

Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio and Mean Platelet Volume in Adults with Hypothyroidism

Hipotiroidizmli Erişkinlerde Nötrofil - Lenfosit Oranı, Platelet- Lenfosit Oranı ve Ortalama Trombosit Hacmi

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ABSTRACT

Objective: The aim of the present study was to investigate neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and mean platelet volume (MPV) in adult patients with hypothyroidism.

Materials and Methods: The records of 496 patients with hypothyroidism and 5677 euthyroid healthy individuals were compared from the laboratory information system between July 10, 2018 and April 09, 2019.

Results: In the hypothyroid group, free triiodothyronine, leukocyte, neutrophil, and NLR values were lower; thyrotropin, platelet, PLR, and MPV values were higher; and free thyroxine and lymphocyte values were similar when compared with the euthyroid healthy group.

Conclusion: Platelet count, PLR, and MPV values are higher in adults with hypothyroidism than in euthyroid healthy individuals, whereas leukocyte, neutrophil, and NLR levels are low, and lymphocyte count is similar.

Keywords: Hypothyroidism, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume

ÖZ

Amaç: Bu çalışmada, hipotiroidili erişkin hastalarda nötrofil/lenfosit oranı (NLO), platelet/lenfosit oranı (PLO) ve ortalama trombosit hacmi (OTH) araştırılmıştır.

Gereç ve Yöntem: Laboratuvar bilgi sisteminden 10 Temmuz 2018 ile 09 Nisan 2019 tarihleri arasındaki kayıtlar incelenerek 496 hipotiroidili ve 5677 ötiroid sağlıklı bireyin verileri karşılaştırılmıştır.

Bulgular: Hipotiroidili grupta ötiroid sağlıklı gruba kıyasla serbest triiodothyronine (s T3), lökosit, nötrofil ve NLO değerleri daha düşük, thyrotropin (TSH), platelet, PLO, OTH değerleri daha yüksek, serbest thyroxine (s T4) ve lenfosit değerleri ise benzer bulunmuştur.

Sonuç: Hipotiroidizmli erişkinlerde platelet sayısı, PLO ve OTH değerleri ötiroid sağlıklı kişilerden yüksek iken lökosit, nötrofil ve NLO değerleri düşüktür ve lenfosit sayısı ise benzer düzeydedir.

Anahtar kelimeler: Hipotiroidi, nötrofil - lenfosit oranı, platelet - lenfosit oranı, ortalama trombosit hacmi

INTRODUCTION

Thyroid hormones affect almost every organ and system and must be present in the plasma at a certain level for them to function properly. Thyroid dysfunction is a common disorder in adults, which is more common in women as 3%-21% of the population are affected (1). Thyrotropin (TSH) level is the most sensitive marker of the individual's thyroid status and associated with negative feedback with free thyroxine (fT4) and free triiodothyronine (fT3). Serum

TSH level increases, and fT4 level decreases in overt hypothyroidism. In subclinical hypothyroidism, TSH level is high, whereas circulating fT4 level is normal (2).

Recently, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have appeared as new inflammatory biomarkers and are related to type 2 diabetes mellitus (3), gestational diabetes mellitus (4), and some thyroid pathologies (5-8).

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Platelets play an important role in atherothrombosis. It is more likely that large platelets will be more reactive, contain more granules, and produce more vasoactive and prothrombotic factors (9). The mean platelet volume (MPV) shows the platelet size and has been reported to be associated with platelet activity (10). In some previous studies, increased MPV was found to be associated with increased cardiovascular risk and thromboembolism in patients with hypothyroidism (8, 11, 12).

The aim of the present study was to investigate the levels of NLR, PLR, MPV, and some other hematological parameters in adult patients with hypothyroidism, which we find only in a limited number of studies in the literature.

MATERIALS AND METHODS

This retrospective study was conducted by examining the records between July 10, 2018 and April 09, 2019 from the laboratory information system of Mengücek Gazi Training and Research Hospital of Erzincan Binali Yıldırım University. Only adults older than 18 years were included in the study. The diagnoses of "E03.9 hypothyroidism, unspec-

ified" and "E03.8 hypothyroidism were defined, other" were searched, and a total of 3009 patients were found. However, in addition to the mentioned diagnoses, any other disease, vitamin deficiency, and diet counseling, such as additional diagnosis of all patients, were excluded, resulting in the data of 496 patients remaining. As an exception, data of 55 patients with the diagnoses of "E03.9 hypothyroidism, unspecified" and "Z00.0 general medical examination" were included in the patient group. Patients who were diagnosed with "E89.0 hypothyroidism, post-operative" and "E03.3 hypothyroidism, post-infection" were also excluded from the study. On the same dates, 31,089 individual data were found when questioned with the diagnosis of only "Z00.0 general medical examination," but only 14,900 of them did not receive an additional diagnosis. Moreover, the results of 5677 individuals with TSH request and within the reference range (TSH: 0.55-4.78 $\mu\text{U/mL}$) were evaluated as the control group. Data of three Sysmex XN_1000 (XN_1000; Sysmex, Kobe, Japan) and one Sysmex XN_2000 (XN_2000; Sysmex, Kobe, Japan) devices in our laboratories for hemogram values and two Siemens Centaur XP (Centaur XP; Siemens, Muenchen, Germany) devices for hormone values were evaluated. In both the patient and control groups, only the number of leukocytes (white blood cell, WBC) with 4000-11,000, the number of neutrophils with 2000-8000, the number of lymphocytes with 1000-5000, and the number of platelets with 150,000-450,000 were included in the study. Therefore, according to the reference ranges of our laboratory, those outside this range are excluded.

Statistical Analysis

Data were analyzed using Statistical Package for Social Sciences version 20.0 (IBM SPSS Corp.; Armonk, NY, USA) for statistical analysis. The Kolmogorov-Smirnov test was used for normal distribution of values. The Mann-Whitney U test was used for comparison of continuous variables with non-normal distribution. The chi-square test was performed to determine the relationship between two categorical variables. A p value <0.05 was accepted as statistically significant.

RESULTS

The median age of the hypothyroidism group was higher than that of the euthyroid healthy control group ($p < 0.001$). The number of women in the hypothyroid group was higher than that of men ($p < 0.001$). The percentage of females in the euthyroid healthy control group was similar. TSH value was higher, FT3 value was lower, and FT4 value was similar in the hypothyroidism group compared with the control group. In addition, WBC, neutrophil, and NLR values were lower; platelet, PLR, and MPV values were higher; and lymphocyte value was similar in the hypothyroid group compared with the control group (Table 1 and Figures 1-3).

Table 1. Demographic and laboratory outcomes of the groups

Parameter	Control group (median 95% CI)	Hypothyroidism group (median 95% CI)	p
Female/male (n)	2940/2737	434/62	<0.001*
Age (years)	37 37-38	42 41-43	<0.001*
TSH (mIU/L)	1.55 1.53-1.58	2.58 2.39-2.84	<0.001*
FT4 (ng/dL)	1.15 1.14-1.16	1.16 1.15-1.18	0.057
FT3 (pg/mL)	3.25 3.19-3.29	2.97 2.89-3.04	<0.001*
WBC (10^3 mm^3)	7.4 7.3-7.5	6.9 6.7-7.0	<0.001*
Platelet (10^3 mm^3)	267 265-268	276 270-281	0.010**
Neutrophil ($10^3/\mu\text{L}$)	4.30 4.24-4.34	3.87 3.73-3.98	<0.001*
Lymphocyte ($10^3/\mu\text{L}$)	2.33 2.31-2.36	2.29 2.23-2.36	0.323
NLR	1.85 1.82-1.87	1.66 1.59-1.74	<0.001*
PLR	113 112-115	118 114-122	0.044**
MPV (fL)	10.2 10.2-10.3	10.4 10.3-10.5	<0.001*

* $p < 0.001$, ** $p < 0.05$. CI: confidence interval; FT4: free thyroxine; FT3: free triiodothyronine; MPV: mean platelet volume; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; TSH: thyrotropin; WBC: white blood cell

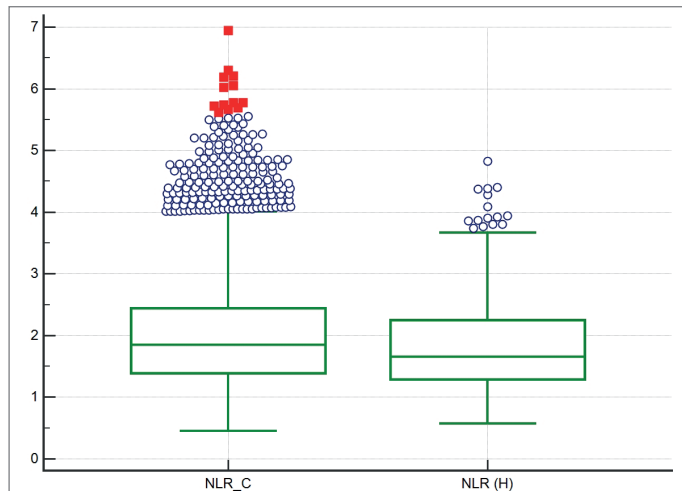


Figure 1. Box-plot of NLR data; groups shown on the x-axis and NLR value on the y-axis. Significant differences were found between the groups. Horizontal line, median; ends of boxes, 25%-75% quartiles; whiskers, range
NLR: neutrophil to lymphocyte ratio; NLR (C): the control group; NLR (H): the hypothyroid group

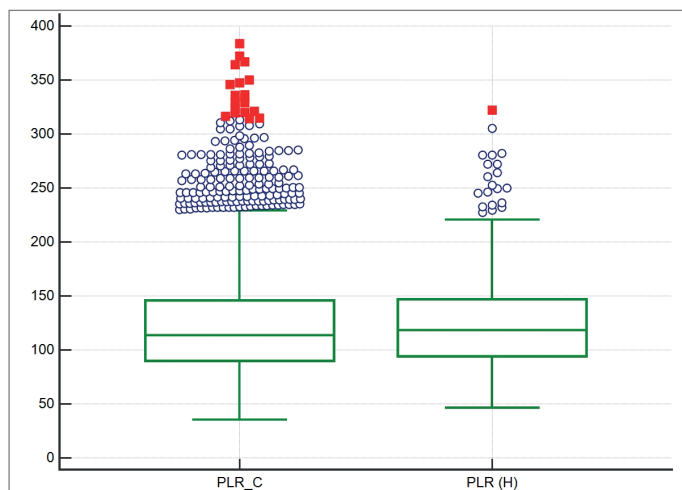


Figure 2. Box-plot of PLR data; groups shown on the x-axis and PLR value on the y-axis. Significant differences were found between the groups. Horizontal line, median; ends of boxes, 25%-75% quartiles; whiskers, range
PLR: platelet to lymphocyte ratio; PLR (C): the control group; NLR (H): the hypothyroid group

DISCUSSION

The results of the present study have shown that platelet, PLR, and MPV values increased; WBC, neutrophil, and NLR values decreased; and lymphocyte value remained unchanged in patients with hypothyroidism. Çoban et al. (13) found that the MPV values of individuals with subclinical hypothyroidism are higher than those of euthyroid individuals. In addition, Yılmaz et al. (11) found that an increased MPV value is associated with increased cardiovascular complications in patients with hypothyroidism. Similarly, Kim et al. (8) found a positive correlation between MPV value and TSH value and suggested that MPV value is related to prothrombotic conditions. Kutluturk et

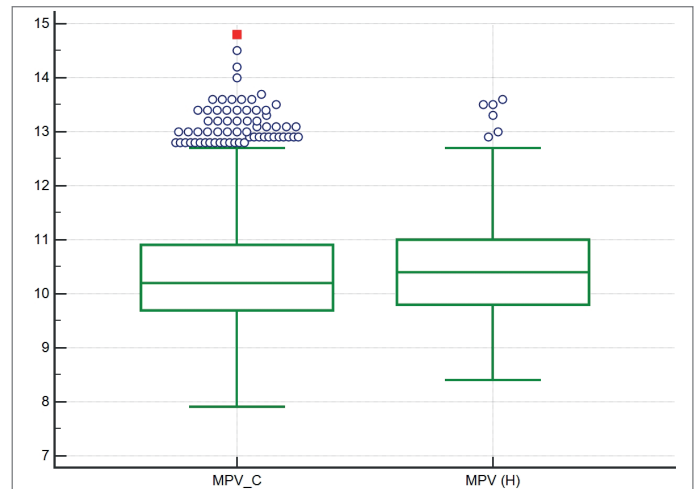


Figure 3. Box-plot of MPV data; groups shown on the x-axis and MPV value on the y-axis. Significant differences were found between the groups. Horizontal line, median; ends of boxes, 25%-75% quartiles; whiskers, range
MPV: mean platelet volume; PLR (C): the control group; NLR (H): the hypothyroid group

al. (12) reported that an increased MPV value is associated with increased cardiovascular complications in patients with hypothyroidism, whereas no relationship was found in platelet count, NLR, and PLR values. All these results related to the MPV value are similar to the current study. However, Kutluturk et al. (12) did not find any difference in platelet count, NLR, and PLR values, as opposed to the present study, which may be related with the number of patients in their study less than the present study. Because they are only based on the data of 58 patients, the subject numbers of the current study are much higher than that.

It has also been suggested that NLR and PLR values increase in Hashimoto's thyroiditis, which is one of the most common causes of hypothyroidism and can be used in combination in the diagnosis (5, 6).

Demir et al. (14) reported that radioiodine therapy changes the NLR, PLR, and MPV values. Moreover, it has been suggested that there is a relationship between NLR value and tumor size and extrathyroidal spread in patients with papillary thyroid cancer (7). In another study, PLR was reported to be associated with lateral lymph node metastasis in women with papillary thyroid cancer (15). In addition, PLR was found to be associated with lymph node metastasis in medullary thyroid carcinoma (16). High NLR and PLR values were claimed to show poor survival in thyroid cancer (17). However, although NLR value increased in thyroid malignancies, both NLR and PLR values were reported to be insufficient in distinguishing malignancies from benign pathologies (18).

According to the results of the present study, increased platelet count, PLR, and MPV values in individuals with

hypothyroidism may be associated with increased cardiovascular diseases and thrombosis as shown in other studies (8, 11, 12). In our study, while the lymphocyte count was not different from the control group, low levels of neutrophil, NLR, and WBC suggest that there may be a relationship between hypothyroidism and decreased neutrophil and WBC count. However, the exact mechanism of this relationship has not been elucidated in the present study. Therefore, this mechanism can be searched in advanced studies.

The fact that it was done retrospectively on records is one of the main limitations of the present study. Because, as it is known, sometimes there may be deficiencies or errors in the records.

In conclusion, the present study showed that platelet count, PLR, and MPV values are higher in adults with hypothyroidism than in euthyroid healthy individuals; WBC, neutrophil, and NLR values are low, and lymphocyte count is similar.

Ethics Committee Approval: Ethics committee approval was received for this study from the local ethics committee.

Informed Consent: Since it is a retrospective study, patient consent was not obtained, however, approval was obtained from the relevant departments of the hospital for data use.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.M., M.K.; Design – C.M., M.K.; Supervision – C.M.; Resources – C.M.; Materials – C.M.; Data Collection and/or Processing – C.M.; Analysis and/or Interpretation – C.M., M.K.; Literature Search – C.M.; Writing Manuscript – C.M.; Critical Review – C.M., M.K.

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Hasta Onamı: Retrospektif bir çalışma olduğu için hasta onamı alınmamıştır ancak hastanenin ilgili birimlerinden veri kullanımı için onay alınmıştır.

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