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RESEARCH ARTICLE

Association Between Serum Ferritin Levels and Thyroid Function Parameters: A Cross-Sectional Observational Study

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Abstract: ***Background***: Iron deficiency and thyroid dysfunction are common endocrine disorders with possible interrelationships. This study aimed to evaluate the association between serum ferritin levels and thyroid function parameters. ***Methods***: A cross-sectional observational study was conducted among individuals aged 18–63 years. Baseline characteristics including age, BMI, blood pressure, serum iron, total iron-binding capacity (TIBC), thyroid hormones (TSH, T3, T4), and Anti-TPO antibodies were recorded. Comparisons between males and females were made using independent t-tests. Associations between ferritin status (normal vs. deficient) and thyroid function markers were assessed using Chi-square tests. Correlations between continuous ferritin levels and thyroid parameters were analyzed using Pearson's correlation. ***Results***: The study found no statistically significant difference in BMI ($p = 0.537$) or systolic blood pressure ($p = 0.369$) between genders. Ferritin status was not significantly associated with TSH ($p = 1.000$), T3 ($p = 0.871$), T4 ($p = 0.407$), or Anti-TPO antibody levels ($p = 1.000$). Correlation analyses showed no significant relationship between serum ferritin and thyroid function parameters. ***Conclusion***: In this cross-sectional study, no significant association was observed between serum ferritin levels and thyroid function markers. These findings suggest that variations in ferritin status may not influence thyroid hormone profiles in the studied population.

Keywords: Serum Ferritin, Thyroid Function, Iron Deficiency, Endocrine Disorders, Correlation Analysis

INTRODUCTION

Iron is an essential micronutrient involved in a wide array of physiological processes, including oxygen transport, enzymatic reactions, and cellular metabolism (1). Ferritin, the primary intracellular iron storage protein, serves as a reliable marker of the body's iron reserves (2). Deficiency in iron, even in the absence of overt anemia, has been associated with systemic effects, including impaired immune function, cognitive disturbances, and metabolic dysregulation (3).

The thyroid gland is another critical regulator of metabolism. Thyroid hormone synthesis requires iron as a cofactor for thyroid peroxidase, the enzyme responsible for iodination and coupling of thyroglobulin to form T3 and T4 hormones (4). Consequently, iron deficiency has the potential to impair thyroid function, leading to subclinical or overt hypothyroidism. Several studies have suggested an association between iron deficiency and altered thyroid hormone profiles, particularly in vulnerable populations such as pregnant women and adolescents (5,6). However, the evidence remains inconsistent, with some studies failing to establish a clear link (7).

Given the overlapping prevalence of iron deficiency and thyroid dysfunction globally, especially in developing regions, there is a growing interest in understanding whether ferritin levels are predictive of thyroid status. An improved understanding of this association could aid in better diagnostic and therapeutic strategies for individuals at risk of dual deficiencies.

The present cross-sectional observational study was undertaken to investigate the association between serum ferritin levels and thyroid function parameters, including TSH, T3, T4, and Anti-TPO antibodies, in a South Indian population.

The primary objective of this study was to assess the association between serum ferritin levels and thyroid function parameters, including thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and anti-thyroid peroxidase (Anti-TPO) antibodies, in the study population. Secondary objectives included comparing body mass index (BMI) and systolic blood pressure between males and females, and evaluating the correlation between continuous serum ferritin levels and thyroid function markers. The prespecified null hypothesis (H_0) was that there is no significant association between serum ferritin levels and thyroid function parameters. The alternative hypothesis (H_1) proposed that a significant association exists between serum ferritin levels and thyroid function markers.

MATERIALS AND METHODS

This study was designed as a cross-sectional observational study conducted to evaluate the association between serum ferritin levels and thyroid function parameters. Data were collected at a single point in time without any interventions or follow-up, ensuring the observational nature of the research.

The study was conducted at Saveetha Medical College and Hospital, Tamil Nadu, India. Data collection took place over a defined period from January 2023 to

December 2023. The setting included outpatient and inpatient departments where routine biochemical investigations, including thyroid function tests and iron studies, were performed as part of clinical evaluation.

Participants included individuals aged between 18 and 63 years who underwent evaluation of thyroid function and serum ferritin levels. Eligibility criteria included adults with available data on serum ferritin, thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and anti-thyroid peroxidase (Anti-TPO) antibody levels. Exclusion criteria included individuals with a known history of chronic inflammatory diseases, recent infections, malignancies, liver disorders, or those on iron or thyroid supplementation therapy. Participants were selected retrospectively from the hospital's laboratory database based on the availability of complete biochemical and clinical parameters.

The primary variables assessed in the study included serum ferritin levels as the exposure variable and thyroid function parameters (TSH, T3, T4, and Anti-TPO antibodies) as outcome variables. Serum ferritin was categorized into normal and deficient groups based on standard laboratory cutoffs. Thyroid function was categorized into normal and abnormal based on institutional reference ranges: elevated TSH, decreased T3, decreased T4, and elevated Anti-TPO antibody levels were considered indicators of thyroid dysfunction. Additional variables included body mass index (BMI), systolic and diastolic blood pressure, serum cholesterol, serum iron, total iron-binding capacity (TIBC), mean corpuscular volume (MCV), fasting blood sugar, urea, and total bilirubin. Potential confounders such as age, gender, and BMI were recorded to assess their influence on the outcomes. Standard diagnostic criteria were used for all laboratory measurements following institutional protocols.

Data for this study were obtained retrospectively from the hospital's electronic laboratory database. For each participant, serum ferritin levels, thyroid function parameters (TSH, T3, T4, Anti-TPO antibodies), and other biochemical markers such as serum iron, total iron-binding capacity (TIBC), fasting blood sugar, cholesterol, urea, and total bilirubin were recorded. Anthropometric measurements including weight, height, and body mass index (BMI) were retrieved from clinical records. Blood pressure readings were recorded using a standardized mercury sphygmomanometer. All biochemical parameters were measured using standardized automated analyzers following internal quality control procedures. Assessment methods were consistent across all participants, ensuring comparability between groups.

To minimize selection bias, all participants who met the inclusion and exclusion criteria within the specified period were included without any further selection based on clinical outcomes. Measurement bias was reduced by using standardized laboratory assays and routine hospital protocols for all tests. Additionally, data extraction was performed by independent reviewers to reduce information bias.

To determine the appropriate sample size for detecting associations between serum ferritin levels and thyroid parameters, several key statistical considerations were accounted for. The calculation was based on an expected difference in the proportion of thyroid dysfunction between two groups—those with high ferritin levels and those with normal ferritin levels. Specifically, the proportion of thyroid dysfunction was anticipated to be 30% ($P_1 = 0.30$) in the high-ferritin group and 10% ($P_2 = 0.10$) in the normal-ferritin group. The desired statistical power was set at 80%, corresponding to a $Z\beta$ value of 0.84, with a significance level (α) of 0.05 ($Z\alpha = 1.96$). Assuming equal group sizes (1:1 ratio), the estimated minimum required sample size was approximately 132 participants per group. Accounting for an expected attrition rate of 15%, the total sample size was rounded to 150 participants to ensure adequate power and validity of the study findings.

Quantitative variables such as serum ferritin, TSH, T3, T4, Anti-TPO, BMI, and blood pressure were initially treated as continuous variables. For specific subgroup analyses, serum ferritin levels were categorized into normal and deficient groups based on established laboratory reference ranges. Thyroid function parameters were categorized as normal or abnormal according to institutional cutoffs. Groupings were chosen to facilitate Chi-square tests and subgroup comparisons while maintaining clinical relevance.

All statistical analyses were performed using SPSS version 23.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation. Independent t-tests were used to compare continuous variables (such as BMI and systolic blood pressure) between males and females. Categorical variables were compared using the Chi-square test to assess associations between ferritin status (normal vs. deficient) and thyroid function parameters (normal vs. abnormal TSH, T3, T4, and Anti-TPO levels).

Pearson or Spearman correlation coefficients were used to evaluate the relationship between continuous serum ferritin levels and thyroid function markers, depending on the normality of the data distribution. Missing data were excluded from the analysis using listwise deletion, as the missing values were minimal and random. No sampling strategy adjustments were required, and no sensitivity analyses were performed as the study primarily aimed to explore potential associations without subgroup stratification beyond gender and ferritin status.

RESULTS

A total of 150 individuals were initially screened for eligibility based on the availability of ferritin and thyroid

function data. After applying the inclusion and exclusion criteria, 136 participants were confirmed eligible and included in the final analysis. Fourteen participants were excluded: eight due to incomplete thyroid profile or ferritin data and six due to a documented history of chronic inflammatory or autoimmune conditions. Since the study was cross-sectional, there was no follow-up period. Missing data for key variables were minimal (less than 5%) and were handled by listwise deletion during statistical analysis.

Table-1

Parameters	Mean	SD	Min	Max
Age	41.73	13.5	18	63
BMI	26.3417	4.3	18.62	34.54
Blood_Pressure_Systolic	127.39	15.3	100	159
Blood_Pressure_Diastolic	80.68	12.2	60	99
Cholesterol_Level	198.636	29.6	153.1	249.8
Outcome_Variable	0.46	0.5	0	1
Serum_Ferritin	147.873	86.4	13.1	293.1
Serum_Iron	114.385	36.3	51.3	179.2
TIBC	324.329	80.4	203.5	449.6
TSH	2.7928	1.4	0.41	4.91
T3	1.4396	0.5	0.62	2.47
T4	8.3853	2.3	4.6	11.89
Anti_TPO	45.33	28.0	0.1	99.3
MCV	90.075	5.6	80.1	99.3
Total_Leucocyte_Count	7162.33	2020.0	4006	10926
Urea	30.97	11.7	10.4	49.3
Total_Bilirubin	0.8603	0.4	0.22	1.49
Fasting_Blood_Sugar	104.009	20.1	70.1	138.4

Table 1 presents the baseline characteristics of the study population, including various biochemical and clinical parameters. The mean age of the participants was 41.73 ± 13.5 years, with a minimum of 18 years and a maximum of 63 years. The average BMI was 26.34 ± 4.3, ranging from 18.62 to 34.54. Regarding blood pressure, the mean systolic blood pressure was 127.39 ± 15.3 mmHg, while the diastolic blood pressure was 80.68 ± 12.2 mmHg. The mean cholesterol level was recorded at 198.64 ± 29.6 mg/dL. Serum iron levels averaged 114.39 ± 36.3 µg/dL, with total iron-binding capacity (TIBC) at 324.33 ± 80.4 µg/dL.

Thyroid function markers showed a mean TSH level of 2.79 ± 1.4 µIU/mL, T3 at 1.44 ± 0.5 ng/mL, and T4 at 8.39 ± 2.3 µg/dL. The Anti-TPO antibody levels varied significantly, with a mean of 45.33 ± 28.0 IU/mL. Mean corpuscular volume (MCV) was 90.08 ± 5.6 fL.

Hematological and metabolic parameters included a mean total leukocyte count of 7162.33 ± 2020.0 cells/mm³, urea at 30.97 ± 11.7 mg/dL, and total bilirubin at 0.86 ± 0.4 mg/dL. The fasting blood sugar levels averaged 104.01 ± 20.1 mg/dL, indicating variability within the study population.

Figure- 1

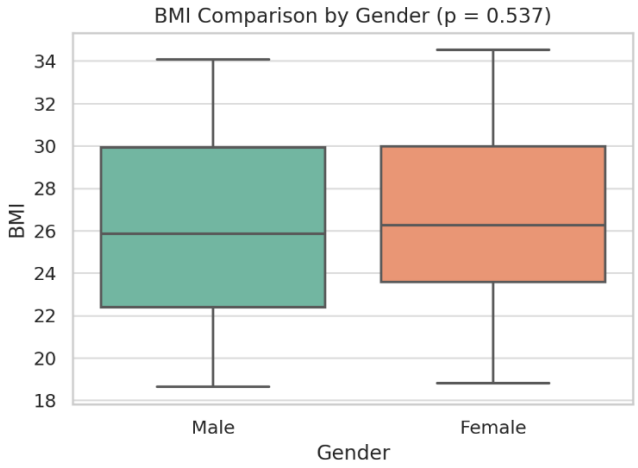


Figure 1 presents a box plot comparison of Body Mass Index (BMI) between males and females. The median BMI values appear similar between the two groups, with a slight variation in interquartile ranges. The whiskers indicate the range of BMI values, showing that both genders exhibit a comparable spread.

A statistical comparison using an independent t-test yielded a p-value of 0.537, suggesting that there is no significant difference in BMI between males and females in the study population. These findings indicate that gender does not appear to be a determining factor in BMI distribution within this cohort.

Figure-2

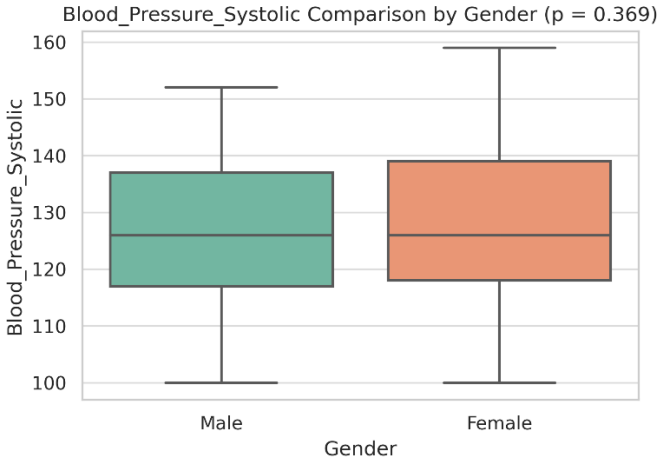


Figure 2 illustrates the comparison of systolic blood pressure between males and females using a box plot. The median systolic blood pressure appears similar between the two groups, with both exhibiting a comparable interquartile range and whisker distribution.

A statistical analysis using an independent t-test yielded a p-value of 0.369, indicating that there is no significant difference in systolic blood pressure between males and females in the study population. These findings suggest that gender does not have a substantial impact on systolic blood pressure levels in this cohort.

Figure- 3

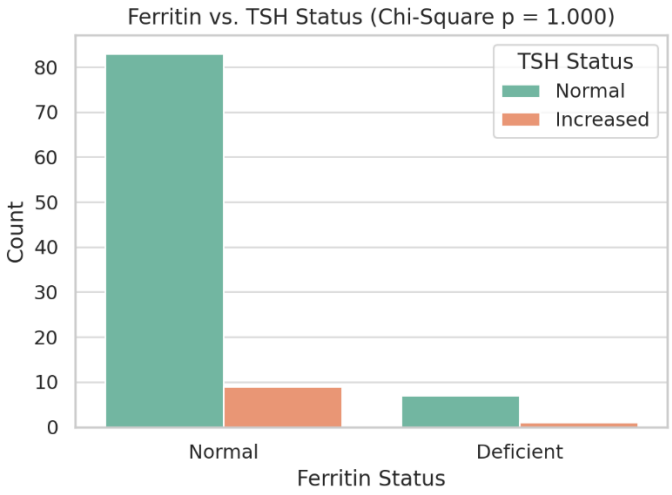


Figure 3 illustrates the distribution of TSH status (Normal vs. Increased) across different ferritin status groups (Normal vs. Deficient). The majority of individuals in both ferritin status groups had normal TSH levels, with only a small proportion exhibiting increased TSH.

A Chi-square test was performed to assess the association between ferritin status and TSH status, yielding a p-value of 1.000, indicating no statistically significant association between these variables. This suggests that variations in ferritin levels do not appear to influence TSH status in this study population.

Figure 4 illustrates the distribution of T3 status (Normal vs. Decreased) across different ferritin status groups (Normal vs. Deficient). Among individuals with normal ferritin levels, the majority exhibited decreased T3 levels (n = 72), while only n = 20 had normal T3 levels. Similarly, in the ferritin-deficient group, most individuals had decreased T3 levels (n = 7), with only n = 1 showing normal T3 levels.

A Chi-square test was conducted to assess the association between ferritin status and T3 status, yielding a p-value of 0.871, indicating no statistically significant relationship between these variables. This suggests that ferritin levels do not significantly influence T3 status within the study population.

Figure- 4

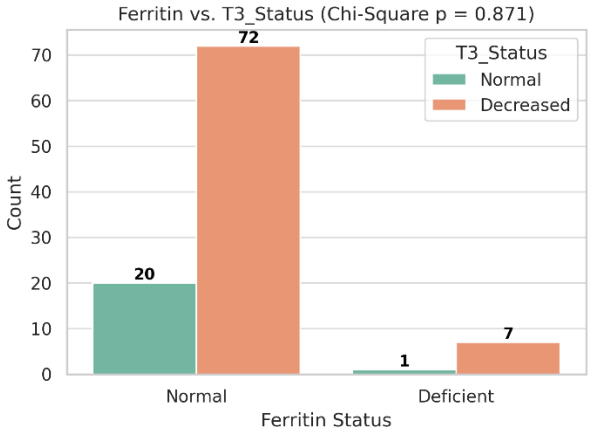


Figure- 5

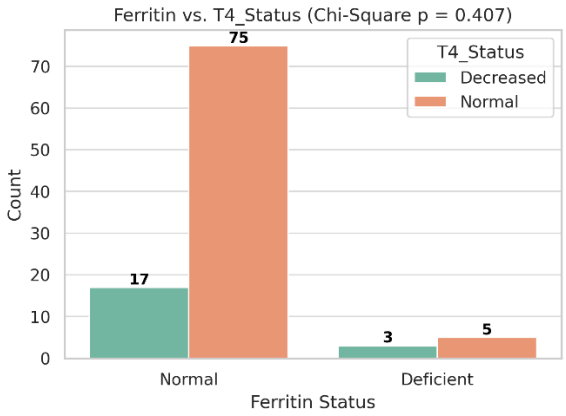


Figure 5 presents the distribution of T4 status (Normal vs. Decreased) across different ferritin status groups (Normal vs. Deficient). Among individuals with normal ferritin levels, n = 75 exhibited normal T4 levels, whereas n = 17 had decreased T4 levels. In the ferritin-deficient group, n = 5 had normal T4 levels, while n = 3 had decreased T4 levels.

A Chi-square test was conducted to examine the association between ferritin status and T4 status, yielding a p-value of 0.407, indicating no statistically significant relationship between these variables. This suggests that ferritin levels do not significantly influence T4 status within the study population.

Figure- 6

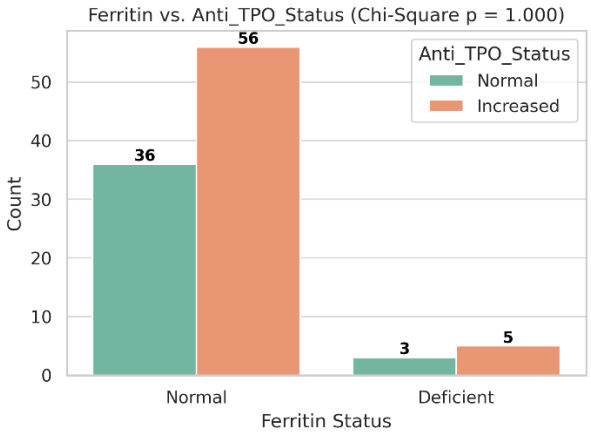
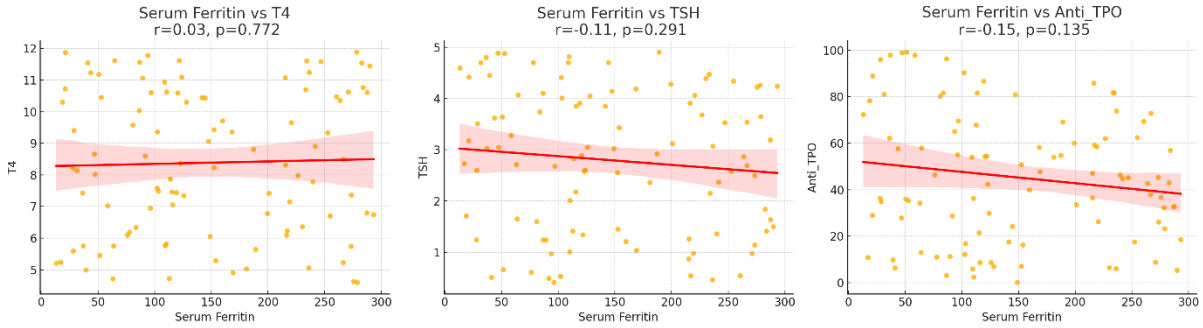


Figure 6 illustrates the distribution of Anti-TPO status (Normal vs. Increased) across different ferritin status groups (Normal vs. Deficient). Among individuals with normal ferritin levels, n = 56 had increased Anti-TPO levels, while n = 36 had normal Anti-TPO levels. In the ferritin-deficient group, n = 5 had increased Anti-TPO levels, whereas n = 3 had normal Anti-TPO levels.

A Chi-square test was conducted to assess the association between ferritin status and Anti-TPO status, yielding a p-value of 1.000, indicating no statistically significant association between these variables. This suggests that ferritin levels do not have a significant influence on Anti-TPO status in this study population.

Figure 7 illustrates scatter plots depicting the correlation between serum ferritin levels and thyroid function parameters, including T4, TSH, and Anti-TPO. The correlation between serum ferritin and T4 was weakly positive ($r = 0.03$, $p = 0.772$), indicating no significant association. Similarly, a weak negative correlation was observed between serum ferritin and TSH ($r = -0.11$, $p = 0.291$), but the association was not statistically significant. Additionally, serum ferritin showed a weak inverse correlation with Anti-TPO levels ($r = -0.15$, $p = 0.135$), though this too lacked statistical significance. These findings suggest that serum ferritin levels do not have a meaningful correlation with thyroid function markers in this dataset.

Figure- 7



DISCUSSION

The primary objective of this cross-sectional study was to assess the association between serum ferritin levels and thyroid function parameters (TSH, T3, T4, and Anti-TPO antibodies) among adults. The study findings demonstrated no statistically significant association between ferritin status and thyroid function parameters. Correlation analysis also revealed no meaningful linear relationship between serum ferritin and thyroid hormones or Anti-TPO antibodies. These results suggest that, within this study population, variations in iron storage as reflected by serum ferritin do not have a significant impact on thyroid function.

Several prior studies have explored the interaction between iron status and thyroid function, with varying outcomes. Beard et al. showed in animal models that iron deficiency impairs thyroid peroxidase activity and alters thyroid hormone metabolism (4). However, clinical studies in non-pregnant adults, such as those conducted by Hess et al have also reported no significant association between serum ferritin levels and thyroid function, supporting the current findings (8). Furthermore, Zimmermann et al demonstrated that while iron deficiency may exacerbate thyroid dysfunction in iodine-deficient populations, isolated iron deficiency without concomitant iodine deficiency may not significantly alter thyroid hormone profiles (6).

Several limitations must be considered when interpreting the results. First, the cross-sectional design restricts the ability to establish causality. Second, the sample size, though adequate for exploratory analysis, may not be sufficient to detect small effect sizes. Third, ferritin is an acute-phase reactant and can be elevated in inflammatory states; although individuals with known inflammatory conditions were excluded, subclinical inflammation might still have influenced ferritin levels (2). Fourth, potential confounders such as dietary iron intake, vitamin A status, or undiagnosed thyroid disease may not have been fully accounted for (1,3). Lastly, laboratory variations and single-point measurements of biochemical parameters could introduce measurement bias, potentially attenuating true associations (9).

The absence of a significant association between serum ferritin and thyroid function parameters in this study aligns with findings from similar cross-sectional studies (7,8). In contrast, studies in specific populations, such as pregnant women (5) and children (10), have reported associations, suggesting that the impact of iron deficiency on thyroid function may be more pronounced in physiologically vulnerable groups. A meta-analysis by Sun et al. indicated that iron supplementation improved thyroid function only in iron-deficient, hypothyroid pregnant women (11). Our findings, together with the variability in the literature, suggest that serum ferritin may not independently predict thyroid dysfunction in the general adult population, especially in iodine-sufficient areas.

Theoretically, iron deficiency could impair thyroid peroxidase activity and thyroid hormone synthesis (12). However, the lack of significant findings in our cohort may reflect the relatively mild degree of iron deficiency among participants, the presence of compensatory mechanisms, or sufficient dietary iodine intake mitigating the effects of iron deficiency on the thyroid axis (6,13).

The generalisability of our findings is moderate. The study population, derived from a tertiary care hospital in South India, represents a semi-urban to urban demographic with access to healthcare services. Thus, the findings may not be directly extrapolated to rural populations, those with high endemic rates of iron deficiency anemia, or iodine-deficient communities (14). Moreover, as the study excluded individuals with chronic diseases and those on supplementation therapy, results may not apply to clinical populations with comorbidities (15). Nonetheless, the use of standardized laboratory methods and inclusion of a broad adult age range support the external validity of the findings to similar outpatient populations in other developing countries (16).

Future longitudinal studies with larger sample sizes, repeated measurements, and inclusion of inflammatory markers are recommended to better delineate the potential dynamic relationship between iron status and thyroid function.

CONCLUSION

This cross-sectional observational study evaluated the association between serum ferritin levels and thyroid function parameters among adults. The findings demonstrated no significant association between ferritin

status and thyroid markers, including thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), and anti-thyroid peroxidase (Anti-TPO) antibodies. Correlation analyses further revealed no meaningful relationship between continuous serum ferritin levels and thyroid function indices. These results suggest that variations in iron storage, as reflected by serum ferritin levels, may not significantly influence thyroid function in the general adult population studied. While iron plays a crucial role in thyroid hormone synthesis at a mechanistic level, the absence of a significant clinical association in this cohort highlights the potential mitigating effects of compensatory mechanisms and adequate iodine intake. Future longitudinal studies involving larger sample sizes and additional variables, such as inflammatory markers and dietary assessments, are warranted to further clarify the complex interplay between iron status and thyroid function.

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