

Neutrophil and platelet to lymphocyte ratio in patients with hypothyroid Hashimoto's thyroiditis

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Summary. *Aim:* Chronic lymphocytic thyroiditis is among the most common causes of hypothyroidism along with HT (Hashimoto's thyroiditis) goitre, which is also named as autoimmune thyroiditis. Our study aims to determine the usefulness of PLR (platelet to lymphocyte ratio) and NLR (neutrophil to lymphocyte ratio), which can be obtained with a hemogram, at the clinical course or the severity of the disease in patients with Hashimoto's thyroiditis. *Materials and Methods:* Our study is a retrospective cross-sectional study that included 121 hypothyroid or subclinical hypothyroid Hashimoto's thyroiditis patients and a healthy control group comprised of 100 individuals. Thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), anti-thyroid peroxidase (anti-TPO), complete blood count (CBC), and C-reactive protein (CRP) results were obtained from patient files for both HT patients and the control group, and we computed PLR and NLR for both groups. *Results:* PLR was lower in patients diagnosed with HT compared to the healthy control group, with statistical significance (respectively, 130.8 ± 50.5 versus 145.3 ± 58.5 ; $p < 0.05$). NLR was higher in patients diagnosed with HT compared to the control group and a statistically significant relationship was determined (respectively, 2.43 ± 0.94 versus 2.11 ± 0.81 ; $p < 0.05$). In addition to the present findings, we determined that PLR and NLR were correlated with anti-TPO, TSH, and FT4, although without statistical significance. *Conclusion:* As values that can be measured with an inexpensive and easily accessible routine hemogram, PLR and NLR can serve as practical and valuable markers at the clinical course or the severity of the disease and other diseases that are autoimmune and progress with chronic inflammation. (www.actabiomedica.it)

Key words: Hashimoto's thyroiditis, platelet/lymphocyte ratio, neutrophil/lymphocyte ratio

Introduction

Chronic lymphocytic thyroiditis is among the most common causes of hypothyroidism along with HT (Hashimoto's thyroiditis) goitre, which is also named as autoimmune thyroiditis (1). While it can primarily be isolated or related to other autoimmune disorders, it can also appear secondarily due to immunomodulator medications such as interferon alpha or monoclonal antibody therapy (2-4). The most common clinical finding is an enlarged thyroid gland, either with or without hypothyroidism. Clinical symptoms of the disease involve decreased levels of thyroid hormones accompanied by goitre that regresses with levothyrox-

ine hormone replacement therapy. Thyroid function at the time of diagnosis shows significant variability, ranging from euthyroidism to hypothyroidism, and rarely, hyperthyroidism (5-7). Neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR), which are ratios that can be easily measured from a complete blood count for a low cost, were shown to be related to many medical pathologies (8-10).

Materials and Methods

This study was approved by the ethics committee of Firat University Medical Faculty (ethics commit-

tee approval date/number 24.01.2019/02-14). The patient and control groups were composed based on data obtained from a retrospective scan of files belonging to patients who presented to the Internal Medicine polyclinic and clinic between January 2018 and November 2018. The study group involved two groups; one group composed of patients with Hashimoto's thyroiditis and a control group composed of healthy individuals. The Hashimoto's thyroiditis group was comprised of patients that presented to the internal medicine polyclinic for Hashimoto's thyroiditis or received a diagnosis of HT at the polyclinic, who had no other diseases. Patients with a different chronic disease (coronary artery disease, hematologic diseases, malignancies, severe liver disease, severe kidney failure, diabetes) were excluded from the study.

The healthy control group consisted of the patients who did not have any disease and who applied to our outpatient clinic for routine screening every 6 months. A retrospective scan of patient files was conducted to obtain TSH, free T4, free T3, Anti TPO levels, hematocrit (hct) count, neutrophil and lymphocyte counts and ratio (NLR), and platelet count (plt). Demographic information (age, gender) of the entire study group was obtained from a scan of polyclinic patient files.

The obtained data were evaluated statistically using the SPSS-22 packaged program. The data were an-

alyzed using descriptive statistical methods, student's t-test, equivalents, and variance analysis. In addition to these, relationships between the variables were evaluated with Pearson's correlation analysis and a p-value below 0.05 was considered significant.

Results

This study included 121 patients (18 male and 103 female) with a diagnosis of HT and a control group with 100 healthy individuals (44 male and 56 female). Of the patients, 18 were male and 103 were female. Mean levels of the obtained data for the patient and control groups were as follows; hematocrit (%): 39.5 ± 4.3 , 41.6 ± 5.6 , leukocyte ($\times 10^9/L$): 7165 ± 2005 , 6788 ± 1800 , lymphocyte ($\times 10^9/L$): 2213 ± 667 , 1972 ± 452 , respectively. CRP levels were respectively determined as 9.48 ± 14.9 and 2.65 ± 2.5 . Laboratory and demographic characteristics of the patient and control groups have been presented in Table 1. NLR was significantly higher in HT patients compared to the control group (respectively, 2.43 ± 0.94 and 2.11 ± 0.81 ; $p < 0.05$) and PLR was significantly lower in HT patients compared to the control group (130.8 ± 50.5 ; 145.3 ± 58.5 ; $p = 0.04$).

Of the HT patients in our study, 35 had thyroid function consistent with hypothyroidism and 86 had subclinical hypothyroidism based on laboratory re-

Table 1. Descriptive statistics and significance levels of the variables in the patient and the control groups

Parameters	Patients (n=121) Mean \pm SD	Controls (n=100) Mean \pm SD	p value
Age (year)	44,5 \pm 14,5	36,6 \pm 10,7	
Gender (M/F)	18/103	44/56	
Hematocrit (%)	39,5 \pm 4,3	41,6 \pm 5,6	0,002
Leukocyte ($\times 10^9/L$)	7165 \pm 2005	6788 \pm 1800	0,1
Neutrophil ($\times 10^9/L$)	4223 \pm 1610	4081 \pm 1455	0,4
Lymphocyte ($\times 10^9/L$)	2213 \pm 677	1972 \pm 452	0,003
Plt ($\times 10^9/L$)	270980 \pm 71697	262020 \pm 55182	0,3
NLR (%)	2,43 \pm 0,94	2,11 \pm 0,81	0,010
PLR (%)	130,8 \pm 50,5	145,3 \pm 58,5	0,049
CRP (mg/dl)	9,48 \pm 14,9	2,65 \pm 2,5	<0,001
FT3 (ng/dL)	3,39 \pm 1,38	2,52 \pm 0,42	<0,001
FT4 (ng/dL)	1,47 \pm 5,52	1,04 \pm 0,18	0,09
TSH (mIU/L)	7,94 \pm 22,5	2,85 \pm 1,14	<0,001

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

sults. Laboratory characteristics of the patient groups have been presented in Table 2. Among the investigated HT patients, the group with hypothyroidism demonstrated higher NLR and PLR values compared to the group with subclinical hypothyroidism, however, without statistical significance (respectively 2.54 ± 1.07 ; 2.38 ± 0.88 ; $p=0.3$ and 138.7 ± 60.8 ; 127.6 ± 45.7 ; $p=0.2$).

In addition to the present findings, we determined that NLR was negatively correlated with anti-TPO, TSH, and FT4, although without statistical significance.

Discussion

Hashimoto's thyroiditis (chronic lymphocytic thyroiditis) is the most common disease that causes hypothyroidism and an enlarged thyroid gland in children and adolescents, and at the same time, is the primary acquired cause of hypothyroidism and goitre

in regions that are non-endemic for iodine deficiency (11-13). Its etiology implicates certain environmental factors such as excess iodine intake, various viral infections, and medications. Based on investigations of HT pathophysiology, the disease develops due to increased T-cell activation and there are relationships between certain groups of tissues such as HLA, DR3, DR4, and DR5. Furthermore, the appearance of the disease is thought to be connected to multiple genetic factors that regulate immunologic reactions and this notion has been supported by numerous studies (13-15).

Neutrophil and lymphocyte counts undergo certain temporary changes under inflammatory conditions. The neutrophil/lymphocyte ratio (NLR) is calculated by dividing the absolute neutrophil count with the absolute lymphocyte count. As a systemic inflammation index, NLR was determined to be a useful index for the differential diagnosis of diseases and the prediction of their prognoses (16, 17). NLR is also an available marker that can communicate important information

Table 2. Descriptive statistics and significance levels of the variables within the subclinical hypothyroidism and overt hypothyroidism groups of HT patients

Parameters	Hypothyroidism (n=35) Mean±SD	Subclinical hypothyroidism (n=86) Mean±SD	p value
Hematocrit (%)	38±3,7	40,2±4,4	<0,05
Leukocyte (x10 ⁹ /L)	7215±2199	7145±1935	0,8
Neutrophil (x10 ⁹ /L)	4286±1592	4197±1626	0,7
Lymphocyte (x10 ⁹ /L)	2142±833	2243±605	0,4
Plt (x10 ⁹ /L)	267600±83117	272350±66987	0,7
NLR (%)	2,54±1,07	2,38±0,88	0,3
PLR (%)	138,7±60,8	127,6±45,7	0,2
FT4 (ng/dL)	0,67±0,19	1,11±0,18	<0,001
TSH (mIU/L)	49,01±58,07	9,64±8,74	<0,001

SD: Standard deviation; NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio; FT4: Free thyroxine; TSH: Thyroid-stimulating hormone

Table 3. Correlations between the variables in the HT group

		TSH	FT4	Anti-TPO
NLR	Pearson's Correlation (r)	.075	-.037	-.112
	P	0.4	0.6	0.2
PLR	Pearson's Correlation (r)	-.028	-.061	.049
	P	0.76	0.50	0.5

NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio; TSH: Thyroid-stimulating hormone FT4: Free thyroxine; TPO: Thyroid peroxidase

about the inflammatory activity of the patient. Certain epidemiological studies have determined that chronic inflammation measured by NLR is correlated with other conventional risk factors such as obesity and hypertension. Recent studies have shown that an abnormal NLR level is related to autoimmune diseases (18).

The platelet/lymphocyte ratio (PLR) is calculated by dividing the absolute platelet count with the absolute lymphocyte count and is recommended as a potential marker to determine inflammation. Similarly to NLR, PLR is also used as an index for the differential diagnosis of certain diseases such as cancer and inflammatory diseases and for the prediction of their prognoses (19). Arpaci D. et al. (20) found that NLR and PLR were significantly different in a group of HT patients compared to healthy individuals ($p < 0.05$) in a study that involved 38 HT patients and 38 healthy controls, (20). A study conducted by Bilge M et al. (21) inspected 145 HT patients and 60 healthy age-matched females. The patient group demonstrated a lower lymphocyte count, whereas platelet count, NLR, and PLR were higher compared to the control group ($p < 0.001$ for all comparisons) (21). In our study, patients diagnosed with HT demonstrated a higher NLR and a lower PLR compared to the healthy control group with statistical significance, conforming with previous literature studies. HT is merely an inflammatory process that is initiated by 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 believe the low PLR levels that do not conform with data in the literature could be connected to the limitations of our study. By determining statistically significant higher NLR and lower PLR values in HT patients compared to the controls, our study can prove that NLR and PLR are useful indices in the detection of autoimmune diseases and inflammation. In addition, there was no negative and positive correlation between NLR and PLR and anti-TPO in our study. Another important point to note is that the incidence of anemia in patients with Hashimoto thyroiditis is statistically significant compared to the healthy control group. We can explain this as follows the relationship and frequency between autoimmune thyroid diseases and anemia are well known.

In our study, we could see that NLR and PLR values changed in relation to the severity of the disease when we examined healthy individuals, hashimoto patients with subclinical hypothyroidism and hashimoto patients with overt hypothyroidism respectively.

Conclusion

In conclusion, we believe that, based on more comprehensive studies that will be conducted, NLR and PLR, which can be measured with an inexpensive and easily accessible routine hemogram, can serve as practical markers at the clinical course of the disease of HT as well as other diseases that are autoimmune and involve chronic inflammation.

Limitations of the study

Our study should be evaluated in the light of several limitations. The presented study was conducted on a retrospective basis and represented single-center experience. The small number of patients is an important limitation of our study. A higher number of patients are needed to achieve higher statistical significance.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Ozsu E, Mutlu RGY, Cizmeci F, Hatun S. Characteristics of our patients with Hashimoto thyroiditis. *Türk Pediatri Arsivi-Turkish Archives Of Pediatrics* 2011; 46(3): 252-5.
2. Gönç EN, Kandemir N. *Guatr. Çocuk Endokrinolojisi*, İstanbul: Nobel Tıp. 2014.
3. Cappa M, Bizzarri C, Crea F. Autoimmune thyroid diseases in children. *J Thyroid Res* 2011; 675703.
4. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: clinical and diagnostic criteria. *Autoimmun Rev* 2014; 13 (4-5): 391-7.
5. Tutuncu N B, Erbas T. Factors associated with bone metabolism in acromegalic patients: hypogonadism and female gender. *Exp Clin Endocrinol Diabetes* 2004; 112(6): 328-32.
6. Çorakçı A. Tiroid Hastalıklarına Yaklaşım. *Türkiye Klinikleri Journal of Endocrinology* 2004; 2(1): 1-3.

7. Van Zuuren EJ, Albusta AY, Fedorowicz Z, Carter B, Pijl H. Selenium Supplementation for Hashimoto's Thyroiditis: Summary of a Cochrane Systematic Review. *Eur Thyroid J* 2014; 3(1): 25-31.
8. Tulgar YK, Cakar S, Tulgar S, et al. The effect of smoking on neutrophil/lymphocyte and platelet/lymphocyte ratio and platelet indices: a retrospective study. *Eur Rev Med Pharmacol Sci* 2016; 20: 3112-8.
9. Koh C-H, Bhoo-Pathy N, Ng K-L, et al. Utility of pretreatment neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as prognostic factors in breast cancer. *Br J Cancer* 2015; 113: 150-8.
10. Akdag S, Akyol A, Asker M, et al. Platelet-to-Lymphocyte Ratio May Predict the Severity of Calcific Aortic Stenosis. *Med Sci Monit* 2015; 21: 3395-3400.
11. Dündar B, Boyacı A, Sangün Ö and Dündar N. Çocuk ve ergenlerde Hashimoto tiroiditi: klinik ve laboratuvar bulgularının değerlendirilmesi. *Türk Ped Arşiv* 2011; 46: 318-21.
12. Dilek E, İşcan B, Ekuklu G, Tütüncüler F. Hashimoto Tiroiditi Tanısı Alan Vakaların Geriye Dönük Değerlendirilmesi. *Journal of the Child/Cocuk Dergisi*. 2011; 11(2).
13. Setian NS. Hypothyroidism in children: diagnosis and treatment. *J Pediatr (Rio J)*, 2007; 83(5 Suppl): 209-16.
14. Demirbilek H, Kandemir N, Gonc EN, Ozon A, Alikasifoglu A, Yordam N. Hashimoto's thyroiditis in children and adolescents: a retrospective study on clinical, epidemiological and laboratory properties of the disease. *J Pediatr Endocrinol Metab* 2007; 20(11): 1199-205.
15. Duntas LH. Environmental factors and autoimmune thyroiditis. *Nat Clin Pract Endocrinol Metab* 2008; 4(8): 454-60.
16. Motomura T, Shirabe K, Mano Y, Muto J, Toshima T, Umemoto Y, et al. The neutrophil-lymphocyte ratio reflects recurrence of hepatocellular carcinoma after liver transplantation via inflammatory micro-medium. *J Hepatol* 2013; 58: 58-4.
17. Balta S, Aparcı M, Öztürk C, Demirkol S, Çelik T. Yararlı bir mortalite belirteci olarak nötrofil lenfosit oranı. *J Emerg Med* 2014; 32 (12): 1546-7.
18. Hu ZD, Sun Y, Guo J, Huang YL, Qin BD, Gao Q, et al. Red blood cell distribution width and neutrophil/lymphocyte ratio are positively correlated with disease activity in primary Sjögren syndrome. *Clin Biochem* 2014; 47 (18): 287-90.
19. Feng JF, Huang Y, Chen QX. Preoperative platelet lymphocyte ratio (PLR) is a predictive factor for neutrophil lymphocyte ratio (NLR) in patients with esophageal squamous cell carcinoma. *World J Surg Oncol* 2014; 12: 58.
20. Arpacı D, Gurol G, Ergenc H, Yazar H, Tocoglu AG, Ciftci IH, Tamer A. A Controversial New Approach to Address Hematological Parameters in Hashimoto's Thyroiditis. *Clin Lab* 2016 Jul 1; 62(7): 1225-1231. doi: 10.7754/Clin. Lab.2015.150927.
21. Bilge M, Yeşilova A, Adas M, Helvacı A. Neutrophil- and Platelet- to Lymphocyte Ratio in Patients with Euthyroid Hashimoto's Thyroiditis. *Exp Clin Endocrinol Diabetes* 2018 Sep 28. doi: 10.1055/a-0723-3441.

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