

## Correlation of Serum Ferritin and Thyroid Hormone Status among Hypothyroidism

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### ABSTRACT

**Background and Objectives:** Thyroid hormone is produced by the thyroid gland; it plays a vital role in human body. Thyroid peroxidase, an iron containing enzyme, is essential for initial two steps of thyroid hormone synthesis. Serum ferritin is an iron storage protein present in almost all cells, the altered level of serum ferritin have been reported in patients with thyroid disease. The objective of our study were to determine and assess the correlation between serum ferritin and thyroid hormone levels among hypothyroid and euthyroid subjects.

**Methods:** This was a cross sectional study conducted on 50 hypothyroid and 50 euthyroid subjects. Thyroid Stimulating Hormone (TSH), Thyroxin (T4), Tri-iodothyronine (T3) and serum ferritin levels were measured in a fully automated analyzer.

**Result:** In the present study, the mean value of TSH ( $33.66 \pm 35.880$ ) was higher among hypothyroid subjects whereas mean value of T4 ( $2.60 \pm 1.246$ ), T3 ( $0.06 \pm 0.233$ ) and ferritin ( $36.09 \pm 28.004$ ) were found be lower among hypothyroid subjects as compared to euthyroid subjects. All parameters showed statistically significant difference between two groups with a p value of  $<0.001$ .

**Conclusion:** The present study showed that, hypothyroid subjects had low serum ferritin levels. Hence estimation of serum ferritin concentration among hypothyroid subjects could be useful in the evaluation of thyroid hormone status.

**Keywords:** TSH, T4, T3, Serum ferritin, Hypothyroid & Euthyroid.

## **INTRODUCTION**

Thyroid gland is a bilobed 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.<sup>[1]</sup>

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.<sup>[2]</sup>

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.<sup>[3]</sup>

For normal thyroid metabolism, few minerals and trace elements like iodine, iron, selenium and zinc are essential in required proportion.<sup>[4]</sup>

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 heme proteins.<sup>[5]</sup>

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.<sup>[6]</sup>

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 heme-dependent TPO.<sup>[4]</sup>

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.<sup>[7]</sup>

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 is could be a positive correlation exists between the levels of T4/T3 and ferritin in the serum.<sup>[8]</sup> Hence the present study was undertaken with the objective of determining serum ferritin and thyroid hormone status among hypothyroid and euthyroid subjects and to correlate the same.

## **MATERIALS AND METHODS**

It was a cross-sectional study; conducted at RV Metropolis diagnostic & Healthcare Centre Private Limited Bangalore. In the present study, based on their TSH values 50 hypothyroid and 50 euthyroid subjects of age group between 25-60 years were included. Subject with TSH value  $<4.94\mu\text{IU/ml}$  was considered as euthyroid and TSH value  $\geq 4.94\mu\text{IU/ml}$  was considered as hypothyroid subjects. Study was conducted from March 2019- May 2019 for a period of 3 months. Written consent from the participants was taken. Before collecting the data, subjects were explained about the plan and intention of the study. Detailed information of the participants like age, family history, past medical history were noted. 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, subjects consuming drugs known to cause hypothyroidism were excluded from the study as they have effect on thyroid hormone and on ferritin level.

### **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 Microparticle Immunoassay (CMIA) technology. The normal range is  $0.25-4.94\mu\text{IU/ml}$ .<sup>[9]</sup>

**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  $4.5-12.6\mu\text{g/dl}$ .<sup>[9]</sup>

**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  $0.4-2.04\text{ng/ml}$ .<sup>[9]</sup>

**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.<sup>[9]</sup>

The collected data was entered in Microsoft excel and the data analyzed by using Epidata software. Descriptive statistics like mean, percentage, standard deviation and Inferential statistics such as chi square test, Independent t test were used. p value < 0.05 will be considered as statistically significant.

## RESULT

**Table 1:** Distribution of study subjects

Sex		Euthyroid	Hypothyroid	Total
Male	No	20	21	41
	%	40%	42%	41%
Female	No	30	29	57
	%	60%	58%	57%
Total	No	50	50	100
	%	100%	100%	100%

In the present study a total of 100 subjects were included, between the ages of 25-60 years. Amongst them 50 were euthyroid and 50 were hypothyroid subjects (**Table 1**).

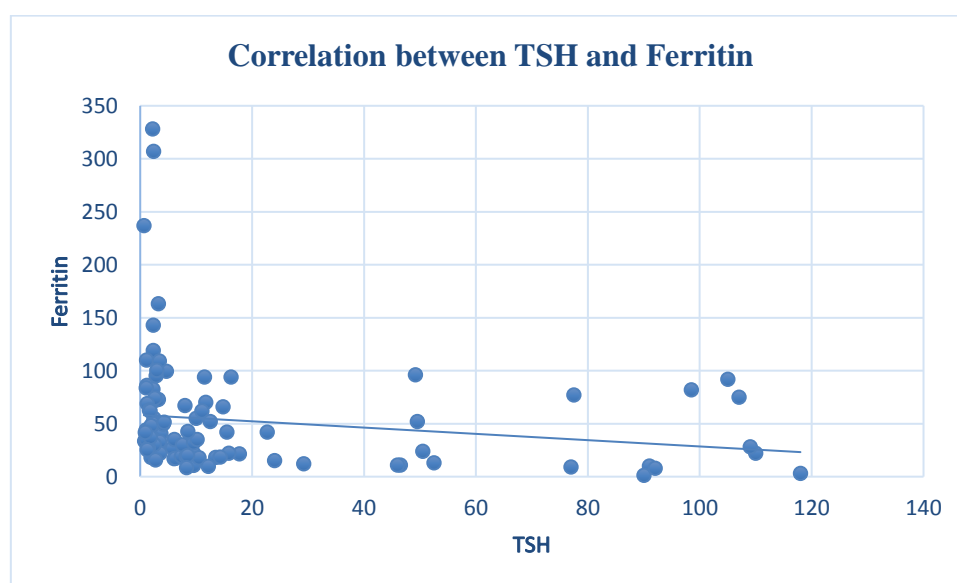
**Table 2:** Correlation of biochemical parameters among study population

TSH cutoff	Euthyroid Mean $\pm$ SD	Hypothyroid Mean $\pm$ SD	p value
<b>TSH</b> $\mu$ IU/ml	2.19 $\pm$ 0.992	33.66 $\pm$ 35.880	<0.001
<b>T4</b> $\mu$ g/dl	7.91 $\pm$ 1.920	2.60 $\pm$ 1.246	<0.001
<b>T3</b> ng/ml	1.06 $\pm$ 0.323	0.06 $\pm$ 0.233	<0.001
<b>Ferritin</b> ng/ml	71.13 $\pm$ 67.666	36.09 $\pm$ 28.004	<0.001

As seen in **Table 2**, mean values of TSH was 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 <0.001.

**Graph 1: Scatter diagram showing correlation between serum TSH and Ferritin among subjects**



As seen in **Graph 1**, there is a negative correlation between TSH and serum ferritin among study subjects ( $r=0.091$ ). As serum TSH levels were increasing serum ferritin levels were decreasing.

## 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 ( $71.13 \pm 67.67$ ng/ml) as compared to the mean value of serum ferritin among hypothyroid subjects ( $36.09 \pm 28.0$  ng/ml) and it was found to be statistically significant. 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.<sup>[10]</sup> 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.<sup>[11]</sup>

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. <sup>[12]</sup>

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.

### **LIMITATION**

Sample size of the present study was small. Though free T4 and free T3 are biological active hormone could not be used in the study.

### **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.

### **REFERENCES:**

- [1] Burtis C A, Ashwood E R, Bruns D E. Tietz Fundamentals of clinical chemistry. 6th ed. Salt lake city,Utah: Loren Wilson;2008.
- [2] Nancy S, Pillai, Jemela B. Prevalence of hypothyroidism amongst pregnant women: a study done in rural set up. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2018 Apr;7(4):1586-1591.
- [3] Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011;15:S78-S81.
- [4] Zimmermann MB and Kohrle J. The Impact of Iron and Selenium Deficiencies on Iodine and Thyroid metabolism: Biochemistry and Relevance to Public Health. N Eng J Med 2002; 12(10): 867-878.
- [5] Winter WE, Bazydlo LA, Harris NS (2014) The molecular biology of human iron metabolism. Lab Med 45: 92–102.
- [6] Granner DK. The diversity of the endocrine System, in RK. Murray, DK Granner, PA Mayes, & VW Rodwell (eds), Harper's Illustrated Biochemistry, 26th edn, McGraw-Hill, United States 2003; 434-455.

- [7] Takamatsu J, Majima M, Miki K, Kuma K, Mozai T. Serum ferritin as a marker of thyroid hormone action on peripheral tissues. *J Clin Endocrinol Metabol* 1985;61(4):672–6.
- [8] Akhter S, Nahar ZU, Parvin S, Alam A, Sharmin S, Arslan MI. Thyroid status in patients with low serum ferritin level. *Bangladesh J Med Biochem* 2012;5(1):5–11.
- [9] Abbott architect kit insert.
- [10] Arvind K, Mishra1, Rohit A, Shailendra P, Verma, Kamlesh K et al. Study of impact of subclinical hypothyroidism on iron status and hematological profile. *International Journal of Advances in Medicine*. 2018 Apr; 5(2): 446-451.
- [11] Ashuma S, Veena S, Isha M, Prasanta SR, Himanshu M, Rajesh N. Association between serum ferritin and thyroid hormone profile in hypothyroidism. *International Journal of Medical Science and Public Health*, 2015; 4(6) 863-865.
- [12] Kiran Dahiy, Monica Verma, Rakesh Dhankhar, Veena Singh Ghalaut, PS Ghalaut, Ashuma Sachdeva, et al. Thyroid profile and iron metabolism: mutual relationship in hypothyroidism. *Biomedical Research*, 2016; 27 (4): 1212-1215.

