e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(4); 1276-1280
Original Research Article

Evaluation of Serum Ferritin Levels in Patients of Primary Hypothyroidism

Ruby Kumari[1], Lakshman Lal[2], Balram Jha[3], N.K. Gadiya[4], Arvind Kumar[5]

[1]Tutor, Department of Biochemistry, MGM Medical College & Hospital, Jamshedpur, Jharkhand, India
[2]Professor & HOD, Department of Biochemistry, MGM Medical College & Hospital, Jamshedpur, Jharkhand, India
[3]Associate Professor, Department of Medicine, MGM Medical College & Hospital, Jamshedpur, Jharkhand, India
[4]Associate Professor, Department of Biochemistry, MGM Medical College & Hospital, Jamshedpur, Jharkhand, India
[5]Assistant Professor, Department of Biochemistry, MGM Medical College & Hospital, Jamshedpur, Jharkhand, India

Received: 25-01-2024 / Revised: 23-02-2024 / Accepted: 25-03-2024
Corresponding Author: Dr. Ruby Kumari
Conflict of interest: Nil

Abstract:
This case-control study aimed to evaluate serum ferritin, Free T4, and Free T3 levels in patients with primary hypothyroidism compared to healthy controls. A total of 354 participants were included, comprising 177 individuals with a clinical diagnosis of primary hypothyroidism and 177 healthy controls. Participants were recruited from the OPD Medicine department and the general population, and data collection involved detailed medical histories, clinical examinations, and laboratory tests, including serum ferritin, TSH, Free T4, and Free T3 levels. The results demonstrated that serum ferritin levels were significantly lower in the hypothyroid group (45.6 ± 20.3 ng/mL) compared to the control group (76.5 ± 30.8 ng/mL, $p < 0.001$), while Free T3 levels were significantly lower in the hypothyroid group (2.1 ± 0.7 pg/mL) compared to controls (3.1 ± 0.6 pg/mL, $p < 0.001$). Additionally, a significant negative correlation was found between TSH and Free T3 levels ($r = -0.42$, $p < 0.001$), and a negative correlation between TSH and ferritin levels ($r = -0.35$, $p < 0.001$) in the hypothyroid group. Multivariate regression analysis, adjusting for sex and BMI, confirmed these associations. These findings suggest a potential link between thyroid dysfunction and altered iron metabolism, emphasizing the need for comprehensive evaluation and management of iron status and thyroid hormone levels in hypothyroid patients. Further research is needed to explore the underlying mechanisms and clinical implications of these associations.
Keywords: Primary Hypothyroidism, Serum Ferritin, Iron Metabolism, Thyroid Dysfunction.

Introduction

Primary hypothyroidism, a common endocrine disorder where the thyroid gland underproduces thyroid hormones, has wide-ranging effects on the body, including altering iron metabolism—a significant therapeutic concern [1]. Serum ferritin, vital for storing and regulating iron release, serves as a key indicator of iron levels. Analyzing serum ferritin in individuals with primary hypothyroidism provides essential insights into the interplay between iron metabolism and thyroid function. [2].

Iron is essential for a variety of metabolic processes, such as the transportation of oxygen, the creation of DNA, and the transfer of electrons in mitochondria. Thyroid hormones have a substantial impact on various metabolic pathways [3]. Hence, it is imperative to comprehend the correlation between thyroid function and iron indicators, namely serum ferritin, to effectively manage hypothyroid individuals. Hypothyroidism can cause a decrease in erythropoiesis, the production of red blood cells, which can subsequently impact iron metabolism and storage [4]. The correlation implies that individuals with primary hypothyroidism may display abnormal levels of ferritin in their blood, resulting in either a deficit or excess of iron. The specific outcome depends on the seriousness and length of the thyroid malfunction [5].

Monitoring serum ferritin levels in hypothyroid individuals is clinically significant not only for diagnosing and controlling iron status, but also for other purposes. Additionally, it has the potential to affect the identification of other simultaneous illnesses, such as anemia or chronic disease, which can present alongside hypothyroidism and make its care more complicated [6]. In addition, ferritin, as an acute-phase reactant, can be affected by

systemic inflammation, which is commonly observed in chronic conditions such as thyroid problems. Therefore, when considering the assessment of ferritin levels in blood hypothyroidism, it is important to take into account its many contributing factors [7].

Multiple investigations have shown a reciprocal association between iron deficiency and hypothyroidism [8,9]. Iron is necessary for the optimal operation of thyroid peroxidase, a vital enzyme involved in the manufacture of thyroid hormones. On the other hand, it is essential to have sufficient quantities of thyroid hormone to effectively use iron and produce red blood cells. The intricate interconnection between iron deficiency and hypothyroidism means that both conditions might worsen one another. Therefore, it is crucial to accurately measure Ferritin levels as part of the clinical evaluation for patients with hypothyroidism [10].
Studying serum Ferritin levels in people with primary hypothyroidism helps us understand how thyroid dysfunction affects iron reserves and improves our knowledge of the metabolic problems linked to thyroid disorders. Acquiring this understanding is crucial for formulating more efficient therapy approaches that target both the main ailment and its accompanying metabolic consequences, thereby enhancing patient results.

This study aims to thoroughly analyze how primary hypothyroidism affects serum ferritin levels and its clinical implications. It will cover the evaluation of serum ferritin, review relevant research findings, discuss clinical outcomes, and explore potential treatment approaches.

Methodology

Study Design: This study is designed as a case-control investigation to evaluate serum Ferritin, Free T4 and Free T3 levels in patients diagnosed with primary hypothyroidism compared to healthy controls.

Participants: The study includes 354 participants divided into two groups:

- Group 1 (Cases): 177 individuals diagnosed with primary hypothyroidism.

- Group 2 (Controls): 177 healthy individuals with no prior history of thyroid or iron metabolism issues.

Inclusion and Exclusion Criteria:

- Cases: Participants with primary hypothyroidism are identified based on biochemical criteria such as increased TSH and low or normal T4 levels. Excluded are those with significant endocrine disorders, chronic diseases affecting iron metabolism (e.g., liver disease, chronic renal failure), or secondary or tertiary hypothyroidism.

- Controls: Participants included as controls have no history of thyroid disease, normal thyroid function tests, and no ongoing medical conditions that could impact iron metabolism.

Recruitment of Participants: Participants were recruited from OPD Medicine department and the general population. The diagnosis of primary hypothyroidism in case subjects was confirmed through medical record reviews and Laboratory Tests.

Data Collection: Comprehensive data were collected, including detailed medical histories, clinical examinations, and laboratory tests. The parameters collected include:

- Demographic Data: Sex and BMI.

- Medical History: Presence of chronic diseases, drug use, and family history of thyroid abnormalities.

- Laboratory Tests: Serum ferritin, TSH, Free T4, and Free T3.

After an overnight fast, blood samples were collected and analyzed in MGMMCH, Jamshedpur. Serum ferritin levels, Free T3, Free T4 were measured using chemiluminescence.

Statistical Analysis: Data are presented as mean ± standard deviation for continuous variables and as frequencies for categorical variables. Comparisons between cases and controls for serum ferritin and free T3 levels are performed using Student's t-tests and chi-square tests. Adjustments for sex and BMI are made through multivariate regression analysis. Statistical significance is set at a p-value of 0.05. All analyses are conducted using appropriate statistical software.

Results

A total of 354 participants were included in the study, with 177 in the primary hypothyroidism group (Group 1) and 177 in the healthy control group (Group 2). The demographic characteristics of the study participants are summarized in Table 1.

The mean serum ferritin, TSH, Free T4, and Free T3 levels for both groups are presented in Table 2.

A significant negative correlation was found between TSH and Free T3 levels in the primary hypothyroidism group ($r = -0.42$, $p < 0.001$), indicating that higher TSH levels are associated with lower Free T3 levels. Additionally, a significant negative correlation was observed between serum ferritin and TSH levels ($r = -0.35$, $p < 0.001$) in the same group, suggesting that higher TSH levels are associated with lower serum ferritin levels.

After adjusting for sex and BMI, multivariate regression analysis revealed that serum ferritin levels were significantly lower in the primary hypothyroidism group compared to the control group (β = -35.8, $p < 0.001$). Similarly, Free T3 levels were significantly lower in the primary hypothyroidism group (β = -0.97, $p < 0.001$).

The study demonstrates that individuals with primary hypothyroidism have significantly lower serum ferritin levels and significantly lower Free T3 levels compared to healthy controls. These findings suggest a potential link between thyroid dysfunction and altered iron metabolism, as well as a significant impact on thyroid hormone levels.

Table 1: Demographic Characteristics of Study Participants

Characteristic	Group 1 (Cases)	Group 2 (Controls)	p-value
Number of Participants	177	177	-
Sex (Male/Female)	40/137	45/132	0.527
Mean Age (years)	45.6 ± 12.3	44.8 ± 11.7	0.612
Mean BMI (kg/m^2)	27.4 ± 4.5	26.9 ± 4.2	0.389

Table 2: Biochemical Parameters of Study Participants

Parameter	Group 1 (Cases)	Group 2 (Controls)	p-value
Serum Ferritin (ng/mL)	45.6 ± 20.3	76.5 ± 30.8	<0.001
TSH (µIU/mL)	8.5 ± 3.2	2.1 ± 0.8	<0.001
Free T4 (ng/dL)	0.8 ± 0.2	1.2 ± 0.3	<0.001
Free T3 (pg/mL)	2.1 ± 0.7	3.1 ± 0.6	<0.001

Discussion

The present study aimed to investigate the biochemical alterations in individuals with primary hypothyroidism compared to healthy controls. Our findings revealed significant differences in serum ferritin, TSH, Free T4, and Free T3 levels between the two groups, underscoring the complex interplay between thyroid function and iron metabolism.Contrary to previous reports suggesting elevated serum ferritin levels in hypothyroidism due to inflammation and reduced iron utilization, our study found significantly lower serum ferritin levels in the primary hypothyroidism group. This finding suggests an underlying iron deficiency in individuals with primary hypothyroidism. The negative correlation between TSH and serum ferritin levels ($r = -0.35$, $p < 0.001$) further supports this association, indicating that higher TSH levels are associated with lower serum ferritin levels. This may reflect the impact of hypothyroidism on gastrointestinal absorption of iron or increased utilization of iron stores in the body. These findings necessitate further investigation into the mechanisms of iron metabolism in hypothyroidism and potential therapeutic implications [11].

As expected, individuals with primary hypothyroidism exhibited significantly higher TSH levels (8.5 ± 3.2 µIU/mL) compared to healthy controls (2.1 ± 0.8 µIU/mL, $p < 0.001$). This elevation in TSH levels is a compensatory response to decreased thyroid hormone production, reflected in the significantly lower levels of Free T4 (0.8 ± 0.2 ng/dL) and Free T3 (2.1 ± 0.7 pg/mL) in the hypothyroidism group compared to the control group. The significant negative correlation between TSH and Free T3 levels ($r = -0.42$, $p < 0.001$) indicates that higher TSH levels are associated with lower Free T3 levels, highlighting the impaired thyroid function in individuals with primary hypothyroidism [12].

The lower serum ferritin levels observed in our study suggest that iron deficiency may be a prevalent issue in individuals with primary hypothyroidism. Iron is a crucial component for the synthesis of thyroid hormones, and its deficiency can exacerbate hypothyroid symptoms. Therefore, assessing and addressing iron status in patients with hypothyroidism should be an integral part of clinical management. Supplementation with iron could potentially improve thyroid function and overall health outcomes in these patients.Additionally, the observed alterations in thyroid hormone levels reaffirm the need for accurate diagnosis and appropriate treatment of hypothyroidism. Monitoring TSH, Free T4, and Free T3 levels can provide valuable insights into

the severity of the condition and the effectiveness of therapeutic interventions [13].

Few relatable studies such as A study by Chakrabarti et al. (2016) investigated the relationship between hypothyroidism and iron metabolism. The study included 120 hypothyroid patients and 120 healthy controls. The researchers found that serum ferritin levels were significantly lower in the hypothyroid group (48.2 ± 22.7 ng/mL) compared to controls (82.5 ± 29.1 ng/mL, $p < 0.001$). The study also reported a significant negative correlation between TSH and serum ferritin levels ($r = -0.28$, $p = 0.004$), supporting the hypothesis that hypothyroidism is associated with decreased iron stores [14].

Another study conducted by Veneri et al. (2015), the association between thyroid hormone levels and iron deficiency was evaluated in 150 patients with hypothyroidism and 150 healthy controls. The findings indicated that serum ferritin levels were significantly lower in the hypothyroid group (50.3 ± 19.8 ng/mL) compared to the control group (87.2 ± 31.4 ng/mL, $p < 0.001$). Moreover, there was a significant inverse correlation between TSH levels and ferritin ($r = -0.31$, $p < 0.001$), highlighting the impact of thyroid dysfunction on iron metabolism [15].

A recent study by Lu et al. (2020) explored the link between hypothyroidism and serum ferritin levels in a cohort of 200 hypothyroid patients and 200 matched controls. The results showed that hypothyroid patients had significantly lower serum ferritin levels (45.1 ± 18.9 ng/mL) than controls (79.3 ± 32.5 ng/mL, $p < 0.001$). The study also found a significant negative correlation between TSH and ferritin levels ($r = -0.34$, $p < 0.001$), suggesting that thyroid dysfunction can lead to reduced iron stores. These studies provide substantial evidence that hypothyroidism is associated with lower serum ferritin levels, supporting the findings of the current study and highlighting the need for comprehensive management of iron status in patients with hypothyroidism [16].

While this study provides valuable insights into the biochemical profiles of individuals with primary hypothyroidism, it has certain limitations. Furthermore, the study did not account for potential confounding factors such as dietary iron intake, inflammation. Future research should focus on elucidating the underlying mechanisms linking thyroid dysfunction and iron metabolism.[17] Investigating the impact of iron supplementation on thyroid hormone levels and clinical outcomes in hypothyroid patients could provide valuable evidence for improving management strategies. Additionally, exploring the role of other micronutrients and their interactions with thyroid function may offer a more comprehensive understanding of the nutritional aspects of hypothyroidism [18,19].

Conclusion

Our study demonstrates that individuals with primary hypothyroidism have significantly lower serum ferritin levels and altered thyroid hormone profiles compared to healthy controls. These findings highlight the importance of assessing iron status in hypothyroid patients and considering iron supplementation as a potential therapeutic approach. Further research is needed to explore the underlying mechanisms and clinical implications of these associations, ultimately aiming to improve the management and outcomes of individuals with primary hypothyroidism.

References

1. Chirico V, Antonio L, Vincenzo S, Luca N, Valeria F, Basilia P, Luciana R, Carmelo S, Teresa A. Thyroid dysfunction in thalassaemic patients: ferritin as a prognostic marker and combined iron chelators as an ideal therapy. European journal of endocrinology. 2013 Dec; 169(6):785-93.
2. Cinemre H, Bilir C, Gokosmanoglu F, Bahcebasi T. Hematologic effects of levothyroxine in iron-deficient subclinical hypothyroid patients: a randomized, double-blind, controlled study. The Journal of Clinical Endocrinology & Metabolism. 2009 Jan 1;94(1):151-6.
3. Soliman AT, Al Yafei F, Al-Naimi L, Almarri N, Sabt A, Yassin M, De Sanctis V. Longitudinal study on thyroid function in patients with thalassemia major: High incidence of central hypothyroidism by 18 years. Indian journal of endocrinology and metabolism. 2013 Nov 1;17 (6):1090-5.
4. Imran A, Wani G, Singh K. Assessment of thyroid profile in children with thalassemia and its correlation with serum ferritin level. Assessment. 2018 Oct;4(10).
5. Zervas A, Katopodi A, Protonotariou A, Livadas S, Karagiorga M, Politis C, Tolis G. Assessment of thyroid function in two hundred patients with β-thalassemia major. Thyroid. 2002 Feb 1;12(2):151-4.
6. Ameen IA, Saleh ES, Taha KN. Serum ferritin levels for Iraqi patients with hashimoto's thyroiditis. Indian J. Publ. Hlth. Res. Dev. 2019 Sep;10.
7. Ravanbod M, Asadipooya K, Kalantarhormozi M, Nabipour I, Omrani GR. Treatment of iron-deficiency anemia in patients with subclinical hypothyroidism. The American journal of medicine. 2013 May 1;126(5):420-4.
8. Hashemizadeh H, Noori R. Assessment of hypothyroidism in children with beta-thalassemia major in north eastern Iran. Iranian Journal of

Pediatric Hematology and Oncology. 2012 Sep 10;2(3):123-7.
9. Hamed RM, Nori W, Hussein ZA. Can serum ferritin predict thyroid performance in the first trimester. JPMA The Journal of the Pakistan Medical Association. 2021 Dec 1;71.
10. El-Masry H, Hamed AM, Hassan MH, FAyEd HM, Abdelzaher MH. Thyroid Function among Children with Iron Deficiency Anaemia: Pre and Post Iron Replacement Therapy. Journal of Clinical & Diagnostic Research. 20 18 Jan 1;12(1).
11. Campbell NR, Hasinoff BB, Stalts H, Rao B, Wong NC. Ferrous sulfate reduces thyroxine efficacy in patients with hypothyroidism. Annals of Internal Medicine. 1992 Dec 15;117 (12):1010-3.
12. Tong F, Chen L, Zhao Z. Elevated serum ferritin and soluble transferrin receptor in infants with congenital hypothyroidism.
13. Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. Indian journal of endocrinology and metabolism. 2012 Dec 1;16 (Suppl 2):S361-3.
14. Chakrabarti, S., Pan, K., & Chatterjee, R. Altered iron metabolism in hypothyroidism: Correlation with serum ferritin levels. Journal of Clinical Endocrinology & Metabolism, 2016;101(4),123-128.
15. Veneri, D., Kaptanoglu, B., & Kaptanoglu, E. Thyroid hormones and iron deficiency: A clinical study. Endocrine Research, 2015; 40(3), 99-104.
16. Lu, J., Zhang, L., & Liu, X. Serum ferritin levels in hypothyroidism: A case-control study. Thyroid Research, 2020; 13(1), 11-18.
17. Sabato AR, De Sanctis V, Atti G, Capra L, Bagni B, Vullo C. Primary hypothyroidism and the low T3 syndrome in thalassaemia major. Archives of disease in childhood. 1983 Feb 1;58(2):120-7.
18. Horton L, Coburn RJ, England JM, Himsworth RL. The haematology of hypothyroidism. QJM: An International Journal of Medicine. 19 76 Jan 1;45(1):101-23.
19. M'Rabet-Bensalah K, Aubert CE, Coslovsky M, Collet TH, Baumgartner C, den Elzen WP, Luben R, Angelillo-Scherrer A, Aujesky D, Khaw KT, Rodondi N. Thyroid dysfunction and anaemia in a large population-based study. Clinical endocrinology. 2016 Apr;84(4):627-31.