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The role of hemogram parameters in predicting diabetic neuropathy risk in patients follow-up with type 2 diabetes mellitus

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ABSTRACT

Aims: Neuropathy, which develops during the course of diabetes mellitus (DM), significantly affects patients' quality of life, making its early diagnosis and detection crucial. Furthermore, it is thought that the impact of neuropathy developing in the course of DM is not localized but has systemic effects. In our study, we will investigate the role of evaluating hemogram parameters and systemic effects in predicting the risk and monitoring the course of diabetic neuropathy in patients followed up with DM.

Methods: Data from patients who presented to the Yozgat Bozok University Neurology Outpatient Clinic between 2024 and 2025 will be scanned. This will include patients diagnosed with diabetic neuropathy and DM, as well as those investigated for but not found to have neuropathy. One hundred individuals will be included in each group. Group 1 was defined as 50 individuals with a diagnosis of diabetic neuropathy, and group 2 as 50 individuals without a diagnosis of diabetic neuropathy. Within the scope of the study, the following data will be recorded from the hospital data system: patients' age, gender, past medical histories, diagnoses, treatments received, and laboratory test results including hemogram, HbA1c, glucose, sedimentation, CRP, ALT, AST, BUN, serum creatinine, B12, vitamin D, folic acid, ferritin, and electrolyte levels. The ratios of neutrophil, platelet, and monocyte counts to lymphocytes will be calculated and analyzed to assess their association with neuropathy. The data will be analyzed using SPSS, with the significance level set at 0.005.

Results: Of the 100 individuals included in the study, 61 (55.5%) were female and 39 (35.5%) were male; the mean age was calculated as 45.77±17.48. The 50 individuals with diabetic polyneuropathy and the 50 individuals in the healthy control group were analyzed as two groups. Among the 100 patient individuals, 44 (48.9%) were within the target HbA1c range, while 46 (51.1%) individuals were observed to have uncontrolled DM. No statistically significant difference was observed between the groups in terms of fasting blood glucose and HbA1c levels (p=0.657). While no statistically significant difference was observed in NLR and PLR, calculated from the same hemogram data in group 1 and group 2 (p=0.647 and p=0.242, respectively), the difference in MLR was found to be statistically significant (p=0.0024).

Conclusion: Although diabetic neuropathy presents with localized symptoms, its effects are systemic. The monocyte-to-lymphocyte ratio (MLR) was evaluated as a usable parameter for the early detection of developing neuropathy and for determining neuropathy risk. Its correlation with next-generation inflammatory biomarkers may be required. As hemogram data is a test that is available and feasible to perform in most medical centers, it could be a suitable tool for monitoring the development of neuropathy in DM patients, and potentially for post-treatment follow-up.

Keywords: Diabetes mellitus, diabetic neuropathy, neutrophil, lymphocyte, monocyte

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a disease characterized by hyperglycemia and associated with microvascular (retinopathy, neuropathy, and nephropathy), macrovascular (coronary artery disease, peripheral artery disease), and neuropathic (autonomic and peripheral) complications.[1,2] Neuropathy, one of the complications of T2DM, holds particular importance due to the subsequent health problems it causes (diabetic foot ulcers, foot amputations, etc.).[3] When these complications occur, they can become a significant source of morbidity and mortality. Furthermore, the economic burden this condition places on national economies is equally important. It has been reported that

in 2002, approximately 20% of healthcare expenditures in the U.S. were allocated to preventing and treating DM and its complications, and this figure is observed to be steadily increasing.[4] For this reason, the early detection of chronic complications of DM, identification of accompanying risk factors, and their prevention have gained even greater importance. Typically, diabetic patients are referred for neurological examination to detect diabetic neuropathy only if they present with neuropathic symptoms. Patients without neuropathic complaints are merely monitored and followed up by clinicians.

Diabetic peripheral neuropathy is one of the common complications of diabetes that can affect almost every tissue in the body and is a significant cause of morbidity and mortality.[5] Early detection of neuropathy and identification of predisposing risk factors in individuals is crucial. The prevalence of neuropathy in diabetic patients is observed to be around 67.6%. The coexistence of complications and their association with morbidity and mortality is also quite high.[6] It is thought that this rate is significantly high since many patients remain undiagnosed. In a recent cross-sectional study aimed at identifying subclinical diabetic neuropathy, the rate of neuropathy was found to be 44.6%.[7] There are various factors that influence the development of neuropathy in diabetic individuals. Glycemic control, duration of diabetes, smoking, alcohol consumption, hypertension, weight, hyperlipidemia, and plasma homocysteine levels have been shown to be potentially influential in different studies.[8-10]

Since neuropathy that develops during the course of diabetes mellitus (DM) affects patients' quality of life, its early diagnosis and detection are highly important. Özütemiz and colleagues[11] proposed that neutrophil, lymphocyte, and platelet values could be used to assess the complications of diabetes. Similarly, Tuncer and colleagues[12] conducted a clinical study to detect increased inflammation in diabetic neuropathy using hemogram data. Çelikdelen and colleagues[13] evaluated the explainability of the relationship between neutrophil/lymphocyte ratio and systemic inflammation in diabetic nephropathy.

The aim of this study is to investigate whether hemogram parameters can be useful in predicting the risk of diabetic neuropathy in patients followed up with T2DM. Unlike previous studies, our research will concurrently evaluate the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR). These ratios will be compared between individuals with DM who have not been diagnosed with neuropathy and those who have, in order to assess their utility in predicting neuropathy risk. It is thought that neuropathy, which occurs as a complication of DM, has systemic effects rather than being merely a localized complication. We will examine whether the underlying cause for this is increased inflammation by investigating the neutrophil-to-lymphocyte, platelet-to-lymphocyte, and MLRs, which can serve as indicators of inflammation.

METHODS

Ethics

The study was initiated after obtaining approval from the Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 02.07.2025, Decision No: 2025-GOKAEK-2513_2025.07.02_531). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Patients who presented to the Yozgat Bozok University Neurology outpatient clinic between 2024 and 2025, including those diagnosed with diabetic neuropathy, those with a diagnosis of DM who were investigated for neuropathy, and those in whom neuropathy was not detected, were included in the study. A total of 100 individuals were to be included in the study, divided into two groups: Group 1 consisted of 50 individuals diagnosed with diabetic neuropathy, and group 2 consisted of 50 individuals without a diagnosis of diabetic neuropathy.

Definitions of DM and Diabetic Neuropathy

Individuals who met the diagnostic criteria for DM, as defined by the Turkish Society of Endocrinology and Metabolism (SEMT), were included in the study. The diagnosis of neuropathy is made through physical examination, which includes an assessment of nerve fiber function by applying 10 grams of pressure. In the clinic, a monofilament test and a vibration sensation test can be performed. However, in cases where typical symptoms are not present or the diagnosis is unclear, electrophysiological tests may be necessary. The diagnosis of diabetic neuropathy is established in all patients only after excluding other causes of neuropathy, such as toxins (e.g., alcohol), neurotoxic drugs (e.g., chemotherapy), vitamin B12 deficiency, hypothyroidism, kidney disease, malignancies (e.g., multiple myeloma, bronchogenic carcinoma), infections (e.g., HIV), chronic inflammatory demyelinating polyneuropathies, hereditary neuropathies, and vasculitis.[1,2]

Data Collection

Within the scope of the study, the following data were recorded from the hospital data system: patients' age, gender, past medical histories, diagnoses, and treatments they received, along with their blood test results including hemogram, HbA1c, glucose, sedimentation, CRP, ALT, AST, BUN, serum creatinine, B12, vitamin D, folic acid, ferritin, and electrolyte levels. The ratios of neutrophil, platelet, and monocyte counts to lymphocytes were examined and their relationship with neuropathy was evaluated. Individuals under the age of 18, those without a DM diagnosis, those without diabetic polyneuropathy, those using anti-inflammatory drugs, those with a diagnosis of myeloproliferative disease, those with electrolyte imbalance, and those with existing vitamin deficiency were excluded from the study.

Statistical Analysis

The data analyses were performed using the SPSS 20.00 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL) software. Descriptive statistics are presented as

mean±standard deviation for continuous variables and as percentages for categorical variables. Whether the groups had a normal distribution or not was determined using the Kolmogorov-Smirnov test. For comparing measurement values between groups, Independent samples t-test and ANOVA tests were used, while categorical variables were assessed using the Chi-square test. However, in cases where the groups were not normally distributed, the Mann-Whitney U and Kruskal-Wallis tests were employed. The relationship between quantitative variables was evaluated using correlation analysis (Pearson, Spearman). A p-value below 0.05 was considered the criterion for statistical significance.

RESULTS

Of the 100 individuals included in the study, 61 (61%) were female and 39 (39%) were male. The minimum age was 21, the maximum age was 80, and the mean age was calculated as 45.77±17.48. The 50 individuals with diabetic polyneuropathy and the 50 individuals in the healthy control group were analyzed as two separate groups.

The results obtained simultaneously from the hemogram data of the groups were evaluated. A statistically significant difference was observed between the groups in white blood cell count, neutrophil count, neutrophil percentage, and monocyte count (p=0.008, 0.037, 0.001, and 0.002, respectively). In contrast, no difference was observed in lymphocyte count, lymphocyte percentage, and platelet levels (p=0.182, 0.169, and 0.682, respectively) (Table 1).

While no statistically significant difference was observed in the NLR and PLR—calculated based on the same hemogram data between group 1 and group 2 (p=0.647 and p=0.242, respectively)—the difference in MLR was found to be statistically significant (p=0.0024) (Table 2).

The HbA1c distribution of the patient individuals included in the study was observed across a wide scale. It was found that 44 out of 100 individuals (44.9%) were within the target HbA1c range, while 46 individuals (51.1%) were identified as having uncontrolled DM based on the age-specific target ranges set by the SEMT (Figure).

An analysis of NLR, PLR, and MLR between the groups achieving and not achieving target HbA1c remission showed no significant difference (p=0.108, p=0.114, and p=0.287, respectively) (Table 3).

Table 2. Analysis of NLR, PLR, and MLR between the groups

	Group 1 (patient)		Group 2 (control)		
	Mean	SD	Mean	SD	p
NLR	5.23	2.18	14.67	2.36	0.647
PLR	295.14	117.78	356.86	130.53	0.242
MLR	0.83	0.26	0.65	0.21	0.024

NLR: Neutrophil-lymphocyte ratio, PLR: Platelet- lymphocyte ratio, MLR: Monocyte- lymphocyte ratio, SD: Standard deviation

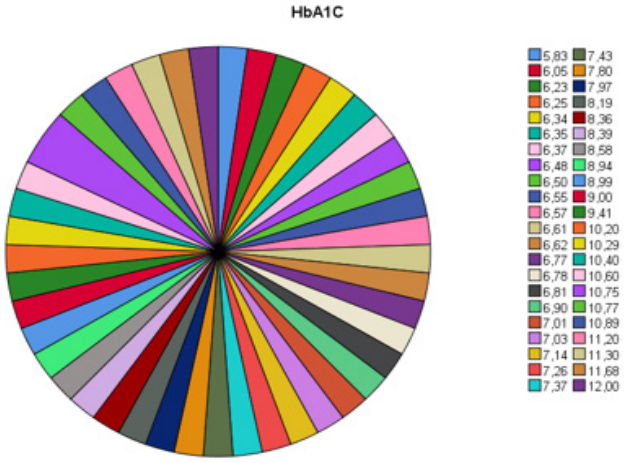

Figure. HbA1c distribution

Table 3. Analysis of NLR, PLR, and MLR according to target HbA1c

	In remission		Not in remission		
	Mean	SD	Mean	SD	p
NLR	1.94	0.67	2.39	1.13	0.108
PLR	108.22	23.25	129.73	59.39	0.114
MLR	0.245	0.073	0.284	0.152	0.287

NLR: Neutrophil-lymphocyte ratio, PLR: Platelet- lymphocyte ratio, MLR: Monocyte- lymphocyte ratio, SD: Standard deviation

The monocyte count showed a correlation with the lymphocyte and neutrophil counts (p=0.001 and p=0.002, respectively). However, no direct correlation was observed for NLR, PLR, or MLR. Furthermore, neutrophil, lymphocyte, and monocyte levels were not found to correlate with the calculations of NLR, PLR, and MLR. A significant correlation was observed between HbA1c and monocyte level (p=0.009), and between glucose level and lymphocyte count (p=0.006) (Table 4).

Table 1. Hemogram parameters of the groups

	Group 1 (patient)				Group 2 (control)				
	Min	Max	Mean	SD	Min	Max	Mean	SD	p
WBC (10^3/mm^3)	3.9	14.90	7.79	2.31	3.72	10.07	6.66	1.79	0.008
Neu #	1.58	10.60	4.70	1.77	1.86	7.48	3.99	1.60	0.037
Neu %	38.8	76.80	59.41	8.59	41.60	88.90	58.30	10.61	0.567
Mono #	0.28	1.13	0.56	0.18	0.24	0.83	0.39	0.13	0.001
Mono %	4.2	16.90	7.37	2.24	3.60	11.30	6.05	1.87	0.002
Lym #	1.02	6.03	2.30	0.82	0.51	3.41	2.11	0.64	0.183
Lym %	14.7	49.40	30.23	7.71	6.00	47.60	32.56	9.06	0.169
PLT (10^3/mm^3)	89	425.00	247.72	60.10	158.00	321.00	243.20	49.27	0.682

Min: Minimum, Max: Maximum, SD: Standard deviation, WBC: White blood cell, Neu: Neutrophil, Mono: Monocyte, Lym: Lymphocyte, PLT: Platelet

Table 4. Correlation between blood glucose levels and hemogram parameters

	HbA1C	Glucose	Hb	WBC	Neu#	Mono#	Lenf#	PLT	NLR	PLR
Glucose	.810**	1								
Hb	0.018	0.171	1							
WBC	0.132	0.177	0.156	1						
Neu#	0.077	0.083	0.118	.924**	1					
Mono#	.268**	0.171	0.124	.581**	.454**	1				
Lenf#	0.121	.271**	0.158	.558**	.217*	.313**	1			
PLT	0.018	0.027	-0.188	0.105	0.089	-0.060	0.128	1		
NLR	-0.110	-0.112	0.049	.251*	.516**	0.003	-.457**	-0.100	1	
PLR	-0.165	-0.160	-0.119	-.226*	0.072	-.254*	-.716**	.321**	.730**	1
MLR	0.057	-0.012	0.051	0.103	.287**	.488**	-.505**	-0.175	.664**	.566**

Hb: Hemoglobin, WBC: White blood count, Neu: Neutrophil, Mono: Monocyte, PLT: Platelet, NLR: Neutrophil-lymphocyte ratio PLR: Platelet- lymphocyte ratio, MLR: Monocyte- lymphocyte ratio

DISCUSSION

In our study, among individuals with T2DM who were diagnosed with diabetic neuropathy, a statistically significant difference was observed between groups in terms of white blood cell count, neutrophil count, neutrophil percentage, and monocyte count (p=0.008, 0.037, 0.001, and 0.002, respectively). In contrast, no significant difference was found in lymphocyte count, lymphocyte percentage, and platelet levels (p=0.182, 0.169, and 0.682, respectively). While no statistically significant difference was observed in the NLR and PLR, calculated from the same hemogram data in group 1 and group 2 (p=0.647 and p=0.242, respectively), the difference in MLR was found to be statistically significant (p=0.0024). The MLR was considered a usable parameter, as it was associated with diabetic neuropathy in diabetic patients. It was postulated that an autoimmunity-mediated condition might be involved, as there is strong evidence for this, particularly in rheumatological diseases. In the study conducted by Hao et al.,[14] hemogram-derived ratios were observed to be usable as diagnostic tools in autoimmune rheumatological diseases, demonstrating the clinical importance of their strong association. Similarly, Yang et al.[15] also demonstrated that hemogram parameters (eosinophil, basophil, and lymphocyte ratios) are valuable in indicating autoimmunity and highlighted their role in rheumatological diseases with a well-established autoimmune pathogenesis. The utility of hematological indices has also been observed in the disease course of systemic conditions that are both rheumatological and involve systemic involvement, such as systemic lupus erythematosus.[16,17] Clinical studies exist that have examined the relationship of proportional evaluation of hemogram data in malignant diseases with both systemic side effects and increased inflammation, as well as with survival.[18,19] Although a disease may be local, it is important to investigate its systemic effects and the adverse outcomes they bring. In our study, it was possible to observe these systemic effects in a highly prevalent disease with significant complications, such as diabetes. The suppression of inflammation in diabetic neuropathy has been identified as highly important for treatment and has become a therapeutic target.[20] Our study highlights that the significant value of proportional evaluations, particularly those based on monocyte levels which were associated with diabetic neuropathy, points to increased inflammation in diabetic neuropathy and suggests a potential role of autoimmunity, even in type 2 diabetes. Our study observed the utility of hemogram data for detecting inflammation and monitoring treatment response. Liu et al.[21] conducted a similar study on diabetic retinopathy, evaluating its association with the NLR and platelet levels. Likewise, Tuncer et al.[12] also investigated hemogram parameters in diabetic neuropathy, as in our study. The difference of our study from the existing one is that it allows for a comparison with a group of DM patients in whom neuropathy was not detected, thus providing results directly related to the complication.

The HbA1c distribution of the patient individuals included in the study was observed across a wide scale. Of the 50 patients, 22 (48.9%) were within the target HbA1c range, while 23 (51.1%) individuals were considered to have uncontrolled DM based on the age-specific target ranges set by the SEMT. This situation indicates that more than half of the individuals are still not regulated, are highly susceptible to complications, and demonstrates how high the risk remains. When NLR, PLR, and MLR were analyzed between the groups in remission and not in remission based on the target HbA1c level for diabetes regulation, no difference was observed (p=0.108; 0.114; 0.287). However, in unregulated individuals, the fact that NLR, PLR, and MLR averages were detected as higher—although the difference was not statistically significant—could be evaluated as being associated with increased inflammation in DM not in remission. Increased inflammation in cases of poor glycemic control was investigated by Hofmann et al.,[22] who also highlighted its detectability in peripheral blood mononuclear cells. This condition has been studied for many years, with a similar study conducted on type 1 DM as early as 2001.[23] While type 1 DM has a well-established autoimmune association, studies have been conducted on undefined autoimmunity underlying the family history in T2DM.[24] It is suggested that poor glycemic control, complicated by an autoimmune background, may bring about numerous complications. Increased microalbuminemia in unregulated DM was associated with the NLR in a study conducted by Öztürk.[25] Furthermore, the fact that the inflammation caused by dyslipidemia in diabetes has also been investigated in diabetic neuropathy using the NLR and PLR demonstrates the utility of these tools in yet another microvascular complication.[26] In our study, although inflammation was found to be somewhat higher when remission was not

achieved, the lack of statistical significance indicates the need for a larger-scale study, suggesting that a clear final result can only be provided in this way.

Based on the data, aside from proportional parameters in peripheral blood, a direct correlation was observed between glucose toxicity and the following: HbA1c showed a correlation with monocyte levels (p=0.009), and glucose levels showed a correlation with lymphocyte count (p=0.006). This result was interpreted as indicating that glucose has adverse effects on bone marrow or on the process of cellular transformation in peripheral blood. A clinical study exists on the effect of insulin resistance on lymphocyte morphology.[27] However, studies generally focus on proportional evaluations. Although Sözel et al.[28] also address glucose toxicity that begins with impaired glucose tolerance, their study likewise discusses proportional hemogram data. The fact that monocyte and lymphocyte levels, which are not directly evaluated in relation to inflammation, are affected by glucose toxicity was considered to be in favor of glucose's adverse effects on the developmental pathway of blood cells. However, obtaining sufficient evidence for this would likely only be possible through bone marrow sampling or by investigating stem cells in peripheral blood.

CONCLUSION

As a result, diabetic neuropathy is an undesirable complication of diabetes, and in individuals currently in remission, it may have occurred as a result of previous long-term glucose toxicity. Early detection and diagnosis of diabetic neuropathy is expected to reduce morbidity and mortality and increase the quality of life of individuals. The MLR was observed to be a usable parameter in this process and was evaluated as a clinically applicable tool, particularly as it was noted not to be directly influenced by raw hemogram data.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated after obtaining approval from the Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 02.07.2025, Decision No: 2025-GOKAEK-2513_2025.07.02_531).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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