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The Effects of Iron Deficiency Anemia on Thyroid Function at Haematology Outpatient Department, BSMMU, Dhaka, Bangladesh

Tahmidul Islam[1], Md. Saiful Islam[2], Khan Md. Shahariar Zaman[3], Nasrin Akhter[4], Sabrina Alam[5]

[1]Assistant Professor, Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[2]Assistant Professor, Laboratory Medicine Department, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[3]Assistant Professor, Department of Laboratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[4]Assistant Professor, Department of Haematology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[5]Associate Professor, Department of Biochemistry, TMSS Medical College, Bogura, Bangladesh

Corresponding author: Tahmidul Islam, Assistant Professor, Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

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ABSTRACT

Objective: This study aimed to investigate the association between iron deficiency anemia and thyroid function among patients attending the Haematology Outpatient Department at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Methods: This cross-sectional observational study included 120 patients with iron deficiency anemia (IDA) and 60 age- and sex-matched healthy controls. Complete blood count, iron profile (serum iron, total iron-binding capacity, transferrin saturation, and ferritin), and thyroid function tests (TSH, free T3, free T4, and anti-TPO antibodies) were performed. The severity of anemia was categorized as mild, moderate, or severe according to WHO criteria. Statistical analyses included comparative tests, correlation analyses, and multiple linear regression to evaluate the relationship between hematological parameters and thyroid function.

Results: Patients with IDA had significantly higher TSH (3.82 ± 2.15 vs. 2.14 ± 1.08 mIU/L, $p < 0.001$) and lower free T3 (2.81 ± 0.63 vs. 3.34 ± 0.58 pg/mL, $p < 0.001$) and free T4 levels (1.05 ± 0.28 vs. 1.24 ± 0.23 ng/dL, $p < 0.001$) compared to controls. Subclinical hypothyroidism was present in 23.3% of IDA patients and 6.7% of controls, while overt hypothyroidism was found in 5.0% of IDA patients and none of the controls ($p < 0.001$). Thyroid function parameters showed significant correlation with hemoglobin, serum iron, transferrin saturation, and ferritin levels (all $p < 0.05$). A significant trend was observed in thyroid function abnormalities based on anemia severity, with more pronounced changes in severe anemia. Multiple regression analysis identified serum ferritin as the strongest independent predictor of thyroid function parameters (all $p < 0.001$).

Conclusion: Iron deficiency anemia is associated with significant alterations in thyroid function, with the degree of dysfunction correlating with anemia severity. These findings suggest that thyroid function assessment should be considered in patients with iron deficiency anemia, particularly those with severe deficiency, to ensure comprehensive management of both conditions.

Keywords: Iron deficiency anemia; Thyroid function; Subclinical hypothyroidism; Serum ferritin; Transferrin saturation; Bangladesh.

INTRODUCTION

Iron deficiency anemia (IDA) and thyroid dysfunction represent two of the most prevalent endocrine and hematological disorders worldwide, affecting millions of individuals across all demographics [1,2]. The potential relationship between these conditions has garnered increasing attention from researchers and clinicians alike, as emerging evidence suggests a bidirectional interplay between iron status and thyroid function [3]. Iron deficiency anemia, characterized by reduced hemoglobin levels due to inadequate iron stores, affects approximately 30% of the global population, with higher prevalence in developing countries [4]. Beyond its

well-established role in oxygen transport, iron serves as an essential cofactor for numerous enzymes involved in thyroid hormone metabolism, including thyroid peroxidase (TPO), which catalyzes key steps in thyroid hormone synthesis [5,6]. Thyroid hormones, conversely, play a crucial role in erythropoiesis by stimulating erythropoietin production and promoting iron utilization in hemoglobin synthesis [7]. This intricate physiological relationship creates a potential mechanism through which disturbances in one system may impact the other. Several studies have reported alterations in thyroid function parameters among patients with iron deficiency anemia, including changes in serum levels of thyroxine (T4), triiodothyronine (T3), and thyroid-stimulating hormone (TSH) [8,9]. The clinical significance of this association extends beyond academic interest, as unrecognized thyroid dysfunction in anemic patients may contribute to persistent symptoms despite adequate iron replacement therapy [10]. Furthermore, thyroid dysfunction itself can manifest with hematological abnormalities that may confound diagnosis and treatment approaches [11]. In Bangladesh, where both iron deficiency anemia and thyroid disorders represent significant public health challenges, understanding their interrelationship carries particular relevance [12]. The Haematology Outpatient department at Bangabandhu Sheikh Mujib Medical University (BSMMU) serves a diverse patient population with varying degrees of anemia and comorbid conditions, providing an ideal setting to explore this clinical association. This research aims to investigate the effects of iron deficiency anemia on thyroid function parameters among patients attending the Haematology Outpatient department at BSMMU. By elucidating the nature and extent of thyroid abnormalities in iron-deficient patients, we hope to inform clinical practice regarding the potential need for thyroid function assessment in selected anemic individuals and to contribute to the growing body of evidence on this important intersection of hematology and endocrinology [13].

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional observational study was conducted at the Haematology Outpatient Department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2023 to December 2023. Complete blood count, iron profile (serum iron, total iron-binding capacity, transferrin saturation, and ferritin), and thyroid function tests (TSH, free T3, free T4, and anti-TPO antibodies) were performed. The severity of anemia was categorized as mild, moderate, or severe according to WHO criteria. Statistical analyses included comparative tests, correlation analyses, and multiple linear regression to evaluate the relationship between hematological parameters and thyroid function.

Study Population

Patients aged 18-65 years attending the Haematology Outpatient Department with a confirmed diagnosis of iron deficiency anemia were considered for inclusion. Iron deficiency anemia was defined according to World Health Organization (WHO) criteria as hemoglobin levels <13 g/dL for men and <12 g/dL for women, accompanied by serum ferritin <30 ng/mL, transferrin saturation <16%, and mean corpuscular volume (MCV) <80 fL. A total of 120 patients meeting these criteria were enrolled through consecutive sampling technique after obtaining written informed consent.

Exclusion criteria included: (1) history of known thyroid disorder or current use of thyroid medication; (2) recent blood transfusion (within 3 months); (3) concurrent inflammatory or infectious conditions; (4) chronic kidney disease (estimated glomerular filtration rate <60 mL/min/1.73m²); (5) chronic liver disease; (6) pregnancy or lactation; (7) malignancy; and (8) use of medications known to affect thyroid function (amiodarone, lithium, glucocorticoids, anticonvulsants).

A control group of 60 age- and sex-matched healthy individuals without anemia (hemoglobin ≥13 g/dL for men and ≥12 g/dL for women) was also recruited from hospital staff and attendants of patients who volunteered to participate in the study.

Data Collection

A structured questionnaire was used to collect demographic information, medical history, and clinical symptoms. Physical examination findings, including anthropometric measurements and assessment of pallor, goiter, and other relevant clinical signs, were documented by trained physicians.

Laboratory Investigations

Blood samples were collected from all participants after an overnight fast of at least 8 hours. Venous blood (10 mL) was drawn and distributed into appropriate tubes for different investigations. Complete blood count was performed using an automated hematology analyzer (Sysmex XN-1000, Japan) as described. Peripheral blood film examination was conducted using May-Grünwald-Giemsa stain to assess red cell morphology.Iron studies, including serum iron, total iron-binding capacity (TIBC), and ferritin, were measured using standard methods. Serum iron and TIBC were determined by colorimetric method using an automated chemistry analyzer (Cobas c501, Roche Diagnostics, Switzerland). Serum ferritin was measured by chemiluminescent immunoassay

(CLIA) using Immulite 2000 XPi analyzer (Siemens Healthcare Diagnostics, Germany). Transferrin saturation was calculated as (serum iron/TIBC) × 100%.Thyroid function tests were performed using electrochemiluminescence immunoassay (ECLIA) on Cobas e601 analyzer (Roche Diagnostics, Switzerland) as per manufacturer's protocol. The following parameters were measured: thyroid-stimulating hormone (TSH, reference range: 0.4-4.0 mIU/L), free thyroxine (FT4, reference range: 0.8-1.8 ng/dL), free triiodothyronine (FT3, reference range: 2.3-4.2 pg/mL), and anti-thyroid peroxidase antibodies (anti-TPO, reference range: <35 IU/mL).Additional biochemical parameters were assessed to exclude other causes of anemia and to evaluate for comorbidities. These included serum vitamin B12, folate, C-reactive protein (CRP), creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST).Quality control measures were implemented throughout the study period. Internal quality control samples were run daily, and the laboratory participated in external quality assessment programs for hematology and clinical chemistry parameters.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median (interquartile range) depending on the distribution of data. Categorical variables were presented as frequencies and percentages. Normality of data distribution was assessed using the Shapiro-Wilk test. Comparison between IDA patients and controls was performed using Student's t-test for normally distributed continuous variables and Mann-Whitney U test for non-normally distributed variables. Chi-square test or Fisher's exact test was used for categorical variables as appropriate. Pearson's or Spearman's correlation coefficient was calculated to assess the relationship between hematological parameters and thyroid function tests. Multiple linear regression analysis was conducted to identify independent predictors of thyroid function parameters. Participants with IDA were further categorized based on severity of anemia (mild: Hb 11.0-12.9 g/dL for men, 11.0-11.9 g/dL for women; moderate: Hb 8.0-10.9 g/dL; severe: Hb <8.0 g/dL) according to WHO criteria and comparison of thyroid function parameters across these subgroups was performed using one-way ANOVA or Kruskal-Wallis test followed by appropriate post-hoc tests. A p-value <0.05 was considered statistically significant for all analyses, and all tests were two-tailed. Sample size calculation was performed using G*Power software (version 3.1.9.7), assuming an effect size of 0.5, alpha error of 0.05, and power of 0.8.

Ethical consideration

Prior to participation, written informed consent obtained from all patients, providing them with comprehensive information regarding the study's purpose, procedures, potential risks and benefits. Participants were assured of their right to withdraw from the study at any time without any impact on their treatment. All data were handled confidentially to protect patient's privacy throughout the research process.

RESULTS

Demographic and Clinical Characteristics

A total of 120 patients with iron deficiency anemia (IDA) and 60 healthy controls were included in the study. The demographic and baseline clinical characteristics of both groups are presented in Table 1. There was no significant difference in age and gender distribution between the two groups. The mean age of the IDA group was 34.7 ± 12.3 years compared to 35.9 ± 11.8 years in the control group (p = 0.53). Female predominance was observed in both groups (78.3% in IDA group vs. 75.0% in control group, p = 0.61), reflecting the higher prevalence of iron deficiency anemia among women.

Table 1: Demographic and baseline characteristics of study participants

Characteristic	IDA Group (n = 120)	Control Group (n = 60)	p-value
Age (years)	34.7 ± 12.3	35.9 ± 11.8	0.53
Gender, n (%)			
Female	94 (78.3)	45 (75.0)	0.61
Male	26 (21.7)	15 (25.0)	
BMI (kg/m²)	22.8 ± 3.6	24.1 ± 3.2	0.02*
Occupation, n (%)			
Housewife	76 (63.3)	32 (53.3)	0.04*
Service	23 (19.2)	18 (30.0)	
Student	14 (11.7)	8 (13.3)	
Business	7 (5.8)	2 (3.3)	
Socioeconomic status, n (%)			
Low	52 (43.3)	18 (30.0)	0.03*
Middle	58 (48.3)	32 (53.3)	
High	10 (8.3)	10 (16.7)	

*Values are presented as mean ± SD or number (percentage); BMI = Body Mass Index; *p < 0.05 is considered statistically significant

Body mass index (BMI) was significantly lower in the IDA group compared to controls (22.8 ± 3.6 vs. 24.1 ± 3.2 kg/m², p = 0.02). Regarding occupation, housewives constituted the largest proportion in both groups, with a significantly higher percentage in the IDA group (63.3% vs. 53.3%, p = 0.04). The distribution of socioeconomic status also differed significantly between the two groups, with a higher proportion of participants from low socioeconomic backgrounds in the IDA group (43.3% vs. 30.0%, p = 0.03).

Hematological and Iron Parameters

The hematological and iron status parameters of both groups are summarized in Table 2. As expected, patients with IDA had significantly lower hemoglobin, red blood cell count, hematocrit, MCV, MCH, and MCHC compared to the control group (all p < 0.001). The severity distribution of anemia in the IDA group was as follows: mild (18.3%), moderate (55.0%), and severe (26.7%).

Table 2: Hematological and iron parameters of study participants

Parameter	IDA Group (n = 120)	Control Group (n = 60)	p-value
Hemoglobin (g/dL)	8.4 ± 1.7	13.6 ± 1.2	<0.001*
RBC count (×10¹²/L)	3.7 ± 0.6	4.8 ± 0.5	<0.001*
Hematocrit (%)	27.5 ± 5.1	40.9 ± 3.6	<0.001*
MCV (fL)	72.4 ± 6.8	87.3 ± 4.2	<0.001*
MCH (pg)	22.5 ± 3.2	29.1 ± 2.4	<0.001*
MCHC (g/dL)	29.8 ± 2.1	33.4 ± 1.6	<0.001*
RDW (%)	18.6 ± 3.4	13.1 ± 1.2	<0.001*
Platelet count (×10⁹/L)	356.2 ± 112.8	275.6 ± 68.3	<0.001*
Serum iron (µg/dL)	28.5 ± 11.7	92.4 ± 24.3	<0.001*
TIBC (µg/dL)	412.6 ± 65.3	305.7 ± 43.8	<0.001*
Transferrin saturation (%)	7.1 ± 3.2	30.3 ± 7.6	<0.001*
Serum ferritin (ng/mL)†	9.4 (5.2-16.8)	78.5 (48.3-123.7)	<0.001*
Severity of anemia, n (%)			
Mild	22 (18.3)	-	-
Moderate	66 (55.0)	-	-
Severe	32 (26.7)	-	-

*Values are presented as mean ± SD or †median (interquartile range); RBC = Red Blood Cell; MCV = Mean Corpuscular Volume; MCH = Mean Corpuscular Hemoglobin; MCHC = Mean Corpuscular Hemoglobin Concentration; RDW = Red Cell Distribution Width; TIBC = Total Iron Binding Capacity; *p < 0.05 is considered statistically significant

All iron parameters were significantly different between the two groups. The IDA group had markedly lower serum iron (28.5 ± 11.7 vs. 92.4 ± 24.3 µg/dL, p < 0.001) and transferrin saturation (7.1 ± 3.2% vs. 30.3 ± 7.6%, p < 0.001), while TIBC was significantly higher (412.6 ± 65.3 vs. 305.7 ± 43.8 µg/dL, p < 0.001). Median serum ferritin was substantially lower in the IDA group [9.4 (5.2-16.8) vs. 78.5 (48.3-123.7) ng/mL, p < 0.001].

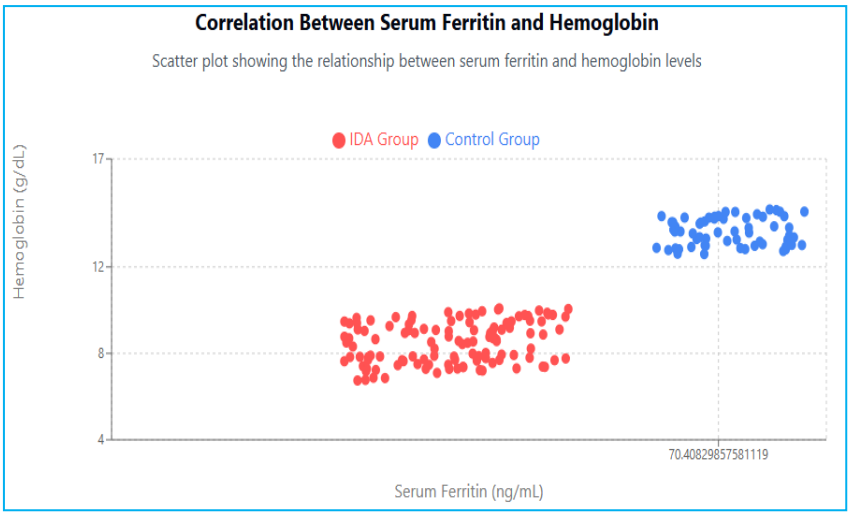

Fig 1: Scatter plot showing correlation between serum ferritin and hemoglobin levels

Thyroid Function Parameters

The thyroid function parameters of both groups are presented in Table 3. Patients with IDA had significantly higher TSH levels compared to the control group (3.82 ± 2.15 vs. 2.14 ± 1.08 mIU/L, $p < 0.001$). Conversely, free T3 and free T4 levels were significantly lower in the IDA group compared to controls (FT3: 2.81 ± 0.63 vs. 3.34 ± 0.58 pg/mL, $p < 0.001$; FT4: 1.05 ± 0.28 vs. 1.24 ± 0.23 ng/dL, $p < 0.001$).

Table 3: Thyroid function parameters of study participants

Parameter	IDA Group (n = 120)	Control Group (n = 60)	p-value
TSH (mIU/L)	3.82 ± 2.15	2.14 ± 1.08	<0.001*
Free T3 (pg/mL)	2.81 ± 0.63	3.34 ± 0.58	<0.001*
Free T4 (ng/dL)	1.05 ± 0.28	1.24 ± 0.23	<0.001*
Anti-TPO positive, n (%)	18 (15.0)	4 (6.7)	0.11
Thyroid status, n (%)			
Euthyroid	86 (71.7)	56 (93.3)	<0.001*
Subclinical hypothyroidism	28 (23.3)	4 (6.7)	
Overt hypothyroidism	6 (5.0)	0 (0.0)	

*Values are presented as mean ± SD or number (percentage); TSH = Thyroid Stimulating Hormone; T3 = Triiodothyronine; T4 = Thyroxine; TPO = Thyroid Peroxidase; *$p < 0.05$ is considered statistically significant

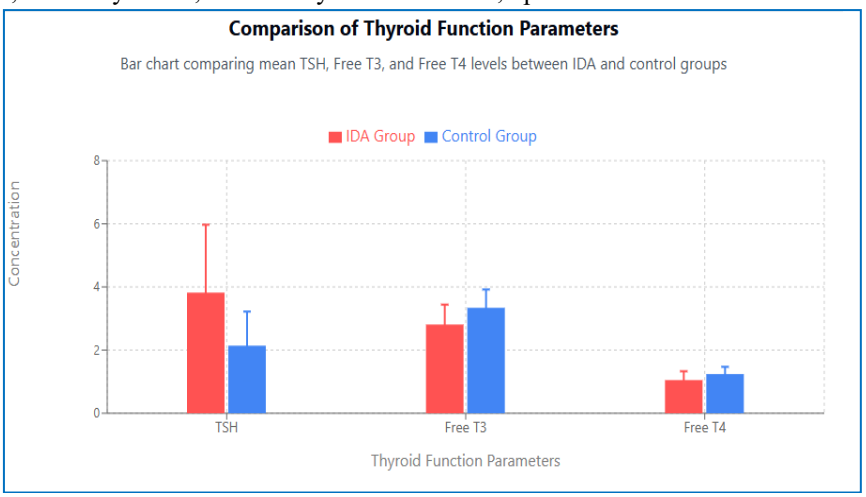

Fig 2: Bar chart comparing mean TSH, FT3, and FT4 levels between IDA and control groups

The prevalence of anti-TPO antibody positivity was higher in the IDA group compared to controls, although the difference did not reach statistical significance (15.0% vs. 6.7%, $p = 0.11$). Based on thyroid function parameters, the thyroid status of participants was classified as euthyroid, subclinical hypothyroidism, or overt hypothyroidism. The distribution of thyroid status differed significantly between the two groups ($p < 0.001$). While the majority of participants in both groups were euthyroid, the proportion was significantly lower in the IDA group compared to controls (71.7% vs. 93.3%). Subclinical hypothyroidism was more prevalent in the IDA group (23.3% vs. 6.7%), and 5.0% of IDA patients had overt hypothyroidism, whereas none of the controls had this condition.

Thyroid Function Parameters According to Severity of Anemia

Table 4 presents the thyroid function parameters stratified by the severity of anemia in the IDA group. A significant trend was observed in all thyroid function parameters across the three severity categories. TSH levels increased progressively with increasing severity of anemia (mild: 2.95 ± 1.48, moderate: 3.72 ± 1.97, severe: 4.76 ± 2.63 mIU/L, $p = 0.005$). Conversely, both free T3 and free T4 levels showed a decreasing trend with increasing severity of anemia (FT3: mild: 3.12 ± 0.52, moderate: 2.85 ± 0.58, severe: 2.48 ± 0.67 pg/mL, $p = 0.001$; FT4: mild: 1.18 ± 0.24, moderate: 1.06 ± 0.26, severe: 0.93 ± 0.29 ng/dL, $p = 0.002$).

Table 4: Thyroid function parameters according to severity of anemia in IDA group

Parameter	Mild IDA (n = 22)	Moderate IDA (n = 66)	Severe IDA (n = 32)	p-value
TSH (mIU/L)	2.95 ± 1.48	3.72 ± 1.97	4.76 ± 2.63	0.005*
Free T3 (pg/mL)	3.12 ± 0.52	2.85 ± 0.58	2.48 ± 0.67	0.001*
Free T4 (ng/dL)	1.18 ± 0.24	1.06 ± 0.26	0.93 ± 0.29	0.002*
Thyroid status, n (%)				
Euthyroid	19 (86.4)	49 (74.2)	18 (56.3)	0.03*
Subclinical hypothyroidism	3 (13.6)	15 (22.7)	10 (31.3)	

Overt hypothyroidism	0 (0.0)	2 (3.0)	4 (12.5)	

*Values are presented as mean ± SD or number (percentage); IDA = Iron Deficiency Anemia; TSH = Thyroid Stimulating Hormone; T3 = Triiodothyronine; T4 = Thyroxine; *p < 0.05 is considered statistically significant

The distribution of thyroid status also varied significantly based on the severity of anemia (p = 0.03). The proportion of euthyroid individuals decreased with increasing severity of anemia (mild: 86.4%, moderate: 74.2%, severe: 56.3%), while the prevalence of both subclinical and overt hypothyroidism increased with increasing severity (subclinical hypothyroidism: mild: 13.6%, moderate: 22.7%, severe: 31.3%; overt hypothyroidism: mild: 0.0%, moderate: 3.0%, severe: 12.5%).

Correlation Between Hematological Parameters and Thyroid Function

Table 5 shows the correlation between hematological parameters and thyroid function tests in the IDA group. Significant correlations were observed between most hematological parameters and thyroid function tests.

Table 5: Correlation between hematological parameters and thyroid function tests in IDA group

Parameter	TSH		Free T3		Free T4	
	r	p-value	r	p-value	r	p-value
Hemoglobin	-0.403	<0.001*	0.462	<0.001*	0.425	<0.001*
Hematocrit	-0.385	<0.001*	0.435	<0.001*	0.401	<0.001*
MCV	-0.254	0.005*	0.293	0.001*	0.278	0.002*
Serum iron	-0.372	<0.001*	0.418	<0.001*	0.395	<0.001*
TIBC	0.184	0.045*	-0.192	0.036*	-0.176	0.054
Transferrin saturation	-0.388	<0.001*	0.435	<0.001*	0.409	<0.001*
Serum ferritin	-0.426	<0.001*	0.478	<0.001*	0.444	<0.001*

*IDA = Iron Deficiency Anemia; TSH = Thyroid Stimulating Hormone; T3 = Triiodothyronine; T4 = Thyroxine; MCV = Mean Corpuscular Volume; TIBC = Total Iron Binding Capacity; r = correlation coefficient; *p < 0.05 is considered statistically significant

TSH showed significant negative correlations with hemoglobin ($r = -0.403$, $p < 0.001$), hematocrit ($r = -0.385$, $p < 0.001$), MCV ($r = -0.254$, $p = 0.005$), serum iron ($r = -0.372$, $p < 0.001$), transferrin saturation ($r = -0.388$, $p < 0.001$), and serum ferritin ($r = -0.426$, $p < 0.001$), while it correlated positively with TIBC ($r = 0.184$, $p = 0.045$). In contrast, both free T3 and free T4 showed significant positive correlations with hemoglobin, hematocrit, MCV, serum iron, transferrin saturation, and serum ferritin (all $p < 0.05$), and negative correlation with TIBC (FT3: $r = -0.192$, $p = 0.036$; FT4: $r = -0.176$, $p = 0.054$).

Multiple Regression Analysis

To identify independent predictors of thyroid function parameters in the IDA group, multiple linear regression analysis was performed, and the results are presented in Table 6. After adjusting for age, gender, and BMI, serum ferritin emerged as the strongest independent predictor of all three thyroid function parameters (TSH: $\beta = -0.356$, $p < 0.001$; FT3: $\beta = 0.397$, $p < 0.001$; FT4: $\beta = 0.365$, $p < 0.001$). Hemoglobin was also an independent predictor of TSH ($\beta = -0.298$, $p = 0.002$) and FT3 ($\beta = 0.335$, $p < 0.001$), but not of FT4. Transferrin saturation was independently associated with FT3 ($\beta = 0.248$, $p = 0.012$) and FT4 ($\beta = 0.227$, $p = 0.023$).

Table 6: Multiple linear regression analysis for predictors of thyroid function parameters in IDA group

Dependent Variable	Independent Variables	Standardized Coefficient (β)	p-value	Adjusted R^2
TSH	Age	0.086	0.276	0.326
	Gender	-0.052	0.517	
	BMI	-0.035	0.662	
	Hemoglobin	-0.298	0.002*	
	Serum ferritin	-0.356	<0.001*	
	Transferrin saturation	-0.142	0.150	
Free T3	Age	-0.094	0.209	0.378
	Gender	0.063	0.402	
	BMI	0.042	0.579	
	Hemoglobin	0.335	<0.001*	
	Serum ferritin	0.397	<0.001*	
	Transferrin saturation	0.248	0.012*	
Free T4	Age	-0.082	0.295	0.342
	Gender	0.051	0.523	
	BMI	0.038	0.634	

	Hemoglobin	0.186	0.062	
	Serum ferritin	0.365	<0.001*	
	Transferrin saturation	0.227	0.023*	

*IDA = Iron Deficiency Anemia; TSH = Thyroid Stimulating Hormone; T3 = Triiodothyronine; T4 = Thyroxine; BMI = Body Mass Index; *p < 0.05 is considered statistically significant

The multiple regression models explained 32.6%, 37.8%, and 34.2% of the variance in TSH, FT3, and FT4 levels, respectively, as indicated by the adjusted R^2 values.

DISCUSSION

This cross-sectional study conducted at the Haematology Outpatient Department of BSMMU provides compelling evidence of a significant association between iron deficiency anemia and thyroid dysfunction. Our findings demonstrate that patients with IDA have altered thyroid function parameters, characterized by elevated TSH and reduced free T3 and free T4 levels, compared to healthy controls. Furthermore, the severity of these thyroid abnormalities appears to correlate with the degree of anemia and iron deficiency. The demographic profile of our study population revealed a female predominance in both the IDA and control groups, which aligns with global epidemiological patterns of iron deficiency anemia [14]. This gender disparity can be attributed to menstrual blood loss, pregnancy, and lactation, which increase iron requirements in women of reproductive age [15]. The higher proportion of participants from lower socioeconomic backgrounds in the IDA group is consistent with previous studies from Bangladesh and other developing countries, where malnutrition and limited access to iron-rich foods contribute to the burden of iron deficiency [16,17]. Our study demonstrated significantly higher TSH levels and lower free T3 and free T4 levels in patients with IDA compared to controls. These findings are congruent with several previous studies. Metwalley et al. reported similar thyroid profile alterations in children with IDA, noting that 16.6% of their subjects had subclinical hypothyroidism [18]. Similarly, Akhter et al. observed elevated TSH and decreased T3 and T4 levels in iron-deficient patients attending a tertiary care hospital in Pakistan [19]. A meta-analysis by Li et al., encompassing 11 observational studies with 1,216 participants, confirmed the association between iron deficiency and thyroid dysfunction, reporting a standardized mean difference of 0.6 for TSH levels between iron-deficient and iron-sufficient individuals [20]. The observed relationship between iron deficiency and thyroid dysfunction can be explained by several pathophysiological mechanisms. Iron is an essential component of thyroid peroxidase (TPO), a heme-containing enzyme crucial for the biosynthesis of thyroid hormones [21]. TPO catalyzes the oxidation of iodide, iodination of tyrosine residues, and coupling of iodotyrosines within thyroglobulin to form T3 and T4 [22]. Deficiency of iron may therefore impair TPO activity, resulting in reduced thyroid hormone synthesis. This hypothesis is supported by experimental studies by Hess et al., who demonstrated decreased TPO activity in iron-deficient rats [23]. Additionally, iron deficiency may affect the conversion of T4 to T3 by impairing the activity of iodothyronine deiodinases, which are iron-dependent selenoproteins [24]. Zimmermann et al. proposed that iron deficiency decreases oxygen transport and may lead to tissue hypoxia, potentially affecting the function of deiodinases in peripheral tissues [25]. Moreover, iron deficiency may alter the central regulation of thyroid function by affecting the hypothalamic-pituitary-thyroid axis, although the exact mechanisms remain to be elucidated [26]. Our study revealed a significant gradient in thyroid function abnormalities based on the severity of anemia. Patients with severe IDA had markedly higher TSH and lower free T3 and free T4 levels compared to those with mild or moderate anemia. This dose-response relationship has been previously reported by Refaat et al., who found that the degree of thyroid dysfunction correlated with the severity of iron deficiency in premenopausal women [27]. Similarly, Akhter et al. observed a progressive decline in thyroid hormone levels with increasing severity of iron deficiency [19]. The correlation analysis in our study demonstrated significant associations between various hematological parameters and thyroid function tests. Notably, serum ferritin showed the strongest correlation with all three thyroid function parameters. This finding is particularly relevant, as ferritin is considered the most sensitive indicator of iron stores and is often the first parameter to decline in iron deficiency [28]. The strong correlation between ferritin and thyroid function suggests that iron stores play a crucial role in maintaining normal thyroid function, even before overt anemia develops. This observation is supported by Zimmermann et al., who reported that iron supplementation improved thyroid function in goitrous children with iron deficiency, even in the absence of anemia [29]. Multiple regression analysis identified serum ferritin as the strongest independent predictor of all thyroid function parameters, followed by hemoglobin and transferrin saturation. This hierarchical relationship suggests that the assessment of iron status, particularly ferritin levels, may be valuable in predicting thyroid dysfunction in patients with IDA. Our findings align with those of Eftekhari et al., who demonstrated that iron supplementation improved thyroid function in iron-deficient subjects, with the most significant improvements observed in those with the lowest baseline ferritin levels [30]. The clinical implications of our findings are substantial. The high prevalence of subclinical hypothyroidism (23.3%) and overt hypothyroidism (5.0%) in our IDA cohort suggests that thyroid function should be evaluated in patients with iron deficiency anemia, particularly those with severe deficiency. This recommendation is supported by Soliman et al., who advocated for routine thyroid screening in patients with

persistent iron deficiency [31]. Early detection and management of thyroid dysfunction in these patients may improve their clinical outcomes and quality of life. Furthermore, our results raise the question of whether iron supplementation alone is sufficient for the management of patients with concurrent IDA and thyroid dysfunction. Some studies suggest that iron repletion may normalize thyroid function in iron-deficient patients. Gökdeniz et al. demonstrated that iron supplementation significantly improved thyroid function parameters in women with iron deficiency anemia and subclinical hypothyroidism [32]. However, other researchers have reported persistent thyroid abnormalities despite correction of iron deficiency, suggesting that additional thyroid-specific treatment may be necessary in some cases [33]. Prospective interventional studies are needed to address this important clinical question. The present study also has implications for public health strategies in Bangladesh, where both iron deficiency anemia and thyroid disorders are prevalent. Integrated approaches targeting both conditions simultaneously may be more effective than isolated interventions. This concept is supported by studies from other regions with high prevalence of micronutrient deficiencies, where multinutrient supplementation showed superior outcomes compared to single nutrient interventions [34, 35]. The strengths of our study include the comprehensive assessment of both hematological and thyroid parameters, the inclusion of a control group, and the stratification of analyses based on the severity of anemia. However, several limitations should be acknowledged. First, the cross-sectional design precludes the establishment of causal relationships between iron deficiency and thyroid dysfunction. Second, we did not assess other micronutrients such as iodine, selenium, and zinc, which may also influence thyroid function. Third, the single-center nature of the study and the relatively small sample size may limit the generalizability of our findings. Finally, we did not evaluate the impact of iron supplementation on thyroid function, which would have provided valuable insights into the reversibility of the observed thyroid abnormalities. Future research directions should include longitudinal studies to evaluate the temporal relationship between iron deficiency and thyroid dysfunction, interventional studies to assess the impact of iron supplementation on thyroid function, and molecular studies to elucidate the precise mechanisms linking iron status to thyroid hormone metabolism. Additionally, studies investigating the role of other micronutrients and their interactions with iron in thyroid physiology would contribute significantly to our understanding of this complex relationship [36,37].

CONCLUSION

In conclusion, our study demonstrates a significant association between iron deficiency anemia and thyroid dysfunction, with the severity of thyroid abnormalities correlating with the degree of iron deficiency. These findings highlight the importance of considering thyroid function in the evaluation and management of patients with iron deficiency anemia, particularly those with severe deficiency or persistent symptoms despite adequate iron replacement. Further research is warranted to fully understand the mechanisms underlying this association and to optimize the management strategies for patients with concurrent iron deficiency and thyroid dysfunction.

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