

# Association between serum ferritin and thyroid hormone profile in hypothyroidism

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## Abstract

**Background:** Ferritin is an iron storage protein found in almost all of the body tissues. Serum ferritin levels also have been reported to be altered in patients with thyroid disease. Thus, changes in the serum concentrations of ferritin reflect thyroid function.

**Objective:** For the synthesis of thyroid hormones, thyroperoxidase requires iron. It has been suggested that there is an association between thyroid profile and ferritin levels, which is the storage protein for iron in the body. This study was undertaken to assess ferritin levels in hypothyroid patients.

**Materials and Methods:** Ferritin levels were estimated in 50 newly diagnosed patients of hypothyroidism using chemiluminescence technique (ADVIA Centaur CP). Total T3 and T4 levels were estimated using radioimmunoassay. Free T3, T4, and thyroid-stimulating hormone (TSH) levels were estimated using chemiluminescence. These were then compared with age- and sex-matched healthy controls. Results were correlated statistically.

**Results:** Serum ferritin levels were found to be significantly reduced in patients with hypothyroidism compared to normal subjects ( $p < 0.001$ ).

**Conclusion:** Hypothyroidism is associated with low serum ferritin levels. The estimation of serum ferritin may help in understanding the etiopathogenesis, diagnosis, and monitoring of hypothyroid patients.

**KEY WORDS:** Ferritin, hypothyroidism, thyroid

## Introduction

Several minerals and trace elements such as iodine, iron, selenium, and zinc are essential for normal thyroid hormone metabolism. Iodine has an important role in the synthesis of thyroid hormones; selenium is a component of the deiodinase enzymes that convert T4 to T3. It also protects the

thyroid gland from damage by excessive iodide exposure. Zinc appears to be involved in thyroid conversion. Low iron, or more specifically, low ferritin, is one of the most overlooked causes of low thyroid function.<sup>[1]</sup> Thyroid hormone (T<sub>3</sub>) plays a central role in differentiation, development, and maintenance of body homeostasis. The actions of T<sub>3</sub>, like the steroid hormones, are mediated through intracellular T3-receptor proteins (TRs), which act predominantly to modulate transcription by binding to specific T<sub>3</sub>-response elements in target genes. T<sub>3</sub> also exerts important effects at the post-transcriptional level to regulate the expression of several genes.<sup>[2]</sup>

Ferritin is an iron storage protein found in almost all of the body tissues. Serum ferritin levels also have been reported to be altered in patients with thyroid disease. Thus, changes in the serum concentrations of ferritin

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reflect thyroid function. Thyroid peroxidase (TPO) is a membrane-bound glycosylated hemoprotein that has a key role in the biosynthesis of thyroid hormones by organification. Iron deficiency has been reported to impair the body's ability to make its own thyroid hormone, which could increase need for thyroid medication.

Several groups have documented an association between  $T_3$  levels and ferritin expression. Furthermore, administration of  $T_3$  to hypothyroid individuals produced a significant increase in the serum ferritin level.<sup>[1]</sup> Although the cause of the  $T_3$ -induced increase in the serum ferritin level in humans is unknown; increased synthesis of ferritin in the liver may well be an important contributor. These links between  $T_3$  and the regulation of ferritin expression suggest that a positive correlation exists between the levels of  $T_4/T_3$  and ferritin in the serum. Thus, it has been suggested that serum ferritin measurement could be useful for the evaluation of thyroid hormone action on peripheral tissues.<sup>[3]</sup>

### Objective

For the synthesis of thyroid hormones, thyroperoxidase requires iron. It has been suggested that there is an association between thyroid profile and ferritin levels, which is the storage protein for iron in the body. This study was undertaken to assess ferritin levels in hypothyroid patients.

### Materials and Methods

The study was carried out in the Department of Biochemistry, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak. A total of 50 newly diagnosed patients with hypothyroidism were included in the study. Blood (5 ml) was taken from the antecubital vein under all aseptic conditions in a red capped plain vacutainer from the subjects and the serum was analyzed for ferritin, thyroid-stimulating hormone (TSH), and free T3 and T4 on chemiluminometer (Advia Centaur CP; Siemens, USA). Total T3 and T4 levels were assessed using radioimmunoassay. All these parameters were compared with age- and sex-matched healthy controls. Patients with pregnancy, hepatic disorder, renal diseases, and polycystic ovarian syndrome were excluded from the study.

**Table 1:** Ferritin levels estimated in newly diagnosed patients with hypothyroidism using chemiluminescence technique

	Controls	Cases	p-Value
S ferritin (ng/ml)	59.89 ± 8.56	21.08 ± 3.18	<0.001
FT3 (pg/ml)	3.12 ± 0.89	2.34 ± 0.06	<0.001
FT4 (ng/dl)	1.07 ± 0.08	0.73 ± 0.03	<0.001
TSH ( $\mu$ IU/ml)	2.76 ± 0.42	6.86 ± 1.16	<0.001
T3 (ng/dl)	126.25 ± 8.53	88.76 ± 6.54	<0.001
T4 ( $\mu$ g/dl)	8.56 ± 1.57	5.17 ± 0.76	<0.001

### Results

Of the 50 subjects, 29 were females and 21 were males. Mean  $\pm$  SD of age among cases and controls were  $32.75 \pm 10.36$  and  $34.69 \pm 12.24$  years with the range of 18–65 years and 19–65 years, respectively. There was no significant difference with respect to age distribution in cases and controls ( $p > 0.05$ ; Table 1).

### Discussion

The present study shows that there is a state of low ferritin concentration in patients with hypothyroidism. It is observed that FT4 level was significantly lowered in cases as compared to controls ( $p < 0.001$ ), suggesting that depletion of iron stores may decrease serum FT4 levels. FT3 levels were also significantly lower in individuals with hypothyroidism as compared to healthy controls. TPO is a membrane-bound glycosylated hemoprotein that has a key role in the biosynthesis of thyroid hormones. This enzyme is responsible for the oxidation of iodide and binding of iodine to tyrosyl residue of thyroglobulin (organification). Two diiodotyrosine (DIT) molecules undergo an oxidative condensation for the formation of thyroxine (T4). Triiodothyronine (T3) is yielded from the coupling of one mono-iodotyrosine and one DIT. A separate coupling enzyme has not been found, and as this is an oxidative process, it is assumed that same thyroperoxidase catalyzes this reaction. This hypothesis is supported by observation that the same drug that inhibits iodide oxidation also inhibits coupling.<sup>[4]</sup>

Thyroid hormone has a central role in differentiation, development, and maintenance of body homeostasis. It has been suggested in various studies that thyroid hormones regulate ferritin expression. The iron regulatory protein (IRP), previously known as the iron-responsive element-binding protein, IRE-BP, and iron-responsive factor, IRF) is a trans-acting RNA-binding protein that binds with high affinity to conserved stem-loop structures, iron-responsive elements (IREs), present in the ferritin, and transferrin receptor (TfR). The IRP has a key role in the regulation of iron (Fe) homeostasis.<sup>[5]</sup> In the absence of iron, the IRP binds to the IRE in the 5'-untranslated region (5'-UTR) of ferritin and represses translation.<sup>[6]</sup> Binding of the IRP to IREs in the 3'-untranslated region (3'-UTR) of TfR mRNA stabilizes the mRNA and prevents its degradation.<sup>[7]</sup> In iron-replete states, the reverse holds, which results in increased ferritin translation and decreased TfR mRNA stability. This reciprocal regulation is achieved at the post-translational level and is independent of new protein synthesis.<sup>[8]</sup>

### Conclusion

Our study suggest that a significant difference in ferritin levels in hypothyroid patients and normal healthy controls could be a reflection of disturbed activities of iron-dependent

enzymes such as TPO, which impairs thyroid hormone metabolism but the mechanism by which thyroid hormone alters ferritin concentration is not well known. Measurement of serum ferritin before and after thyroid hormone therapy may provide useful information in the diagnosis of thyroid disease.

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