothalamic-pituitary axis, combined with chronic hypoxia and oxidative stress, leads to gradual “impairment of thyroid function. Clinically, this may present as either subclinical hypothyroidism (elevated TSH with normal free T4 and T3) or overt hypothyroidism (elevated TSH with low free T4 and/or T3). Left untreated, thyroid dysfunction can lead to growth retardation, delayed puberty, and impaired neurocognitive development,

particularly concerning in a pediatric population [3,4]. Several studies have highlighted the early onset of thyroid dysfunction among thalassemic children, often before clinical symptoms appear. For instance, Mahmoud et al. (2021) reported thyroid abnormalities in 9.17% of multi-transfused children aged 12 years or younger, indicating that endocrine complications can arise earlier than previously thought [1]. Similarly, Pirinççioğlu et al. (2011) detected subclinical hypothyroidism in children as young as 7 years, even in the absence of overt goiter or autoimmune thyroiditis [4]. These findings emphasize the need for early and routine screening for thyroid dysfunction in children with transfusion-dependent beta-thalassemia.

Besides age, high level of serum ferritin and low adherence to chelation therapy have always been associated with high prevalence of thyroid abnormalities. Children, whose serum ferritin levels are above 2000 ng/mL, have a dramatic potential of acquiring thyroid dysfunction compared to those with few concentrations. Besides, it has been indicated that incidence of endocrine complications might be minimized by a combined approach of chelation in contrast to monotherapy, which altogether confirms the vitality of a personalized course of therapy. Due to the paucity of age and country specific data (in the Indian population especially) regarding the thyroid functions of the transfusion dependent children with thalassemic anemia, it becomes necessary to evaluate the thyroid function of the transfusion dependant thalassemic children in a systematic manner. The early identification of subclinical or overt hypothyroidism provides the opportunity to intervene early enough, thus enhancing the growth outcome and the general living status. This study aims to assess the thyroid function status among children with beta-thalassemia major, exploring its correlation with serum ferritin levels and transfusion parameters, to better inform clinical practice and long-term management strategies.

Methodology

Study Design and Setting: This was a cross-sectional, observational study conducted in the Department of Pediatrics, Daffodils by Artemis Hospitals, New Delhi, India. The study aimed to assess thyroid function in transfusion-dependent children diagnosed with beta-thalassemia major.

Study Population: A total of 100 children with transfusion-dependent beta-thalassemia major were included in the study. The sample size was determined based on previous regional studies evaluating endocrine dysfunction in pediatric thalassemia patients, ensuring sufficient statistical power to detect significant differences in thyroid function status across various clinical parameters.

Inclusion & Exclusion Criteria

Inclusion Criteria

- Children aged 6–18 years.
- Confirmed diagnosis of beta-thalassemia major.
- History of regular blood transfusions (every 2–4 weeks) for a minimum of 5 years.
- Parental or guardian consent obtained.

Exclusion Criteria

- Children with thalassemia minor or intermedia.
- Children with acute illness at the time of assessment.
- Known family history of thyroid disorders.
- Children currently on thyroid hormone or other hormonal therapies.

Data Collection

Detailed patient data were collected using a pre-designed case proforma. Variables recorded included:

- Age at diagnosis and age at first transfusion.
- Frequency and volume of transfusions per year.
- Pre-transfusion hemoglobin levels (averaged over the last 6 months).
- Compliance with chelation therapy (evaluated through patient records and parent interviews).

Anthropometric Assessment: All enrolled participants underwent a thorough anthropometric evaluation. Body weight was measured using a calibrated digital weighing scale, and height was recorded using a stadiometer, with participants standing upright without footwear. Body Mass Index (BMI) was calculated using the formula:

$$\text{BMI} = \frac{\textbf{Weight (kg)}}{\textbf{Hieght(m)}^{\textbf{2}}}$$

The obtained anthropometric measurements were plotted on the WHO growth charts for age- and sex-specific percentiles. Nutritional status was categorized based on WHO z-score classification:

- **Normal**: BMI-for-age z-score between -2 SD and +1 SD
- **Underweight**: BMI-for-age z-score < -2 SD
- **Overweight**: BMI-for-age z-score > +1 SD
- **Obese**: BMI-for-age z-score > +2 SD

This assessment provided insight into the growth and nutritional status of transfusion-dependent thalassemic children, as malnutrition is a common comorbidity in chronic hemolytic disorders.

Laboratory Investigations: Peripheral venous blood samples (5 mL) were drawn under aseptic precautions from the median cubital vein before the scheduled transfusion to avoid post-transfusion biochemical alterations. The collected blood was transferred into plain vacutainers, allowed to clot at room

temperature, and centrifuged at 3000 rpm for 10 minutes to separate serum.

The following biochemical parameters were assessed:

- Free Triiodothyronine (FT3)
- Free Thyroxine (FT4)
- Thyroid-Stimulating Hormone (TSH)
- Serum Ferritin

Assay Techniques: FT3, FT4, and TSH were estimated using third-generation enzyme-linked fluorescent immunoassay (ELFA) kits on the VIDAS® system (BioMérieux, France), which offers high specificity and sensitivity with a coefficient of variation (CV) <5%. Serum Ferritin was measured using chemiluminescent immunoassay (CLIA) on the ADVIA Centaur® system (Siemens Healthcare Diagnostics, Germany).

Normal Reference Ranges (as per kit guidelines):

- FT3: 4.0 – 8.3 pmol/L
- FT4: 9.0 – 20.0 pmol/L
- TSH: 0.25 – 5.0 µIU/mL

Serum Ferritin: 12 – 300 ng/mL (age-specific values considered)

Classification of Thyroid Status:

Euthyroid: Normal FT3, FT4, and TSH values.

Subclinical Hypothyroidism: Elevated TSH with normal FT3 and FT4 levels.

Overt Hypothyroidism: Elevated TSH with decreased FT3 and/or FT4 levels.

These laboratory evaluations were essential for determining the functional status of the thyroid gland and estimating iron overload, which is a known etiological factor in the pathogenesis of endocrine dysfunction in beta-thalassemia major.

Statistical Analysis: Data were entered in Microsoft Excel and analyzed using SPSS version 16.0. Mean and standard deviation were calculated for continuous variables. Differences between groups (euthyroid vs. hypothyroid) were analyzed using the Student's t-test. Pearson's correlation coefficient was used to assess associations between serum ferritin and thyroid function parameters. A p-value of <0.05 was considered statistically significant.

Results

Table 1 summarizes the key demographic and clinical features of the 100 transfusion-dependent thalassemic children enrolled in the study. The mean age of the cohort was 11.2 ± 3.1 years, with a slight male predominance (60%). The average age at diagnosis was 11.6 months, and blood transfusions were typically initiated by 13.8 months of age. The children had received transfusion therapy for an average of 8.4 years. The mean pre-transfusion hemoglobin level was 8.3 g/dL, indicating suboptimal transfusion targets in many cases. The mean annual transfusion volume was approximately 240.5 mL/kg/year. In terms of iron chelation, 48% of children were on oral deferasirox, 22% on parenteral desferrioxamine, and 30% received a combination of both. These baseline characteristics reflect a typical profile of pediatric beta-thalassemia major patients in a resource-constrained clinical setting.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Participants (n = 100)

Parameter	Value
Age (years)	11.2 ± 3.1
Gender	Male: 60 (60%)
	Female: 40 (40%)
Age at diagnosis (months)	11.6 ± 4.3
Age at first transfusion (months)	13.8 ± 5.2
Duration of transfusion therapy (years)	8.4 ± 2.7
Average pre-transfusion hemoglobin (g/dL)	8.3 ± 0.5
Annual transfusion volume (mL/kg/year)	240.5 ± 34.2
Type of iron chelation therapy	
Deferasirox	48 (48%)
Desferrioxamine	22 (22%)
Combined (Deferasirox + Desferrioxamine)	30 (30%)

Table 2 shows that the majority of the children (74%) were euthyroid, while 26% demonstrated some form of thyroid dysfunction. Specifically, 18% of participants had subclinical hypothyroidism, and 8% had overt hypothyroidism. This indicates a substantial burden of thyroid dysfunction in transfusion-dependent thalassemic children, consistent with previous literature. The higher proportion of subclinical cases also underscores the importance of routine screening, as these children may be asymptomatic yet still at risk for progression to overt disease.

Table 2: Thyroid Function Status of Study Participants (n = 100)		
Thyroid Status	**Number of Children (n)**	**Percentage (%)**
Euthyroid	74	74%
Subclinical Hypothyroidism	18	18%
Overt Hypothyroidism	8	8%
Total	**100**	**100%**

Table 3 presents a comparative analysis between euthyroid and hypothyroid children. Children with thyroid dysfunction had significantly higher serum ferritin levels (2835.4 ± 885.2 ng/mL) compared to euthyroid counterparts (1980.6 ± 620.3 ng/mL), suggesting a strong association between iron overload and thyroid impairment ($p < 0.01$). Furthermore, hypothyroid children had elevated TSH levels (6.98 ± 1.9 µIU/mL) and reduced FT4 and FT3 levels, with all differences being statistically significant ($p < 0.01$). This supports the hypothesis that iron-induced damage to the thyroid gland is a key factor in the pathogenesis of hypothyroidism in thalassemia major.

Table 3: Comparison of Mean Biochemical Parameters in Euthyroid vs. Hypothyroid Groups			
Parameter	**Euthyroid (n = 74)**	**Hypothyroid (n = 26)**	**p-value**
Serum Ferritin (ng/mL)	1980.6 ± 620.3	2835.4 ± 885.2	<0.01
TSH (µIU/mL)	3.12 ± 0.8	6.98 ± 1.9	<0.001
FT4 (pmol/L)	13.2 ± 2.4	10.4 ± 1.7	<0.01
FT3 (pmol/L)	6.3 ± 1.3	4.6 ± 1.0	<0.01

Table 4 categorizes patients based on their serum ferritin levels. Among children with ferritin levels >2000 ng/mL, 38.2% exhibited thyroid dysfunction, compared to only 11.1% in those with ferritin ≤2000 ng/mL. This reinforces the positive correlation between elevated ferritin levels and increased risk of thyroid dysfunction. It suggests that maintaining ferritin below 2000 ng/mL could be a potential threshold for reducing endocrine complications in this population.

Table 4: Association of Thyroid Dysfunction with Serum Ferritin Levels			
Serum Ferritin Range (ng/mL)	**Number of Patients (n)**	**Hypothyroidism Present (n)**	**Prevalence (%)**
≤ 2000	45	5	11.10%
> 2000	55	21	38.20%
Total	**100**	**26**	**26%**

Table 5 outlines the nutritional status of the participants. While 52% of children had normal BMI-for-age, a significant proportion (42%) were underweighted, indicating a high prevalence of malnutrition. Only 6% were classified as overweight or obese. Malnutrition can further complicate growth and endocrine outcomes in thalassemia, including exacerbating the impact of thyroid dysfunction. These findings underscore the need for integrated nutritional support in the management of chronically transfused children.

Table 5: Nutritional Status Based on BMI-for-Age (WHO Classification)		
Nutritional Category	**Number of Patients (n)**	**Percentage (%)**
Normal	52	52%
Underweight (Z < -2 SD)	42	42%
Overweight / Obese (Z > +1 SD)	6	6%
Total	**100**	**100%**

Discussion

This study evaluated the thyroid function status among transfusion-dependent children with beta-thalassemia major and examined its correlation with iron overload. The findings confirm that hypothyroidism—both subclinical and overt—is a significant endocrine complication in this population, with an overall prevalence of 26%. This is in agreement with previous studies conducted globally and within India, highlighting the endocrine vulnerability of children with chronic transfusional iron overload.

The prevalence of subclinical hypothyroidism (18%) and overt hypothyroidism (8%) observed in our study is consistent with the results reported by Pirinççioğlu et al. (2011), who found thyroid dysfunction in 21% of chronically transfused children,

with a predominance of subclinical forms [4]. Similarly, a study by Raghupathy (2017) conducted in a tertiary center in northern India reported thyroid dysfunction in 16.6% of transfusion-dependent thalassemia patients aged 5–18 years [5]. Another study by Zakaria et al. (2023) analyzing endocrine complications in 1,058 thalassemic patients across several countries found hypothyroidism in 4.2% of cases, highlighting regional variation in prevalence, possibly due to differences in chelation practices, transfusion protocols, and early detection strategies [6].

Our study also demonstrated a significant association between elevated serum ferritin levels and the presence of thyroid dysfunction. Hypothyroid children had a mean ferritin level of 2835.4 ng/mL compared to 1980.6 ng/mL in euthyroid children ($p < 0.01$), echoing the findings of Anwar et al., (2025), who emphasized that subclinical hypothyroidism in thalassemia was significantly linked to poor iron control [7]. A study by De et al. (2017) also showed that serum ferritin >2500 ng/mL significantly increased the risk of endocrine disorders, including hypothyroidism, reinforcing the critical need for effective chelation to reduce iron burden [8].

Most of our cohort patients (65.3 percent) were undergoing chelation therapy, although 30 percent were obtaining combined therapy a head indicating that monotherapy might not be sufficient in controlling iron load in patients. The excellent results of combination chelation studies (deferasirox mixed with desferrioxamine) were confirmed by Salimi et al. (2024) and report higher iron control and minimized endocrine complications [9].

The other area of concern in our study is the nutritional status as 42 percent of the children were underweighted. Beta-thalassemia malnutrition is multifactorial: incomplete endocrinopathy, metabolic demand, and chronic anemia are Conf Beijing. Inefficient nutrition may also lower the thyroid, which may be aggravated by iron caused thyroid injury. Sharma et al. (2022) investigated the connection between hypothyroidism and malnutrition and reported delayed growth and adolescent starters among the star Eva adolescents with thyroid dysfunction that remained untreated [10].

Also, subclinical hypothyroidism is widespread at high numbers, which seals the need to screen and monitor early before symptoms develop. Most of the thalassemic children can only be symptomatic when a considerable glandular destruction happens, and at that point, the restoration of a functional state may not occur fully even with chelation or with the thyroxine treatment, as noted by De et al. (2017) [11]. When combined, our findings are in line with the evidence of a growing number of researchers regarding the fact that thyroid problems are becoming one of the first preventable consequences of the progressive case of thalassemia in the transfusion-dependent group. Thus, diagnostic identification of potentially subtle thyroid dysfunction at an early stage by means of regular thyroid functional tests, intensive chelation, and nutrition are very important to better long-term health outcomes.

Conclusion

The present research demonstrates a high prevalence of thyroid dysfunction, and especially subclinical hypothyroidism, in transfusion-dependent children with thalassemia. There was also a strong correlation between high serum ferritin levels, which is a marker of levels of total body iron, with impaired thyroid function and again" points to iron overload as a factor in endocrine complications. Routine screening can identify thyroid dysfunction early, along with effective iron chelation and dietary support to prevent thyroid dysfunction from progressing, improve quality of life and health outcome. As well, children with thalassemia should routinely have thyroid function monitored in their standard care protocols to secure early intervention with endocrine dysfunction and in the long-term optimization of health in this vulnerable population.

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