Original Research Article

A Study on Serum Ferritin and Hypothyroidism among Patients Attending A Tertiary Care Hospital With Special Emphasis On Effect Of Thyroid Hormone Replacement Therapy

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Abstract

Introduction: Thyroid gland is a bi-lobed endocrine gland and it secretes thyroxin (T4) and tri-iodothyronine (T3) hormones and it is under the regulation of thyroid stimulating hormone (TSH). Iron is one of the important elements required for normal functioning of thyroid gland and it is stored in the body in the form of ferritin and it is an intracellular protein. Present study is an attempt to find out correlation, if any between serum ferritin and hypothyroidism and also changes of serum ferritin level after correction of the disorders with levothyroxine therapy. **Materials and Methods:** A cross-sectional study was conducted by Department of Biochemistry, Darbhanga Medical College, Laheriasri, Bihar. Study was conducted from December 2021 to May 2022. Written informed consent was obtained from each participant before inclusion in the study. Prior ethical approval was obtained from the Institutional Ethics Committee. The study population comprised of 100 hypothyroid and 100 euthyroid subjects of age >18 years. Blood sample was collected from the study participants who visited the laboratory for their thyroid hormone. From the selected subjects, under aseptic precautions, 3ml of venous blood sample was drawn into a non-vacuum plain tube with clot activator. These tubes were allowed to stand for specific period of about 15-20 minutes. Then tubes were centrifuged for 3500rpm for 15- 20 min. The collected data was entered in Microsoft excel and the data analyzed by using Statistical Package for Social Sciences ver. 20.0 (IBM, Chicago). **Results:** The mean values of TSH were higher among hypothyroid subjects as compared to euthyroid subjects. Whereas T4, T3 and ferritin were found be lower among hypothyroid subjects as compared to euthyroid subjects. TSH, T4, T3 and ferritin showed statistically significant difference between euthyroid and hypothyroid subjects with a p value of <0.05. There was a negative correlation between TSH and serum ferritin among study subjects (r= 0.07) implying that as serum TSH levels were increasing serum ferritin levels kept on decreasing. **Conclusion:** In our study we found that there is a significant difference in serum ferritin levels between hypothyroid and euthyroid subjects. Hence measurement of serum ferritin before and after thyroid hormone therapy may provide useful information with regard to diagnosis and prognosis of thyroid disease.

Key Words: Serum Ferritin, Hypothyroidism, Thyroid Hormone Replacement Therapy.

Introduction

Thyroid gland is a bi-lobed endocrine gland and it secretes thyroxin (T4) and tri-iodothyronine (T3) hormones and it is under the regulation of thyroid stimulating hormone (TSH). Synthesis and secretion of hormone is controlled by negative feedback mechanism. T3 and T4 in the circulation are bound reversibly to carrier proteins and it constitutes for about 99.97 % of T4 and 99.7% of T3. Thus only a small fraction of these hormones are free in circulation and are known as free T3 (fT3) and free T4 (fT4) which are biologically active[1]. Decreased production of thyroid hormones by the thyroid gland is called as hypothyroidism; it could be either primary or secondary. Primary hypothyroidism refers to the abnormality in the thyroid gland itself and secondary is due to hypothalamic or pituitary disease. When there is an increase in serum TSH above 10mIU/L along with a decreased concentration of serum T4 and T3 is called as an overt hypothyroidism and in Sub-clinical hypothyroidism there is an increase in serum TSH usually between 4-10mIU/L associated with a normal concentration of serum T4 and T3[2]. According to recent population-based study in India, it was found that the prevalence of hypothyroidism and subclinical hypothyroidism in adults is 3.9% and 9.4% respectively[3]. For normal thyroid metabolism, few minerals and trace elements like iodine, iron, selenium and zinc are essential in required proportion[4].

Iron is one of the important elements required for normal functioning of thyroid gland and it is stored in the body in the form of ferritin and it is an intracellular protein. All cell of the body contains ferritin and acts as a reserve of iron and small amounts are secreted into the serum for formation of hemoglobin and other hemi proteins[5]. The initial two steps of biosynthesis of thyroid hormone require an iron containing enzyme called as Thyroid peroxidase (TPO), which is a membrane-bound glycosylated hemoprotein[6]. During iron deficiency, tissue iron start diminishing at the earliest. In turn synthesis of thyroid hormone is impaired by altering the activity of enzyme called hem dependent TPO[4].

Patient with thyroid disease have shown altered serum ferritin levels. Similarly changes in thyroid hormone levels have reflected if there is an alteration in the concentration of serum ferritin. Furthermore, there is an increase in the concentration of serum ferritin level after the administration of T3 to hypothyroid patient[7]. Even though the mechanism of T3-induced increase in the serum ferritin level in humans is not known; but increased synthesis of ferritin in the liver could be a one of the contributor. Thus there could be a positive correlation exists between the levels of T4/T3 and ferritin in the serum[8]. Present study is an attempt to find out correlation, if any between serum ferritin and hypothyroidism and also changes of serum ferritin level after correction of the disorders with levothyroxine therapy.

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Materials and methods

A cross-sectional study was conducted by Department of Biochemistry, Darbhanga Medical College, Laheriasri, Bihar. Study was conducted from December 2021 to May 2022. Written informed consent was obtained from each participant before inclusion in the study. Prior ethical approval was obtained from the Institutional Ethics Committee. The study population comprised of 100 hypothyroid and 100 euthyroid subjects of age >18 years. Participants with conditions like acute illness, recent history of blood transfusion, anemia, diabetes mellitus, hypertension, renal and hepatic failure, history of thyroidectomy, radiotherapy, radioactive iodine therapy, pregnant women, and subjects consuming drugs known to cause hypothyroidism were excluded from the study. Subjects with TSH value <4.94µIU/ml was considered as euthyroid and TSH value ≥4.94µIU/ml was considered as hypothyroid subjects. Detailed information of the participants like age, family history, past medical history was noted.

Procedure

Blood sample was collected from the study participants who visited the laboratory for their thyroid hormone. From the selected subjects, under aseptic precautions, 3ml of venous blood sample was drawn into a non-vacuum plain tube with clot activator. These tubes were allowed to stand for specific period of about 15-20 minutes. Then tubes were centrifuged for 3500rpm for 15- 20 min.

The serum was separated and tested for the below listed biochemical parameters by various enzymatic method as mentioned in the fully automated Abbott architect analyzers. Quality check for control materials were assayed before processing with study participants samples and the participants were informed about their results along with appropriate advice.

Biochemical parameters

TSH: TSH assay is a two-step immunoassay to determine the presence of TSH in human serum using Chemiluminescent Micro particle Immunoassay (CMIA) technology. The normal range is 0.25-4.94 µIU/ml.

Total T4: Total T4 assay is a two-step immunoassay to determine the presence of total T4 in human serum using CMIA technology. The normal range of total T4 is 4.5-12.6 µg/dl.

Total T3: Total T3 assay is a two-step immunoassay to determine the presence of total T3 in human serum using CMIA technology. The normal range of total T3 is 0.4-2.04 ng/ml.

Ferritin: Ferritin assay is a two-step immunoassay to determine the presence of ferritin in human serum using CMIA technology. The normal range of ferritin for male is 20-250 ng/ml and for female is 10-120 ng/ml.

The collected data was entered in Microsoft excel and the data analyzed by using Statistical Package for Social Sciences ver. 20.0 (IBM, Chicago). Descriptive statistics like mean, percentage, standard deviation and inferential statistics was performed. A p value < 0.05 will be considered as statistically significant.

Results

In the present study a total of 200 subjects were included. Amongst them 100 were euthyroid (Group A) and 100 were hypothyroid (Group B) subjects. The patients were selected such that the male to female ration in both the groups was 1, implying there were 50 males and 50 females in each group. The mean (SD) age was 31.4 (11.2) and 32.8 (8.9) years respectively for patients of group A and B (p value > 0.05). Hence, both the groups were matched for age and sex.

The mean values of TSH were higher among hypothyroid subjects as compared to euthyroid subjects. Whereas T4, T3 and ferritin were found be lower among hypothyroid subjects as compared to euthyroid subjects. TSH, T4, T3 and ferritin showed statistically significant difference between euthyroid and hypothyroid subjects with a p value of <0.05. [Table 1]

There was a negative correlation between TSH and serum ferritin among study subjects (r= 0.07) implying that as serum TSH levels were increasing serum ferritin levels kept on decreasing. [Figure 1]

Patients were given levothyroxine therapy (doses varying with their TSH levels). They were asked to repeat the test after 6 months and come for follow-up. 89 patients out of 100 turned up for the follow-up visits. [Table 2]

Table 1: Value of various biochemical markers among patient of both the groups

Biochemical test	Thyroid status		p value
	Group A (n = 100) Mean (SD)	Group B (n = 100) Mean (SD)	
TSH (µIU/ml)	2.3 (1.1)	29.8 (17.3)	< **0.05**
T4 (µg/dl)	7.5 (1.8)	2.5 (1.4)	< **0.05**
T4 (ng/ml)	1.1 (0.4)	0.04 (0.3)	< **0.05**
Ferritin (ng/ml)	70.3 (65.4)	33.6 (24.3)	< **0.05**

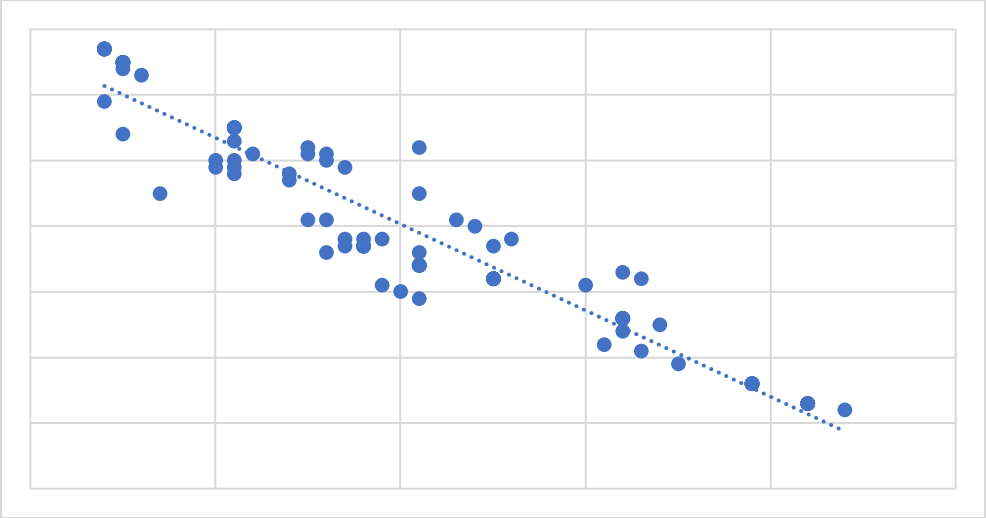

Figure 1: Correlation between TSH and Ferritin

Table 2: Effect of levothyroxine replacement therapy on TSH and serum ferritin levels

Biochemical test	Pre-treatment (N = 100)	Post – treatment (N = 89)	p value
TSH (µIU/ml)	29.8 (17.3)	11.4 (20.6)	< **0.05**
Ferritin (ng/ml)	33.6 (24.3)	50.4 (13.8)	< **0.05**

Discussion

In recent year, thyroid disorders are one of the most common endocrine disorders and its prevalence is increasing worldwide with female preponderance. In our study, we found that mean value of serum ferritin concentration in euthyroid subjects was higher as compared to the mean value of serum ferritin among hypothyroid subjects and it was found to be statistically significant. We also found that the mean serum ferritin level significantly increased with levothyroxine replacement therapy. It is observed that the mean serum ferritin level in after treatment is greater than before treatment. Our results were in concurrence with the study done by Arvind K et al, they showed that mean hemoglobin, serum ferritin and red blood cell indices were significantly decreased in subclinical hypothyroid patient in comparison to euthyroid group[9]. Another study conducted by Ashuma S et al, on assessment between serum ferritin and thyroid hormone profile in hypothyroidism, they found that serum ferritin levels were found to be statistically significantly reduced in patients with hypothyroidism as compared to normal subjects[10]. A similar study conducted by Kiran D et al, on Thyroid profile and iron metabolism: mutual relationship in hypothyroidism. They concluded that the levels of iron and ferritin were found to be significantly decreased while the levels of total iron binding capacity were observed to be significantly increased in hypothyroid patients as compared to healthy individuals[12].

Serum ferritin levels also have been reported to be altered in patients with thyroid disease. Recently, it has been reported that the serum level of ferritin is high in hyperthyroidism andlow in hypothyroidism, and changes in the serum concentrations affect thyroid function. Ferritinlevel is estimated before iron supplements. Iron is also used by bacteria and cancer cells. Iron works in conjunction with iodine and has stimulatory effect on thyroid peroxidase and deiodinase that convert T4 to T3. Therefore levothyroxine prescription in such cases reverses the deleterious effect of hypothyroidism in iron deficiency. The study results demonstrated that treatment of patients with hypothyroidism and iron-deficiency anemia with a levothyroxine resulted in a favorable outcome. Ferritin as the leading indicator for improvement in anemia and thyroid stimulating hormone as an indicator for hypothyroidism both improved significantly. IT has been suggestedthose people with thyroid disorder should have routine screening of hematological, biochemical and hormonal profile assay and simultaneously proper management of this metabolic disease.

It is said that ferritin and its formation can protect against iron toxicity, thus causing decrease in oxidative stress. Lowering of ferritin levels accompanies release of free iron which may contribute to increasing oxidative stress thereby may oxidatively damaged thyroid follicular cells and reducing the synthesis of T3. It may have a role to up regulate hepatic ferritin gene expression which may in part contribute to low serum ferritin in hypothyroidism. Though molecular mechanism to explain regulation of ferritin mRNA by T3 is still not clear.

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 withHashimoto's disease when euthyroidism was achieved with L-T4 therapy. Administration of 75 micrograms T3 daily for 1 week to 11 euthyroid subjects resulted in a 23-243% (mean +/-SD, 117 +/- 70%) increases in serum ferritin above basal values. 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 T3 therapy may prove useful in the diagnosis of thyroid hormone resistance[7].

Thyroid hormone plays an important role in maintaining body homeostasis. In thyroid hormone biosynthesis, TPO acts as key enzyme, which is an iron dependent. The present study showed that hypothyroid subjects had significantly lower serum ferritin concentration as compared to euthyroid subjects.

Conclusion

In our study we found that there is a significant difference in serum ferritin levels between hypothyroid and euthyroid subjects. The mechanism by which thyroid hormone alters ferritin concentration in the blood is still not clear. Hence measurement of serum ferritin before and after thyroid hormone therapy may provide useful information with regard to diagnosis and prognosis of thyroid disease. Further studies are required with large sample size to know the serum ferritin level before & after thyroid hormone supplements.

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Conflict of interest

None declared

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