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Investigation Of Full Blood Count Parameters, Neutrophil Lymphocyte Ratio And Platelet Lymphocyte Ratio In Patients With Metabolic Syndrome

Metabolik Sendromlu Hastalarda Tam Kan Sayımı Parametreleri, Nötrofil Lenfosit Oranı Ve Trombosit Lenfosit Oranının Araştırılması

Akif Doğantekin[1], Yunus Gören[2], Nevzat Gözel[3], Esin Doğantekin[4], Osman Ersin Avcı[5]

1 Private Gaziantep Emek Hospital, Clinic of Internal Medicine, Gaziantep, Türkiye, https://orcid.org/0000-0001-6078-540X

2 Gaziantep Public Health Laboratory, Biochemistry Laboratory, Gaziantep, Türkiye, https://orcid.org/0000-0003-0344-2456

3 Fırat UniversityFaculty of Medicine, Department of General Internal Medicine, Elazig, Türkiye, https://orcid.org/0000-0001-7326-6860

4 Gaziantep Public Health Laboratory, Microbiology Laboratory, Gaziantep, Türkiye, https://orcid.org/0000-0002-3989-0421

5 Ankara Atatürk Senatorium Training and Research Hospital, Department of Pediatrics, Ankara, Türkiye, https://orcid.org/0009-0005-4838-3076

Abstract

Introduction: Metabolic syndrome is a fatal endocrino pathy that starts with insulin resistance and is accompanied by systemic disorders. Neutrophil-lymphocyteratio (NLR) and platelet-lymphocyte ratio (PLR) can be a determinant in inflammation as an alternative to white bloodcell count.

Aim: In this study, metabolic syndrome characterized by endothelial dys function, subclinical inflammation and hypercoagulability and systemic inflammation indicator; It is aimed to show there lationship between neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR).

Method: The study was carried out by retrospectively examining the demographic information and laboratory records of the patients who applied to Gaziantep Private Emek Hospital Internal Medicine Polyclinic between 01/10/2022-30/12/2022 for general health controlor Type 2 DM follow-up. The cases were divided into 2 groups as metabolic syndrome and control group. 63 patients with metabolic syndrome and 53 healthy (control group) patients were included in thestudy.

Results: The neutrophil-lymphocyte ratio (NLR) was 3.44 (2.87-4.1) in the metabolic syndrome group (n=63), and the NLR was 1.81 (1.65-2.04) in the control group (n=53), and there was a statistically significant difference ($p<0.001$). The platelet-lymphocyte ratio (PLR) was 198 (169.5-228.5) in the metabolic syndrome group and 101 (87.7-114.2) in the control group and was statistically significant ($p<0.001$).

Conclusion: Metabolic syndrome, which is the cause of low-grade chronic inflammation, and NLR and PLR levels, which are easily and in expensively accessible indicators of inflammation, were compared, and NLR and PLR levels were found to be significantly higher in the metabolic syndrome group. This result shows us that these two inflammation parameters can be used as prognostic indicators in chronic diseases.

Keywords: Metabolic Syndrome, Neutrophil Lymphocyte Ratio, Platelet Lymphocyte Ratio.

Corresponding Author: Akif Doğantekin, e-mail: akifdogantekin@gmail.com
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Özet

Giriş: Metaboliksendrom insülin direnci ile başlayan ve sistemik bozuklukların eşlik ettiği ölümcül bir endokrinopatidir. Nötrofil-lenfosit oranı (NLR) ve trombosit-lenfosit oranı (PLR), lökosit sayısına alternatif olarak inflamasyonda belirleyici olabilir.
Amaç: Bu çalışmada endoteldisfonksiyonu,subklinikinflamasyon, pıhtılaşma artışı ve sistemik inflamasyon göstergesi ile karakterize metaboliksendrom; nötrofil-lenfosit oranı (NLR) ile trombosit-lenfosit oranı (PLR) arasındaki ilişkinin gösterilmesi amaçlanmaktadır.
Yöntem: Çalışma, Gaziantep Özel Emek Hastanesi Dahiliye Polikliniğine 01/10/2022 - 30/12/2022 tarihleri arasında genel sağlık kontrolü veya Tip 2 DM takibi için başvuran hastaların demografik bilgileri ve laboratuvar kayıtları retrospektif olarak incelenerek yapılmıştır. Olgular metaboliksendrom ve kontrol grubu olarak 2 gruba ayrıldı. Çalışmaya 63 metabolik sendromlu hasta ve 53 sağlıklı (kontrol grubu) hasta dahil edildi.
Bulgular: Metaboliksendrom grubunda (n=63) nötrofil-lenfosit oranı (NLO) 3,44 (2,87-4,1), kontrol grubunda (n=53) NLO 1,81 (1,65-2,04) ve istatistiksel olarak anlamlı bir farktı ($p<0.001$). Trombosit-lenfosit oranı (PLR) metaboliksendrom grubunda 198 (169,5-228,5), kontrol grubunda 101 (87,7-114,2) olup istatistiksel olarak anlamlıydı ($p<0,001$).
Sonuç: Düşük dereceli kronik inflamasyonun nedeni olan metaboliksendrom ile inflamasyonun kolay ve ucuz ulaşılabilir göstergeleri olan NLR ve PLR düzeyleri karşılaştırılmış ve metabolik sendromda NLR ve PLR düzeylerinin anlamlı olarak yüksek olduğu saptanmıştır. Bu sonuç bize bu iki inflamasyon parametresinin kronik hastalıklarda prognostik göstergeler olarak kullanılabileceğini göstermektedir.

Anahtar Kelimeler: Metabolik Sendrom, Nötrofil Lenfosit Oranı, Platelet Lenfosit Oranı.

INTRODUCTION

Metabolic syndrome (MetS) is a complex of diseases characterized by decreased insulin sensitivity as the main pathology and root cause, weight gain, onset of diabetes, high cholesterol, high blood pressure, and accumulation of oxidized low-density lipoprotein (LDL-Cholesterol) in the heart vessels. The formation of foam cells by macrophages is the most important step in the formation of oxidized LDL. These foam cells accumulate in the subendothelial tissue and form fatal prothrombotic lesions. Since it is the disease of our modern age, it would be correct to call it the disease of civilization complex. It attracted attention for the first time in the 1980s, and scientists had problems in naming it due to the coexistence of all metabolic diseases affecting the cardiovascular bed, and it was called unidentified (X) disease. Obesity, subclinical inflammation, and insulin resistance are features that define the MetS (1).

One of the mechanisms involved in the pathogenesis of metabolic syndrome is a chronic inflammatory process. In abdominal obesity, prothrombotic and inflammatory responses are triggered by fatty tissue-derived metabolic products, hormones and cytokines. Leukocytosis is the hemogram value that best shows acute and chronic inflammation in the body. NLR and PLR can be a determinant in inflammation as an alternative to white blood cell count. NLR may be elevated due to the potential conditions that create atheroma plaque in the entire vascular bed of the body, such as diabetes, hypertension, sedentary lifestyle, western diet, carbohydrate-heavy diet, family history of cardiovascular disease and metabolic diseases. It is an indicator of inflammation that can show the course of cardiovascular diseases and predict the risk of death. NLR is a value that is directly affected by the increase in other inflammatory indicators such as procalcitonin, C-Reactive Protein (CRP), and systemic inflammation index (SII) (2).

Both NLR and PLR, as well as CRP and procalcitonin levels were found to be high in patients with bipolar disease, mania, depression and panic attacks. In addition, these markers increased in the age group of children with attention deficit.We know that the reason for subclinical chronic inflammation in all these mood disorders is the intake of foods high in sugar and

carbohydrates, and the leaching of pesticides into the soil, vegetables and fruits. We call these foods and ingredients inflammatory foods (3). In patients with metabolic syndrome, glycated low-density lipoprotein (GLDL-C) is directly related to platelet count and PLR (4).

The inflammatory indices NLR, PLR and SII are complete blood count rates and diseases that have predictive importance in MetS and oncological diseases (5).

In this study, metabolic syndrome characterized by endothelial dysfunction, subclinical inflammation and hypercoagulability and systemic inflammation indicator; It is aimed to show the relationship between NLR and PLR.

METHOD

The study was carried out by retrospectively examining the demographic information and laboratory records of patients who applied to Gaziantep Private Emek Hospital Internal Medicine Polyclinic between 01/10/2022 and 30/12/2022 for general health check-up or Type 2 diabetes mellitus (DM) follow-up. First of all, blood pressure measurement and waist circumference measurements were recorded in terms of National Cholesterol Education Program/Adult Treatment Panel (NCEP-ATP III) criteria of the patients who applied to the outpatient clinic, and they were evaluated for the presence of MetS (6) (Table 1).

Table 1. NCEP-ATP III Diagnostic Criteria For Metabolic Syndrome.

Parameter	Criteria
Abdominal obesity	Waist circumference ≥102 cm in male and ≥88 cm in female
Triglyceride (TG)	≥ 150 mg/dl
HDL-cholesterol	<50 mg/dl in female and <40 mg/dl in male, or take medication for it
Blood pressure	≥130/85 mmHg
Fasting blood glucose	≥100 mg/dl

The cases were divided into 2 groups as MetS and control group. The control group consisted of individuals with normal body mass index (BMI), no hypertension, diabetes, insulin resistance and known chronic disease, HbA1c < 5.7% and no drug prescribed for the last 6 months. Those with hemoglobinopathy, anemia were not included in the study. In total, 63 patients with metabolic syndrome, 53 healthy; 116 patients with available biochemical data were included in the study. Complete blood count parameters, NLR and PLR of both groups were compared. Body mass indexes of the patients were calculated using the formula BMI = kg/m². Age, gender, weight and height values and waist circumference of the patients were recorded and fasting blood glucose, Hba1c, lipid profile, hemogram, sedimentation and CRP levels were examined in both groups (blood taken after 8-12 hours of fasting).

The IBM Statistical Package for the Social Sciences (SPSS) version 25 was used for the statistical analysis of our study. The Kolmogorov-Smirnov test was used to determine whether the values we obtained were suitable for normal distribution. While defining the results, standard deviation and mean for those with normal distribution, and median and quartile range (IQR) forms for the others were used. The group comparison of the values with normal distribution was made with Student-T, while the Mann Whitney U test was used in the others. If the P value was below 0.05, the result was said to be significant.

RESULTS

The gender distribution ratios of the 116 participants included in the study are shown in Table 2. The mean age was 42±12 years in the MetS group and 43.6±11.76 years in the control

group. Since the cases were selected from similar age groups, there was no difference between the mean ages (p=0.45).

Table 2. Age And Gender Distribution By Groups

Group Name	MetS group	Control group
Average age	42±12	43,6±11,76
Gender distribution (Female/Male)	33/30	28/25
Total count of patients	63	53

When the NLR of the groups are examined; The NLR was 3.44(2.87-4.1) in the MetS group and 1.81 (1.65-2.04) in the control group (p<0.001).When we have a detailed look at thePLR values of the groups; PLR was 198 (169.5-228.5) in the MetS group and PLR 101 (87.7-114.2) in the control group (p<0.001). Absolute neutrophil count was 5.77±0.75 (10^3mm^3) in the MetS group and 3.89±0.79 (10^3mm^3) in the control group, (p<0.001). Absolute lymphocyte count was 1.69±0.29 (10^3mm^3) in the MetS group and 2.09±0.31 (10^3mm^3) in the control group (p<0.001). The platelet count was 340 (299-381) (10^3mm^3) in the MetS group and 210 (189-238) (10^3mm^3) in the control group (p<0.001). The CRP level in the MetS group was 4.1 (3.9-4.6) mg/dL, and the CRP level in the control group was 1.6 (1.07-1.8) mg/dL (p <0.001). The sedimentation level in the MetS group was 17 (15-19) (1st hour), and the sedimentation level in the control group was 7 (5-10) (1st hour) (p<0.001).

FBG level 168 (146.5-195.8) mg/dL and HbA1c level 7.8% (7.1-8.6) in the MetS group, FBG level 89 (85-93) mg/dL and HbA1c level % in the control group; It was found to be 5.3 (5-5.5) (p<0.001 for each 2 values).

When the blood pressure levels of the groups were compared, the systolic blood pressure level was 136 (126-143) mmHg and the diastolic blood pressure level was 85 (77-92) mmHg in the MetS group, the systolic blood pressure level was 111 (108-118) mmHg and the diastolic blood pressure level was 65(58-70) mmHg in the control group (p<0.001 for both values).

Table 3. Comparison Of Metabolic Syndrome And Control Group In Terms Of Study Parameters

Group Name	MetS group (n=63)	Control group (n=53)	p
FBG (mg/dL)	168 (146,5-195,8)	89 (85-93)	<0,001
HbA1c (%)	7,8 (7,1-8,6)	5,3 (5-5,5)	<0,001
BMI(kg/m^2)	33,3 (31,9-34,6)	23,2 (22,5-23,7)	<0,001
Waist circumference (cm)	103,3 (94,1-110,4)	79,2 (77,2-86,4)	<0,001
Waist circumference-female (cm)	94,3 (91,5-98,8)	77,4 (75,3-78,2)	<0,001
Waist circumference-male (cm)	111,5±8,5	86,6±2,09	<0,001
Systolic blood pressure (mmHg)	136 (126-143)	111 (108-118)	<0,001
Diastolic blood pressure(mmHg)	85 (77-92)	65 (58-70)	<0,001
Triglyceride (mg/dL)	250±50,8	121±14,5	<0,001
HDL-Cholesterol(mg/dL)	40±5,79	65±4,85	<0,001
HDL-Cholesterol-female(mg/dL)	42,5±5,4	66,6±4,8	<0,001
HDL-Cholesterol-male(mg/dL)	37±4,82	62,5±3,93	<0,001
CRP (mg/dL)	4,1 (3,9-4,6)	1,6 (1,07-1,8)	<0,001
Sedimentation (1st hour)	17 (15-19)	7 (5-10)	<0,001
Neutrophil (absolute) count (10^3mm^3)	5,77±0,75	3,89±0,79	<0,001
Platelet count (10^3mm^3)	340 (299-381)	210 (189-238)	<0,001
Lymphocyte (absolute) count (10^3mm^3)	1,69±0,29	2,09±0,31	<0,001
Neutrophil-Lymphocyte ratio (NLR)	3,44 (2,87-4,1)	1,81 (1,65-2,04)	<0,001
Platelet-Lymphocyte ratio (PLR)	198 (169,5-228,5)	101 (87,7-114,2)	<0,001

When the lipid profiles of the groups were compared, the triglyceride level was 250±50.8 mg/dL and HDL-cholesterol level was 40±5.79 mg/dL in the MetS group, while the triglyceride level was 121±14.5 mg/dL and HDL-cholesterol level was 65±4.85 mg/dL in the control group ($p<0.001$ for both values).

When the waist circumference and body mass index (BMI) of the groups were compared, the waist circumference in the MetS group was 103.3 (94.1-10.4) cm and the BMI was 33.3 (31.9-34.6) kg/m². In the control group, waist circumference was 79.2 (77.2-86.4) cm and BMI was 23.2 (22.5-23.7) kg/m² ($p<0.001$ for both values) (Table 3).

DISCUSSION

MetS is a group of combined diseases that give signs and symptoms with high blood sugar, decrease in insulin sensitivity, increase in body fat mass, high blood pressure, high cholesterol, apple-type adiposity in which the lower extremities are thin and the body is thick, and eventually progress to cardiovascular diseases. It also includes endothelial dysfunction, prooxidant, prothrombotic and inflammatory processes. With the formation of low-grade subclinical systemic inflammation, increase in inflammatory parameters, oxidation, that is, premature aging, continues with damage to the vascular bed that feeds the vital organs (7, 8).

NLR is a commonly used test, even in Grade 1 healthcare facilities. NLR is thought to be an indicator of subclinical inflammation (9). Studies have shown that there is a subclinical inflammation in diseases such as diabetes mellitus, hypertension, hyperlipidemia, metabolic syndrome, endothelial dysfunction and NLR is an indicator of this inflammation (10). As inflammatory markers, NLR and PLR are frequently preferred in studies conducted in different clinical pathologies and patient groups. Conditions such as malignancy, neurodegeneration, acute systemic infection, smoking addiction can be included in these study groups (11).

These two inflammatory parameters have been used to determine the course of cardiovascular system diseases, high blood sugar and malignancies (12). NLR is used to determine the general condition and course of the patient after treatment of malignant disease and MetS. It can also determine whether metabolic syndrome will develop in a healthy individual in the future (13). It is known that NLR and high sensitivity CRP (hs-CRP) levels are higher in patients with metabolic syndrome than in normal individuals (14). MetS is associated with chronic inflammation, high CRP, sedimentation, leukocytes and NLR (15).

In our study, confirming this, the NLR value in the MetS group [3.44 (2.87-4.1)] was detected to be higher than the control group [1.81 (1.65-2.04)] ($p<0.001$). Likewise, CRP level [4.1 (3.9-4.6)] mg/dL in the MetS group was detected to be increased in the other group[1.6 (1.07-1.8)] mg/dL ($p<0.001$). When the leukocyte counts were examined, in accordance with the literature, the leukocyte count in the MetSgroup (7.78±0.78) 10^3mm^3 was detectedto be increased in the other group(6.43±0.85) 10^3mm^3 ($p<0.001$). When the sedimentation levels were examined, it was found that it was 17 (15-19) (1st hour) in the MetS group and 7 (5-10) (1st hour) in the control group ($p<0.001$).

In a study, it was determined that both platelet and PLR did not increase in patients with MetS(16). In our study, the platelet count [340 (299-381)] was higher in the metabolic syndrome group compared to the control group [210 (189-238)] ($p<0.001$). In addition, PLR [198 (169.5-228.5)] was found to be higher in the metabolic syndrome group compared to the control group [101 (87.7-114.2)] ($p<0.001$).

In a study by Varol et al., NLR showed a negative correlation with high-density lipoprotein (HDL), which has anti-inflammatory activity. Patients with low HDL-cholesterol had significantly higher NLR compared with control participants (17). In our study, HDL-cholesterol level with anti-inflammatory effect was 40±5.79 mg/dl in the metabolic syndrome group and 65±4.85 mg/dl in the control group ($p<0.001$).

The lymphocyte/HDL ratio was found to be increased in metabolic syndrome and is an effective predictor of metabolic syndrome. Again in the same study, it was observed that the platelet-lymphocyte ratio did not increase (18). In our study, in accordance with this literature, the lymphocyte/HDL-Cholesterol ratio [0.041 (0.035-0.052)] in the MetS group was detected to be 0.0233 increased in the other group (0.03-0.035) in the in the other group($p<0.001$).

Inflammation is closely associated with insulin resistance due to excess adipose tissue that produces proinflammatoryadipokines that result in low-grade chronic inflammation, impair the tissue response to insulin, and lead to type 2 diabetes. HbA1c levels >7% are associated with a higher risk of irreversible, organic injury, but HbA1c certainly does not predict inflammatory processes (19,20). In our study, HbA1c level [7.8% (7.1-8.6)] in the metabolic syndrome group was found to be higher than >7% and higher and statistically significant compared to the control group [5.3% (5-5.5)]. ($p<0.001$).

In the study of Atak et al., the platelet-lymphocyte ratio can be used to detect low-grade inflammation caused by diabetes. It was determined that PLR was increased in cases with high sugar levels for many years compared to normal individuals. It has been found that PLR and 3-month sugar indicator are directly related to each other in cases with high blood sugar. The PLR value is an indicator of the course of the disease in diabetics and whether it harms other organs. As the sugar level rises as a result of the diabetic's weakness in the use of medication and not paying attention to his diet, PLR and similar indicators increase with the sugar level (21). In our study, direct relationshipwas detected between HbA1c and PLR in accordance with this literature ($p=0.03$).

PLR, and especially NLR, has been associated with microvascular and macrovascular complications in diabetes, most notably with disease progression and metabolic deterioration. In a study by Sefil et al., it showed a positive correlation with NLR and HbA1c levels. This study showed a difference in the proportions of hyperglycemic subjects with HbA1c <7.0% and hyperglycemic subjects with HbA1c ≥7.0% (22). In our study, a positive correlation was found with NLR and HbA1c levels in accordance with this literature ($p=0.02$).

Obesity has become a growing problem around the world and is turning into a pandemic. It is a component of the complex of metabolic diseases. Obesity is a precursor disease for vascular bed diseases, osteoporosis, uterine and breast malignancies. If obesity is treated, all the conditions it causes are also treated. Ratios such as NLR, PLR and SII obtained from complete blood count (CBC) and its results have been associated with obesity and obesity-related diseases (23). In our study, the BMI level was 33.3 (31.9-34.6) kg/m² in the obese group with metabolic syndrome and 23.2 (22.5-23.7) kg/m² in the control group ($p<0.001$). In our study, NLR and PLR were found to be higher and statistically significant in the obese group with metabolic syndrome compared to the control group in accordance with the literature ($p<0.001$ for both values).

In many studies, leukocyte count has been found to be an independent risk indicator for diabetes, insulin resistance, metabolic syndrome, obesity and coronary artery diseases (24). In human and animal experiments, it has been determined that increased leukocyte and neutrophil counts are associated with obesity and metabolic disorders triggered by obesity

(25). An increased leukocyte count is a direct risk factor for the development of MetS (26). When the leukocyte counts were examined in our study, the leukocyte count in the MetSgroup (7.78±0.78) was found to be higher than 10^3mm^3 and the control group (6.43±0.85) 10^3mm^3, in accordance with the literature ($p<0.001$).

In a study by Furuncuoğlu et al., it was determined that there was no statistically significant relationship between the degree of obesity and PLR and NLR. However, white blood cells, neutrophils, lymphocytes, platelets, and plateletcrit (PCT) levels were statistically significantly affected by the increase in body mass index (27). In some previous studies, it was observed that neutrophil and lymphocyte counts increased in patients with obesity and MetS compared to control groups, and NLR increased, but this was not very significant (28). In our study, the plateletcrit (PCT) level in the MetS group was 0.31±0.03%, 0.20±0.02% in the control group ($p<0.001$).

Mean platelet volume (MPV) indicates the mean volume and functionality of platelets. It can be used as an inflammatory marker such as NLR and PLR. There are close links between MPV, metabolic syndrome and cardiometabolic risk. The incidence of MetS in women was higher in the low MPV group than in the high MPV groups (29). In our study, the MPV level was found to be 11.3±0.68 fL in the MetS group and 8.7±0.59 fL in the control group ($p<0.001$).

CONCLUSION

In conclusion, in our study, the relationship between metabolic syndrome and inflammation markers NLR, PLR, CRP and sedimentation was investigated and inflammatory markers were detected to be increased in the group with metabolic syndrome. It is thought that NLR and PLR can be used as simple, effective and low-cost hematological tests in the follow-up of MetS and its components and in determining the burden of disease. Large-scale and multicenter studies in mass of peopleare needed for the use of NLR and PLR in follow-up and prognosis in metabolic syndrome.

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