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To study the hematological parameters and assess the prevalence and pattern of anemia among patients diagnosed with primary hypothyroidism

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Abstract

Introduction: Thyroid function disorders are among the most common endocrine diseases worldwide and occur more frequently in females, particularly during the reproductive age group. Hypothyroidism is the most prevalent thyroid disorder, with a reported global prevalence of 2–5%. Thyroid hormones play a vital role in the regulation of metabolism and are essential for the normal functioning of virtually all body tissues. Their deficiency can impair bone marrow hematopoiesis, leading to various hematological abnormalities. Anemia is one of the most frequently observed hematological manifestations in patients with primary hypothyroidism. **Objectives:** To evaluate the hematological profile and assess the prevalence and pattern of anemia in patients with primary hypothyroidism. **Materials and Methods:** This cross-sectional study was conducted on 110 newly diagnosed patients with primary hypothyroidism aged between 28 and 60 years. Based on serum TSH levels, patients were categorized into subclinical hypothyroidism (n = 40) and overt hypothyroidism (n = 70). Patients fulfilling the inclusion and exclusion criteria were evaluated using thyroid function tests (T3, T4, and TSH) and hematological investigations including complete blood count (CBC) and peripheral blood film (PBF). **Results:** The overall prevalence of anemia among patients with hypothyroidism was 56.5%, which is higher than the World Health Organization–reported global prevalence of anemia. Normocytic normochromic anemia was the most common type observed, followed by microcytic anemia, while macrocytic anemia had the lowest prevalence. Subgroup analysis revealed no statistically significant difference between subclinical and overt hypothyroid patients with respect to hematological parameters or the pattern of anemia. **Conclusion:** Anemia is highly prevalent in patients with hypothyroidism, and correction of anemia may be difficult without appropriate diagnosis and treatment of the underlying thyroid disorder. The findings highlight the importance of screening for hypothyroidism during the evaluation of patients presenting with anemia.

Keywords: Hypothyroidism, Subclinical hypothyroidism, Overt hypothyroidism, Anemia, Hematological profile, Thyroid disorders.

INTRODUCTION

Hypothyroidism is a clinical disorder characterized by insufficient production of thyroid hormones by the thyroid gland. It may result from conditions directly affecting the thyroid gland (primary hypothyroidism) or from disorders involving the hypothalamic–pituitary axis (secondary hypothyroidism). Since thyroid hormones play a crucial role in growth, development, and regulation of numerous cellular functions, their deficiency can have widespread systemic effects. Common clinical manifestations of hypothyroidism include cold intolerance, fatigue, constipation, bradycardia, depression, weight gain, and menstrual irregularities in women [1].

Hypothyroidism is relatively common in India, affecting nearly one in ten individuals, although prevalence varies across geographical regions. The prevalence of hypothyroidism is reported to be 4.6% in the United States, approximately 2% in the United Kingdom, and significantly higher in India at around 11%. Within India, coastal cities such as Chennai, Mumbai, and Goa report a lower prevalence (9.5%) compared to inland cities including Delhi, Ahmedabad, Bengaluru, and Hyderabad, where prevalence rates reach approximately 11.7% [2].

Anemia is a widespread clinical problem, with prevalence reaching up to 10% in certain populations, particularly among women of reproductive age and the elderly. Anemia is defined as a reduction in the number of red blood cells or hemoglobin concentration, resulting in decreased oxygen-carrying capacity of blood. According to World Health Organization (WHO) criteria, anemia is diagnosed when hemoglobin levels fall below 12.0 g/dL in women and 13.0 g/dL in men. Based on mean corpuscular volume (MCV), anemia is classified as normocytic (80–100 fL), microcytic (<80 fL), or macrocytic (>100 fL) [3–5].

Globally, the WHO estimates the prevalence of anemia to be approximately 24.8%, with a higher burden in developing countries [3,6]. Studies have reported a significantly increased prevalence of anemia in patients with hypothyroidism, with rates of 26.6% in subclinical hypothyroidism and 73.2% in overt hypothyroidism, indicating that hypothyroidism is an important risk factor for anemia [6]. Thyroid hormones influence hematopoiesis both directly, by stimulating erythroid progenitor cells, and indirectly, by enhancing erythropoietin production [5]. Anemia in hypothyroid patients is not solely attributable to nutritional deficiencies but also results from reduced thyroid hormone levels, leading to diminished bone marrow activity, impaired tissue oxygenation, and decreased erythropoietin synthesis [7,8].

Thyroid hormones play a significant role in bone marrow function and the regulation of hematopoietic cells [9,10]. Thyroid disorders have long been associated with various hematological abnormalities. As early as 1979, Fein reported anemia in patients with Graves' disease [11]. Earlier, Charcot and Kocher described anemia in patients with primary hypothyroidism and post-thyroidectomy hypothyroidism [12,13]. Horton observed a reduction in peripheral red blood cell counts following thyroidectomy, and anemia has been reported in 20–60% of patients with hypothyroidism [14]. While anemia is common in hypothyroidism, hyperthyroidism is more frequently associated with erythrocytosis [15]. Several studies have demonstrated normalization of hematological parameters following restoration of euthyroid status, although contradictory findings have also been reported [16]. Additionally, mild leukopenia,

neutropenia, and thrombocytopenia have been observed in some hypothyroid patients [16].

Despite extensive research over the past century exploring the relationship between thyroid function and hematopoiesis, available data remain fragmented and, at times, contradictory. Anemia associated with hypothyroidism poses a diagnostic challenge, as it may precede other clinical manifestations or develop later during the disease course. Moreover, overlapping symptoms of anemia and hypothyroidism may obscure diagnosis. Without appropriate identification and treatment of the underlying thyroid dysfunction, correction of anemia is often incomplete.

Therefore, the present study was undertaken to evaluate the hematological profile and assess the pattern of anemia in patients with primary hypothyroidism.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based, cross-sectional study was conducted in the Department of Pathology, Chandulal Chandraker Memorial Medical College, Durg (Chhattisgarh). The study included patients diagnosed with primary hypothyroidism.

Study Population

A total of **110 patients** aged **20–60 years** with primary hypothyroidism were enrolled after fulfilling the inclusion criteria. Based on serum TSH levels, patients were categorized into:

- **Subclinical hypothyroidism:** 40 patients
- **Overt hypothyroidism:** 70 patients

Inclusion Criteria

- Patients diagnosed with primary hypothyroidism (subclinical or overt)
- Patients included irrespective of age, sex, and thyroid status

Exclusion Criteria

Patients with the following conditions were excluded:

- Anemia due to other causes such as hemolytic anemia, malignancy, acute blood loss (gastrointestinal or genitourinary)
- Comorbid conditions including chronic kidney disease, coronary heart disease, diabetes mellitus, tuberculosis, liver disorders
- Endocrine disorders other than thyroid disease
- Hemoglobinopathies, bleeding diathesis, bone marrow suppression
- Autoimmune disorders such as rheumatoid arthritis and celiac disease
- History of blood transfusion in the preceding 3 months
- Current or prior treatment with iron, vitamins, or other hematinic therapy
- Pregnant and lactating women

- Cigarette smokers

Data Collection

The study was conducted after obtaining approval from the Institutional Ethics Committee of Chandulal Chandraker Memorial Medical College, Durg. Written informed consent was obtained from all participants. Relevant demographic and clinical details were collected using a structured questionnaire and from patients' medical records.

Study Variables and Methods of Measurement

Blood Sample Collection

Venous blood samples were collected under aseptic conditions after cleaning the venipuncture site with 70% alcohol. Two early-morning blood samples (2 mL each) were collected:

- One sample in an EDTA vial for hematological analysis
- One sample in a plain vial for thyroid function tests
- A peripheral blood smear was prepared immediately.

Thyroid Function Tests

Blood samples collected in plain vials were centrifuged at 3000 rpm for 20 minutes. Separated serum samples were stored at −20°C until analysis. Serum levels of T3, T4, and TSH were measured using commercial ELISA kits. The reference ranges provided by the manufacturer were:

- TSH: 0.27–4.20 μIU/mL
- Total T4: 66–181 nmol/L
- Total T3: 1.30–3.10 nmol/L
- Free T3: 0.22–6.78 pmol/L
- Free T4: 10.3–35 pmol/L

Subclinical hypothyroidism was defined as elevated TSH (>5 μIU/mL) with normal circulating thyroid hormone levels and absence of classical symptoms.
Overt hypothyroidism was defined as elevated TSH with reduced serum T3 and/or T4 levels along with clinical features.

Hematological Evaluation

EDTA samples were analyzed using a **Sysmex automated hematology analyzer**, based on electrical impedance and optical light scatter techniques. Parameters assessed included hemoglobin, RBC indices, total RBC count, WBC count, and platelet count.Anemia was defined according to WHO criteria as hemoglobin <12 g/dL in women and <13 g/dL in men.

Peripheral Blood Smear Examination

Peripheral blood smears were stained using Field's and Leishman's stains and examined microscopically to corroborate automated analyzer findings.

Statistical Analysis

Data were analyzed using **SPSS software**. Continuous variables were expressed as mean ± standard deviation. Comparisons between subclinical and overt hypothyroid groups were performed using **Student's t-test**. A p-value ≤0.05 was considered statistically significant.

RESULTS

This observational cross-sectional study included **110 patients** with primary hypothyroidism aged 20–60 years. Of these, **40 patients (36.4%)** had subclinical hypothyroidism and **70 patients (63.6%)** had overt hypothyroidism. The mean age of patients in the subclinical and overt hypothyroid groups was **39.3 ± 11.9 years** and **41.3 ± 11.2 years**, respectively.

The study population comprised **28% males** and **72% females**, with a male-to-female ratio of **1:5**. The subclinical hypothyroid group included 11 males and 29 females, while the overt hypothyroid group consisted of 20 males and 50 females.

Anemia was observed in **56%** of patients with hypothyroidism, which is markedly higher than the **24.8% global prevalence** reported by the World Health Organization. Anemia was detected in **23 patients** with subclinical hypothyroidism and **44 patients** with overt hypothyroidism. However, there was **no statistically significant difference** in the prevalence of anemia between the two groups (p = 0.203).

Comparison of hematological parameters—including hemoglobin, hematocrit, RBC indices, total RBC count, WBC count, and platelet count—showed **no statistically significant difference** between subclinical and overt hypothyroid patients (Table 1).

Table 1: Demographic and hematological parameters of hypothyroid patients

	Subclinical Hypothyroidism	**Overt Hypothyroidism**	**P-value**
Number of cases	40	70	-
Age (years)	39.3±11.9	41.3±11.2	0.38
Gender (male:female)	11:29	20:50	-
TSH (0.27-4.2 µIU/mL)	7.9±2.5	34.9±10.9	0.0001
Hemoglobin (g/dL)	11.8±2.3	11.2±2.4	0.203
Hematocrit (%)	35.2±11.3	33.9±10.2	0.538
RBC (×106 /µl	4.16±1.3	4.01±1.35	0.571
MCH (pg)	27.3±6.4	27.8±6.3	0.691
MCV (fl)	84.8±6.4	86.2±6.8	0.291
MCHC (g/dl)	32.5±9.5	31.7±9.4	0.67
WBC (×103 /µl)	7.5±2.4	6.9±2.2	0.186

Platelets (×103 /µl)	270.8±20.6	265.6±20.2	0.2

The pattern of anemia observed in patients with hypothyroidism is shown in **Table 2**. Analysis of the types of anemia revealed that **anemia of chronic disease** was the most common, accounting for **50.7%** of cases. **Microcytic hypochromic anemia (iron deficiency anemia)** was the second most frequent type (**43.3%**), while **macrocytic anemia** was observed in **6%** of patients.

Subgroup analysis demonstrated that anemia of chronic disease was the most prevalent type in both overt and subclinical hypothyroid patients. The proportion of this anemia was **54.5%** in patients with overt hypothyroidism and **43.5%** in those with subclinical hypothyroidism. Microcytic anemia was observed in **36.4%** of overt hypothyroid patients and **56.5%** of subclinical hypothyroid patients. Macrocytic anemia was found in **9.1%** of overt hypothyroid patients, whereas no cases were identified in the subclinical hypothyroid group. There was **no statistically significant difference** between subclinical and overt hypothyroid groups with respect to the **type of anemia** observed (**Table 2**).

Table 2: Type of anemia in primary hypothyroid patients.

Type of anemia	Subclinical Hypothyroidism	Overt Hypothyroidism	Total
Normocytic Normochromic (MCV 80-100 fl) (MCHC 30-36 %	10 (43.5%)	24 (54.5%)	34 (50.7%)
Microcytic Hypochromic (MCV <80 fl) (MCHC < 30)	13 (56.5%)	16 (36.4%)	26 (43.3%)
Macrocytic (MCV > 100 fl)	0 (0.0%)	4(9.1%)	4 (6%)
Total	23 24 (54.5%)	44(100%)	67 (100%)

DISCUSSION

Hypothyroidism represents a significant global health problem and manifests with a wide spectrum of clinical features, ranging from asymptomatic disease to life-threatening multisystem involvement. These diverse manifestations reflect the essential role of thyroid hormones in regulating metabolic and cellular functions throughout the body [17]. Based on serum thyroxine and thyroid-stimulating hormone (TSH) levels, hypothyroidism is classified into subclinical and overt forms. Subclinical hypothyroidism is characterized by elevated TSH with normal circulating thyroid hormone levels and minimal or absent clinical symptoms, making its diagnosis challenging. In contrast, overt hypothyroidism is associated with elevated TSH and reduced thyroid hormone levels, accompanied by overt clinical manifestations [18].

Thyroid hormones play a crucial role in normal erythropoiesis. Consequently, thyroid hormone deficiency can impair red blood cell production and lead to anemia. Normocytic normochromic anemia is reported as the most common hematological abnormality in hypothyroid patients; however, microcytic and macrocytic anemias have also been documented [19]. Multiple mechanisms may contribute to anemia in hypothyroidism, including nutritional deficiencies, chronic inflammatory states, and reduced erythropoietin production. Nevertheless, the etiology remains unexplained in a substantial proportion of cases [20]. Previous studies have reported anemia in 23–60% of hypothyroid patients [19]. Importantly, several reports indicate improvement or complete resolution of anemia following levothyroxine therapy, emphasizing the role of thyroid hormone deficiency in its pathogenesis [21]. These observations provided the rationale for the present study.

In our study, the overall prevalence of anemia among patients with hypothyroidism was **56.5%**, which lies within the range reported in previous literature. Rabet-Bensalah et al. [22] reported one of the lowest prevalence rates, whereas Anand et al. [19] documented a higher prevalence of 62.14%. According to World Health Organization (WHO) data, the global prevalence of anemia is approximately **24.8%** [23]. The markedly higher prevalence observed in our study supports the notion that hypothyroidism may be an important risk factor for anemia. However, the existing evidence remains limited and heterogeneous, warranting further well-designed studies. The reduced basal metabolic rate and diminished tissue oxygen consumption seen in hypothyroidism may lead to decreased erythropoietin secretion, resulting in reduced hemoglobin synthesis and the development of normocytic, microcytic, or macrocytic anemia depending on associated comorbidities [24].

Analysis of anemia patterns in our study revealed that **normocytic normochromic anemia** was the most prevalent type, followed by **microcytic anemia**, while **macrocytic anemia** was least common. These findings are consistent with previous studies [19]. The predominance of normocytic anemia may be attributed to impaired erythroid colony formation caused by thyroid hormone deficiency, reduced erythropoietin levels, and decreased oxygen delivery to tissues [25].

Conflicting reports exist regarding the predominant type of anemia in hypothyroid patients, with some studies describing macrocytic anemia as most common, while others report microcytic anemia predominance. This variability highlights the importance of thorough evaluation of anemia etiology in hypothyroid patients. Cinemre et al. [26] emphasized the role of hypothyroidism, particularly subclinical hypothyroidism, in patients with iron-deficiency anemia unresponsive to iron therapy. They demonstrated a significantly greater improvement in hemoglobin levels in patients treated with a combination of iron and levothyroxine compared to iron supplementation alone.

In subgroup analysis, our study found **no statistically significant difference** in the prevalence or pattern of anemia between subclinical and overt hypothyroid patients. Although the overall prevalence of anemia in hypothyroidism was higher than that reported by WHO for the general population, the prevalence within each hypothyroid subgroup was comparable to global population estimates. This observation suggests that factors other than thyroid dysfunction, including coexisting comorbidities, may contribute to anemia in these patients. Therefore, while hypothyroidism appears to be

associated with anemia, its independent contribution—particularly in subclinical disease—requires further investigation.

CONCLUSION

Anemia is a common hematological abnormality in patients with hypothyroidism, with **normocytic normochromic anemia** being the most frequently observed pattern. The high overall prevalence of anemia in hypothyroid patients underscores the importance of considering thyroid dysfunction during the evaluation of patients presenting with anemia, especially when the cause is unclear or the anemia is refractory to standard treatment. Early diagnosis and appropriate management of hypothyroidism may facilitate effective correction of anemia. However, current evidence remains insufficient to establish a definitive causal relationship, highlighting the need for larger prospective studies to further elucidate the association between hypothyroidism and anemia..

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