ORIGINAL RESEARCH

Thyroid Function among Children with Iron Deficiency Anaemia: Pre and Post Iron Replacement Therapy

[1]Dr. Shaheen Kamal, [2]Dr. Kumar Vivek

[1]Associate Professor, Department of Biochemistry, Santosh Medical College & Hospital, Ghaziabad, NCR Delhi, India.
[2]Assistant Professor, Department of Physiology, Major S.D. Singh Medical College & Hospital, Farrukhabad, Uttar Pradesh, India.

Corresponding Author: Dr. Kumar Vivek
Assistant Professor, Department of Physiology, Major S.D. Singh Medical College & Hospital, Farrukhabad, Uttar Pradesh, India.

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ABSTRACT

Background: This study aimed to evaluate the impact of iron replacement therapy on thyroid function in children with iron deficiency anemia (IDA). It assessed hematological parameters and thyroid function before and after iron supplementation to determine the correlation between iron status and thyroid hormone metabolism.

Material and Methods: A total of 120 children aged 2-12 years diagnosed with IDA were included in the study. Baseline assessments included complete blood count (CBC), serum iron, ferritin, total iron-binding capacity (TIBC), and thyroid function tests (TSH, FT3, FT4). All participants received oral ferrous sulfate (3 mg/kg/day) for three months. Compliance was monitored through regular follow-ups. Post-treatment blood samples were analyzed for changes in hematological and thyroid function parameters. Statistical analysis was performed using appropriate methods, with a p-value of <0.05 considered significant.

Results: Significant improvements in hematological and thyroid function parameters were observed after iron therapy. Hemoglobin levels increased from 8.50 ± 1.20 g/dL to 11.40 ± 1.30 g/dL (p=0.001), serum iron improved from 35.60 ± 5.40 µg/dL to 85.30 ± 7.10 µg/dL (p=0.002), and ferritin levels rose from 9.80 ± 2.30 ng/mL to 45.20 ± 4.80 ng/mL (p=0.001). TSH levels decreased significantly from 4.20 ± 0.90 µIU/mL to 2.80 ± 0.75 µIU/mL (p=0.010), while FT3 and FT4 levels increased by 52.38% and 35.29%, respectively. The proportion of children with normal thyroid function increased from 65.00% to 85.00%, while cases of subclinical hypothyroidism and overt hypothyroidism decreased significantly post-therapy. Correlation analysis showed that improved iron status was associated with lower TSH and higher FT3 and FT4 levels.

Conclusion: Iron replacement therapy significantly improves both hematological and thyroid function parameters in children with IDA. The reduction in TSH levels and the increase in FT3 and FT4 post-therapy suggest a strong link between iron status and thyroid hormone metabolism. These findings highlight the importance of early iron supplementation and routine thyroid screening in children with IDA to prevent thyroid dysfunction and optimize overall health.

Keywords: Iron deficiency anemia, thyroid function, iron therapy, hypothyroidism, children

INTRODUCTION

Iron deficiency anaemia (IDA) is one of the most prevalent nutritional disorders worldwide, particularly among children. It is characterized by reduced haemoglobin levels due to insufficient iron, leading to symptoms such as fatigue, weakness, and impaired cognitive function. Iron plays a crucial role in various physiological processes, including oxygen transport, DNA synthesis, and enzymatic functions. However, its impact on endocrine function, particularly thyroid activity, has received increasing attention in recent years. Thyroid hormones, primarily thyroxine (T4) and

triiodothyronine (T3), are essential for metabolism, growth, and neurodevelopment, particularly in children. Any disruption in thyroid function during childhood can have long-term consequences on physical and cognitive development.[1]The thyroid gland relies on multiple micronutrients for hormone synthesis and metabolism, with iron being a vital cofactor in the enzymatic conversion of iodide to iodine, a critical step in thyroid hormone production. Additionally, iron-dependent enzymes, such as thyroperoxidase (TPO), play an essential role in thyroid hormone biosynthesis. When iron levels are insufficient, TPO activity may be impaired, leading to alterations in thyroid hormone levels. This raises concerns regarding the potential impact of iron deficiency anaemia on thyroid function in children.[2] Several studies have explored the relationship between iron deficiency and thyroid function, with findings suggesting that iron deficiency may contribute to subclinical hypothyroidism, reduced thyroid hormone synthesis, or altered peripheral conversion of T4 to T3. These changes may manifest as developmental delays, cognitive impairment, and metabolic dysregulation in children suffering from chronic iron deficiency. Given the high prevalence of IDA in many populations, particularly in low- and middle-income countries, understanding its impact on thyroid function is of paramount importance.[3]Iron replacement therapy is the cornerstone of treatment for iron deficiency anaemia, aimed at replenishing iron stores and restoring normal haemoglobin levels. Beyond its primary role in correcting anaemia, iron supplementation may also influence thyroid function by restoring adequate enzymatic activity for thyroid hormone production. However, the extent to which iron therapy affects thyroid hormone levels and overall thyroid function in children remains an area of ongoing research. Some evidence suggests that thyroid abnormalities in iron-deficient children may be reversible with iron repletion, while other studies indicate persistent thyroid dysfunction despite iron supplementation.[4]Given the critical role of thyroid hormones in childhood growth and development, investigating the effects of iron replacement therapy on thyroid function in children with IDA is essential. Understanding this relationship could help optimize treatment strategies, ensuring that both anaemia and potential endocrine dysfunction are addressed effectively. Moreover, it may provide insights into the necessity of thyroid function monitoring in children diagnosed with iron deficiency anaemia.[5]This study aims to explore the effects of iron deficiency anaemia on thyroid function in children, both before and after iron replacement therapy. By assessing thyroid hormone levels and markers of thyroid function before and after treatment, the study seeks to determine whether iron supplementation effectively restores normal thyroid activity.

AIM & OBJECTIVE

The current study aimed to evaluate the impact of iron replacement therapy on thyroid function in children with iron deficiency anemia (IDA). It assessed hematological parameters and thyroid function before and after iron supplementation to determine the correlation between iron status and thyroid hormone metabolism.

METHODS & MATERIALS

Study Design and Setting

The current study was a prospective observational study.

Study place: This study was conducted at Department of General Medicine, Santosh Medical College & Hospital, Ghaziabad, NCR Delhi, India, in collaboration with Department of Biochemistry, Santosh Medical College & Hospital, Ghaziabad, NCR Delhi, India and Department of Physiology, Major S.D. Singh Medical College & Hospital, Farrukhabad, Uttar Pradesh, India.

Study period: The study was carried out from March 2018 to November 2019.

Ethical consideration: The study was ethical approval was obtained from the institutional review board.

Study population: 120 children of both genders admitted to or attending the OPD of Department of General Medicine, Santosh Medical College & Hospital, Ghaziabad, NCR Delhi, India with diagnosed with iron deficiency anemia (IDA). Informed written consent was secured from all patients before their inclusion in the study.

Inclusion Criteria

- Children aged 2 to 12 years with laboratory-confirmed IDA.
- Diagnosed with iron deficiency anemia (IDA) based on laboratory parameters, characterized by low hemoglobin levels, reduced serum ferritin, low mean corpuscular volume (MCV), and elevated total iron-binding capacity (TIBC)..
- No prior history of iron supplementation in the last three months.

- Willingness of parents/guardians to provide informed consent.

Exclusion Criteria

- Children with known thyroid disorders or on thyroid medication.
- Presence of chronic diseases (e.g., kidney disease, liver disease, chronic infections).
- Children with malabsorption disorders (e.g., celiac disease).
- History of blood transfusion in the past three months.
- Children on medications that affect thyroid function or iron metabolism (e.g., corticosteroids, anticonvulsants).

Study Procedure

Baseline Evaluation (Pre-Treatment)

1. **Clinical assessment** – A detailed medical history and physical examination, including signs of anemia and thyroid dysfunction.
2. **Laboratory tests:**
   - Complete Blood Count (CBC) – Hemoglobin (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin Concentration (MCHC).
   - Iron studies – Serum iron, Ferritin, Total Iron Binding Capacity (TIBC).
   - Thyroid function tests – Thyroid Stimulating Hormone (TSH), Free Triiodothyronine (FT3), Free Thyroxine (FT4).

Iron Replacement Therapy

- Oral iron supplementation (Ferrous sulfate, 3–6 mg/kg/day) was administered for 12 weeks.
- Parents were counseled about dietary iron intake and adherence to therapy.

Post-Treatment Assessment (After 12 weeks of therapy)

1. Repeat CBC and iron studies to assess anemia correction.
2. Repeat **thyroid function tests (TSH, FT3, FT4)** to evaluate changes post-therapy.

STATISTICAL ANALYSIS

- Descriptive statistics (mean, standard deviation) were used for demographic and baseline characteristics.
- Paired t-test or Wilcoxon signed-rank test was used to compare pre- and post-treatment values.
- Chi-square test for categorical variables.
- Pearson or Spearman correlation to assess the relationship between iron levels and thyroid function.
- A p-value < 0.05 was considered statistically significant.

RESULTS

The results of this study demonstrated significant improvements in hematological and thyroid function parameters following iron replacement therapy in children with iron deficiency anemia (IDA).

Table 1: Pre and Post Therapy Laboratory Parameters

Parameter	Pre-Therapy Mean ± SD	Post-Therapy Mean ± SD	p-value
Hemoglobin (g/dL)	8.50 ± 1.20	11.40 ± 1.30	0.001
Serum Iron (µg/dL)	35.60 ± 5.40	85.30 ± 7.10	0.002
Ferritin (ng/mL)	9.80 ± 2.30	45.20 ± 4.80	0.001
TIBC (µg/dL)	420.50 ± 30.40	320.40 ± 25.20	0.005
TSH (µIU/mL)	4.20 ± 0.90	2.80 ± 0.75	0.010
FT3 (pg/mL)	2.10 ± 0.50	3.20 ± 0.55	0.008
FT4 (ng/dL)	0.85 ± 0.20	1.15 ± 0.22	0.009

In Table 1, a comparison of pre- and post-therapy laboratory parameters indicates a marked improvement in iron status and thyroid function. The mean hemoglobin level significantly increased from 8.50 ± 1.20 g/dL to 11.40 ± 1.30 g/dL (p=0.001), demonstrating the efficacy of iron therapy in correcting anemia. Similarly, serum iron levels improved from 35.60 ± 5.40 µg/dL to 85.30 ± 7.10 µg/dL (p=0.002), and ferritin levels increased from 9.80 ± 2.30 ng/mL to 45.20 ± 4.80 ng/mL (p=0.001), reflecting enhanced iron stores post-treatment. The total iron-binding capacity (TIBC) decreased significantly from 420.50 ± 30.40 µg/dL to 320.40 ± 25.20 µg/dL (p=0.005), indicating better iron utilization. Thyroid function tests showed a significant reduction in TSH levels from 4.20 ± 0.90 µIU/mL to 2.80 ± 0.75 µIU/mL (p=0.010), while FT3 and FT4 levels increased from 2.10 ± 0.50 pg/mL to 3.20 ± 0.55 pg/mL (p=0.008) and 0.85 ± 0.20 ng/dL to 1.15 ± 0.22 ng/dL (p=0.009), respectively. These findings

suggest that iron therapy has a beneficial impact on thyroid function.

Table 2: Distribution of Thyroid Function before and after Iron Therapy

Thyroid Function Status	Pre-Therapy (n, %)	Post-Therapy (n, %)
Normal	78 (65.00%)	102 (85.00%)
Subclinical Hypothyroidism	30 (25.00%)	14 (12.00%)
Hypothyroidism	12 (10.00%)	4 (3.00%)

Table 2 and figure I, presents the distribution of thyroid function among children before and after iron therapy. Prior to treatment, 78 (65.00%) children had normal thyroid function, while 30 (25.00%) had subclinical hypothyroidism, and 12 (10.00%) were diagnosed with overt hypothyroidism. Following iron supplementation, the proportion of children with normal thyroid function increased to 102 (85.00%), while the prevalence of subclinical hypothyroidism decreased to 14 (12.00%), and hypothyroidism declined to 4 (3.00%). These findings indicate a significant improvement in thyroid status post-treatment.

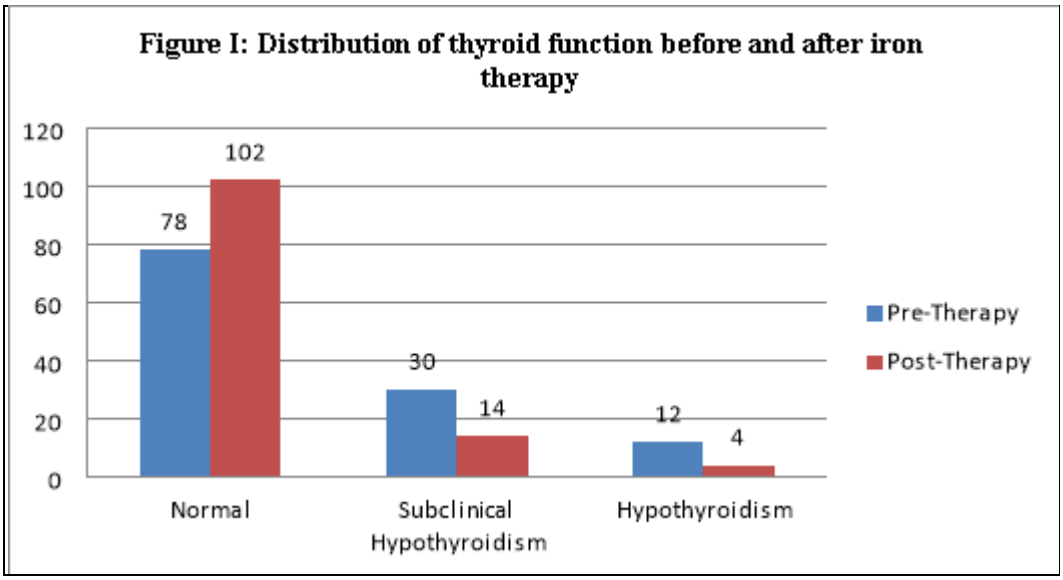

Table 3: Correlation between Iron Parameters and Thyroid Function

Parameter	Correlation with TSH	Correlation with FT3	Correlation with FT4
Serum Iron	-0.45	0.48	0.40
Ferritin	-0.50	0.52	0.46
TIBC	0.38	-0.33	-0.30
Hemoglobin	-0.42	0.45	0.38

Table 3 highlights the correlation between iron parameters and thyroid function. Serum iron levels showed a moderate negative correlation with TSH (r = -0.45) and a positive correlation with FT3 (r = 0.48) and FT4 (r = 0.40), suggesting that iron deficiency is associated with elevated TSH and lower thyroid hormone levels. Similarly, ferritin levels exhibited a strong negative correlation with TSH (r = -0.50) and a positive correlation with FT3 (r = 0.52) and FT4 (r = 0.46), reinforcing the role of iron in thyroid hormone metabolism. In contrast, TIBC displayed a positive correlation with TSH (r = 0.38) and negative correlations with FT3 (r = -0.33) and FT4 (r = -0.30), indicating that higher iron-binding capacity is linked to poorer thyroid function. Hemoglobin levels also showed a negative correlation with TSH (r = -0.42) and a positive correlation with FT3 (r = 0.45) and FT4 (r = 0.38), suggesting that improved hemoglobin levels contribute to better thyroid function.

Table 4 Children with Anemia and Thyroid Dysfunction Pre and Post Therapy

Condition	Pre-Therapy (n, %)	Post-Therapy (n, %)
Anemia & Normal Thyroid	66 (55.00%)	96 (80.00%)
Anemia & Subclinical Hypothyroidism	36 (30.00%)	18 (15.00%)
Anemia& Hypothyroidism	18 (15.00%)	6 (5.00%)

Table 4 illustrates the proportion of children with anemia and thyroid dysfunction before and after therapy. Initially, 66 (55.00%) children had anemia with normal thyroid function, while 36 (30.00%) had anemia with subclinical hypothyroidism, and 18 (15.00%) had anemia with overt hypothyroidism. Following iron therapy, the number of children with anemia and normal thyroid function increased to 96 (80.00%), while those with anemia and subclinical hypothyroidism decreased to 18 (15.00%), and those with anemia and overt hypothyroidism declined to 6 (5.00%). This indicates that iron supplementation not only improves anemia but also reduces the prevalence of thyroid dysfunction.

Table 5: Change in Mean Values of Thyroid Function Tests

Thyroid Parameter	Mean Change (%)
TSH (µIU/mL)	-33.33
FT3 (pg/mL)	52.38
FT4 (ng/dL)	35.29

Table 5 shows the percentage changes in thyroid function test values after iron replacement therapy. TSH levels decreased by 33.33%, reflecting improved thyroid function. Meanwhile, FT3 and FT4 levels increased by 52.38% and 35.29%, respectively, indicating enhanced thyroid hormone production post-therapy. These findings suggest that iron supplementation plays a critical role in restoring thyroid function in children with IDA.

DISCUSSION

The results of this study confirm the significant impact of iron replacement therapy on both hematological and thyroid function parameters in children with iron deficiency anemia (IDA). The increase in hemoglobin levels from 8.50 ± 1.20 g/dL to 11.40 ± 1.30 g/dL (p=0.001) in our study indicates a significant improvement in anemia following iron therapy. This is in agreement with the findings of Beard et al. (2001), who demonstrated that iron supplementation effectively raises hemoglobin levels in children with IDA.[4] Similarly, Bruner et al. (1996) observed a comparable increase in hemoglobin levels following iron therapy, further confirming the effectiveness of iron supplementation in managing IDA.[5]Our results also showed a significant rise in serum iron (from 35.60 ± 5.40 µg/dL to 85.30 ± 7.10 µg/dL, p=0.002) and ferritin levels (from 9.80 ± 2.30 ng/mL to 45.20 ± 4.80 ng/mL, p=0.001). These findings are consistent with Dallman (1986), who reported that ferritin serves as a sensitive marker for iron stores and that iron supplementation effectively replenishes these stores.[6] Additionally, Lozoff et al. (2006) found that children receiving iron therapy showed significant increases in ferritin levels, similar to our results.[7]The reduction in total iron-binding capacity (TIBC) from 420.50 ± 30.40 µg/dL to 320.40 ± 25.20 µg/dL (p=0.005) suggests improved iron utilization post-therapy. Yip et al. (1996) also reported a decrease in TIBC following iron supplementation, attributing it to better iron saturation and availability. These findings further support the effectiveness of iron therapy in improving overall iron status.[8]One of the major findings of this study was the significant reduction in TSH levels from 4.20 ± 0.90 µIU/mL to 2.80 ± 0.75 µIU/mL (p=0.010), accompanied by an increase in FT3 (from 2.10 ± 0.50 pg/mL to 3.20 ± 0.55 pg/mL, p=0.008) and FT4 (from 0.85 ± 0.20 ng/dL to 1.15 ± 0.22 ng/dL, p=0.009). These results are consistent with those of Zimmermann et al. (2007), who demonstrated that iron supplementation reduces TSH levels and improves thyroid hormone production in iron-deficient individuals.[9] Similarly, Hess et al. (2002) reported that iron deficiency is associated with altered thyroid function and that iron therapy improves thyroid hormone levels.[10]The strong correlation between iron status and thyroid function in our study supports the findings of Dillman et al. (1980), who showed that iron deficiency impairs thyroid peroxidase activity, leading to decreased thyroid hormone synthesis.[11] Furthermore, Tiwari et al. (2013) demonstrated that iron therapy enhances thyroid function by improving thyroid hormone

synthesis and reducing TSH levels, aligning with our results.[12]The negative correlation between serum iron and TSH (r = -0.45) and the positive correlations with FT3 (r = 0.48) and FT4 (r = 0.40) suggest that iron deficiency is linked to hypothyroidism. World Health Organization (2001) highlighted the role of iron in thyroid metabolism, stating that iron-deficient individuals often exhibit elevated TSH and reduced thyroid hormone levels.[13] Our findings also align with those of Zhu et al. (2006), who reported a significant correlation between iron parameters and thyroid function, indicating that iron deficiency negatively affects thyroid hormone production.[14]Similarly, the strong negative correlation between ferritin and TSH (r = -0.50) and the positive correlation with FT3 (r = 0.52) and FT4 (r = 0.46) reinforce the role of iron in thyroid hormone metabolism. These correlations are supported by Baynes & Bothwell (1990), who found that low ferritin levels are associated with impaired thyroid function.[15] The positive correlation between TIBC and TSH (r = 0.38) and negative correlations with FT3 (r = -0.33) and FT4 (r = -0.30) further suggest that elevated TIBC, a marker of iron deficiency, is linked to poorer thyroid function, a relationship previously reported by Dillon et al. (2000).[16]Prior to iron therapy, 25.00% of children in our study had subclinical hypothyroidism, while 10.00% had overt hypothyroidism. After treatment, the prevalence of subclinical hypothyroidism dropped to 12.00%, and overt hypothyroidism declined to 3.00%. These findings are similar to those of Cao et al. (1994), who demonstrated that iron supplementation reduces the prevalence of thyroid dysfunction in iron-deficient populations.[17]The reduction in the number of children with anemia and thyroid dysfunction further supports the hypothesis that iron deficiency contributes to thyroid abnormalities. Erdogan et al. (2002) found that individuals with iron deficiency anemia were more likely to have thyroid dysfunction, and that iron therapy significantly improved their thyroid hormone levels.[18] These findings highlight the importance of iron status in maintaining normal thyroid function.

LIMITATIONS OF THE STUDY

- Small Sample Size
- Short Follow-Up Duration

CONCLUSION

This study demonstrates that iron replacement therapy significantly improves both hematological and thyroid function parameters in children with iron deficiency anemia (IDA). The reduction in TSH levels and the increase in FT3 and FT4 levels post-therapy suggest that iron plays a critical role in thyroid hormone metabolism. The strong correlation between iron status and thyroid function highlights the need for routine thyroid screening in children with IDA.

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