

Could neutrophil to lymphocyte ratio be a marker in Hashimoto's thyroiditis?

Erhan Onalan, Mehmet Aslan

Abstract

Objective: To determine the applicability of neutrophil/lymphocyte ratio as diagnostic and prognostic marker in patients with Hashimoto's thyroiditis.

Methods: The retrospective cross-sectional study was conducted at Elazig Firat University, Elazig, Turkey, and comprised data of Hashimoto's thyroiditis patients aged 18 years or more admitted between January 1, 2017, and November 1, 2018. A healthy control group was also included to work as controls. Thyroid-stimulating hormone, free triiodothyronine, free thyroxine, anti-thyroid peroxidase, complete blood count, and C-reactive protein results were obtained from patient files for both the cases and the controls, and neutrophil/lymphocyte ratio was computed NLR for both the groups. Data was analysed using SPSS 22.

Results: Of the 477 subjects, 377(79%) were cases with a mean age of 45.3 ± 13.8 years, and 100(21%) were controls with a mean age of 36.6 ± 10.7 ($p < 0.001$). Neutrophil/lymphocyte ratio was statistically higher in the cases compared to the controls ($p < 0.05$). Neutrophil/lymphocyte ratio had a negative correlation with thyroid-stimulating hormone, free thyroxine and anti-thyroid peroxidase but it was non-significant ($p > 0.05$)

Conclusion: Neutrophil/lymphocyte ratio was found to be an effective low-cost marker in the diagnosis and follow-up of Hashimoto's thyroiditis.

Keywords: Hashimoto's thyroiditis, Neutrophil/lymphocyte ratio, Chronic inflammation.
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Introduction

Hashimoto's thyroiditis (HT) is a chronic organ-specific inflammatory autoimmune disease identified in 1912 following the histopathological evaluation of thyroid tissues of four patients, which manifested distinct histological characteristics (diffuse lymphocytic infiltration, formation of lymphoid follicles, destruction of epithelial cells, and fibrous tissue proliferation).¹ Chronic lymphocytic thyroiditis is among the most common causes of hypothyroidism alongside HT goitre, which is also named as autoimmune thyroiditis.² HT is defined by diffuse mononuclear cell infiltration, fibrosis with a decrease in thyroid follicles, presence of large thyrocytes with granular and pink cytoplasm that are named as Hurthle cells, and the presence of thyroid antibodies anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) in blood circulation, as well as the detection of an enlarged thyroid gland, morphological changes in thyroid ultrasonography (USG), and abnormal thyroid function.³ Excess iodine

intake, viral infections and medications are among the many factors that trigger the emergence of the disease. The most common clinical finding is the enlargement of the thyroid gland, either with or without hypothyroidism. The clinical symptoms of the disease involve low thyroid hormone levels accompanied by goitre that regresses with levothyroxine replacement therapy. Thyroid function at the time of diagnosis shows significant variability, ranging from euthyroidism to hypothyroidism, and rarely, hyperthyroidism.^{1,3,4}

Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and thrombocyte indices are ratios that can be easily accessed through a complete blood count (CBC) at a low cost and are shown to be related to many medical conditions and pathologies.⁵⁻⁷ There are reports suggesting that these indices and ratios are correlated with metabolic and endocrine disorders.^{8,9} Inflammatory processes play a key role in chronic diseases, primarily in cardiovascular diseases, cancer, chronic kidney disease, and diabetes mellitus (DM).¹⁰ Studies have identified the NLR as a systemic marker of inflammation. Moreover, NLR has been

Department of Internal Medicine, Firat University, Elazig, Turkey.

Correspondence: Erhan Onalan. Email: drakdeniz@msn.com

shown to be a significant marker for predicting long-term cardiovascular mortality and the prognosis in cancer patients.^{11,12}

The current study was planned to determine the applicability of NLR as a diagnostic and prognostic marker in HT patients.

Patients and Methods

The retrospective cross-sectional study was conducted at the Internal Medicine Department, Elazig Firat University, Elazig, Turkey, and comprised data of HT patients aged 18 years or more admitted to the polyclinics between January 1, 2017, and November 1, 2018. After determining the sample size in the light of previous studies,^{13,14} the patient group was raised using simple random sampling.

A control group was also raised that included healthy individuals who visited the institution for routine check-ups. Diagnosis of HT was established with a combination of relevant history and findings in physical examination that were supported by characteristic findings on USG scan, like diffuse enlargement of the gland and decreased echo pattern, and elevated serum anti-TPO or anti-Tg levels.

Record of patients with other chronic diseases like coronary artery disease, haematological diseases, malignancies, severe liver disease, severe kidney failure, diabetes were excluded.

General characteristics and laboratory data of all participants were obtained from the computerised database of the clinics. White blood cell (WBC) count, neutrophil count (Neu), lymphocyte count (Lym), haemoglobin (Hb), haematocrit (Htc) and platelet count (PLT) were recorded for all participants. NLR was calculated by simply dividing the Neu value by the Lym value.

Statistical analysis was performed using SPSS 22. Descriptive tools like student's t-test, equivalents, and variance analysis were used. Pearson's correlation was used to determine the relationships between the variables and $P < 0.05$ was considered significant.

Results

Of the 477 subjects, 377(79%) were cases with a mean age of 45.3 ± 13.8 years, and 100(21%) were controls with a mean age of 36.6 ± 10.7 ($p < 0.001$). Mean levels of all parameters were noted (Table). NLR was significantly higher in HT patients compared to the controls ($p < 0.05$). NLR had a negative correlation with anti-TPO, TSH and

Table: Descriptive statistics and significance levels of the variables in the patient and the control groups.

Parameters	Patients (n=377) Mean±SD	Controls (n=100) Mean±SD	(95%CI)	p value
Gender(M/F)	38/339	44/56		
Age (year)	45.3 ± 13.8	36.6 ± 10.7		< 0.001
Haematocrit(%)	39.5 ± 4.4	41.6 ± 5.6	39.5-40.4	< 0.001
Leukocyte($\times 10^9/L$)	7280 ± 2056	6788 ± 1800	6.9-7.3	0.03
Neutrophil($\times 10^9/L$)	4322 ± 1648	4081 ± 1455	4.1-4.4	0.18
Lymphocyte($\times 10^9/L$)	2204 ± 667	1972 ± 452	2-2.2	0.001
Plt($\times 10^9/L$)	289968 ± 86950	262020 ± 55182	276.7-291.4	0.002
NLR (%)	2.60 ± 1.78	2.11 ± 0.81	2.3-2.6	0.008
CRP (mg/dl)	8.76 ± 15.02	2.65 ± 2.5		< 0.001
FT3 (ng/dl)	3.39 ± 1.38	2.52 ± 0.42	3.1-3.3	< 0.001
FT4 (ng/dl)	1.47 ± 5.52	1.04 ± 0.18	0.9-1.8	
TSH (mIU/L)	7.94 ± 22.5	2.85 ± 1.14	0.02	5-8.6

SD: Standard deviation; NLR: Neutrophil/lymphocyte ratio; CRP: C-reactive protein; FT3: Free triiodothyronine; FT4: Free thyroxine; TSH: Thyroid-stimulating hormone.

FT4, but it was not significant ($p > 0.05$).

Discussion

HT is the most common disease that results in hypothyroidism and an enlarged thyroid gland in children and adolescents, and at the same time, is the most prominent acquired cause of hypothyroidism and goitre in regions not endemic for iodine deficiency.¹⁵⁻¹⁷ Certain environmental factors, such as excess iodine intake, various viral infections and medications, have been implicated in its aetiology. Investigations of HT patho-physiology revealed that the disease developed due to increased T-cell activation, and determined relationships between certain groups of tissue such as human leukocyte antigen (HLA), DR3, DR4, and DR5. Moreover, multiple genetic factors that regulate immunological reactions have been held accountable for the appearance of the disease and this notion has been corroborated by numerous studies.¹⁷⁻¹⁹

NLR, PLR and thrombocyte indices are ratios that can be easily accessed through CBC at a low cost and have been shown to be related to many medical conditions and pathologies.⁵⁻⁷ There are reports suggesting that these indices and ratios are correlated with metabolic and endocrine disorders.^{8,9} Inflammatory processes play a key role in chronic diseases, primarily in cardiovascular diseases, cancer, chronic kidney disease, and DM.¹⁰ Studies have identified NLR as a systemic marker of inflammation. Moreover, it was shown to be a significant marker for predicting long-term cardiovascular mortality and the prognosis in cancer patients.^{11,12} Uslu et al.²⁰ determined

that the NLR was higher in patients with rheumatoid arthritis compared to the healthy control group, and suggested that it could be a marker for inflammatory autoimmune diseases (20A study¹³ involved 38 HT patients and 38 healthy controls, and reported that NLR and PLR were significantly different in patients compared to controls ($p < 0.05$). Bilge M et al.¹⁴ evaluated 145 HT patients and 60 healthy age-matched females. The patient group manifested a lower lymphocyte count and higher thrombocyte count, NLR and PLR compared to healthy individuals ($p < 0.001$). In our study, patients diagnosed with HT demonstrated a higher NLR compared to the healthy controls. HT is simply an inflammatory process that emerges due to the stimulation of T lymphocytes by the autoimmune system, and while we think that the increase in NLR could be related to the similar mechanisms involved in this process, we were not able to prove our hypothesis with the data obtained in this study. Our theory involving NLR and autoimmunity was not supported by the negative correlation between NLR and the thyroid autoantibody anti-TPO we determined in addition to the present findings, which did not demonstrate statistical significance.

There are some limitations to our study as it was conducted on a retrospective basis and represented a single-centre data. The sample size was not calculated scientifically. Lack of power analysis is another limitation of the study. Despite the limitations, they study was able to determine a higher NLR value in HT patients compared to healthy controls.

Conclusion

NLR, which can be measured with an inexpensive and easily accessible routine hemogram, can serve as a practical and valuable marker in the diagnosis and follow-up of HT and other diseases that are autoimmune and involve chronic inflammation.

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Conflict of Interest: None.

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