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Ferritin and Thyroid stimulating hormone in subclinical hypothyroidism: A prospective study

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Abstract

Introduction: Subclinical hypothyroidism (SCH) is defined as having elevated thyroid-stimulating hormone (TSH), normal levels of thyroxine (T4) and triiodothyronine (T3), and little to no hypothyroidism symptoms or indicators. In essence, it is a laboratory-based diagnosis. Microcytic anemia coupled with hypothyroidism is related to iron deficiency arising from malabsorption and menorrhagia. The body's iron reserves are indicated by serum ferritin (SF). Based on these data, we decided to investigate serum ferritin levels and their relationship to TSH in individuals with subclinical hypothyroidism.

Materials and Methods: The study was carried out at AIMSR, Bathinda's Department of Biochemistry in partnership with the Department of Medicine. The study included 100 euthyroid controls and 100 cases of subclinical hypothyroidism.

Results: In this investigation, there was a noteworthy distinction (p=0.001) in the TSH levels in the patients (7.7 ± 1.9 uI/ml) and controls (2.3 ± 1.1 uI/ml). Serum ferritin levels in cases (9.3 ± 1.7 ng/dl) and controls (101±5.6 ng/dl) differed significantly (p=0.001). In the cases, there was a non-significant negative correlation (r = -0.09, p = 0.79) between serum ferritin and TSH.

Conclusion: The non-significant negative correlation between ferritin and TSH in subclinical hypothyroidism can be explained by several factors, such as the mild nature of thyroid dysfunction in subclinical hypothyroidism, the influence of inflammation and autoimmunity on ferritin levels, iron status variability and inflammatory markers across individuals, and study design limitations.

Keywords: Subclinical hypothyroidism, ferritin, inflammation

1. Introduction

Worldwide, thyroid disorders are common and impact about 42 million people in India. A prevalent thyroid condition, hypothyroidism, has been the focus of recent research conducted in India [1]. Subclinical hypothyroidism (SCH) is defined as having elevated thyroid-stimulating hormone (TSH), normal levels of thyroxine (T4) and triiodothyronine (T3), and little to no hypothyroidism symptoms or indicators. In essence, it is a diagnosis from a lab [2]. An estimated 9.4% of Indians are thought to have SCH [3]. Microcytic anemia coupled with hypothyroidism is

related to iron deficiency arising from malabsorption and menorrhagia. The body's iron reserves are indicated by serum ferritin (SF) [4]. Thyroid peroxidase (TPO), an iron-containing enzyme necessary for the synthesis of thyroid hormones, can become dysfunctional due to insufficient iron [5]. Based on these data, we decided to investigate serum ferritin levels and their relationship to TSH in individuals with subclinical hypothyroidism.

2. Materials and Methods

This study was carried out at the Adesh Institute of Medical Sciences and Research (AIMSR), Bathinda, a tertiary care teaching hospital in Punjab, India, in collaboration with the departments of medicine and biochemistry. The Institutional Ethical Committee gave its approval. (AE/EC_BHR/2K24/636)

Study design

This was intended to be a prospective observational study conducted in a hospital.

Data collection

Patients with subclinical hypothyroidism (SCH) who were admitted to the AIMSR hospital and exhibited a subclinical thyroid profile in their biochemistry reports were given ferritin tests. Subjects with subclinical hypothyroidism had their complete medical histories and clinical examinations recorded. CLAI performed quantitative measurements of serum ferritin, T3, T4, and TSH on SNIBE MAGLUMI. The usual range of TSH is 0.3-4.5 microIU/mL, T3 is 80-220 ng/dl, T4 is 5-12 microgm/dl, and SF is 30-400 ng/ml for males and 13-150 ng/ml for females, according to the manufacturer.

Sample size

The actual sample size was calculated based on the average prevalence rate of SCH (9%) by using Cochran's formula [3]:

Z^2 pq/e^2

Where Z is Z score (1.96), p is prevalence of subclinical hypothyroidism, q was (1-p), e was precision value.

The sample size came out to be 78, but it was increased to 100 to ensure adequate power and to draw significant conclusions.

Statistical Analysis

The mean, standard deviation, and percentage for categorical variables, as well as frequency, were determined using descriptive statistics. The correlation coefficient between variables was determined using Pearson's method. For every statistical outcome, a significance threshold of $p \leq 0.05$ was deemed appropriate.

Inclusion criteria

Subjects with normal thyroid levels and TSH levels between 4.5 to 10 microIU/mL were enrolled in the study.

Exclusion criteria

Individuals who satisfy specific requirements include those who have recently undergone a blood transfusion, have undergone a thyroidectomy in the past, are over 60 years of age, have familial hyperlipidemia, coagulation disorders, severe systemic disease, fever of any kind, systemic arterial hypertension, are smokers, have diabetes mellitus, have renal failure, have an underlying known cardiac disorder, are pregnant, have connective tissue disease, are taking medications known to cause hypothyroidism, and are taking an acute illness.

3. Results

The piece of enquiry was a prospective observational study undertaken in the Department of Biochemistry, Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India. A total of 100 SCH patients and 100 euthyroid controls were recruited for the study. Out of 100 SCH patients, 71 were female and 29 were male. In the control group, there were 66 females and 34 males. The range of age of the subjects was 10-59 years, with a mean age of 32 ±5.5 years. There was no statistically significant difference in gender and age between the two groups. The present study showed a highly significant difference ($p= 0.001$) in TSH levels between cases (7.7 ± 1.9 uI/ml) and controls (2.3±1.1 uI/ml). (Table 1 and Figure 1) T3 and T4 showed a non-significant difference in cases and controls. A significant difference ($p=0.001$) in serum ferritin levels was seen in cases and controls. TSH and serum ferritin levels showed a negative, non-significant correlation in levels in the cases compared to controls ($p=0.79$). (Table 2 and Figure 2)

Table 1. Biochemical parameters in the cases of subclinical hypothyroidism

Variable	Cases	Controls	p value
TSH (uI/ml)	7.7 ±1.9	2.3 ± 1.1	0.001**
T3 (ng/dl)	1.5 ±1.7	1.6 ± 0.2	0.45
T4 (ug/dl)	8.2 ±1.7	9.5 ± 1.8	0.46
Ferritin (ng/dl)	9.3 ± 1.7	101.2 ± 56.0	0.001**

p>0.05 indicates no significant correlation

p<0.05 indicates significant correlation,

**p<0.001 indicates Highly significant correlation.

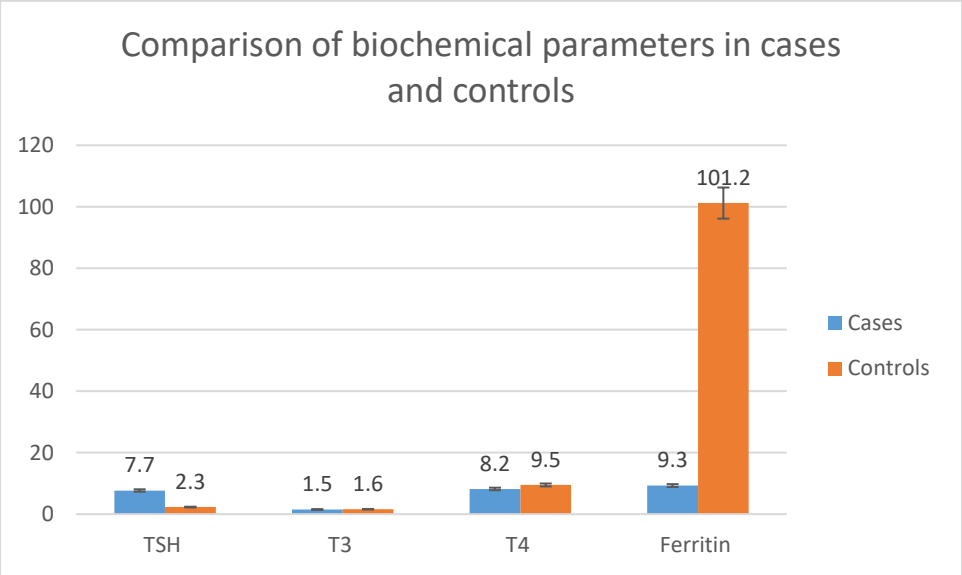


Figure 1 . Comparison of biochemical parameters in cases and controls

Table 2. Correlation of TSH and Ferritin in the cases of subclinical hypothyroidism

Variable	Cases	r value	p value
TSH (uI/ml)	7.7 ±1.9	-0.09	0.79 *
Ferritin (ng/dl)	9.3 ± 1.7		

*p>0.05 indicates no significant correlation

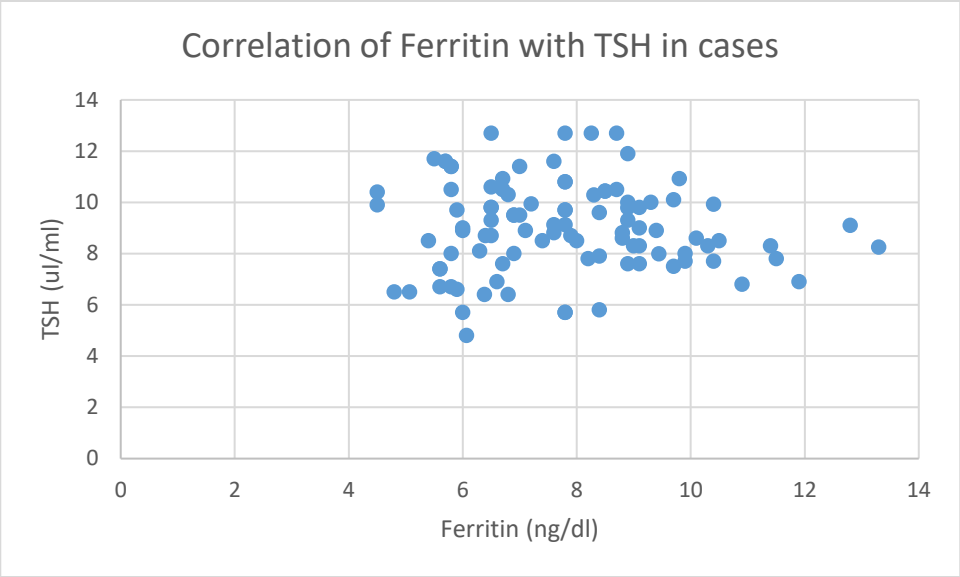


Figure 2. correlation of TSH and serum ferritin in cases

4. Discussion

The TSH levels in patients (7.7 ± 1.9 uI/ml) were significantly higher (p=0.001) compared to controls (2.3 ± 1.1 uI/ml) in the current study (Table 1 and Figure 1). Between the patients and controls, T3 and T4 did not indicate a significant difference. Serum ferritin levels in patients were significantly lower than those in controls (p=0.001). Patients with thyroid illness may have changes in serum ferritin, an indicator of iron stores, as a result of iron loss from menorrhagia and malabsorption brought on by hypothyroidism [7, 8] .

Studies have revealed the role of thyroid hormones in the regulation of ferritin expression. Thyroid hormone binding elements are documented upstream of the ferritin gene, and the binding of thyroid hormones to these elements enhances ferritin synthesis. One possible explanation for iron deficiency anemia in hypothyroidism could be due to less ferritin synthesis. Because ferritin is an iron storage protein, low levels of ferritin decrease iron storage in the body [9].

In a retrospective study, A. K. Mishra et al. (2018) discovered that SCH patients had significantly lower mean hemoglobin, serum ferritin, and red blood cell indices than the euthyroid group, which supported our study. In India, hypothyroidism and other diseases can exacerbate anemia, which is a public health concern. [10] They recommended early detection of anemia in SCH in order to facilitate its early management [11].

Similar findings were reported by Swapnil TG et al. [12] and D Shiva Krishna et al. [13].

TPO activity is significantly reduced due to iron deficiency, as iron is a component of TPO. There is a reduction in the incorporation of iodine into thyroglobulin and coupling of iodothyronine to form thyroid hormones as a result of decreased TPO activity. [11] As a result, there is a common picture of iron deficiency (serum ferritin as a marker for iron stores) and hypothyroidism. A study by Akhter et al. shows that there is a considerable variation in thyroid hormone status in persons with iron shortage. The disruptions in iron-dependent enzymes, such as TPO, influence the overall metabolism of thyroid hormones [14].

A non-significant negative correlation (r = -0.09, p= 0.79) was observed between TSH and SF in the cases. (Table 2and Figure 2). In the present study, out of total of 100 cases, 52 had SF levels below the reference range. And out of 52 cases of hypoferritinemia, 38 were female. Our findings are comparable to that reported by Farooq MS et al. [15] who also reported a statistically insignificant negative correlation between serum ferritin and TSH.

The non-significant negative correlation between ferritin and TSH in subclinical hypothyroidism can be explained by several factors: Firstly, Subclinical hypothyroidism is characterized by mildly elevated TSH with normal thyroid hormone levels (FT3, FT4).

Elevated TSH and normal T3 and T4 are the hallmarks of subclinical hypothyroidism. [2] This mild dysfunction may not strongly impact ferritin metabolism or iron status, leading to weaker correlations. Secondly, ferritin levels are influenced by inflammation and autoimmunity. Anti-TPO positivity in hypothyroidism can elevate ferritin levels independently of TSH levels, masking any direct correlation. Hashimoto's thyroiditis, or chronic autoimmune thyroiditis, is the main cause of SCH. It is specifically associated with anti-TPO antibodies. It is characterized by inflammation and thyroid gland destruction brought on by antibodies directed against the individual's own thyroid gland [7]. Ferritin is a well-known indicator of inflammation that is secreted from injured cells. Untreated chronic inflammation can harm the thyroid gland and result in hypothyroidism. Systemic organ damage and clinical symptoms of hypothyroidism are significantly influenced by chronic inflammation [6]. A number of studies suggest that iron deficiency, thyroid dysfunction, and autoimmunity may be related, particularly in certain patient populations. [15,16] Ferritin concentration in SCH is influenced by an individual's level of inflammation. Ferritin concentrations were lower in anti-TPO negative hypothyroidism but higher in anti-TPO positive cases, according to another study [17].

Thirdly, ferritin reflects iron stores but is also an acute-phase reactant. Variability in iron status and inflammatory markers across individuals may dilute the correlation between ferritin and TSH [6, 7, 8]. Lastly, differences in sample size, population characteristics, and methodology across studies can contribute to inconsistent findings.

The lack of significant relationship between ferritin and TSH levels in hypothyroidism may be due to different regulatory mechanisms for iron metabolism and thyroid function. More research is needed to fully understand the relationship between subclinical hypothyroidism and ferritin levels. The impact of inflammation on SF may have an impact on iron status and thyroid function. Iron indicators are difficult to interpret when inflammation is present, especially serum ferritin. Actually, a number of pro-inflammatory cytokines boost serum ferritin synthesis, which raises iron uptake in cells as a result. Thus, when iron deficiency is present, inflammation lowers ferritin's predictive values [18].

5. Conclusion

Ferritin levels were significantly decreased in subclinical hypothyroid patients. Thyroid hormones can influence ferritin expression. The non-significant negative correlation between ferritin and TSH in subclinical hypothyroidism can be explained by several factors like mild nature of thyroid dysfunction in subclinical hypothyroidism, inflammation and autoimmunity affecting ferritin levels, iron status variability and inflammatory markers across individuals, and study design limitations.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Author's contributions

All authors equally contributed to preparing this article.

Conflict of interest

Authors declare no conflict of interest.

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