Section: Biochemistry

Original Research Article

A STUDY OF ASSOCIATION OF SERUM FERRITIN WITH HYPOTHYROIDISM AND EFFECT OF THYROID HORMONE REPLACEMENT THERAPY IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Thyroid hormones synthesized and released by the thyroid gland, have a vital role in regulating the metabolism of body. Hypothyroidism is a condition in which thyroid gland does not produce adequate quantity of thyroid hormones. Hypothyroidism can become a serious and life-threatening medical condition if it is not treated on time. **Materials and Methods:** The type of study is observational prospective study in which 50 patients were included in the Department of Biochemistry, Nalanda Medical College, Patna, a tertiary care hospital. The duration of the study was from November 2021 to October 2022.A total of 50 newly diagnosed patients with hypothyroidism were included in the study. Blood (10 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. **Result:** 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. Mean ± SD of age among cases and controls were 31.73 ± 11.34 and 33.67 ± 13.22 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 ($p <0.001$; Table 1).**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.

INTRODUCTION

Thyroid hormones synthesized and released by the thyroid gland have a vital role in regulating the metabolism of body. Synthesis of these thyroid hormones requires an iron containing enzyme, thyroid peroxidase (TPO). Thus, iron inadequacy can affect the proper functioning of the TPO enzyme that further affect the thyroid hormone production. Serum ferritin, an index of iron store is present in almost all cells; however, it has been reported that an alteration in ferritin levels occurs in patients with thyroid disease. Worldwide, thyroid diseases are common and in India too, there is a significant burden of thyroid disease.[1]

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.[2] Thyroid hormone (T3) plays a central role in differentiation, development, and maintenance of body homeostasis. The actions of T3, like the steroid hormones, are mediated through intracellular T3-receptor proteins (TRs), which act

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predominantly to modulate transcription by binding to specific T3 -response elements in target genes. T3 also exerts important effects at the post-transcriptional level to regulate the expression of several genes.[3]

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. 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.[4-8]

Several groups have documented an association between T3 levels and ferritin expression. Furthermore, administration of thyroid hormone to hypothyroid individuals produced a significant increase in the serum ferritin level.[1] Although the cause of the thyroid hormone -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 thyroid hormone and the regulation of ferritin expression suggest that a positive correlation exists between the levels of T4 /T3 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.[4]

Estimation of serum ferritin is simple, reliable, economic, and sensitive and can be used as a marker of thyroid hormone action.[9,10]

Present study is an attempt to find out correlation if any between serum ferritin and hypothyroidism and also changes of serum ferritin level if any after correction of the disorders with levothyroxine therapy.[11-13]

Aim and Objective

General objective of this study is to assess whether serum ferritin can be a biomarker of thyroid dysfunction.

Specific Objectives

1. To establish association of serum ferritin level with serum FT3, FT4and TSH level in control group as well as in study group.
2. To detect whether any change occurs in serum ferritin level with Levothyroxine therapy in the study group.

MATERIALS AND METHODS

The type of study is observational prospective study in which 50 patients were included who attended the Department of Biochemistry Lab, Nalanda Medical College, Patna, a tertiary care hospital. The duration of the study was from November 2021 to December 2022. A total of 50 newly diagnosed patients with hypothyroidism were included in the study. Out of 50 patients 34 were Females and 16 were males, the ratio of female and male is 2.13. 10 ml blood was drawn from the antecubital vein under 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. All these parameters were compared with age and sex matched healthy controls. All the above parameters will estimate in study group before commencement of Levothyroxine therapy and after six months (at least) of therapy. Patients with pregnancy, hepatic disorder, renal diseases, and polycystic ovarian syndrome were excluded from the study.

RESULTS

A total of 50 newly diagnosed patients with hypothyroidism were included in the study. Out of the 50 subjects, 34 were females and 16 were males. Mean ± SD of age among cases and controls were 31.73 ± 11.34 and 33.67 ± 13.22 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 ($p < 0.001$)[Table 1].

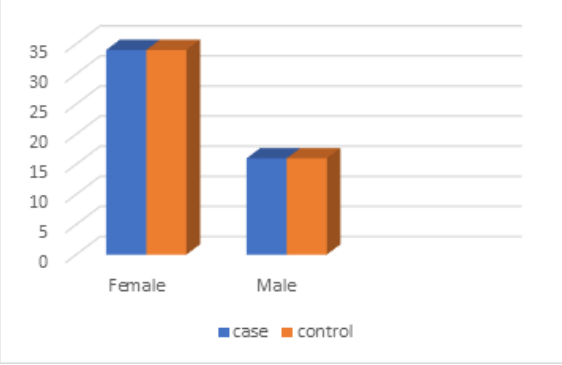

Figure 1: Association between sex with case and control was not statistically significant (p≤0.001).

Table 1: Distribution of sex in two groups.

Sex	Male	Female	Total
Case	16	34	50

Table 2: Ferritin levels estimated in newly diagnosed patients with hypothyroidism using chemiluminescence technique.

	Controls	Cases	p-Value
S ferritin (ng/ml)	58.85±7.35	20.06±2.16	p<0.001

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FT3 (pg/ml)	3.09± 0.57	2.30±0.84	p<0.001
FT4 (ng/dl)	1.05±0.06	1.04±0.06	P<0.001
TSH (µIU/ml)	2.74±0.40	1.85±0.32	p<0.001
T3 (ng/dl)	124.23±6.51	120±8.50	p<0.001
T4 (µg/dl)	6.54±1.54	6.50±0.57	p<0.001

DISCUSSION

The type of study is observational prospective study in which 50 patients were included in the Department of Biochemistry in Tertiary Care Hospital.

In this study the association of serum ferritin with hypothyroidism and effect of thyroid has been conducted to determine the association if any between serum ferritin and hypothyroidism and whether ferritin level change after correction of hypothyroidism with levothyroxine therapy.

Thyroid hormones are essential for cell growth, differentiation and metabolism, as well as for maintaining body homeostasis. Serum ferritin levels have been observed to change in subjects with thyroid diseases, indicating a link between serum ferritin concentration and thyroid functions. This study focussed to find correlation between serum ferritin and TSH levels in hypothyroid patients.

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 haemoprotein 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 thyroperoxidasecatalyzes this reaction. This hypothesis is supported by observation that the same drug that inhibits iodide oxidation also inhibits coupling.[5]

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 transacting 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.[5,14,15] In the absence of iron, the IRP binds to the IRE in the 5′-untranslated region (5′-UTR) of ferritin and represses translation.[6,13] Binding of the IRP to IREs in the 3′-untranslated region (3′-UTR) of TfR mRNA stabilizes the mRNA and prevents its degradation.[16-20] 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.[8,20-24]

Increased oxidative stress has been reported in hypothyroidism. Hypothyroidism causes immunosuppression that may lead to oxidative stress. Ferritin has an important role in iron sequestration with some antioxidant properties.[9,10,11,16] TSH, at higher concentration is known to induce inflammatory cytokines and decrease the concentration of antioxidants in the body, as seen in clinical hypothyroidism.[16,18,22,23]This may be an additional reason for decrease in ferritin levels in these patients.The study done by Takamatasu J et al suggested that serum ferritin measurements were evaluated as a marker of thyroid hormone action on peripheral tissues. Furthermore, a significant inter-individual correlation between serum levels of ferritin and T4 or T3 was found in 2 patients with thyrotoxic Graves' disease in whom levels were measured serially throughout the course of therapy. Similarly, serum ferritin levels increased in all 12 hypothyroid patients with Hashimoto's disease when euthyroidism was achieved with L-T4therapy. Administration of 75 micrograms thyroid hormone daily for 1 week to 11 euthyroid subjects resulted in a 23-243% (mean +/-SD, 117 +/- 70%)increases in serum ferritin above basal values. In contrast, in 3 patients with thyroid hormone resistance, the same treatment produced rises in serum ferritin concentrations of only 2%, 5% and 15%.Their data suggest that alterations in thyroid status in a given individual produce changes in serum ferritin levels. Measurement of this protein before and after thyroid hormone therapy may prove useful in the diagnosis of thyroid hormone resistance.[25]

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

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therapy may provide useful information in the diagnosis of thyroid disease.

Hypothyroidism causes immunosuppression that may lead to oxidative stress. Ferritin has an important role in iron sequestration with some antioxidant properties.

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