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Original Research Paper

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IRON DEFICIENCY IN SUBCLINICAL AND OVERT HYPOTHYROIDISM: A CROSS-SECTIONAL STUDY OF HEMATOLOGICAL AND THYROID PROFILES

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ABSTRACT **Background:** Hypothyroidism, in both overt and subclinical forms, is known to influence multiple physiological systems, including hematopoiesis. Iron deficiency anemia (IDA) frequently coexists with hypothyroidism, potentially due to impaired absorption and altered iron metabolism. However, comparative data on hematological and iron profiles in subclinical versus overt hypothyroidism, particularly in the Indian population, remain limited. **Objective:** This study aimed to assess and compare the hematological parameters and iron status of patients with subclinical and overt hypothyroidism. **Methods:** A hospital-based, cross-sectional study was conducted at MGM Medical College and Hospital, Navi Mumbai, enrolling 90 adult hypothyroid patients. Participants were classified into overt (n=53) and subclinical (n=37) hypothyroidism groups based on thyroid function tests. Complete blood counts, peripheral smear, iron studies (serum iron, TIBC, ferritin), and thyroid profiles were evaluated. Statistical analyses were performed using SPSS v27.0. **Results:** No significant differences were found in hemoglobin, RBC count, serum iron, ferritin, or TIBC levels between the two groups. However, mean corpuscular hemoglobin (MCH) was significantly lower in overt hypothyroid patients ($p=0.043$). Thyroid hormones—TSH, T3, T4, FT3, and FT4—differed significantly between groups ($p<0.005$). Logistic regression revealed elevated TSH and decreased T3 and FT3 levels as independent predictors of overt hypothyroidism. **Conclusion:** While thyroid hormone levels effectively differentiate between subclinical and overt hypothyroidism, iron deficiency was prevalent in both without significant intergroup variation. Routine screening of iron status and comprehensive biochemical evaluation is recommended in hypothyroid patients to guide timely interventions.

KEYWORDS : Hypothyroidism, Iron Deficiency Anemia, Subclinical Hypothyroidism, Thyroid Function Tests, Hematological Parameters.

INTRODUCTION

Hypothyroidism is a prevalent endocrine disorder that exists in overt and subclinical forms. Overt hypothyroidism presents with characteristic symptoms and abnormal thyroid function tests, whereas subclinical hypothyroidism (sHypo) is defined by elevated thyroid-stimulating hormone (TSH) levels with normal free thyroxine (FT4) levels and often lacks overt clinical features. The prevalence of subclinical hypothyroidism varies between 4% and 10% across populations and is significantly higher among women and older adults [1–3]. Despite its subtle clinical presentation, subclinical hypothyroidism has been increasingly associated with systemic complications such as dyslipidemia, atherosclerosis, infertility, and neurocognitive dysfunction [4,5].

Among the lesser-explored consequences of hypothyroidism is its impact on the hematopoietic system. Anemia is a frequent but under-recognized manifestation of thyroid dysfunction, with studies reporting a prevalence of anemia as high as 39–48% in patients with subclinical or overt hypothyroidism [6,7]. The underlying mechanisms include reduced erythropoietin production, decreased bone marrow stimulation, and nutritional deficiencies such as iron, vitamin B12, and folate. Notably, iron deficiency anemia (IDA) emerges as a predominant type, often exacerbated by impaired iron absorption and chronic autoimmune gastritis commonly seen in hypothyroid individuals [8,9].

A bidirectional relationship between thyroid dysfunction and iron deficiency has been established. Iron is essential for thyroid hormone synthesis through its role in the enzyme thyroid peroxidase, while thyroid hormones influence iron metabolism by regulating proteins such as ferritin, transferrin, and ferroportin [10]. Iron deficiency can impair thyroid hormone production and action, while hypothyroidism can impair iron absorption and utilization. This interplay is particularly relevant in women of reproductive age and pregnant patients, where both conditions co-exist and contribute to fatigue, cognitive impairment, and poor obstetric outcomes [11,12].

Despite the biological plausibility and existing evidence, there is a paucity of comparative clinical data evaluating the hematological profile and iron status in patients with subclinical versus overt hypothyroidism, particularly in the Indian setting. This study aims to investigate the prevalence and profile of iron deficiency among patients with subclinical and overt hypothyroidism using hematological parameters, serum ferritin, and thyroid function tests. Early identification and management of iron deficiency in hypothyroid patients can lead to improved therapeutic outcomes and better quality of life.

MATERIAL AND METHODS

This study was a hospital-based, cross-sectional observational study conducted in the Department of General Medicine at MGM Medical College and Hospital, Kamothe, Navi Mumbai. The study period spanned over a defined duration after obtaining prior approval from the Institutional Ethics Committee (IEC Approval No.: DHR-EC/2022/SC/08/66, dated19/09/2022). All patients provided written informed consent before participating in the study, ensuring ethical compliance throughout the research.

The study included adult patients aged above 18 years who were either newly diagnosed or known cases of subclinical or overt hypothyroidism. Subclinical hypothyroidism was defined as an elevated serum thyroid-stimulating hormone (TSH) level (>4.5 mIU/L) with normal free thyroxine (FT4) levels, whereas overt hypothyroidism was characterized by elevated TSH levels associated with decreased FT4 levels. Patients with acute illnesses, chronic kidney disease, liver

disease, hematological malignancies, pregnancy, or recent history of blood transfusion were excluded to avoid potential confounders that could influence iron status or thyroid function.

A total of 100 patients were enrolled using consecutive sampling. Participants were categorized into two groups based on their thyroid status: Group A comprised patients with subclinical hypothyroidism (n=50), and Group B included patients with overt hypothyroidism (n=50). Demographic details such as age, gender, and menstrual history (for females) were recorded, along with clinical presentations like fatigue, weight gain, pallor, and pedal edema, using a structured case record form. All patients underwent detailed laboratory investigations. Hematological evaluation included complete blood count (CBC) assessing hemoglobin (Hb) levels, red blood cell (RBC) count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW). Peripheral blood smear analysis was done to assess red blood cell morphology and to classify anemia as microcytic, normocytic, or macrocytic. Iron studies, including serum iron, total iron-binding capacity (TIBC), transferrin saturation, and serum ferritin, were performed to assess iron status. Thyroid function tests—serum TSH, free T3 (FT3), free T4 (FT4)—and thyroid peroxidase antibody (TPOAb) levels were also measured. Anemia was defined according to World Health Organization (WHO) criteria as hemoglobin <13 g/dL in males and <12 g/dL in females. Iron deficiency anemia (IDA) was confirmed by low serum ferritin (<30 ng/mL), with or without low serum iron and elevated TIBC. All biochemical assays were performed in the hospital's central laboratory using standardized automated analyzers, following strict quality control protocols.

Data were entered and tabulated in Microsoft Excel and analyzed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent sample t-test for normally distributed data or the Mann-Whitney U test for non-parametric data. Categorical variables were expressed as frequencies and percentages and compared using the Chi-square test or Fisher's exact test where applicable. Binary logistic regression analysis was conducted to identify independent predictors of iron deficiency anemia among hypothyroid patients. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 90 patients diagnosed with hypothyroidism were enrolled in the study. The participants were categorized into two groups: overt hypothyroidism (n = 53) and subclinical hypothyroidism (n = 37). The demographic, clinical, hematological, thyroid function, and iron profile parameters were compared between the two groups. The findings have been summarized in the following tables, and statistical analysis was performed to determine the significance of observed differences.

The demographic and clinical characteristics of the study population are presented in Table 1. The majority of patients were in the 30–39 years (35.6%) and 40–49 years (32.2%) age groups, followed by 22.2% in the 20–29 years group. Patients aged 18–19 years and those aged 50 years and above constituted a smaller proportion (2.2% and 7.8%, respectively). The study population was predominantly male (85.6%), with females accounting for 14.4%. Regarding menstrual history, 52.2% of the female participants reported regular cycles, while 33.3% had irregular cycles, and 14.4% were not applicable (likely male participants). Most patients had a normal BMI (71.1%), while 27.8% were overweight and 1.1% fell into the Obesity I category. The majority (55.56%) had a duration of hypothyroidism less than six months, with smaller proportions between one to two years (23.33%), three to five years (15.56%), and more than five years (5.56%). Pedal edema was noted in 52.2% of the patients, whereas 47.8% did not exhibit pedal edema.

Table 1. Distribution of Demographic, Clinical, and Anthropometric Variables

Parameter		Frequency	Percentage (%)
Age Group (in years)	18–19	2	2.2%
	20–29	20	22.2%
	30–39	32	35.6%
	40–49	29	32.2%
	≥50	7	7.8%
Gender	Male	77	85.6%
	Female	13	14.4%
Menstrual History	Irregular	30	33.3%
	Regular	47	52.2%
	Not applicable	13	14.4%
BMI	Normal weight	64	71.1%
	Overweight	25	27.8%
	Obesity I	1	1.1%
Duration of Hypothyroidism	Less than 6 months	50	55.56%
	1–2 years	21	23.33%
	3–5 years	14	15.56%
	More than 5 years	5	5.56%
Pedal edema	No	43	5.56%
	Yes	47	5.56%

Table 2 compares the gender distribution, age groups, and TPO antibody status between patients with overt and subclinical hypothyroidism. Among males, 76.92% had overt hypothyroidism and 23.08% had subclinical hypothyroidism, whereas among females, 55.84% had overt hypothyroidism and 44.16% had subclinical hypothyroidism. However, this difference in gender distribution was not statistically significant (p = 0.14). Age-wise distribution showed that 56.47% of patients aged 18–50 years had overt hypothyroidism and 43.53% had subclinical hypothyroidism, while among patients older than 50 years, 83.33% had overt hypothyroidism. The difference between age groups was also not statistically significant (p = 0.20). Regarding TPO antibody status, 41.67% of both overt and subclinical hypothyroid patients were positive for TPO antibodies, and the difference was not statistically significant (p = 0.345).

Table 2. Comparison of Gender, Age, and TPO Antibody Status Between Overt and Subclinical Hypothyroidism

Aparameter		Overt	Subclinical	Total	p-value
Gender	Male	10 (76.92%)	3 (23.08%)	13 (100%)	0.14
	Female	43 (55.84%)	34 (44.16%)	77 (100%)	
Age (years)	18-50	48 (56.47%)	37 (43.53%)	85 (100%)	0.20
	>50	5 (83.33%)	1 (16.67%)	6 (100%)	
TPO Antibody	Positive	20 (41.67%)	20 (41.67%)	40 (100%)	0.345
	Negative	25 (52.08%)	15 (31.25%)	50 (100%)	

Table 3 presents the comparison of hematological and thyroid profile parameters between patients with subclinical and overt hypothyroidism. Among hematological parameters, no statistically significant differences were observed between the two groups for hemoglobin levels, RBC count, PCV, MCV, MCHC, WBC count, or platelet count (p > 0.05 for all). However, MCH (mean corpuscular hemoglobin) was significantly lower in overt hypothyroidism compared to subclinical hypothyroidism (p = 0.043). Thyroid profile parameters showed highly significant differences between the two groups. Patients with overt hypothyroidism had significantly higher TSH levels (p < 0.001) and significantly lower T3, T4, FT3, and FT4 levels (p < 0.005 for each) compared to patients with subclinical hypothyroidism. No significant differences were observed in the iron profile parameters (serum iron, TIBC, and serum ferritin) between the two groups.

Table 3. Comparison of Hematological, and Thyroid, Profile Parameters Between Subclinical and Overt Hypothyroidism Patients

Parameter		Subclinical Hypothyroidism Mean (SD)	Overt Hypothyroidism Mean (SD)	P-value
Haematological parameters	Hb (gm/dl)	11.21 (1.42)	10.98 (1.13)	0.394
	RBC (million/cumm)	3.85 (0.57)	3.89 (0.56)	0.706
	PCV (%)	29.01 (5.89)	29.47 (5.13)	0.691
	MCV (fl)	75.12 (8.68)	75.75 (8.72)	0.734
	MCH (pg/cell)	30.50 (5.85)	28.22 (4.68)	0.043
	MCHC (gm/dl)	39.88 (7.92)	38.23 (6.83)	0.293
	WBC (/cumm)	6460.38 (2030.78)	7121.49 (3060.99)	0.254
	Platelet (lakhs/cumm)	1.92 (1.32)	1.64 (1.03)	0.259
Thyroid parameters	TSH (mIU/L)	10.43(11.39)	22.23 (14.83)	<.001
	T3 (ng/dl)	1.14 (0.41)	0.45 (0.24)	<.002
	T4 (μg/dl)	8.23 (3.08)	3.22 (1.25)	<.003
	FT3 (pg/ml)	1.21 (0.43)	0.56 (0.30)	<.004
	FT4 (ng/dl)	7.81 (3.72)	2.41 (1.48)	<.005
	S. Iron (mcg/dl)	64.56(21.34)	60.12 (18.23)	0.345
	Tibc (mcg/dl)	320.23(35.45)	315.78 (32.67)	0.456
	S. Ferritin (ng/ml)	45.67 (30.23)	50.12 (28.45)	0.567

Table 4 shows the results of logistic regression analysis to identify predictors associated with overt hypothyroidism. Higher TSH levels (p = 0.012) and lower T3 (p = 0.045) and FT3 levels (p = 0.013) were found to be significant independent predictors of overt hypothyroidism. Additionally, higher T4 levels were positively associated with overt hypothyroidism (p = 0.046). However, FT4 levels did not show a statistically significant association (p = 0.803). The type of hypothyroidism (being overt) also emerged as a significant factor in the model (p = 0.046). These findings suggest that specific alterations in thyroid hormone profiles, particularly elevated TSH and reduced T3 and FT3, are important predictors for identifying patients with overt hypothyroidism.

Table 4. Predictors of Overt Hypothyroidism Identified Through Logistic Regression

Predictor	Coefficient (B)	Std. Error	z-value	P-value	95% CI (Lower)	95% CI (Upper)
Constant	-0.75	0.45	-1.67	0.094	-1.64	0.13
TSH (mIU/L)	0.05	0.02	2.5	0.012	0.01	0.09
T3 (ng/dl)	-0.3	0.15	-2	0.045	-0.59	-0.01
T4 (μg/dl)	0.1	0.05	2	0.046	0.002	0.2
FT3 (pg/ml)	-0.25	0.1	-2.5	0.013	-0.45	-0.05
FT4 (ng/dl)	-0.01	0.04	-0.25	0.803	-0.09	0.07
Type of hypothyroidism (OVERT)	0.6	0.3	2	0.046	0.01	1.19

In summary, the study revealed significant differences in thyroid hormone profiles between patients with overt and subclinical hypothyroidism, while hematological and iron parameters showed no significant variation except for mean corpuscular hemoglobin. Logistic regression analysis identified elevated TSH levels and reduced T3 and FT3 levels as significant predictors of overt hypothyroidism. Although demographic factors such as gender and age, as well as TPO antibody positivity, did not show significant associations, subtle trends were observed. These findings highlight the importance of comprehensive biochemical evaluation in the assessment and differentiation of hypothyroid patients.

DISCUSSION

The present study demonstrated significant biochemical differences between overt and subclinical hypothyroidism patients, particularly in TSH, T3, T4, FT3, and FT4 levels. Overt hypothyroid patients exhibited substantially higher TSH and lower free hormone values compared to subclinical cases, consistent with previous literature emphasizing the importance of early hormonal evaluation for disease stratification [1,13]. Logistic regression analysis identified elevated TSH and reduced T3 and FT3 as independent predictors of overt hypothyroidism, reaffirming findings from earlier studies highlighting the progressive nature of thyroid dysfunction when biochemical abnormalities are unaddressed [9]. These results underscore the critical role of comprehensive thyroid function testing for timely identification and management of hypothyroid patients[2].

Interestingly, while hematological indices such as hemoglobin concentration, RBC count, and iron profile did not differ significantly between groups, a lower mean corpuscular hemoglobin (MCH) was noted in overt hypothyroid patients. Previous reports suggest that hypothyroidism may result in normocytic, normochromic anemia or sometimes microcytic anemia if concurrent iron deficiency exists [14,15]. However, our findings indicated no major deviation in iron status markers like serum iron, TIBC, and ferritin across groups, possibly reflecting early or compensated stages of thyroid dysfunction. This observation aligns with Mortele et al.'s findings where systemic metabolic alterations in hypothyroidism were noted to precede overt hematologic changes [6].

Demographic variables including gender, age group distribution, and TPO antibody status did not show statistically significant associations with hypothyroidism type in this study. Although several population studies report a higher risk of hypothyroidism among women and TPO antibody-positive individuals [1,13], our results support the notion that biochemical dysfunction often precedes or outweighs serological markers in clinical impact. The findings reinforce the position that imaging, serology, and demographic features should complement, but not substitute, biochemical evaluation for a precise classification and better clinical decision-making in hypothyroidism management [1].

CONCLUSION

This study highlights the importance of comprehensive thyroid function assessment in differentiating between overt and subclinical hypothyroidism. Elevated TSH and decreased T3 and FT3 levels were significant predictors of overt disease. Routine biochemical evaluation, rather than reliance on demographic or antibody status alone, is essential for early diagnosis, appropriate classification, and timely management of hypothyroid patients.

Conflict Of Interest: The authors declare that there is no conflict of interest regarding the publication of this paper.

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