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Evaluation of blood parameters in the management of patients with thyroid disease

Abazar Yari [1], Morteza Ahmadi [1], Mahdieh Mehrpouri [2*]

1. Department of Anatomy, Faculty of Medicine, Alborz University of Medical Sciences, Karaj, Iran
2. Department of Laboratory Sciences, School of Allied Medical Sciences, Alborz University of Medical Sciences, Karaj, Iran
* Correspondence: Mahdieh Mehrpouri. Department of Laboratory Sciences, School of Allied Medical Sciences, Alborz University of Medical Sciences, Karaj, Iran. Tel: +989128826488; Email: mahdiyemehrpoori@gmail.com

Abstract

Background: Thyroid hormones play a critical role in hematopoiesis, and thyroid disorders such as hypothyroidism and hyperthyroidism can affect blood parameters. Therefore, this study aimed to evaluate the effect of thyroid dysfunction on various blood parameters.

Methods: This case-control study included 194 subjects who were classified into three groups based on TSH levels: hypothyroid (n=70), hyperthyroid (n=56), and control (n=68). Conditions that affect blood parameters, including pregnancy, inherited or acquired red blood cell abnormalities, chronic inflammatory diseases, evidence of nutritional deficiencies, and underlying diseases such as cancer, as well as patients unwilling to participate in the study, were excluded. Hematological parameters were measured using a cell counter, and the results were analyzed using SPSS software.

Results: The results showed that 78% of the participants were female and 22% were male, aged 4 to 89 years. The analyses revealed that RBC, Hb, HCT, WBC count, and WBC differential count were significantly different between the three groups (P-value <0.05), but the differences were not significant for MCV, MCH, MCHC, RDW, PLT, and MPV (P-value >0.05). Correlation analysis indicated a significant correlation between TSH and Hb, HCT, WBC, PLT, neutrophils, lymphocytes, monocytes, and eosinophils (P<0.05).

Conclusion: Since thyroid hormones play a critical role in hematopoiesis, thyroid dysfunction can affect many hematological parameters. Therefore, the management of patients with thyroid disease should include the CBC test. In addition, patients with poor responses to anemia treatment may have an underlying thyroid disorder.

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Introduction

Thyroid hormones (THs) play essential roles in the development, growth, metabolism, and physiological function of all organs and tissues. TH binds to thyroid hormone receptors (TRs), which are members of the nuclear hormone receptor superfamily (1). Notably, in hematopoiesis in the bone marrow, THs have a regulatory effect through the TR-Krüppel-like factor 9 axis (2). Thyroid dysfunction is among the most common endocrine disorders and is mainly divided into hypothyroidism and hyperthyroidism (1,3). Hypothyroidism is the most common thyroid disorder, in which insufficient THs are released into the bloodstream, resulting in many clinical manifestations including lipid abnormalities, cardiac dysfunction, atherosclerosis, and changes in blood parameters. Due to these variations in clinical manifestations, the diagnosis of hypothyroidism is primarily biochemical (3-5). Hyperthyroidism is characterized by the overproduction of THs due to autoantibodies or excessive secretion by a functional thyroid nodule. This condition is diagnosed and managed using thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3) measures (3). The association between thyroid dysfunction and abnormalities in blood parameters has been noted in patients with thyroid dysfunction. However, the exact mechanism for the action of THs on human hematopoiesis remains to be elucidated, although their important role in hematopoiesis, especially erythropoiesis, has long been identified. THs have the potential to influence the activity of delta-aminolevulinic acid synthase (ALA synthase-the rate-limiting enzyme in the synthesis of heme), thereby playing a role in hemoglobin (Hb) synthesis. Moreover, thyroid status can also play a role in heme degradation and the maturation of Hb in the fetus (6). Of particular interest, a causal association between hypothyroidism and different types of anemia has been shown in humans, indicating lower Hb or erythropoietin (EPO) levels (7). A previous study found that both hypo- and hyperthyroidism change the expression of TR gene expression in hematopoietic progenitor cells in vivo, and TH reduction resulted in a decrease in total blood counts (8). This study was conducted to evaluate the effect of various types of thyroid dysfunction on different blood parameters and compare them to the healthy individual group, as well as to explore a possible correlation between thyroid dysfunction and various blood parameters.

Methods

The present study was designed as a case-control study and included 194 subjects who were admitted to the medical diagnostic laboratory of Imam Ali Medical Center, Karaj, Iran, from December 2020 to December 2021.

The participants were classified into hypothyroid (n=70), hyperthyroid (n=56), and control groups (n=68). The inclusion criteria for this study were TSH > 5 mIU/mL for hypothyroidism, TSH < 0.25 mIU/mL for hyperthyroidism, and normal TSH levels for the control group. This study was conducted following the ethics committee approval of Alborz University of Medical Sciences (IR.ABZUMS.REC.1400.167), and informed consent was obtained from all patients in accordance with the Helsinki Declaration. The exclusion criteria included conditions that affect blood parameters, such as pregnancy, inherited or acquired red blood cell (RBC) abnormalities, chronic inflammatory diseases (e.g., diabetes, hypertension, and coronary artery disease), evidence of nutritional deficiencies, and underlying diseases such as cancer, as well as unwillingness to participate in the study. Two ml of ethylenediaminetetraacetic acid (EDTA)-anticoagulated blood and five ml of whole blood were collected from each patient and control individual under aseptic conditions for complete blood count (CBC) and thyroid function tests, respectively, and placed in Becton Dickinson tubes. CBC was analyzed immediately after blood collection using an automated cell counter (Sysmex KX21-N; Sysmex Corporation, Kobe, Japan) at the laboratory of Imam Ali Medical Center. The hematological parameters studied included RBC count, hematocrit (HCT), Hb, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), white blood cell (WBC) count, platelet count (PLT), and mean platelet volume (MPV). Whole blood was centrifuged for 10 min at 1000 g, and serum was collected. Chemiluminescence immunoassay was performed to analyze thyroid function tests, including TSH, T3, and T4 (Roche Diagnostics, Germany). The reference ranges for T3, T4, and TSH hormones were 0.8-1.9 ng/mL, 5-13 µg/dL, and 0.50-5.06 mIU/mL, respectively. Statistical analysis was performed using SPSS software (Version 21), and the results were presented as mean ± standard deviation (SD). The normal distribution of the variables was assessed by the Kolmogorov-Smirnov test. One-way analysis of variance (ANOVA) was used to compare the three groups, including the hypothyroid, hyperthyroid, and control groups. Pearson's correlation analysis was used to determine the correlation between hematological parameters and thyroid function tests. A P-value < 0.05 was considered statistically significant.

Results

In the present study, a total of 194 subjects participated, of whom 78% were female and 22% were male, aged between 4 and 89 years. Cases were categorized into three groups based on the thyroid function test TSH, including hypothyroid, hyperthyroid, and control. There were 70 hypothyroid patients, 56 hyperthyroid

patients, and 68 individuals in the control group. The demographic characteristics of hypothyroid patients, hyperthyroid patients, and the control group are provided in Table 1. The levels of TSH in hypothyroid patients showed a significant increase compared to healthy controls (p=0.000). Hypothyroid patients also had significantly lower levels of T4 (p=0.000). Moreover, there was no significant difference in the mean T3 levels between hypothyroid patients and controls (p=0.58) (Table 1). ANOVA analyses were used to compare RBC, WBC, PLT, neutrophil, and lymphocyte parameters among the three groups. In addition, the non-parametric Kruskal-Wallis test was applied to compare Hb, HCT, MCV, MCH, MCHC, RDW, MPV, monocyte, eosinophil, and basophil parameters between the hypothyroid, healthy control, and hyperthyroid groups. The results showed significant differences in RBC, Hb, and HCT among the three groups; specifically, healthy controls had higher RBC, Hb, and HCT levels compared to hypothyroid and hyperthyroid patients (p=0.000). Regarding other RBC parameters, the analyses indicated no significant differences in MCV, MCH, MCHC, and RDW among the three groups (p>0.05). The results further indicated that PLT and MPV levels showed no significant differences between healthy controls and patients. The analyses also revealed significant differences in WBC count and WBC differential count among the three groups, except for basophil percentages, which showed no significant differences (Table 2).

The bivariate Pearson correlation indicates a significant correlation between TSH and WBC, PLT, neutrophil, and lymphocyte parameters (P<0.05). Moreover, Spearman's rank-order correlation was used to assess the association between TSH and non-parametric parameters, indicating a significant correlation between TSH with Hb, HCT, monocyte, and eosinophil (Table 3).

Table 1. Demographic characteristics and thyroid hormones level in three groups

Parameter	Hypothyroid (n=70)	Hyperthyroid (n=56)	Control group (n=68)
Age (Mean ± SD)	36.55±17.36	46.62±18.04	36.00±14.18
Gender (Male/Female)	10/60	9/47	24/44
TSH (Mean ± SD)	7.92±3.66	0.09±0.07	2.32±0.98
T4 (Mean ± SD)	8.33±1.88	6.53±1.25	7.17±1.60
T3 (Mean ± SD)	1.15±0.42	1.11±0.19	1.11±0.19

Table 2. Comparison of CBC parameters in three groups

Parameter	Hypothyroid (n=70) (Mean ± SD)	Hyperthyroid (n=56) (Mean ± SD)	Control group (n=68) (Mean ± SD)	P-value
RBC	4.91±0.49	4.71±0.55	5.16±0.58	0.000
Hb	13.56±1.57	12.98±1.62	14.28±1.68	0.000
HCT	40.23±4.92	38.70±4.37	42.57±4.28	0.000
MCV	82.67±4.66	82.57±5.31	82.97±6.88	0.240
MCH	27.78±2.29	27.52±2.33	27.77±3.31	0.364
MCHC	33.57±1.38	33.39±1.41	33.61±1.14	0.769
RDW	13.56±2.14	13.63±1.78	13.20±1.50	0.327
PLT	264140±64480	273980±72190	259750±64580	0.489
MPV	10.45±0.85	10.60±0.86	10.48±1.35	0.349
WBC	7.31±1.52	9.05±2.15	7.84±1.78	0.000
Neutrophil percent	51.95±10.36	68.25±13.26	55.18±9.47	0.000
Lymphocyte percent	37.77±10.03	23.23±11.61	33.64±10.49	0.000
Monocyte percent	7.62±1.90	6.71±2.19	7.72±1.62	0.007
Eosinophil percent	2.40±1.64	1.40±1.35	2.93±3.1	0.001
Basophil percent	0.51±0.22	0.47±0.42	0.51±0.25	0.729

Table 3. Correlation assessment between TSH and CBC parameters

Parameter	Correlation coefficient	P-value
RBC	- 0.024	0.742
Hb	0.178	0.013
HCT	0.181	0.012
MCV	- 0.053	0.466
MCH	- 0.002	0.983
MCHC	0.038	0.599
RDW	- 0.003	0.964
PLT	- 0.180	0.012
MPV	- 0.039	0.585
WBC	- 0.272	0.000
Neutrophil percent	- 0.277	0.000
Lymphocyte percent	0.275	0.000
Monocyte percent	0.164	0.022
Eosinophil percent	0.220	0.002
Basophil percent	0.106	0.142

Discussion

The thyroid gland is a vital endocrine gland, with the secretion of THs playing a critical role in the metabolism, growth, and development of the human body. In erythropoiesis, THs can induce the production of EPO and the proliferation of erythroid progenitors, thereby increasing the oxygen-carrying capacity of the blood (9). Of particular interest, anemia and other abnormal blood parameters are common in thyroid disorders. Due to the autoimmune nature of many thyroid disorders, thyroid dysfunction is more common in females than males, with 12.5% of women ultimately developing a thyroid problem during their lifetime (10). In this regard, this study was conducted to assess the effects of thyroid diseases (Hypothyroidism and hyperthyroidism) on CBC parameters. In the present study, the female gender predominated (78%) over the male gender (22%), similar to most articles, such as those by Dorgalaleh et al. and Ahmed et al., although in Iddah et al., the male-to-female ratio was higher, around 1:10.9 (11-13). In our study, the age of the participants ranged from 4 to 89 years, which was higher than in the previous study (2 to 34 years) (12). We evaluated the patients from December 2020 to December 2021, which included 70 hypothyroid patients and 56 hyperthyroid patients. It is generally estimated that hypothyroid cases outnumber hyperthyroid patients when patients are selected randomly. Our results revealed that RBC, Hb, and HCT were significantly lower (P=0.000) in hypothyroid and hyperthyroid patients compared with healthy controls. Similarly, a previous study showed that Hb levels are affected by thyroid dysfunction, with about one-third of patients with thyroid disease being anemic (12). In a study by Dorgalaleh et al., Hb and HCT were significantly lower in patients with thyroid dysfunction compared to healthy controls, although no significant difference in RBC was observed between patients and the control group (11). Notably, anemia is a common clinical condition in thyroid disease, partly due to the critical role of THs in erythropoiesis, and various types of anemia may develop in thyroid dysfunction (14). MCV and MCH measure the average amount of Hb in RBCs and the average size of red blood cells, respectively. Moreover, RDW reflects the erythrocyte size distribution. These parameters are valuable in explaining the etiology of anemia (15). In the present study, we did not observe any significant differences in RBC indices, including MCV, MCH, MCHC, and RDW, between patients and healthy controls. Studies have found that normocytic anemia with normal indices is the most common type of anemia in patients with thyroid dysfunction, while macrocytic or microcytic anemia occurs less frequently. In hypothyroidism, anemia may be caused by bone marrow failure, reduced production of EPO, comorbid diseases, or concurrent deficiencies of iron, folate, or cobalamin. However, oxidative stress and altered iron metabolism may result in anemia in hyperthyroid patients (14).

According to the obtained results, PLT and MPV showed no significant differences between patients and normal controls. Supporting our data, Dorgalaleh et al. indicated that PLT did not show a statistically significant difference between hypothyroid and hyperthyroid patients (P-value > 0.05) (11). Ahmed et al. found that PLT was independent of thyroid dysfunction and did not change following thyroid abnormalities (12).

It seems that the reason that platelets are less affected by thyroid function is that platelets are non-nucleated cells with a short lifespan, and thyroid dysfunction mainly affects the megakaryopoiesis process. Nevertheless, some studies have found an inverse association between thyroid hormone levels and MPV. Erikci et al. indicated that patients with subclinical hypothyroidism had significantly higher MPV and platelet distribution width (PDW) than the control group, suggesting that MPV and PDW play a significant predictive role in subclinical hypothyroidism (16). Yilmaz et al. showed that the MPV value was significantly higher (P-value < 0.001) in the subclinical hypothyroidism group, which decreased after subclinical hypothyroid patients were converted to euthyroid (17). Regarding leukocytes, analysis of the acquired data revealed a statistically significant difference among the three groups of patients in WBC count and different types of WBCs, except for basophils. In the study by Ahmed et al., they indicated that WBC was among the parameters strongly affected by thyroid function status (12). However, in a study by Dorgalaleh et al., they did not find statistically significant differences in WBC parameters in patients with hypothyroidism and hyperthyroidism (P-value > 0.05) (11).

Conclusion

In conclusion, our data suggest that THs play a critical role in hematopoiesis, as thyroid dysfunction has the potential to change many hematological parameters, including RBC, Hb, HCT, and WBC, although RBC indices such as MCV, MCH, MCHC, and RDW, as well as platelets, are less affected by thyroid status. Therefore, while many patients with thyroid disorders are anemic, their anemia is often normochromic and normocytic. The management of patients with thyroid disease should include the CBC test and WBC differential count. Furthermore, it can be concluded that patients who respond poorly to anemia treatment may have an underlying thyroid disorder.

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Ethical statement

The study was conducted at Imam Ali Medical Center (Karaj, Iran) from December 2020 to December 2021 and was approved by the ethics committee of Alborz University of Medical Sciences (IR.ABZUMS.REC.1400.167).

Conflicts of interest

The authors declare no potential conflicts of interest.

Author contributions

AY supervised the work and edited the draft. MA drafted the paper and contributed to data gathering. MM conceptualized the study and provided the study design and statistical analysis. All authors contributed to the discussions and writing of the manuscript.

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