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Association between Serum Ferritin and Thyroid profile in Radiologically proven patients with Goitre with Thyroiditis

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Abstract

Introduction: Thyroid peroxidase (TPO) is a membrane-bound glycosylated hemoprotein that has a key role in the biosynthesis of thyroid hormones by organification. 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.

Objective: The aim of this study is to establish a correlation between serum ferritin and thyroid hormones in thyroid disorder patients.

Materials and Method: This cases, visiting medical outpatient department of SGT Medical College and Hospital, Budhera, Gurugram, Haryana. Patients were subjected to ultrasound. Radiologically proven Thyroid disorder patients sample were analysed for the measurement of T_3, T_4, TSH (by CLIA) and Serum Ferritin (by ELISA).

Results: The mean T_3, T_4, TSH and serum ferritin levels showed highly significant difference with $p<0.001$ in hypothyroid group compared to controls

Conclusion: Low serum ferritin levels are associated with hypothyroidism. The estimation of iron storage protein ferritin may help in understanding the pathiphysiology, diagnosis and treatment of thyroid disorders.

Keywords: Serum Ferritin, Thyroid Profile, Hypothyroidism.

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 converts T_4 to T_3. 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 thyroid dysfunction.[1]

Thyroid hormones plays a central role in differentiation, development, and maintenance of body homeostasis.[2] Thyroid hormone performs a role in hemoglobin synthesis in adults and maturation of hemoglobin in fetus; and hypothyroidism leads to anemia via reducing oxygenation process through disturbing hematopoietic process.[3] It is considered that thyroid hormones influence hematopoeisis through an increase in erythropoietin generation or hematopoietic factors by non-erythroid cells. The actions of T_3, like steroid hormones, are mediated through intracellular T_3-receptor proteins (TRs), which act predominantly to modulate transcription by binding to specific T_3 response elements in target genes. T_3 also exerts important effects at the post-transcriptional level to regulate the expression of several genes.[4]

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.[2]

Several studies 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.[1] Although the cause of T_3-induced increase in the serum ferritin levels in human 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 serum. Thus, it has been suggested that serum ferritin measurement could be useful for the evaluation of thyroid hormone action on peripheral tissues.[5] Therefore the present study was designed to assess serum ferritin levels in hypothyroid patients.

Materials and Method

The study was carried out in the Department of Radiodiagnosis and Department of Biochemistry, SGT Medical College, Budhera, Gurugram, Haryana. A total of 40 newly diagnosed thyroid disorder patients were compared with 40 age and sex matched normal healthy controls. A written informed consent was also taken from the cases with detailed history.

Inclusion Criteria: Clinically and radiologically diagnosed patients with Goitre with Thyroiditis in the age group of 20-60 years.

Controls: Healthy controls in the age group of 20-60 years.

Exclusion criteria:

- Pregnancy
- Hepatic disorder
- Renal diseases
- Polycystic ovarian syndrome

On Ultrasound, diffuse or multifocal decrease in echogenicity was the hallmark of many types of Thyroiditis. On color Doppler study increased blood flow was noted throughout the gland Enlargement of the gland was also noted. From the radiologically proven thyroid disorder patients, 4 ml of fasting blood sample was collected and centrifuged for serum separation. Thyroid function was assessed by quantitative estimation of T3, T4 and TSH levels in serum performed using SEIMENS-Centaur CP analyzer based on chemiluminescent immuno assay (CLIA). Serum ferritin was assessed by ELISA method by commercially available kit provided by Calbiotech.

Statistical Analysis: Statistical analysis was done using the SPSS software version 24. The data was represented by counts, percentage and mean± standard deviation. Statistical analysis of the biochemical parameters, T_3, T_4, TSH and serum ferritin were done by t-test to compare these parameters in cases and controls. A *p*-value of <0.05 was considered significant and *p*-value >0.05 as non-significant.

Results

Of the 40 cases 27 were females and 17 were males. Mean ±SD of age among cases and controls were 33.65± 9.46 years and 35.78± 11.28 years respectively. There was no significant difference with respect to age distribution in cases and controls ($p>0.05$).

Table 1: Ferritin levels in newly diagnosed hypothyroid patients

Parameters	Controls	Cases	p-Value
T_3 (ng/ml)	1.23± 0.78	0.51±0.87	<0.001
T_4 (µg/dl)	9.87±1.68	4.23±0.86	<0.001
TSH (mIU/ml)	2.68±0.34	8.95±1.14	<0.001
Serum Ferritin (ng/ml)	72.43±9.20	19.10±3.40	<0.001

The mean T_3, T_4, TSH and serum ferritin levels showed highly significant difference with $p<0.001$ in hypothyroid group compared to controls (Table 1).

Discussion

Thyroid gland has a critical effect on erythropoiesis by induction of erythropoietin production and proliferation of erythroid progenitors.[6,7] Several studies showed a relationship between body iron status (indulging iron metabolism, ferritin, and serum iron) and thyroid hormones function.[8,9]

Our study shows that there is a state of low ferritin concentration in patients with hypothyroidism. It is observed that serum T_3 and T_4 levels were significantly lower in cases as compared to healthy controls ($p<0.001$), suggesting that depletion of iron stores may decrease these hormones. Our results are consistent with various studies.[2,10,11] Iron deficiency impairs thyroid hormone synthesis by reducing activities of heme-dependent thyroid peroxidase (TPO). TPO is a membrane-bound glycosylated hemoprotein that plays 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).[12]

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 a role in the regulation of iron homeostasis.[13] In the absence of iron, the IRP binds to the IRE in the 5'-untranslated region (5'-UTR) of ferritin and represses translation.[14] Binding of the IRP to IREs in the 3'-untranslated region (3'-UTR) of TfR mRNA stabilizes the mRNA and prevents its degradation.[15] 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.[16]

Conclusion

Our study suggest that a significant difference in ferritin levels in hypothyroid patients could be a reflection of disturbed activities of iron dependent thyroid peroxidase (TPO) enzyme which impairs the metabolism of thyroid hormones but the mechanism by which thyroid hormone status alters ferritin levels is not well known. There is a need for further studies to evaluate the affect of thyroid hormones on ferritin metabolism for the diagnosis and treatment of thyroid illness.

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