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Original Article

Evaluate the Hematologic Parameters, Neutrophil-to-Lymphocyte Ratio, and Platelet-to-Lymphocyte Ratio in Patients with Autoimmune Hypothyroidism from Amara City, Southern Iraq

Nidhal Abdullah Hashim, Younus Jasim Abdullah, Ali Abdullah Sayhood

Department of Medical Laboratory Technology, Amara Medical Institute, Southern Technical University, Maysan Province, Amara City, Iraq

Abstract

Background: Thyroid diseases are affecting 3%–5% of the women general population. Autoimmune thyroid diseases such as Graves' disease (GD) and Hashimoto's disease were detected to be the commonest disorders affecting thyroid function. **Objectives:** This study is a case–control study that aimed to estimate the effect of HT on hematological parameters. **Materials and Methods:** A total of 100 persons (50 HT patients and 50 euthyroid groups) of both sexes aged between 15 and 50 years were included in this study during the period April 2021–April 2022. Samples of venous blood (5 mL) were obtained from the study participants and used for the estimation of serum thyroid-stimulating hormone (TSH), FT3, and FT4 levels, as well as anti-thyroid peroxidase (TPO), anti-thyroglobulin (TG) concentration, as well as hematologic parameters. **Results:** The results of this study showed that HT patients had significantly higher levels of TSH as well as thyroid autoantibodies (anti-TPO and anti-TG) and significantly lower levels of FT3 and FT4. A considerable decrease was found in the hematocrit, hemoglobin, and mean corpuscular volume among HT patients, whereas no significant differences were found between the HT patients and the euthyroid group in total red blood cell count, total white blood cell count, neutrophils, lymphocytes, monocytes, basophils, platelet counts, MPV, mean distribution width, plateletcrit, and PLCR. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) values were significantly higher in the HT patients compared with the euthyroid group. **Conclusions:** The current study concluded that Hashimoto's thyroiditis is associated with significant elevation in the serum concentrations of anti-TPO and anti-TG antibodies, high TSH levels, and decreased FT3 and FT4 levels. Hashimoto's disease resulted in a significant decrease in the hemoglobin concentration; hence, patients with HT could be at risk to have anemia. Also, HT was associated with elevated NLR and PLR values; therefore, NLR and PLR ratios could be used as routine, inexpensive, easily accessible markers at the clinical course or the severity of autoimmune diseases that progress with chronic inflammation.

Keywords: Hashimoto's disease, NLR, PLR, TG, TPO, TSH

Introduction

The thyroid is described as an endocrine gland responsible for the secretion of thyroid hormones thyroxine (T4) and triiodothyronine (T3) and affecting normal growth, tissue differentiation, and metabolism. The production of thyroid hormones is regulated by thyroid-stimulating hormone (TSH), which is secreted by the pituitary gland.[1] Also, a defect in the hypothalamus gland may lead to hypothyroidism.[2] Thyroid diseases are shown to affect 3%–5% of the women general population. The most common diseases affecting thyroid functions are autoimmune thyroiditis of which the most prevalent disorders were Graves' disease (GD) and Hashimoto's

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Address for correspondence: Dr. Younus Jasim Abdullah, Department of Medical Laboratory Technology, Amara Medical Institute, Southern Technical University, Amara City, Iraq.
E-mail: younusjasim@stu.edu.iq

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hypothyroidism (HT).[3] In females, the incidence ratio for HT is approximately 8:1. The pathogenesis of HT involved both cell-mediated and humeral autoimmune immune responses where dendritic cells expose thyroid antigens to T-cells as heterologous antigens, which causes these cells to multiply and differentiate into thyroid antigen specialized lymphocytes, which then causes inflammation of the thyroid, cytotoxicity, and antibody formation.[4] Hypothyroidism is also common in patients who are subjected to thyroidectomy.[5]

Thyroid hormones have been shown to regulate hematopoiesis in the bone marrow, as well as participate in the generation of hemoglobin in adults and fetal hemoglobin maturation. As a result, problems in thyroid hormone synthesis are accompanied by red blood cell (RBC) abnormalities.[6] They promote erythropoiesis by encouraging erythroid progenitor cells to proliferate. They promote erythropoietin (EPO) secretion via influencing EPO gene expression and EPO secretion by the kidneys.[7] Therefore, it is critical for patients with thyroid dysfunction to analyze their hematologic indices to better manage refractory anemia. Hence, the aim of the present study was to evaluate the hematologic parameters in patients suffering from autoimmune hypothyroidism.

Materials and Methods

Study participant

One hundred persons were enrolled in the current case–control study (50 patients with hypothyroidism and 50 euthyroid group) during the period of April 2021–April 2022. The study participants were aged between 15 and 50 years, and they were of both genders (males and females). The diagnosis of Hashimoto thyroiditis was achieved using serological tests for the detection of TSH level, anti-thyroid peroxidase (TPO-Abs), and anti-thyroglobulin antibodies (TG-Abs). Subjects with inherited or acquired red cell abnormalities, thyroid disorders, anemia, chronic illnesses, children under the age of 12, pregnant women, and anyone who refused to take part in the study were all omitted from the analysis.

Sample collection

Venous blood samples of 5 mL were collected from the study subjects and divided into portions (2 mL in ethylene diamine tetra acetic acid tube and 3 mL in plane tube). The first 2 mL were used to analyze blood indices, whereas the second 3 mL were utilized to estimate the levels of TSH, and concentration of thyroid autoantibodies anti-TPO and anti-TG using serology.

Serological detection of TSH and thyroid hormones

Using the electrochemiluminescence immunoassay (ECLIA) method, the serum levels of the thyroid hormones free triiodothyronine (fT3), free thyroxine (fT4), and TSH were assessed on the same day as blood collection (Cobas, Comp., Penzberg, Germany). The data have been expressed in IU/mL, as stated in the manufacturer's instructions.

Serological detection of thyroid autoantibodies

Estimation of serum anti-TPO and anti-TG concentration was achieved by the ECLIA technique. Kits for anti-TPO and anti-TG were provided by Roche Austria GmbH, Vienna, Austria.

Detection of hematologic indices

Hematologic parameters of HT patients and euthyroid group were obtained by applying 2 mL of fresh uncoagulated blood into the hematology auto analyzer Sysmex KX-21 (Sysmex Corporation, Kobe, Japan). The results for each participant were then recorded and analyzed.

Statistical analysis

SPSS package version 20 (performed by IBM Co., Chicago, IL, USA) software was applied for statistical analysis of data obtained in this study. The significance of the difference in means was examined using independent *t* tests. When the *P* value was less than 0.05, statistical significance was found.

Ethical statement

The present study complied with the ethical standards outlined by the healthcare institution, according to the Declaration of Helsinki. Blood samples from participants were collected under the observation of a public health technician. The patient consent form was read and signed by all study participants, and the study was approved by the Amara Medical Institute's Committee on Scientific Research Ethics, by the document numbered 42437 in the date of April 4, 2021.

Results

The findings of the current study showed, as shown in Table 1, that TSH levels were considerably higher in HT patients than in the euthyroid group ($P = 0.001$), whereas the levels of thyroid hormones FT3 and FT4 were decreased significantly ($P = 0.023$ and 0.045, respectively). Also, the concentrations of both thyroid autoantibodies (TPO and TG) were significantly higher in HT patients than in the euthyroid group ($P = 0.001$).

The RBCs indices in HT patients and the euthyroid group are presented in Table 2. From this table, no significant differences were found between HT patients and euthyroid group in the total RBC count. However, considerable differences were found in all of hematocrit, hemoglobin, mean corpuscular hemoglobin concentration, red cell distribution width - standard deviation (RDW-SD), and red cell distribution width-coefficient of variation, as all of these parameters were decreased significantly in HT patients compared with the euthyroid group.

Table 1: Serum levels of TSH, TPO, and TG in HT patients and euthyroid group

Parameter	HT patients	Euthyroid group	*P* value
	Mean ± SD	Mean ± SD	
TSH (μIU/ml)	6.93 ± 1.61	2.35 ± 0.82	<0.001[a]
FT3 (pmol/L)	3.25 ± 1.50	8.32 ± 2.32	0.023[b]
FT4 (pmol/L)	14.12 ± 4.15	17.67 ± 4.89	0.045[b]
TPO-Abs (IU/L)	40.57 ± 18.45	4.39 ± 1.50	<0.001[a]
TG-Abs (IU/L)	8.41 ± 2.91	5.85 ± 1.14	<0.001[a]

SD: standard deviation.
[a]Results are significant at 0.01 level.
[b]Results are significant at 0.05 level

Table 2: RBC total count and RBC indices in HT patients and euthyroid group

Parameter	HT patients	Euthyroid group	*P* value
	Mean ± SD	Mean ± SD	
RBC total (×10⁶)	4.79 ± 0.49	4.90 ± 0.46	0.815
HCT (%)	37.54 ± 4.67	40.08 ± 2.86	0.019[a]
HB (g\dL)	11.64 ± 1.96	12.69 ± 1.00	0.001[a]
MCV (fL)	78.70 ± 9.75	81.14 ± 8.49	0.067
MCH (pg)	24.39 ± 4.08	27.34 ± 9.23	0.991
MCHC (g\dL)	30.82 ± 2.05	31.69 ± 1.35	0.032[b]
RDW-SD (fL)	42.03 ± 3.29	41.70 ± 1.91	0.000[a]
RDW-CV (%)	15.25 ± 2.21	14.15 ± 1.26	0.017[a]

HB: hemoglobin, HCT: hematocrit, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, MCV: mean corpuscular volume, RDW-CV: red cell distribution width - coefficient of variation, RDW-SD: red cell distribution width - standard deviation, SD: standard deviation.
[a]Results are significant at 0.01 level.
[b]Results are significant at 0.05 level

On the other hand, findings of Table 3 revealed that there were no appreciable differences between the HT group and the euthyroid group in terms of the total white blood cell (WBC) count, neutrophils, lymphocytes, monocytes, and basophils. Additionally, patients' eosinophil counts were considerably greater than those of the euthyroid group (*P* value = 0.014).

Moreover, the findings presented in Table 4 showed that there are no considerable differences detected between HT patients and euthyroid group in relation to the platelets counts, MPV, mean distribution width, plateletcrit, and PLCR.

According to the current findings, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were both substantially greater in the HT patients than in the euthyroid group (*P* = 0.029 and *P* = 0.047, respectively) as seen in Table 5.

Discussion

The present study pointed that Hashimoto's patients have significant elevation in the serum concentrations of

Table 3: Count of WBC, neutrophils, lymphocytes, monocytes, eosinophils, and basophils in HT patients and euthyroid group

Parameter	HT patients	Euthyroid group	*P* value
	Mean ± SD	Mean ± SD	
WBC total (×10³)	7.43 ± 2.14	8.35 ± 2.27	0.429
Neutrophil (×10³)	4.00 ± 1.51	4.75 ± 1.67	0.168
Lymphocytes (×10³)	2.47 ± 0.77	2.68 ± 0.82	0.602
Monocytes (×10³)	0.67 ± 0.02	0.66 ± 0.03	0.545
Eosinophils (×10³)	0.28 ± 0.01	0.23 ± 0.02	0.014[a]
Basophils (×10³)	0.017 ± 0.001	0.018 ± 0.002	0.917

SD: standard deviation.
[a]Results were significant at 0.01 level

Table 4: Platelets count and platelet-related parameters in HT patients and euthyroid group

Parameter	HT patients	Euthyroid group	*P* value
	Mean ± SD	Mean ± SD	
PLT (×10³)	301.78 ± 99.07	311.82 ± 81.30	0.627
MPV (fL)	11.07 ± 0.86	10.66 ± 1.28	0.433
PDW (fL)	14.07 ± 2022	13.00 ± 3.55	0.174
PCT	0.32 ± 0.08	0.33 ± 0.08	0.806
PLCR	33.18 ± 6.17	32.30 ± 5.83	0.514

PCT: plateletcrit, PDW: mean distribution width, PLT: platelet count SD: standard deviation

Table 5: Comparison between HT patients and euthyroid group in NLR and PLR

Parameter	HT patients	Euthyroid group	*P* value
	Mean ± SD	Mean ± SD	
NLR (%)	1.85 ± 0.71	1.67 ± 0.53	0.029[a]
PLR (%)	128.65 ± 42.42	121.15 ± 31.47	0.047[a]

SD: standard deviation.
[a]Results were significant at 0.05 level

thyroid autoantibodies (TPO and TG) and TSH as well as considerable decreased levels of the thyroid hormones (FT3 and FT4), as presented in Table 1.

The main antithyroid antibody in Hashimoto's disease is called TPO. Future clinical signs of illness progression have been linked to the development of anti-TPO antibodies.[8] According to studies, the serum of HT patients had higher levels of anti-TPO and anti-Tg antibodies. However, these antibodies may not be present in the circulation in 10% of Hashimoto's disease patients. The limited generation of thyroid autoantibodies to the thyroid gland has been associated to these situations.[9,10] In addition, Siriwardhane *et al*.[11] came to the conclusion that serum levels of anti-Tg and anti-TPO can be used as markers for early thyroid autoimmunity development prediction, and they also suggested including these tests in the same list of thyroid function tests that also includes FT3, FT4, and TSH.

From the above results, it is clear that all of hematocrit, hemoglobin, mean corpuscular hemoglobin concentration, RDW-SD, and RDW-CV values were significantly differed in the patients with autoimmune hypothyroidism compared with the euthyroid group, as presented in Table 2. Comparable results were recorded by Bashir *et al*.[12] and Kadgi *et al*.[13] Moreover, Wopereis *et al*.[14] concluded that adult patients with hypothyroidism and hyperthyroidism are at high risk for developing anemia, whereas Gamal *et al*.[15] reported that primary school aged children with iron deficiency anemia are at high risk to develop thyroid dysfunction in the future.

The thyroid hormones are crucial for controlling the production of RBCs, so when a person has hypothyroidism, their production is reduced, which disturbs the hematological parameters. However, the precise mechanism by which thyroid hormones affect erythropoiesis has not yet been fully understood.[16] In this context, the pervasiveness of anemia in subclinical and overt hypothyroid groups was 26.6% and 73.2% individually as indicated by Mehmet *et al*.[17] Thus, the recurrence of anemia in subclinical hypothyroidism is higher than in general population. Hence, hypothyroidism could be a risk factor for anemia.[18]

According to the results of this study, no significant differences were found between HT patients and euthyroid group in the total and differential WBC count. Consistent results were found by Dorgalaleh *et al.*,[19] Olt *et al.*,[20] and Rezk *et al*.[21] Other studies reported that WBCs and platelets were significantly lower in patients with hypothyroidism with and without autoimmune thyroid disease.[22,23] Hematological indicators such hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and WBC count are all found to be affected by thyroid dysfunction as indicated by Kawa *et al*.[24] Earlier studies have found that leukocytopenia, neutropenia, and thrombocytopenia are conditions that are more likely to develop in people with hyperthyroidism and hypothyroidism.[25,26] These findings may vary from research to study due to genetic factors, sample size, methodology, sociodemographics of the study population, and study design.

Results of this study also noticed that the NLR and PLR values were significantly higher among the HT patients than the euthyroid group. These findings closely matched those of Bilge *et al*.[27] and Ozmen *et al*.,[28] who found that patients with Hashimoto's thyroiditis have elevated levels of both NLR and PLR in addition to C-reactive protein. It is stated that inflammatory diseases cause brief alterations in neutrophil and lymphocyte numbers; hence, NLR could to be a helpful index for the differential diagnosis of diseases and the forecasting of their prognoses as a systemic inflammation index.[29] Additionally, both thyroid inflammation and cancer outcomes from the PLR and NLR were comparable. Using these characteristics, it appears to be challenging to distinguish between inflammatory episodes and malignancy. They can be used to help diagnose thyroid papillary carcinoma or inflammation.[30,31]

Our results suggest that NLR and PLR may serve as additional routine, inexpensive, easily accessible, and valuable markers that could determine the severity and progression of the autoimmune inflammatory condition. Moreover, WBC, neutrophil, NLR, and PLR values should be evaluated in patients with GD to determining its role as inflammatory parameters indicating the progress of the autoimmune hyperthyroidism.

Conclusion

Hashimoto's thyroiditis is associated with significant elevation in the serum concentrations of TPO, TG antibodies, high TSH level, and decreased FT3 and FT4 levels. Hashimoto's disease was associated with significant decrease in the hemoglobin concentration; hence, patients with HT could be at risk to have anemia suggesting a necessary follow-up to avoid complications. Also, HT was associated with elevated NLR and PLR values; therefore, NLR and PLR ratios could be used as routine, inexpensive, easily accessible, practical, and valuable markers at the clinical course or the severity of autoimmune diseases that progress with chronic inflammation.

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Conflicts of interest

There are no conflicts of interest.

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