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INVESTIGATION OF THE RELATIONSHIP BETWEEN INFLAMMATION PARAMETERS AND BLOOD GROUPS IN NEWLY DIAGNOSED TYPE 2 DIABETES PATIENTS

YENİ TANI ALAN TİP 2 DİYABET HASTALARINDA İNFLAMASYON PARAMETRELERİNİN KAN GRUPLARI İLE İLİŞKİSİNİN İNCELENMESİ

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ABSTRACT

Objective: Type 2 diabetes mellitus (T2DM) is a chronic disease with an increasing prevalence, accounting for 90-95% of all diabetics. It is considered that the disease is induced by inflammation. In this study, we aimed to investigate the inflammation parameters and the relationship of these parameters with blood groups in newly diagnosed T2DM patients.

Methods: The study included 80 newly diagnosed T2DM patients and 80 healthy volunteers. Demographic characteristics, body mass indexes (BMI), biochemistry and hemogram test results, C-reactive protein (CRP) values, and blood groups of the patient and control groups were recorded and compared between the groups.

Results: The mean age was 51.64 years and 53.8% of the patients were male in the newly diagnosed T2DM group. The counts of white blood cells (WBC), neutrophils, lymphocytes, platelets, and monocytes, the values of the monocyte/HDL ratio (MHR) and the systemic immune-inflammatory index (SII), and the CRP levels of T2DM patients were statistically significantly higher than those of the control group ($p<0.05$). Of the T2DM patients, the platelet counts were statistically significantly higher in the blood type B group compared to the blood type O group ($p=0.022$).

Conclusion: We think that the hematological parameters of inflammation and the high MHR and SII ratios the presence of chronic systematic inflammation in newly diagnosed T2DM patients before the development of complications. Therefore, these parameters may guide the diagnosis and preventive treatment in prediabetic patients.

Keywords: Type 2 diabetes mellitus, inflammation, blood group

ÖZ

Amaç: Tip 2 diyabetes mellitus (T2DM), inflamasyonun indüklediği düşünülen, tüm diyabetlilerin %90-95'ini oluşturan prevelansı giderek artan kronik bir hastalıktır. Bu çalışmada yeni tanı almış T2DM olan hastalarda inflamasyon parametrelerini ve bu parametrelerin kan grupları ile ilişkisini araştırmayı amaçladık.

Yöntem: Bu çalışmaya 80 yeni tanı almış T2DM hastası, 80 sağlıklı gönüllü dâhil edildi. Hadta ve kontrol grubunun demografik özellikleri, vücut kitle indeksi (VKİ) biyokimya, hemogram, C-reaktif protein (CRP) ve kan grupları kayıt gruplar arasında karşılaştırıldı.

Bulgular: Yeni tanı diyabet alan T2DM hatalarının yaş ortalaması 51,64'dü ve hastaların %53,8'i erkekti. T2DM hastaların beyaz kan hücresi (BKH), nötrofil, lenfosit, platelet, monosit, monosit/HDL oranı (MHO), sistemik immün-inflamatuar indeks (Sİİ) ve CRP düzeyleri kontrol grubundan istatistiksel olarak anlamlı derecede yüksek saptandı ($p<0,05$). T2DM'li hastalarda kan grubu B olanların platelet değerleri, kan grubu O olan gruptan istatistiksel olarak anlamlı derecede yüksek saptandı ($p=0,022$).

Sonuç: Yeni tanı T2DM hastalarında inflamasyonu gösteren hematolojik parametrelerin ve MHO ve Sİİ oranlarındaki yüksekliğinin, hastalarda komplikasyon gelişmeden kronik sistemik inflamasyonun varlığını gösterdiğini, prediyabetik hastalarda tanıda ve koruyucu tedaviye başlamada yol gösterici olabileceğini düşünüyoruz.

Anahtar Kelimeler: Tip 2 diyabetes mellitus, inflamasyon, kan grubu.

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Introduction

Diabetes mellitus is a chronic metabolic and systemic disorder characterized by impairments in fat metabolism, protein and carbohydrate due to partial or complete insulin deficiency and/or insulin resistance leading to chronic hyperglycemia.[1] Type 2 diabetes mellitus (T2DM) accounts for 90-95% of all diabetes cases. Despite the evidence for the significant role of genetics, the prevalence of T2DM is on the rise, especially in children and young adults, due to increasing obesity rates.[2]

Significant evidence has been established in recent years showing that low-grade inflammation is an important pathogenic determinant of T2DM.[3] Although the underlying mechanisms have not been clarified yet, supporting evidence is available for the hypothesis that the increase in central fat mass due to chronic inflammation and the production of proinflammatory cytokines such as Tumor Necrosis Factor-alpha (TNFα) and Interleukin-1 (IL-1) constitute the risk factors for the development of T2DM.[4,5] Furthermore, acute phase proteins and certain cytokines are involved in several metabolic pathways such as insulin regulation and the functioning of lipoprotein lipases and adipocytes, contributing to the development of insulin resistance.[6] In recent years, easily accessible and cost-effective biomarkers have been investigated such as neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) for their association with T2DM.[7] Some studies have shown the association of the NLR ratio with glucose control in T2DM.[8]

It has been suggested in the literature that ABO blood group antigens may play a role in the pathogenesis of cancers and cardiovascular, endocrine, and metabolic disorders.[9,10] It has been documented in studies that the increased levels of plasma lipids and inflammatory markers are associated with the variants of ABO gene loci, especially of the A and B antigens and that they are well-known risk factors for DM.[11,12] The inflammatory mechanisms in the development of T2DM and the relationship of ABO blood groups with diabetes and inflammation have not been fully elucidated, yet. In this study, we aimed to investigate the inflammatory parameters and the relationship of these parameters with blood groups in newly diagnosed T2DM patients.

Methods

The study was approved by Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (2021-11/123/04). All procedures were conducted in accordance with the principles of the Declaration of Helsinki. The study included 80 patients, who presented to the internal medicine outpatient clinic for routine examinations and were diagnosed with T2DM for the first time based on relevant laboratory parameters. Patients with a history of chronic disease (hypertension, hematologic disorders, or chronic diseases of the liver, kidney, heart, lung, or thyroid), immunodeficiency, acute or chronic inflammatory diseases, oncological diseases, thalassemia, infections in the past 1 month, pregnant women, or those with a history of drug use were not included in the patient group. In the control group, 80 healthy volunteers, who presented to the outpatient clinic for routine check-up visits were included.

Demographic characteristics, the results of biochemistry and hemogram tests, C-reactive protein (CRP) levels, and blood groups of the patients and healthy controls were recorded. PLR indicates the ratio of platelet to lymphocyte, NLR indicates the ratio of neutrophil to lymphocyte, and MHR indicates the ratio of monocyte to high-density lipoprotein (HDL). Systemicimmune-inflammation index (SII) = neutrophil count X platelet count/lymphocyte count.[13] SII = neutrophil count X platelet count/lymphocyte count. The measurement of HDL and fasting plasma glucose levels of the study population after 12-hour fasting was conducted by enzymatic colorimetric assay. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Diabetes mellitus was diagnosed in patients with a blood glucose value of ≥126 mg/dL and a Hemoglobin A1c (HbA1c) value of ≥ 6.5% mmol/mol, both of which were measured after at least 8 hours of fasting.[1]

Statistical Analysis

Study data were collected from 160 people, of whom 80 were patients and 80 were healthy controls. Descriptive statistics (median, mean, standard deviation) and frequencies (percentage, number) were used for categorical and numerical variables, respectively. IBM SPSS Statistics 26 package software were used for analyzes.

Kolmogorov Smirnov test of normality was used for the normality assumptions of the numerical variables and it was found that the variables were not normally distributed. Therefore, non-parametric statistical methods were used in the study. Spearman's Rho Correlation coefficient was used for the relationships between two independent numerical variables. Chi-square analyses were used for the relationships between two independent categorical variables. Differences among more than two independent groups were evaluated with the Kruskal-Wallis test. Differences between two independent groups were evaluated with the Mann-Whitney U Test. Statistical significance was interpreted at the 0.05 level.

Results

The mean age was 51.64±10.145 years and 48.54±11.966 years in the T2DM and control groups, respectively. Males constituted 53.8% of the T2DM patients and 56.3% of the individuals in the control group. BMI was 30.60±4.610 kg/m² in the T2DM group and 24.11±3.236 kg/m² in the control group ($p<0.001$). The distribution of blood types

was not different between the T2DM and control groups (p>0.05) (Table 1).

Table 1. Demographic characteristic of patients (N=160).

	T2DM (n=80) Mean±SD	Control (n=80) Mean±SD	Z	p
Age (years)	51.64±10.145	48.54±11.966	-1,682	0,093
BMI	30.60±4.610	24.11±3.236	-8,286	**0,000***
	N (%)	**N (%)**	**Chi-Square**	**p**
Gender				
Female	37 (46.3)	35 (43.8)	0.101	0.751
Male	43 (%53.8)	45 (56.3)		
Blood Group				
A	25 (31.3)	30 (37.5)	4.792	0.188
B	25 (31.3)	14 (17.5)		
AB	13 (16.3)	12 (15.0)		
0	17 (21.3)	24 (30.0)		

Z: Mann Whitney U Analizi *: p<0,05 BMI: Body mass index, T2DM: Type 2 diabetes mellitus

The values of glucose and HbA1c; the counts of white blood cells (WBC), neutrophils, lymphocytes, platelets, and monocytes; and the levels of MHR, SII, and CRP were statistically significantly higher in the T2DM patients compared to the control group (p<0.05). HDL levels of T2DM patients were significantly lower than those of individuals in the control group (p<0.001) (Table 2).

The comparison of the blood types with the inflammatory parameters in the T2DM group revealed that diabetes patients with blood type B had statistically significantly higher platelet counts compared to those with blood type O (p=0.022) (Table 3).

Table 2. Biochemical Test Results and Differences by Groups (N=160)

	T2DM (n=80) Mean±SD	Control (n=80) Mean±SD	Z	p
Glucose (mg/dl)	243.00±79.261	93.43±8.918	-10.923	**0.000***
HbA1c (%)	9.98±2.765	5.23±0.730	-10.925	**0.000***
WBC (×10³ µl)	8.22±1.562	7.18±1.586	-3.625	**0.000***
Neu (×10³ µl)	5.07±1.349	4.04±1.152	-4.780	**0.000***
Lym (×10³ µl)	2.50±0.820	2.22±0.696	-2.123	**0.034***
Plt (×10³ µl)	293.34±74.732	258.39±70,783	-2.386	**0.017***
Mon (×10³ µl)	0.53±0.759	0.46±0.686	-2,403	**0.016***
HDL (mg/dl)	46.09±11.049	54.55±12.975	-4.238	**0.000***
NLR	2.27±1.007	1.96±0.794	-1.853	0.064
PLR	130.81±58.81	124.81±46.332	-0.183	0.855
MHR	0.01±0.023	0.01±0.012	-4.107	**0.000***
SII	670.46±374.772	497.38±222.013	-3.100	**0.002***
CRP (mg/l)	0.64±0.740	0.26±0.387	-6.580	**0.000***

Z: Mann Whitney U Analysis, *:p<0,05, T2DM: Type 2 diabetes mellitus, HbA1c: Hemoglobin A1c, WBC: White blood cell, Neu: Neutrophils, Lym: Lymphocytes, Plt: Platelets, Mon: Monocytes, HDL: High-density lipoprotein, NLR: Neutrophil/lymphocyte ratio, , PLR: Platelet/lymphocyte ratio, MHR: Monocyte/HDL ratio, SII: Systemic immune-inflammation index, CRP: C-reactive protein

Discussion

It is predicted that T2DM will continue to be on the rise in the coming years, mostly in individuals between the ages of 45-64 years and more commonly in developing countries.[14] Although there are some differences in gender ratios across countries, T2DM is usually diagnosed in males at a lower age and with low body

Table 3. Biochemical Results According to Blood Groups in T2DM patients (N=80)

	1) A group Mean±SD	2) B group Mean±SD	3) AB group Mean±SD	4) 0 group Mean±SD	KW	p
WBC (×10³ µl)	8.37±1.723	8,36±1.256	8.27±1.794	7.75±1.585	1.522	0.677
Neu (×10³ µl)	5.14±1.405	5.13±1.158	5.33±1.643	4.7±1.333	2.268	0.519
Lym (×10³ µl)	2.75±0.96	2.44±0.759	2.55±0.76	2.16±0.647	4.971	0.174
Plt (×10³ µl)	293.68±80.15	311.36±70.488	317.38±86.58	247.94±41.198	9.661	**0.022* 0-B**
Mon (×10³ µl)	0.46±0.14	0.72±1.34	0.47±0.144	0.38±0.121	4.585	0.205
HDL	48.06±13.089	47.44±9.337	42.69±7.488	43.82±12.218	3.35	0.341
NLR	2.06±0.748	2.38±1.159	2.32±1.03	2.39±1.123	0.723	0.868
PLR	118.96±50.559	143.98±70.849	137.1±65.699	124.06±43.645	2.18	0.536
MHR	0.01±0.008	0.02±0.04	0.01±0.005	0.01±0.002	2.173	0.537
SII	603.9±271,653	755.32±477.361	736.4±407.479	593.12±297.318	2.126	0.547
CRP(mg/l)	0.68±0.537	0.77±1.158	0.52±0.411	0.48±0.256	1.612	0.657
BMI	31.12±4.746	31.52±4,265	27.62±4.835	30.74±4.164	6.848	0.077

Z: Mann Whitney U Analysis, *:p<0,05, T2DM: Type 2 diabetes mellitus, HbA1c: Hemoglobin A1c, WBC: White blood cell, Neu: Neutrophils, Lym: Lymphocytes, Plt: Platelets, Mon: Monocytes, HDL: High-density lipoprotein, NLR: Neutrophil/lymphocyte ratio, , PLR: Platelet/lymphocyte ratio, MHR: Monocyte/HDL ratio, SII: Systemic immune-inflammation index, CRP: C-reactive protein

mass indexes. Obesity, which is the most significant risk factor, is more common in women.[15] The mean age of newly diagnosed T2DM patients in our study was 51.64 years and 53.8% of our patients were men. The majority of patients, who were diagnosed with T2DM, were obese with a mean BMI of 30.60 kg/m², which was significantly higher than that of the control group.

Evidence obtained from studies shows that there is a relationship between the diabetes risk and the total peripheral WBC or leukocyte count, which is a non-specific inflammatory marker.[16] Zhang et al. reported significantly increased total counts of WBC, neutrophils, and lymphocytes in patients with newly diagnosed diabetes compared to those without diabetes.[17] Similarly, we found significantly higher counts of WBC, neutrophils, lymphocytes, and monocytes in newly diagnosed T2DM patients compared to the control group in our study. Studies have shown evidence that CRP levels are predictive of developing diabetes, indicating the relationship between inflammation and glycemic control in patients with T2DM.[18,19] It has been observed in T2DM patients that the activation, adhesion, and aggregation of platelets increase due to the dysregulation of various signaling pathways.[20] Thus, platelets have become proinflammatory entities that cause inflammation in T2DM.[21] In our study, we found that platelet counts and CRP levels in newly diagnosed T2DM patients were significantly higher than those of the control group, suggesting that these increased levels represented the indicators of inflammation.

Various studies with diabetic patients have shown that inflammatory ratios such as NLR and PLR are predictive of diabetes-related microvascular and atherosclerotic complications and that such ratios have prognostic values.[22,8] In our study, there were no significant differences in NLR and PLR values between newly diagnosed T2DM patients and the control group but MHR and SII values were found to be significantly higher in T2DM patients. There are only a few studies in the literature investigating the relationship of hematological parameters such as MHR and SII with T2DM. In a study, Cardoso et al. reported an association between MHR and an increased risk for cardiovascular mortality in patients with T2DM.[23] Wang et al. showed that a high SII value may be a risk factor for depression in diabetic patients.[24] In our study, we have thought that a high SII value and increased MHR in newly diagnosed T2DM patients compared to the control group have indicated the presence of chronic systemic inflammation before the development of diabetic complications and that these parameters can be used as predictive markers in the diagnosis of prediabetic patients.

Blood group antigens are considered among hereditary indicators, playing a vital role in understanding genetics and disease susceptibility.[25] In recent years, the relationship between blood types and T2DM has been investigated to identify susceptible groups. Although some studies have reported conflicting results, B and O blood types have been associated with increased and decreased risk of developing T2DM, respectively.[26, 27] In our study, no differences were found in blood types between the patients with T2DM and the control group. However, when the blood groups and inflammation markers were compared in the patient group with T2DM, platelet counts were found to be statistically significantly higher in individuals with group B compared to those with group O. We thought that these results were associated with a higher risk of inflammation in patients with B blood group compared to O blood group among T2DM patients. Although studies have reported different results regarding the relationship between susceptibility to inflammatory diseases and ABO blood group antigens, it has been shown that the risk of developing thromboembolic and cardiovascular disease is lower in people with O blood group compared to other blood groups[28].

Our study is not free of limitations. The study sample is not large because of the inclusion of only newly diagnosed diabetic patients in the study and the strict exclusion criteria. Another limitation of the study is the retrospective design.

Conclusions

In conclusion, we suggest that the inflammatory hematological parameters in newly diagnosed T2DM patients and the high MHR and SII ratios indicate the presence of chronic systemic inflammation in patients before the development of complications and that such parameters and ratios may lead to the diagnosis and starting preventive treatment in prediabetic patients. We think that, among newly diagnosed T2DM patients, higher platelet counts in individuals with B blood group compared to individuals with group O are associated with an increased risk of inflammation and that comprehensive studies with large samples will contribute further to the early diagnosis and the prediction of prognosis.

Compliance with Ethical Standards

Ethics committee approval of the study was obtained from the Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (Decision no: 01-11-2021/123/04).

Conflict of Interest

The author declares no conflicts of interest.

Author Contribution

OS: Study idea, hypothesis, study design; Material preparation, data collection and analysis; Writing the article; Critical review and publication process

Financial Disclosure

None

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