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Original Article

A comparison of neutrophil-lymphocyte ratio and body fat percentage in hashimoto's disease induced hypothyroid patients

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Abstract

Aim: Inflammatory mechanisms are activated when the body mass index is increased and in cases of Hashimoto's Thyroiditis (HT). The neutrophil-lymphocyte ratio (NLR), which is used as a new and easily accessible inflammatory marker, may be related to the body mass index. The objective of this study is to compare the NLR and body fat percentage in patients with Hashimoto's disease induced hypothyroidism.

Material and Methods: The study consisted of 29 patients diagnosed with HT induced hypothyroidism based on the clinical and laboratory findings. The control group consists of 29 healthy individuals who do not suffer from any disease known to increase TSH level. Body analysis is performed for all cases that are included in the study, and the height, weight, body fat percentage, lean body mass, visceral adiposity, basal metabolic rate, and body fluid percentages are calculated, and complete blood count, TSH, FT3, FT4, Anti-TPO tests were performed following 3-4 cc venous blood sample collection from all cases.

Results: There were not any significant difference between the patient and control group in terms of gender, BMI, body fat percentage, lead body mass, visceral adiposity, fluid percentage, and basal metabolic rate data ($p>0.05$). NLR rate was 1.95±1.37 in patient group and 2.52±1.40 in control group. Significant difference was identified in NLR ($p=0.025$), fat percentage ($p=0.002$), lean mass ($p=0.002$) and visceral adiposity data ($p=0.006$) between the HT patients and control group when the male patients were removed from the groups. NLR was identified statistically significantly low in the patient group when compared to the control group ($p<0.012$). There was no significant correlation between NLR and lean mass, TSH, BMI, visceral adiposity, fluid percentage, and age parameters in both groups.

Conclusion: NLR, like other common inflammatory markers, is an inexpensive and easily accessible marker that can be used in hospitalized patients. However, it would be more appropriate to evaluate the conditions that may have effects on the results such as patients drug use and bone marrow suppression. It can be said that more evidence is needed to use NRL as a marker for HT management.

Keywords: Hashimoto's thyroiditis; neutrophil-lymphocyte ratio; body fat percentage

INTRODUCTION

Hashimoto's thyroiditis (HT) is the most frequent type of acquired hypothyroidism, and histopathologically characterized by diffused mononuclear cell infiltration, fibrosis, parenchymal atrophy and oxyphilic cell metaplasia in thyroid parenchyma (1, 2). Reduction in the lean body masses and body fat percentages of patients with hypothyroidism was detected following hormone replacement treatment. Such reduction in the body fat percentages was also verified with bioelectrical impedance method (3).

HT is still a complicated disease whose etiology and pathogenesis are investigated. Illumination of these aspects can make a significant contribution to the treatment and prevention steps (4, 5). Neutrophil-lymphocyte ratio (NLR) is a widely studied and frequently used new inflammatory marker due to its inexpensive, easy accessible and easy identifiable nature.

Lymphocytes increase in inflammatory conditions under the influence of multiple factors and inflammatory cytokines such as interferons and interleukins (IL). There are many cytokines observed to increase both in subacute

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and chronic inflammation like IL-1. These factors lead to developing cellular and specific humoral immune responses to the pathogenic agent in the damaged tissue area. As another example of the inflammatory process, factor IL-6 which is produced by cells, such as T cells, mononuclear phagocytes and fibroblasts, plays the role of activating and differentiating T cells. These factors lead to developing cellular and specific humoral immune responses to the pathogenic agent in the damaged tissue area. It is reported that one of the most important effects of IL-6 is to inhibit TNF production and increase chronic inflammation by limiting the acute inflammatory response by the feedback effect and this can be observed in some chronic inflammatory diseases like thyroiditis and diabetes mellitus type 1 (6-8).

In many studies, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio and systemic immune inflammatory index, etc. has been associated with various diseases (9). It is seen in the literature review that the NLR increases in many diseases related to acute and chronic inflammation. While tumoral cases (10) come first, there is literature demonstrating that they can be used as an indicator of inflammation in many types of diseases such as ischemic stroke (11), acute myocardial infarction (12), atherosclerotic diseases (13), acute pancreatitis (14). It is reported that NLR may be helpful in risk classification and prognosis of patients diagnosed with acute coronary syndrome (12). Various studies manifest that NLR is an independent indicator of mortality in acute heart failure, and may serve as a marker indicating subclinical inflammation in cardiac and non-cardiac diseases (12, 15).

The objective of this study is to evaluate the probable relations of NLR as an indicator of subclinical inflammation in patients with HT induced hypothyroidism with thyroid functions, body mass index and body fat percentage.

MATERIAL and METHODS

The patients who have applied to Harran University Faculty of Medicine Family Medicine and Endocrinology Outpatient Clinic between the dates of October 2016 and April 2017 and consented to participate in the study were, included in this cross-sectional study. These 29 patients included in the study were those diagnosed with hypothyroidism due to HT, based on clinical and laboratory findings. The control group consists of 29 healthy individuals who do not suffer from any disease known to increase the TSH level. Harran University Faculty of Medicine research ethics committee approval was obtained for the study, and written consents of the individuals participating in the study composing the patient group and the healthy group were obtained by specifying the objective of the study.

Patients, who were previously or newly diagnosed with HT were included in the study. HT was diagnosed in all patients using clinical findings, TSH, fT3, fT4, and Anti-TPO values tested from the venous blood sample collections, and the ultrasonographic imaging methods. Sociodemographic characteristics of the patients (age, sex, educational background, profession, number of children, drinking and smoking habits) were recorded. The study was planned prospectively and routine tests requested from these patients were used for evaluation. Participants were asked questions such as weight gain, weakness, fatigue, facial edema, constipation, skin dehydration-cracking, etc. in order to evaluate the clinical findings of HT. Body analysis was performed in the patient and control groups participating in the study using bioelectrical impedance analysis device, and height, weight, body fat percentage, lean body mass, visceral adiposity, basal metabolic rate, and body fluid percentage was calculated. Exclusion criteria were determined as existence of another accompanying chronic disease such as DM, HT, previous thyroid operation, and pregnancy.

Serum T3, T4 and TSH levels were measured using Centaur Xp Analyzer system and Chemiluminescent Microparticle Immunoassay (CMIA) method. Serum anti-TPO levels were measured using Immulite 2000 electrochemiluminescence immunoassay method. Complete blood count was performed using a full-automatic Ruby (Abbott, USA) complete blood count analyzer. In this study, TANITA BC 418 Body Composition Monitor, Tokyo, Japan was used. This device is a safe, quick, portable and noninvasive. Body composition analysis of all patients were performed on this device calculating the height, weight, body fat percentage, lean body mass, visceral adiposity, basal metabolic rate and body fluid percentage.

SPSS 20.0 statistics software was used to analyze the data. Figures were expressed as arithmetic mean ± standard deviation; and categorical data were expressed in figures and percentages. The data were tested using Kolmogorov-Smirnov test as to whether they conform to normal distribution or not. Data manifesting parametric characteristics were analyzed using Student T-Test if they are distributed normally, using Mann Whitney U test if not distributed normally, and the categorical data were analyzed with chi-square test. Correlation between data was analyzed using Spearmen correlation analysis.

RESULTS

Data of Hashimoto patients with hypothyroidism and the control group participating in this study were compared. The patient group of the study was composed of 5 male (17.2 %) and 24 female (82.7 %) individuals, and the mean age was 35.96 ± 10.61 years old. The control group was composed of 6 male (20.6 %), and 23 female (79.4 %) participants, and the mean age was 29.72 ± 8.81. It is identified that there is no statistically significant difference between the sexes when the patient group and the control group was compared ($p>0.05$), however, mean age of the patient group was statistically higher than control group ($p=0.018$).

The patient group had a mean height of 162.58 ± 7.49 cm, mean weight of 71.20 ± 13.60 kg, and mean BMI of 27.09 ± 5.65 kg/m^2, while the control group had a mean height

of 166.27±8.91 cm, mean weight of 68.17 ± 15.78 kg, and mean BMI of 24.58 ± 4.38 kg/m^2. Demographic data of the patients are given in Table 1. As seen in Table 1, there is no significant difference identified between the two groups in terms of demographic data except for age.

Body analyses were performed in the patient and control groups by using bioelectrical impedance analysis device. There is no statistically significant difference identified between the analyzed body fat percentage, lean body mass, visceral adiposity, fluid percentage, and basal metabolic rate data as seen in Table 1.

While the most frequent complaint of the applying patients was swollen neck, the physical examination revealed goiter (55.7 %), weakness (40 %), weight gain (30 %), cold intolerance (13.8%), and dry hair (12.5 %). Of 22 patients examined using ultrasonography, 19 of them had reduced thyroid echo intensity (90 %), 10 of them had thin fibrous bands (45 %), and 12 of them had grade II increased pattern vascularity.

Hashimoto patient group had a mean fT3 value of 2.91±0.95 pg/ml, fT4 value of 1.05±0.46 ng/dl, TSH value of 18.44±30.44 µIU/ml, and Anti-TPO value of 580.15±395.56 IU/ml. Control group had a mean fT3 value of 3.42±0.42 pg/ml, fT4 value of 1.13±0.13 ng/dl, TSH value of 1.45±0.65 µIU/ml, and Anti-TPO value of 10.91±2.46 IU/ml. A significant difference was identified in mean fT3 ($p<0.011$), TSH ($p<0.001$) and Anti-TPO ($p<0.001$) values when both groups are compared. No significant difference was identified in cholesterol, glucose, creatinine and ALT values between the patient and control groups ($p>0.05$) (Table 2).

Table 1. Comparison of Hashimoto and Control Group Demographic Data

	Hashimoto	Control	P Value
Age (Years)	35.96± 10.61	29.72± 8.81	0.018
Sex (F/M)	24/5	23/6	>0.05
Height (cm)	162.58±7.49	166.00±8.91	>0.05
Weight (kg)	71.20±13.60	68.17±15.78	>0.05
BMI (kg/m2)	27.09±5.65	24.58±4.38	>0.05
Fat Percentage (%)	31,21±12.00	26.23±8.67	>0.05
Lean Mass (%)	68.79±11.99	73.76±8.67	>0.05
Fluid Percentage (%)	50.36±8.79	54.00±6.34	>0.05
Basal Metabolic Rate (Kcal)	1456.13±176.34	1525.10±345.44	>0.05

Table 2. Comparison of Biochemical and Hematological Data of Hashimato and Control Group

	Hashimoto	Control	P Value
TSH (mIU/L)	18.44±30.47(n:29)	1.45±0.65(n:29)	<0.001
fT3 (pg/ml)	2.91±0.95(n:29)	3.42±0.42(n:29)	<0.011
fT4 (pg/dl)	1.05±0.46(n:29)	1.13±0.13(n:29)	>0.05
AntiTPO (IU/ml)	580.15±395.56(n:29)	10.91±2.46(n:29)	<0.001
LDL (mg/dl)	94.48±12.62(n:9)	112.05±36.25(n:13)	>0.05
Glucose (mg/dl)	94.04±26.56(n:23)	92.35±15.14(n:14)	>0.05
Creatinin (mg/dl)	0.67±0.10(n:23)	0.69±0.08(n:22)	>0.05
ALT (U/L)	16.08±6.36(n:23)	18.45±14.67(n:22)	>0.05
Triglycerides (mg/dl)	139.55±80.92(n:9)	129.35±54.73(n:14)	>0.05
T.Cholesterol (mg/dl)	170.00±21.09(n:9)	188.71±44.88(n:14)	>0.05
HDL (mg/dl)	47.60±10.63(n:9)	43.68±9.10(n:12)	>0.05
WBC (10e3/uL)	8.20±1.92	8.58±2.05	>0.05
NEU (10e3/uL)	4.57±1.53	5.31±1.78	>0.05
LYM (10e3/uL)	2.74±0.88	2.40±0.70	>0.05
HCT (%)	40.96±4.08	43.59±4.02	<0.015
HGB (g/dl)	12.92±1.82	14.11±1.60	<0.010
PLT (10e3/uL)	301.35±119.53	304.30±69.58	>0.05
NLR	1.90±1.26	2.43±1.28	0.012

Complete blood count levels of the patient and control groups of the study were compared (Table 2). No significant difference was identified in white blood cell, thrombocyte, lymphocyte, and neutrophil values (p>0.05). However, hemoglobin value was elevated in the control group, and the elevated hematocrit values were identified in the Hashimoto group (p values are respectively p<0.010 and p<0.015). Furthermore, NLR was identified as significantly lower in the Hashimoto group when compared to the control group (p<0.012) (Table 2).

In the comparison made after excluding male patients from the HT patient and control group, a significant difference was found between the two groups in terms of NLR, fat percentage, lean mass and visceral fat (p=0.025, p=0.002, p=0.002 and p=0.006, respectively) (Table 3).

Furthermore, a correlation analysis between the NLR value and TSH, BMI, lean mass, body fat percentage visceral adiposity, fluid percentage, and age parameters was made between the two groups in our study and no significant correlation was identified between NLR and other parameters in both groups (Table 4).

Table 3. Comparison of NLR, Fat Percentage, Lean Mass, Visceral Adiposity Values of Female Patients in Hashimoto and Control Group

	Hashimoto	Control	P Value
NLR	1.95±1.37	2.52±1.40	0.025
Fat Percentage (%)	34.95±9.30	28.04±8.71	0.002
Lean Mass (%)	65.06±9.31	71.95±8.71	0.002
Visceral Adiposity (%)	6.25±3.24	3.78±3.98	0.006

Table 4. Correlation Analysis of NLR between Age, TSH, BMI, Fat Percentage, Lean mass, Visceral Adiposity and Liquid Percentage in Hashimoto and Control Group

	Age		TSH		BMI		Fat percentage		Lean mass		Visceral adiposity		Fluid percentage	
NLR	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**	**r**	**p**
Hashimoto	-0.222	>0.05	0.114	>0.05	0.312	>0.05	0.209	>0.05	-0.222	>0.05	0.312	>0.05	-0.222	>0.05
Control	-0.155	>0.05	-0.136	>0.05	-0.118	>0.05	0.155	>0.05	-0.155	>0.05	-0.118	>0.05	-0.155	>0.05

r=Pearson correlation coefficient

DISCUSSION

Hashimoto's disease is typically detected in women between the ages of 30 and 50, and manifests familial characteristics. In our study, the mean age of the cases with Hashimoto's thyroid was identified as 35.96 ± 10.61 years old. The mean age of the cases with Hashimoto's thyroid included in our study is similar to previous studies (16). HT is 8 to 10 times more common in women than men and 95 % of cases are women (17-20). Similarly, 82.7 % of the cases with suspected Hashimoto's thyroid in this study consisted of women. While thyroglobulin antibodies of 190 patients diagnosed with Hashimoto's thyroiditis were positive at the rate of 85.53 % in the study conducted by Lastrzebska-Bohaterewicz E, et al., thyroperoxidase antibodies were identified as positive at the rate of 78.89 %. It is reported that both autoantibodies were negative in 1.83 % of the patients with Hashimoto's thyroiditis. Anti-thyroglobulin antibody (anti-TG) and anti-TPO positivity rates of 79 patients with Graves' disease were identified as 62 % and 91.13 % respectively (21). It is reported in the studies conducted by Vural, et al. that anti-TPO positivity is 10.57 %, anti-TG positivity is 22.41 %, and the rate of patients with positive values for both antibodies is 67.02 % (20). In this study, anti-TPO was identified as positive in 86 % of the patients with Hashimoto's thyroiditis, and it is seen that the study is consistent with most of the studies in the literature.

In HT, reduced thyroid functions are associated with degradation in the thyroid gland. Weight gain associated with reduced thyroid function occurs in the process. In particular, gain weight despite reduced appetite is linked to decreased basal metabolic rate and increased fluid in myxoedematous tissues (22). In the study conducted by Arpacı, et al., the mean BMI value of the patients was identified as 27.39 ± 5.62 kg/m^2 and as 24.11 ± 3.59 kg/m^2 in the control group, and the BMI of the case group was identified higher compared to the BMI of the control group (5). In our study there was no difference between, the mean BMI of the patient group was 27.09 ± 5.65 kg/m^2, and the mean BMI of the control group was 24.58 ± 4.38 kg/m^2.

Seppel, et al. report increased fat mass percentage

and total body water percentage in patients with hypothyroidism compared to euthyroid patients (23). Sartorio, et al. argued in a study that the body analysis performed with bioimpedance measurements are more valuable than anthropometric measurements in patients with hypothyroidism, and such measurements may be in direct relation with the lean tissue (24). In the present study, we have measured the body fat percentages, lean masses, water percentages, and basal metabolic rates of the patient and control groups. The mean water percentage was identified as 45.73 % in Hashimoto group female patients and as 64.88 % in Hashimoto group male patients, and mean water percentage was identified as 46.64% in the control group female patients, and as 58.09% in the control group male patients. The fat percentages of the patient group of this study manifest extremely high distribution and the water percentages manifest low distribution, and the fat percentages of the control group manifest normal distribution in ages 20 to 40 and 40 to 49, and high distribution in ages 30 to 39, and the water percentages manifest low distribution. No statistically significant difference was identified when the fat percentages and water percentages of the healthy group and the patient group were compared. In the measurements made in HT female patients, the fat rate was found to be significantly higher.

A study conducted by Binay, et al. identifies that 30-40% of the patients diagnosed with Hashimoto's thyroiditis has anemia associated with impaired erythropoiesis. Macrocytic anemia was frequently encountered in addition to hypochromic or normochromic anemia. They believed that such macrocytic anemia may be associated with accompanying B12 and folate deficiency (25). Similarly, lower hemoglobin value was identified in the patients with HT compared to the control group in the presented study.

Güneş et al. has identified in a study that a subclinical inflammation occurs in hypothyroidism, however, there is no significant change in the NLR percentage among the groups (26). While Acay, et al. have identified a correlation between HT and CRP in a study investigating the importance of NLR in identifying systemic inflammation in HT patients, they were unable to identify a significant correlation with NLR (27). Bilge et al. found NLR higher than the control group in their study on euthyroid HT patients (28). Aktaş et al. found NLR higher in the HT group than the control group (29). Arpacı, et al. have reported in a study conducted with 92 patients that there is a positive correlation between NLR and anti-TG and anti-TPO. They have concluded that the NLR and PLR combination is a promising biomarker for safe diagnosis of HT (5). Lower NLR value was identified in the HT group in the present study. Bone marrow suppression, using of drug and delayed inflammation may be the cause of lower NLR in the HT patient group.

Bahadır et al. reported that there was no correlation between BMI and NLR in patients with obesity and metabolic syndrome. Similarly, in our study, there was no significant relationship between BMI and NLR (30). In the study of Koca, a negative correlation was reported between BMI and NLR in normal and overweight patients (31).

The limitation of the study is the limited number of patients and the fact that significant difference was identified between the mean ages. We believe that there is a need for prospective studies in which similar age groups and broader participation is ensured.

CONCLUSION

NLR, like other common inflammatory markers, is an inexpensive and easily accessible sign that can be used in hospitalized patients. In our study, NLR values were found to be significantly lower in the Hashimato group. Since there were contrary results in the literature, more evidence is needed to use NRL as a marker for HT management. It would be more appropriate to evaluate conditions that may affect our results, such as drug use and bone marrow suppression.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: Harran University Faculty of Medicine research ethics committee approval was obtained for the study, and written consents of the individuals participating in the study composing the patient group and the healthy group were obtained by specifying the objective of the study.

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