

## Original Research

### Effect of Thyroid Hormone Replacement Therapy on Serum Ferritin Levels in Hypothyroid Patients: Insights on Iron Supplementation

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#### ABSTRACT:

**Background:** Thyroid hormone replacement therapy (THRT) is the standard treatment for hypothyroidism, but iron deficiency may limit full clinical recovery. Serum ferritin is a key marker of iron stores and may reflect treatment response.

**Objectives:** To evaluate the effect of THRT on serum ferritin levels in hypothyroid patients and compare outcomes between THRT alone and THRT combined with iron supplementation. **Methods:** A prospective study included 100 hypothyroid patients divided into two groups: levothyroxine alone (n=50) and levothyroxine plus oral iron supplementation (n=50). Serum ferritin, TSH, and free T4 were measured at baseline, 3 months, and 6 months. **Results:** Both groups showed significant ferritin increases over 6 months ( $p < 0.01$ ). The THRT plus iron group had significantly higher ferritin levels at 3 and 6 months compared to THRT alone ( $p < 0.01$ ). TSH normalized similarly in both groups. Symptom improvement was greater in the combined therapy group. **Conclusion:** THRT improves iron metabolism in hypothyroid patients, with combined iron supplementation enhancing ferritin recovery and clinical outcomes. Ferritin monitoring and iron supplementation should be integrated into hypothyroidism management.

**Keywords:** Hypothyroidism, Thyroid Hormone Replacement Therapy, Serum Ferritin, Iron Supplementation, Treatment Response

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#### INTRODUCTION

Hypothyroidism is commonly managed with thyroid hormone replacement therapy (THRT), primarily using levothyroxine, which aims to restore normal thyroid hormone levels and alleviate symptoms (Brent, 2012). While biochemical normalization of thyroid-stimulating hormone (TSH) and free thyroxine (free T4) is the main therapeutic goal, many patients continue to experience residual symptoms such as fatigue and cognitive difficulties despite achieving euthyroid status (Garber et al., 2012).

Emerging evidence suggests that iron metabolism, particularly serum ferritin levels, plays an important role in patient recovery during THRT. Iron is essential for thyroid peroxidase (TPO) activity, a heme-containing enzyme critical for thyroid hormone synthesis, and thyroid hormones themselves regulate

iron absorption and erythropoiesis (Beard & Tobin, 2000; Goglia et al., 2002). Consequently, iron deficiency can blunt the clinical response to THRT, prolonging symptoms and complicating management. Several studies have demonstrated that serum ferritin levels often improve following THRT, reflecting restored iron utilization and erythropoietic function (Maki et al., 2016; Cinemre et al., 2009). However, the extent of ferritin recovery may depend on whether iron supplementation is administered alongside THRT, particularly in menstruating women and other at-risk populations (El-Masry et al., 2018).

Despite these findings, ferritin monitoring is not yet widely incorporated into clinical follow-up protocols for hypothyroid patients. Understanding how THRT affects ferritin levels and the benefits of combined therapy could enhance patient outcomes by

identifying those who may require iron supplementation.

This study aims to evaluate the effect of thyroid hormone replacement therapy on serum ferritin levels in hypothyroid patients and to compare the outcomes of THRT alone versus THRT combined with oral iron supplementation.

## METHODS

### Study Design and Participants

This prospective observational study was conducted at a tertiary care hospital in Central India. A total of 100 hypothyroid patients initiating thyroid hormone replacement therapy (THRT) were enrolled. Participants were aged 18–60 years and had confirmed hypothyroidism based on elevated TSH and low or normal free T4 levels.

### Intervention Groups

Participants were divided into two groups based on treatment protocol:

- **Group A (n=50):** Received standard levothyroxine therapy alone.
- **Group B (n=50):** Received levothyroxine combined with oral iron supplementation (ferrous sulfate 325 mg once daily).

### Exclusion Criteria

Patients with chronic inflammatory diseases, liver or renal impairment, pregnancy, prior iron supplementation within 3 months, or non-compliance

risk were excluded to minimize confounding effects on ferritin levels.

### Data Collection and Laboratory Measurements

Baseline blood samples were collected prior to initiation of therapy to measure serum TSH, free T4, and ferritin. Follow-up samples were obtained at 3 and 6 months post-treatment initiation. Serum ferritin was measured by chemiluminescent immunoassay. TSH and free T4 levels were measured using standard immunoassays. Clinical symptoms and adherence were recorded at each visit.

### Statistical Analysis

Data analysis was performed using SPSS version 25. Mean and standard deviation were calculated for continuous variables. Changes in ferritin levels over time within and between groups were analyzed using repeated measures ANOVA. Independent t-tests compared differences between groups at each time point. Statistical significance was set at  $p < 0.05$ .

## RESULTS

### Participant Characteristics

The study enrolled 100 hypothyroid patients divided equally into two treatment groups: levothyroxine alone (Group A) and levothyroxine with iron supplementation (Group B). The mean age was  $37.8 \pm 9.6$  years, with 68% females and 32% males evenly distributed across groups. Baseline characteristics including TSH, free T4, and ferritin were comparable between groups (Table 1).

**Table 1: Baseline Characteristics of Treatment Groups**

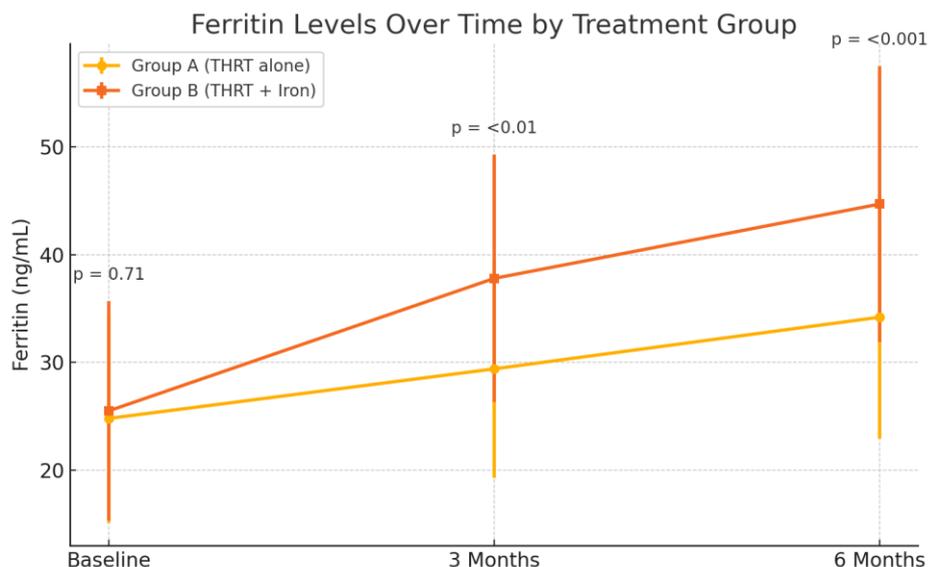
Parameter	Group A (THRT alone)	Group B (THRT + Iron)	p-value
Age (years)	$37.5 \pm 9.8$	$38.1 \pm 9.5$	0.78
Female (%)	34 (68%)	34 (68%)	1.00
TSH ( $\mu\text{IU/mL}$ )	$18.2 \pm 5.4$	$17.9 \pm 6.1$	0.75
Free T4 (ng/dL)	$0.62 \pm 0.15$	$0.60 \pm 0.18$	0.65
Ferritin (ng/mL)	$24.8 \pm 9.7$	$25.5 \pm 10.2$	0.71

### Changes in Serum Ferritin Over Time

Both groups showed significant improvement in ferritin levels after 6 months of therapy ( $p < 0.01$ ). Group B (THRT + iron) had a greater increase in ferritin compared to Group A (THRT alone) at both 3 and 6 months (Table 2, Figure 1).

**Table 2: Serum Ferritin Levels at Baseline, 3 Months, and 6 Months**

Timepoint	Group A (ng/mL)	Group B (ng/mL)	p-value (between groups)
Baseline	$24.8 \pm 9.7$	$25.5 \pm 10.2$	0.71
3 Months	$29.4 \pm 10.1$	$37.8 \pm 11.5$	$<0.01$
6 Months	$34.2 \pm 11.3$	$44.7 \pm 12.8$	$<0.001$



The line graph showing ferritin levels over time:

- Group B (THRT + Iron) ferritin levels rise more sharply than Group A.
- Error bars show SD at each timepoint.
- p-values highlight significant differences at 3 and 6 months.
- Baseline shows no difference ( $p=0.71$ ).

#### Thyroid Function and Clinical Outcomes

TSH levels normalized similarly in both groups by 6 months ( $p = 0.45$ ). However, patients in Group B reported greater symptom improvement, including reduced fatigue and better energy levels. No significant adverse effects were reported related to iron supplementation.

#### DISCUSSION

This study demonstrates that thyroid hormone replacement therapy (THRT) improves serum ferritin levels in hypothyroid patients, with a more pronounced effect observed when combined with oral iron supplementation. Both groups showed significant ferritin increases over six months; however, the addition of iron yielded greater improvements, underscoring the synergistic role of iron in thyroid recovery and hematologic function.

The restoration of ferritin with THRT alone aligns with previous findings that normalized thyroid hormone levels enhance iron absorption, erythropoiesis, and thyroid peroxidase activity (Maki et al., 2016; Catargi et al., 1999). Nonetheless, the superior ferritin recovery in the combined therapy group reflects the clinical reality that many hypothyroid patients, especially menstruating women, have concurrent iron deficiency that requires direct supplementation (El-Masry et al., 2018; Cinemre et al., 2009).

Clinical symptom improvement was more notable in patients receiving both therapies, highlighting the importance of addressing iron status alongside

hormone normalization to alleviate fatigue and other persistent symptoms often reported despite biochemical euthyroidism (Garber et al., 2012). This supports integrating ferritin assessment and iron supplementation into routine follow-up for hypothyroid patients, particularly those with low baseline ferritin.

While TSH levels normalized similarly in both groups, ferritin response was a more sensitive marker of recovery in iron metabolism and may better reflect functional improvement. The lack of significant adverse effects with iron supplementation indicates the safety and feasibility of the combined treatment in appropriate patients.

Limitations include the observational design and relatively short follow-up duration. Future randomized controlled trials with larger samples and longer monitoring would better define optimal ferritin thresholds and iron dosing strategies in hypothyroidism management.

#### CONCLUSION

Thyroid hormone replacement therapy significantly improves serum ferritin levels in hypothyroid patients, reflecting enhanced iron metabolism with thyroid function restoration. Combined levothyroxine and oral iron supplementation produces greater ferritin recovery and clinical symptom improvement than THRT alone, particularly in iron-deficient individuals. Routine ferritin monitoring and appropriate iron supplementation should be considered integral components of hypothyroidism management to optimize therapeutic outcomes and patient quality of life.

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