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ASSOCIATION BETWEEN SERUM FERRITIN AND THYROID HORMONE PROFILE IN HYPOTHYROIDISM IN PAKISTANI POPULATION

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Abstract

Objective: *To determine the association between serum ferritin levels and thyroid hormone profile (TSH, fT3, fT4) among patients with hypothyroidism*

Study Design: *Analytical Cross-sectional Study*

Place and Duration of Study: *Department of Internal (General) Medicine, Pak Emirates Military Hospital, Rawalpindi, from November 2024 to April 2025.*

Methodology: *Adults between 18 and 65 years of age, with newly diagnosed or untreated hypothyroidism were included. Patients who had chronic liver or kidney disease, acute or chronic infection or on drugs that alter thyroid function (lithium, steroids) were excluded. Demographic information (gender and age) and relevant clinical history, including comorbid conditions and previous therapy, were recorded using a structured proforma. A 5 mL fasting venous blood sample was drawn for serum TSH, free triiodothyronine, free thyroxine, and serum ferritin were measured using the chemiluminescence immunoassay technique.*

Results: *Among the ninety patients, the majority, 59 (65.56%) were females. The included patients had a mean age of 42.76±11.63 years, median ferritin levels were 84.00 (32.75-147.00) ng/ml, and the median TSH was 7.10 (5.60-13.10) IU/l. Serum TSH and Serum ferritin showed a statistically significant negative correlation (r= -0.589, p<0.001). Free T4 had an insignificant negative correlation (r= -0.133, p=0.211). However, there was positive correlation between serum ferritin and free T3 (r=0.255, 0=p=0.025). Additionally, strong positive correlation was observed between cardiovascular disease and serum TSH (p<0.001).*

Conclusion: *Serum ferritin was significantly correlated with serum thyroid-stimulating hormone and serum free tri-iodothyronine.*

Introduction

Hypothyroidism is among the most common endocrine disorders affecting people worldwide and is particularly prevalent in South Asian populations like Pakistan, with 4.1% for hypothyroidism and 5.1% for hyperthyroidism.[1,2] Hypothyroidism refers to reduced levels of thyroid hormones (T3 and T4) with a rise in thyroid-stimulating hormone (TSH) via a negative feedback mechanism. These are metabolically active hormones as they directly

Frontier in Medical & Health Research

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regulate the body's metabolic rate, thrombogenesis, and blood pressure.[3, 4]

Researchers have found different electrolyte and minerals abnormalities such potassium, calcium, sodium and phosphorus.[5, 6] Similarly, growing evidence suggests a strong biochemical link between iron metabolism (reflected by serum ferritin) and thyroid function. Ferritin, a major iron-storage protein, is essential for the activity of thyroid peroxidase. A strong negative correlation was seen between serum ferritin levels and TSH levels (r = −0.855). Similarly, a comparatively weaker positive correlation was observed for free T3 (r = 0.488). For free T4, a similar trend was seen (r= 0.366).[7] In coherence, hypothyroidism was found to be associated with decreased ferritin levels (p<0.0001).[8] These studies show significantly lower serum ferritin levels in hypothyroid patients and an inverse correlation between ferritin and TSH levels.[7, 8] In another study by Chatterjee *et al.*, there was a negative correlation between serum TSH and ferritin (r=-0.343); however, a statistically insignificant correlation was found between serum TSH and iron (p=0.057).[9]

Despite the high burden of hypothyroidism, nutritional deficiencies, and anemia in Pakistan, local evidence on ferritin and thyroid hormone relationships is scarce. Understanding this association will improve diagnostic accuracy, guide supplementation strategies, and help clinicians differentiate iron deficiency-related thyroid hormone dysfunction from inherent thyroid gland and its feedback pathway-related pathologies.

Methodology:

This analytical cross-sectional study was conducted at Department of Internal (General) Medicine, Pak Emirates Military Hospital, Rawalpindi, Pakistan from November 2024 to April 2025. The study was conducted in accordance with the principles laid down by the Declaration of Helsinki and local guidelines for human research. The sample size was calculated using the WHO sample size calculator, with an expected correlation (r = –0.34) between ferritin and TSH, a 95% confidence level, 80% power, and a target sample size of 90 patients.[7] A non-probability consecutive sampling technique was used to enrol patients after informed consent. Patient anonymity was maintained at all levels, from data collection to laboratory investigations and data synthesis.

Inclusion Criteria: Adults between 18 and 65 years of age, both males and females, with newly diagnosed or untreated hypothyroidism (TSH > 4.5 mIU/L and low free T4 < 7 pmol/L) were included in this research.

Exclusion Criteria: Patients who had chronic liver or kidney disease, acute or chronic infection or on drugs that alter thyroid function (lithium, steroids) were excluded. Moreover, pregnant females and patients who are known to have haematological disorders like hemochromatosis, thalassemia, HLH, acute/ chronic myeloid leukaemia were excluded. Patients receiving iron therapy, multivitamins, or nutritional supplements were also excluded.

The relevant data for this study were gathered prospectively over 6 months at the outdoor and indoor patient departments. All patients presenting with hypothyroidism were assessed for eligibility, and those who met the criteria and provided informed consent were enrolled. Demographic information (gender and age) and relevant clinical history, including comorbid conditions and previous therapy, were recorded using a structured proforma. A 5 mL fasting venous blood sample was drawn under aseptic conditions. The collected blood was allowed to clot, and serum was separated for laboratory analysis. Serum levels of TSH, free triiodothyronine (fT3), free thyroxine (fT4), and serum ferritin were measured using the chemiluminescence immunoassay technique. Serum ferritin was the primary variable in this study to assess its association with thyroid hormone levels. Patients were labelled hypothyroid if serum TSH > 4.5 mIU/L and low free T4 < 7 pmol/L. Similarly, the ferritin was considered low <30 ng/mL.

Data was entered into the Statistical Package for Social Sciences (SPSS) version 25. Numerical variables, such as age, TSH levels, fT4, fT3, haemoglobin, and serum ferritin, were represented as mean ± standard deviation (SD) or median (interquartile range). Categorical variables, such as gender and the presence of comorbid conditions, were presented as frequencies and percentages. The

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Shapiro-Wilk test was used to check the normality of data. The Chi-square test or Fisher's exact test was used for the categorical variables (gender and comorbid conditions). Spearman's and Pearson's correlations, as appropriate, were used to assess the relationship between serum ferritin and the thyroid profile (TSH, fT4, and fT3). Stratification of the data was performed by age, gender, and Hb to adjust for potential confounders. A p-value < 0.05 was considered significant.

Characteristics	Descriptive Statistics
Age, years	42.76±11.63
Gender, n (%)	
Male	59 (65.56%)
Female	31 (34.44%)
Median Duration of Illness, months	5.00 (3.00-8.25)
Hypertension, n (%)	
Yes	30 (33.33%)
No	60 (66.67%)
Diabetes mellitus, n (%)	
Yes	26 (29.89%)
No	64 (71.11%)
Cardiovascular Disease, n (%)	
Yes	20 (22.22%)
No	70 (77.78%)
Median TSH, IU/l	7.10 (5.60-13.10)
Median Ferritin, ng/ml	84.00 (32.75-147.00)
Median Free T3, pmol/l	1.85 (1.20-2.60)
Median Free T4, pmol/l	4.80 (3.50-6.35)

RESULTS

A total of 103 patients were enrolled in the study. Out of these, 7 were found to have subclinical hypothyroidism, 2 patients were lost to follow-up, and 1 patient refused to participate in the study as he was already enrolled in another research project. Among the ninety (n=90), the majority of patients, 59 (65.56%) were females, and 31 (34.44%) were males. The included patients had a mean age of 42.76±11.63 years, and a median illness duration of 5.00 (3.00-8.25) months. The median ferritin levels were 84.00 (32.75-147.00) ng/ml, and the median TSH was 7.10 (5.60-13.10) IU/l, as shown in Table-I with other parameters.

Table-I: Baseline and biochemical parameters of the included population (n=90)

TSH: Thyroid stimulating hormone, T3: Triiodothyronine, T4: Thyroxine

Serum TSH and Serum ferritin showed a statistically significant negative correlation (r= -0.589, p<0.001). Similarly, free T4 had a negative correlation (r= -0.133, p=0.211). However, there was positive correlation between serum ferritin and free T3 (r=0.255, 0=p=0.025). A strong positive correlation was observed between cardiovascular disease and serum TSH (p<0.001). Details are shown in Table-II.

Table-II: Spearman's correlation between thyroid profile and serum ferritin (n=90

Variable	Correlation coefficient (r)	p-value
TSH	-0.589	<0.001
T3	0.255	0.015
T4	0.133	0.211
Hb	0.505	<0.001

Frontier in Medical & Health Research

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TSH: Thyroid stimulating hormone, T3: Triiodothyronine; T4: Thyroxine

DISCUSSION

Hypothyroidism has long been recognized as influencing multiple aspects of iron metabolism through reduced erythropoietin production, impaired intestinal iron absorption, diminished gastric acid secretion, and altered iron utilization. The present study investigated the association between serum ferritin and thyroid hormone profile among patients with overt hypothyroidism. The principal findings demonstrate a significant inverse association (r = -0.589) between serum ferritin concentrations and serum TSH, and a modest positive correlation (r = 0.255) between serum ferritin concentrations and free T3 concentrations. No statistically significant association (p = 0.211) was observed between serum ferritin and free T4 levels. Collectively, these findings suggest TSH concentrations are associated with declining body iron stores and support the growing evidence of an interaction between thyroid hormone homeostasis and iron metabolism. In addition, we observed, serum TSH and serum ferritin levels were strongly correlated (r = 0.442, p<0.001) and (r = 0.457, p<0.001) with cardiovascular diseases. Again, highlighting the metabolic role of thyroid hormones and iron metabolism in cardiovascular health and morbidity.

The inverse relationship between serum ferritin and TSH observed in the present study is consistent with several previous investigations. Studies conducted in patients with overt and subclinical hypothyroidism have demonstrated significantly lower ferritin concentrations compared with euthyroid controls and have reported that ferritin levels tend to decrease with increasing TSH concentrations.[10, 11] A study by Shukla et al. found that iron status was significantly associated with thyroid hormone levels, especially in hypothyroid individuals.[12] In Iraqi females suffering from hypothyroidism, ferritin, total iron binding capacity, and haemoglobin showed a statistically significant decline.[13] A case-control study conducted by Akhter et al. in Bangladesh found a significant correlation between serum ferritin and serum TSH; however, the same was not observed among cases.[14] Irrespective of significance, the correlation was negative in both groups. Serum free T3 and T4 showed a statistically non-significant positive correlation. In contrast to our study, in which a significant positive correlation was observed between serum ferritin and serum free T3, no association was observed with serum free T4. In coherence, serum TSH showed a strong negative association with serum ferritin (P<0.001). These observations support the hypothesis that hypothyroidism adversely affects iron homeostasis through impaired gastrointestinal iron absorption, decreased metabolic activity, and reduced erythropoietic stimulation.[15, 16] Furthermore, normalization of thyroid function following levothyroxine replacement has been shown to improve iron metabolism in several longitudinal studies, suggesting that thyroid dysfunction itself contributes substantially to alterations in ferritin concentrations rather than representing an incidental association.[15] The difference in findings may be due to different patient demographics, comorbid conditions and racial differences.

Serum TSH has been found to be positively correlated with cardiovascular disease, suggesting that the higher the serum TSH, the higher the risk of cardiovascular-related events, morbidity and mortality. Several studies have supported this finding. Thyroid dysfunction increases the risk of cardiovascular diseases, including heart failure, coronary heart disease, and atrial fibrillation.[17-19] They impair heart function and alter cardiovascular risk factors like atherosclerosis, hypertension, and dyslipidaemia, contributing to the risk of stroke associated with atrial fibrillation.[17] Similarly, serum ferritin and haemoglobin showed a positive correlation, underscoring the role of iron stores in erythropoiesis. A study by Nabeela et al., found a positive correlation between serum ferritin and haemoglobin.[20] The clinical implications of our findings are noteworthy. Routine assessment of serum ferritin in patients with newly diagnosed hypothyroidism may facilitate early identification of concomitant iron deficiency, particularly among women and individuals with persistent symptoms despite appropriate therapy. Correction of iron deficiency has the potential to improve haematological status,

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optimize thyroid hormone metabolism, and enhance responsiveness to thyroid hormone replacement. Therefore, integrated evaluation of thyroid function and iron status may represent a practical approach to improving patient outcomes.

LIMITATIONS OF STUDY

The present study has several strengths. It prospectively evaluated a well-defined cohort of patients with overt hypothyroidism using standardized biochemical measurements and demonstrated consistent associations between serum ferritin and multiple thyroid function parameters. The exclusion of patients with subclinical hypothyroidism and incomplete follow-up minimized heterogeneity and enhanced the internal validity of the study population. Nevertheless, certain limitations should be acknowledged. The cross-sectional design precludes establishing a causal relationship between thyroid dysfunction and reduced ferritin concentrations. The study was conducted at a single tertiary care center with a relatively modest sample size, which may limit the generalizability of the findings to other populations. Furthermore, additional biomarkers of iron metabolism, including serum iron, transferrin saturation, total iron-binding capacity, hepcidin, vitamin B12, and inflammatory markers such as C-reactive protein, were not measured and could have provided a more comprehensive assessment of iron homeostasis. Future multicentre longitudinal studies incorporating these biomarkers may clarify the causal relationship between thyroid and iron metabolism. These studies might determine whether correction of iron deficiency favourably influences thyroid function and clinical outcomes.

CONCLUSION

In conclusion, our findings demonstrated a significant inverse relationship between serum ferritin and TSH concentrations, together with a positive association between ferritin and free T3 levels among patients with hypothyroidism. These results support the physiological interaction between thyroid function and iron metabolism.

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