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EVALUATING ANEMIA IN THYROID DISEASE: A STUDY OF HEMATOLOGICAL PARAMETERS

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ABSTRACT

Background: Both anemia and thyroid disorders are widespread clinical issues that can significantly affect patients' health. Investigating the interplay between these conditions is essential for accurate diagnosis and treatment.

Objective: To assess the prevalence and specific characteristics of anemia in individuals with thyroid dysfunctions.

Materials and Methods: In this retrospective study, we examined 140 clinical data of patients with diagnosis of thyroid diseases at our hospital, from January 2019 to December 2023. After ethical approval, the record was assessed for thyroid parameters e.g., thyroid stimulating hormone, and free thyroxine or free T_4. Likewise, hematological parameters were also analyzed. The data was analyzed using SPSS 25.0. A p-value of <0.05 was taken as statistically significant.

Results: A total of 140 patients were involved in current study. The cohort comprised 102 females and 38 males. Majority of patients were having diagnosis of primary hypothyroidism, followed by primary hyperthyroidism. The overall frequency of anemia was 40% with 75.3% of anemic patients having some form of hypothyroidism, and 28.8% having some form of hyperthyroidism.

Conclusion: The normocytic anemia was commonly seen in patients with thyroid diseases, with hyperthyroidism cases approaching microcytosis. There was a statistically significant difference in erythrocytes counts among males having hypothyroidism and those with hyperthyroidism. Additionally, hypothyroidism showed significant association with cardiovascular disorders, diabetes, and hypertension.

Keywords: Anemia, hypothyroidism, hyperthyroidism, investigation.

Introduction

Thyroid disorders, such as hypothyroidism and hyperthyroidism, are usually encountered in primary healthcare and are one of the most widespread medical conditions. These disorders can present with clinical symptoms or be detected through laboratory tests that reveal subclinical states, including subclinical hyperthyroidism or hypothyroidism[1]. The hypothyroidism is characterized by a deficiency or absence of circulating thyroid hormones, T4 (thyroxine) and T3 (triiodothyronine), which are important for normal bodily functions[2]. Conversely, hyperthyroidism is marked by an overactive thyroid glands, resulting in elevated free T3 and T4 levels in the circulation. The predominant cause of hypothyroidism is autoimmune devastation of thyroid gland, where antibodies wither damage the gland or inhibit thyroid hormone production. Other causes include surgical removal of the thyroid, treatments for hyperthyroidism, hypothalamic-pituitary insufficiency, and iodine deficiency. Hyperthyroidism is often caused by conditions such as diffuse thyroid hyperplasia linked with Grave's disease, hyperfunctioning multinodular goiter, as well as hyperfunctioning thyroid adenoma[3].

Between 21% and 60% individuals with hypothyroidism experience anemia, which is primarily due to reduced erythrocytes production, diminished erythropoietin stimulation, and decreased oxygen demand by the body. The symptoms of anema i.e., fatigue, weakness, and shortness of breath, are often mild and can go unnoticed, frequently overlapping with the clinical signs of hypothyroidism, such as cold intolerance, tiredness, and lethargy[4]. Anemia is defined by a lower-than-normal hemoglobin concentration in the blood for an individual's age, sex, and physiological status (e.g., pregnancy). It can result from various factors, including impaired erythrocyte production, shortened erythrocyte lifespan due to hemolysis or blood loss, increased retention or sequestration of erythrocytes in an enlarged spleen, and interactions with hemoglobinopathies[5].

The coexistence of anemia and thyroid dysfunction presents a significant clinical challenge, though the connection between these conditions is not fully understood. Thyroid hormones are known to directly influence hematopoiesis by stimulating the proliferation of erythrocyte precursors and the production of erythropoietin in the kidneys. Various forms of anemia, including normocytic, macrocytic, and microcytic anemia, can occurs in thyroid dysfunctions, with normocytic anemia being the most common. The concurrence of anemia with thyroid disorders is a notable clinical issue. Thyroid hormones play a critical role in erythropoiesis, and several factors and comorbidities to anemia in thyroid diseases[6]. Autoimmune conditions, such as pernicious anemia, where parietal cells are destroyed leading to reduced vitamin B12 absorption, and conditions like celiac disease, which impairs nutrient absorption and can cause iron deficiency anemia, further complicate the scenario[7]. This research aimed to assess the prevalence and characteristics of anemia in patients with thyroid dysfunctions. Hematological biochemical, and hormonal data was analyzed and correlated with

thyroid dysfunctions in patients diagnosed with hypothyroidism and hyperthyroidism.

Materials and Methods

This research utilized a retrospective cross-sectional design, carrier out at a tertiary care hospital. It focused on patients diagnosed with various forms of hypothyroidism and hyperthyroidism. The study used data from both outpatients and inpatients data records. The records chosen ere from patients who had been diagnosed with thyroid dysfunctions during their initial visit and met the inclusion criteria, with period ranging from January 2019 to December 2023. The study included male and female patients of all aged who were diagnosed with hypothyroidism and hyperthyroidism. Patients were excluded if their medical records were unavailable or if the records did not include the specific indication of thyroid dysfunction.

The study assessed several laboratory parameters, primarily focusing on thyroid function tests, including thyroid-stimulating hormone (TSH) and free thyroxine (FT4). Hematological parameters analyzed included hemoglobin levels, mean corpuscular volume (MCV), red blood cell count (RBC), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular hemoglobin (MCH), hematocrit (Hct) values, red blood cell distribution width (RDW), and cytomorphological changes in red blood cells. Additionally laboratory data considered was serum iron and ferritin levels.

Patients were classified into anemia and non-anemic groups based on World Health Organization (WHO) criteria[8]. Descriptive statistics were used to present continuous variables through measures of central tendency and dispersion. The normality of continuous variables was assessed using the Shapiro-Wilk test. Statistical analysis included Chi-square and Fisher's exact tests, as well as Mann-Whitney U test. A p-value of <0.05 was considered as statistically significant.

Results

A total of 140 patients were included in this study. Our analysis revealed distinct hematological profiles among patients with hypothyroidism and hyperthyroidism. Table 1 provides the median values of key hematological parameters stratified by gender and disease. Notable, patients with hypothyroidism exhibited lower median values of red blood cell count (RBC), with values ranging from 3.70 to 4.30 x $10^6/mm^3$, and hemoglobin concentration (Hb), with values ranging from 10.80 to 12.50 g/dL, compared to reference values, suggesting a tendency towards anemia. Conversely, patients with hyperthyroidism showed slightly elevated median values of RBC and Hb, indicating potential erythrocytosis.

Further classification of hematological data based on the type of anemia revealed intriguing insights as depicted in Table 2 and 3. Normocytic anemia was prevalent among patients with hypothyroidism, with median values ranging from 3.70 to 3.90 x $10^6/mm^3$ and Hb ranging from 12.20 to 12.50 g/dL. These findings underscore the

complex interplay between thyroid function and erythropoiesis. Our study also investigated the prevalence of comorbidities associated with thyroids disorders, as summarized in Table 4. Hypothyroidism was significantly associated with comorbidities, such as diabetes (17.76%), hypertension (24.34%), and cardiovascular diseases (5.95%), highlighting the systemic nature of thyroid dysfunction. In contrast, hyperthyroidism showed weaker associations with comorbidities, albeit still notable, including hypertension (13.86%) and diabetes (10.14%).

Table 1: Median of Hematological Parameters for Hypothyroidism and Hyperthyroidism Patients, Stratified by Disease and Gender (n=140)

Parameter	Hypothyroidism (Median)		Hyperthyroidism (Median)	
	Female	*Male*	*Female*	*Male*
RBC (x 10^6/$mm^{3)}$	4.20	4.30	4.30	4.60
Hemoglobin (g/dL)	12.35	12.45	12.45	13.55
Hct (%)	37.10	37.90	37.80	40.50
MCV (fL)	90.00	89.50	87.00	87.50
MCH (pg)	30.00	30.20	28.50	30.00
MCHC (g/dL)	33.20	33.50	33.00	34.60
RDW (%)	13.50	14.00	14.20	13.30

Hct, hematocrit; MCH; mean corpuscular hemoglobin; MCHC; mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; RDW; red cell distribution width

Table 2: Description of Hematological Parameters in Hypothyroidism and Hyperthyroidism, Stratified by Type of Anemia (n=140)

Parameter	Hypothyroidism			Hyperthyroidism		
	Normocytic (n=30)	*Microcytic (n=20)*	*Macrocytic (n=15)*	*Normocytic (n=25)*	*Microcytic (n=18)*	*Macrocytic (n=20)*
RBC (x 10^6/$mm^{3)}$	3.70	3.30	3.35	3.91	3.28	3.21
Hemoglobin (g/dL)	10.80	10.71	11.70	10.20	10.15	10.12
Hct (%)	32.50	31.40	34.70	36.10	35.20	33.52
MCV (fL)	89.00	69.00	110.30	87.10	71.10	113.41
MCH (pg)	28.70	26.80	29.30	29.20	29.70	28.60
MCHC (g/dL)	32.80	33.00	33.20	33.40	33.30	33.25
RDW (%)	13.80	15.20	14.10	11.50	14.12	14.20

Table 3: Comparison of Hypothyroidism and Hyperthyroidism according to Type of Anemia (n=140)

Type of anemia	Hypothyroidism	Hyperthyroidism	p-value
Normocytic	20	25	0.312
Microcytic	15	18	0.547
Macrocytic	7	8	0.729

Table 4: Comorbidities and Their Association with Hyperthyroidism and Hyperthyroidism (n=140)

Co-morbid condition	Hypothyroidism (%)	Hyperthyroidism (%)	p-value
Pre-existing anemia	1.32	0.73	0.98
Asthma	0.66	0.73	0.64
Diabetes	17.76	10.14	0.003
Dyslipidemia	2.65	1.47	0.12
Cardiovascular diseases	5.95	2.20	0.03
COPD	1.32	0.73	0.12
Chronic kidney disease	1.32	1.23	0.91
Gout	0.66	0	-
Hypertension	24.34	13.86	0.002
Obesity	8.87	7.32	0.21
Smoking	7.89	7.59	0.45

Discussion

Thyroid dysfunctions are associated with alterations in blood composition, with anemia emerging as the most prevalent. Nevertheless, research exploring the correlation between anemia and thyroid disorders remains sparse, often presenting conflicting findings regarding its manifestations in patients with hypothyroidism or hyperthyroidism. Challenges in gathering hematological, biochemical, and hormonal data of this study limited the number of participants analyzed, with numerous medical records lacking essential information required to assess the link between thyroids function and anemia. The demographic distribution of sex and age in this study corresponds with existing literature. Predominantly female participants align with the established trend of thyroid disorders affecting women more frequently. These findings underscore the connection between anemia and thyroids disorders, particularly in older individuals. Prior studies indicate that older adults, especially those with thyroid disorders, often exhibit diminished levels of hemoglobin, red blood cells, and hematocrit, suggesting a

potential correlation between the disease's pathophysiology and aging[9–11]. Moreover, the skewed gender ratio towards females in thyroid disorders supports literature findings, further discounting alternative mechanisms linking erythropoiesis to endocrine function[6,9,12].

Analysis of this study indicates a higher prevalence of hypothyroidism among participants, consistent with literature suggesting a greater incidence of hypothyroidism diagnoses compared to hyperthyroidism[13]. This trend is attributed to the complexities in managing hyperthyroidism effectively, often necessitating interventions like thyroidectomy or radioactive iodine, which may inadvertently induce hypothyroidism. Primary hypothyroidism emerges as the most prevalent subtype observed in this study. Anemia is characterize by hemoglobin levels below 13 g/dL for men or 12 g/dL for women, with reduced red blood cells, hemoglobin concentration or hematocrit. Hemoglobin values more prevalent in a significant proportion of hypothyroid and hyperthyroid patients in this study, surpassing reported frequencies of anemia in thyroid disorders in the existing literature. Additionally, a noteworthy number of patients with thyroid disorder were diagnosed with anemia in this study compared to previous research.

Only two patients' medical records in this study documented preexisting anemia, hinting at a potential link between anemia and thyroid disorders. Hematological findings in anemia patients align with existing literature, with normocytic and normochromic anemia predominating[14]. Notable, the presence of ovalocytes, previously unreported, suggest a potential avenue for further investigation. Anemia in hypothyroidism predominantly arise from deficiencies in erythropoietic stimulation due to insufficient thyroid hormone levels, resulting in diminished erythropoietic activity in the bone marrow. Conversely, hyperthyroidism triggers increased erythropoietic stimulation by thyroid hormones, leading to bone marrow hyperplasia and alterations in erythrocyte morphology and function. Iron plays a pivotal role in thyroid function, being a crucial component of heme[6]. However, this study did not find direct evidence linking thyroid deficiency with iron or ferritin levels. Elevated serum ferritin levels observed suggest chronic disease anemia, commonly associated with thyroid disorder.

Analysis also highlights associations between thyroid disorders and comorbidities such as hypertension, diabetes, and cardiovascular diseases, with patients with hypothyroidism exhibiting a higher likelihood of these conditions compared to those with hyperthyroidism. Thyroid hormones influence myocardial function and vascular resistance, potentially contributing to cardiovascular disease development[15,16].

Conclusion

The findings of this study resonate with the documented variances in anemia prevalence among individuals with thyroid disorders as reported in existing literature. This adds weight to the understanding of the unique features of anemia in this population, notably in relation to hemoglobin and mean corpuscular volume

(MCV) levels. A notable proportion of patients diagnosed with both hypothyroidism and hyperthyroidism exhibited anemia, highlighting the intricate regulation of erythropoiesis influenced by diverse factors, with thyroid hormones playing a pivotal role in governing both erythropoiesis and erythropoietin concentrations. The anemia observed in this study cohort displayed characteristics of normocytic and normochromic profiles, presenting challenges to clinicians to discerning its underlying causes. Data collection unveiled numerous instances wherein clinicians grappled with unraveling the elusive origins of anemia in these patients. Moreover, beyond the scope of hematologic, hormonal, and biochemical assessments, the prevalence of specific comorbidities, particularly in hypothyroid cases, hints at the direct impact of thyroid disorders on metabolic processes, consequently affecting the functionality of other bodily systems, with potential implications for erythropoiesis.

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