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ORIGINAL ARTICLE

Can neuropathy be predicted by halp score in diabetic patients?

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ABSTRACT

Objective: In the pathogenesis of diabetes mellitus, insufficient insulin secretion, improper glucose utilization, and insulin resistance in tissues lead to oxidative stress and inflammation and cause neuropathy in peripheral nerves. Hemoglobin, albumin, lymphocyte, and platelet (HALP) scores give an idea of nutritional and inflammatory status. In this report, we aimed to evaluate the relationship between HALP score and diabetic polyneuropathy.

Materials and Methods: Patients admitted to our electrophysiology laboratory between 2022 and 2024 with a prediagnosis of polyneuropathy due to type 2 diabetes were included in the study. Demographic data (age, gender), hemogram (hemoglobin, lymphocyte, monocyte, platelet), biochemical values (fasting blood glucose, HbA1c, urea, creatinine, albumin, cholesterol, triglyceride), and electromyography results were retrospectively reviewed from the hospital information system.

Results: The study included 155 type 2 diabetic patients with a prediagnosis of distal symmetric polyneuropathy; 79 had sensorimotor polyneuropathy, while 76 did not. Mean age was similar between groups, but males were more prevalent in the neuropathy group ($p = 0.002$). Cholesterol ($p = 0.001$) and platelet levels ($p < 0.001$) were higher in the group without neuropathy, whereas HbA1c was higher in the neuropathy group ($p = 0.03$). No significant difference was observed in HALP scores between the two groups according to the presence of neuropathy ($p = 0.327$).

Conclusion: The HALP score is known as a prognostic indicator, especially in patients with malignancy and ischemic stroke. This study found no statistically significant difference between the patient groups with diabetic polyneuropathy and those without diabetic polyneuropathy in terms of HALP scores. Comprehensive and more detailed studies are needed to investigate the potential of the HALP score to predict the development of diabetic neuropathy.

Keywords: HALP Score, Diabetic Neuropathy, Inflammation, Nutritional Status.

INTRODUCTION

The most common subtype (approximately 90%) of Diabetes Mellitus, a metabolic disease characterized by chronic hyperglycemia exposure, is type 2 diabetes mellitus (T2DM) [1]. Diabetic peripheral neuropathy (DPNP) is one of the prominent and common microvascular complications of DM [1].

It has been reported that the prevalence of DPNP, which is the most common type of neuropathy universally, varies between 6% and 51% in recent studies in Europe and the United States [1]. Several risk factors contribute to the development of neuropathy, including age, diabetes duration, glycemic control, and comorbid conditions such as hypercholesterolemia, hypertension, obesity, and smoking [1]. The pathogenesis of neuropathy is complex and multifactorial. It is well-established that hyperglycemia and prolonged diabetes are linked to microvascular complications, and the diabetic microenvironment is thought to involve ongoing low-grade inflammation activated by the immune system [2]. Immune cells, cytokines, chemokines, soluble adhesion molecules, and other inflammatory markers are elevated in peripheral nerve or cerebrospinal fluid samples from patients with diabetic neuropathy [3]. Inflammation,

driven by reactive oxygen species produced due to elevated glucose levels and impaired energy production, contributes to oxidative stress [4]. Additionally, hyperglycemia and free radicals can lead to changes in albumin concentration and structural modifications in albumin, impairing its antioxidant function and exacerbating oxidative stress [5].

The HALP score (hemoglobin [g/L] × albumin [g/L] × lymphocyte count [cells/L] / platelet count [cells/L]) has recently been used to predict prognosis, particularly in cancer [6]. In studies involving diabetic retinopathy and nephropathy, higher HALP scores were associated with a lower incidence of these microvascular complications [7,8].

Our study aimed to evaluate the relationship between HALP score and diabetic polyneuropathy.

METHODS

This study was designed retrospectively, and the Declaration of Helsinki conducted it; ethics committee approval was obtained from the Kastamonu Training and Research Hospital Clinical Research Ethics Committee (date: 10/12/2024 and endorsement number: 2024-KAEK-123). Between 01.Jan.2022 and 01.Sep.2024, adults who applied to Kastamonu Training and Research Hospital and Tepecik Training and Research Hospital Electrophysiology laboratory, diagnosed with T2DM according to WHO / ADA diagnostic criteria and referred to us with a preliminary diagnosis of polyneuropathy were included. Patients were included in the study retrospectively. Patients with type-1 diabetes mellitus, neoplastic and hematological diseases, active or chronic immunosuppressive drugs, severe hepatic and renal dysfunction, acute infection findings, or rheumatological diseases were excluded. Demographic data (age, gender), complete blood count (hemoglobin, lymphocyte, neutrophil, neutrophil, monocyte, platelet), biochemical parameters (fasting blood glucose, HbA1c, urea, creatinine, albumin, cholesterol, triglyceride), and electromyography results were recorded retrospectively. Patients diagnosed with sensorimotor polyneuropathy, characterized by nerve conduction abnormalities in at least three limbs and predominantly axonal involvement in the lower and distal extremities, were assigned to the polyneuropathy group. In contrast, patients whose nerve conduction studies showed normal results on electromyography were placed in the non-polyneuropathy (non-PNP) group. The HALP Score was calculated using the formula [(hemoglobin x serum albumin x lymphocyte count) / Platelet count] [9]. The data from both the polyneuropathy and non-polyneuropathy groups were compared.

The data were analyzed using SPSS version 26.0 (IBM Statistics for Windows, Chicago, IL, USA). Descriptive statistics were employed to assess the clinical characteristics of the participants. The chi-square test was used to compare data between the two groups for categorical variables. Differences in mean and median values were analyzed using the Mann-Whitney U test and independent samples t-test. Results were considered significant at a 95% confidence interval and a p-value of less than 0.05.

RESULTS

The study included 155 adults, 76 patients without polyneuropathy, and 79 patients with polyneuropathy. Demographic data revealed that women comprised 58.9% of the non-polyneuropathy group, while men represented 66.7% of the polyneuropathy group (Table 1).

The cruel age was 63 ± 9.6 within the polyneuropathy gather and 60.5 ± 12.2 within the non-PNP gather, with no factually noteworthy distinction between the bunches (p = 0.106) (Table 2).

Table 1. The gender distribution of neuropathy

	Gender			
	Male (n:60)	**Famele (n:95)**	**Total (n:155)**	**P value**
Non-PNP*	20 (%33,3)	56 (%58,9)	76 (%49)	0.002
PNP	40 (%66,7)	39 (%41,1)	79 (%51)	

Chi-Spuare test

*PNP: Polyneuropathy

Table 2. The age distribution by neuropathy

	PNP median/mean ± SD	**Non-PNP median/mean ± SD**	**Test statistic**	**p value**
Age	64/ 63 ± 9,6	59,5/ 60,5 ± 12,2	1,627	0.106

Independent samples t test – median / mean ± SD

Table 3. Comparison of laboratory values based on the presence of neuropathy

	PNP	Non-PNP	p
Hemoglo-bin	13 ± 2	13.1 ± 1.7	0.593[3]
Hematocrit	39.5 ± 5.8	39.5 ± 4.6	0.996[3]
Neutrophil	4.7 (1.7- 174) / 78.43	4.8 (2.5- 10.4) / 75.47	0.680[4]
Lympho-cyte	2.2 (0.5- 4.2) / 70.41	2.4 (0.8- 5,2) / 84.03	0.057[4]
Monocyte	0.6 (0.2- 1.2) / 79.20	0.6 (0.3- 1.2) / 74.66	0.526[4]
Glucose	163 (65- 792) / 82.22	140.5 (81- 393) / 71.43	0.132[4]
Cholesterol	174.5 (100- 301) / 62.07	209.5 (124- 316) / 85.25	0.001[4]
Ttriglycer-ide	155.5 (57- 667) / 70.53	179 (51- 915) / 82.79	0.086[4]
Hba1c	7.5 (5.7- 13.5) / 81.83	7.2 (5.2- 15) / 66.55	0.030[4]
BUN	33 (16- 164) / 83.65	29 (11- 112) / 69.91	0.055[4]
Creatinine	0.8 (0.2- 4.2) / 76.90	0.9 (0.3- 1.7) / 77.11	0.977[4]
Albumine	4.2 (2.4- 4.9) / 71.65	4.2 (2.4- 4.9) / 83.66	0.093[4]
Platelet	237 (10- 403) / 63.75	**280.5 (133- 739) / 91.15**	**<0.001[4]**

[3] Independent samples t test – median (min-max) / mean ± SD

[4] Mann-Whitney U test- median (min-max) / mean ± SD

Table 4. The relationship between the presence of neuropathy and the HALP score

	PNP	Non-PNP	p value
HALP score	49.2 (7.3 - 268.3)	45.9 (21.3 - 151.4)	0.327

Mann-Whitney U test- median (min-max) / mean ± SD

Cholesterol and platelet levels were higher within the non-polyneuropathy bunch, whereas HbA1c levels were raised within the polyneuropathy gather. The difference between laboratory values according to the presence of neuropathy is shown in Table 3.

No measurably critical distinction was found when comparing the two bunches concerning the HALP score (p = 0.327). The relationship between the presence of neuropathy and the HALP score is shown in Table 4.

DISCUSSION

The most common microvascular complication of T2DM, which continues to climb with the aging population, is DPNP [2]. It is length-dependent damage to peripheral nerves. In the complex pathogenesis of DPN, impaired metabolism and inflammatory processes in peripheral nerve axons constitute the main elements [2]. In our study, the predictive role of the HALP score, which is used to estimate cancer prognosis and is thought to play a role in the mechanisms involved in pathogenesis, in diagnosing diabetic PNP was investigated, and no significant predictive value was determined in the presence of neuropathy.

Diabetic polyneuropathy (DPN), characterized by peripheral nerve dysfunction, is explained by three pathophysiological mechanisms [10]. First, inflammation activates signaling pathways such as nuclear factor kappa B, activator protein 1, and mitogen-activated protein kinases [10]. Second, hyperglycemia induces oxidative stress, triggering the activation of pathways including polyol, hexosamine, protein kinase C, advanced glycosylation end products, and glycolysis [10]. Third, mitochondrial dysfunction leads to increased production of reactive oxygen and nitrogen species, resulting in lipid peroxidation, protein modifications, nucleic acid damage, and, ultimately, axonal degeneration and segmental demyelination [10].

It is suggested that chronic inflammation plays a role in the pathogenesis of diabetic neuropathy. This has led to a focus on immune system-associated cells, such as neutrophils, lymphocytes, and platelets [11]. Parameters such as neutrophil-lymphocyte (NLR) ratio and platelet-lymphocyte (PLR) ratio have been examined. The systemic immune-inflammation index (SII), which combines these three cells, has also been studied in diabetic neuropathy and other microvascular complications of diabetes [11,12].

Albumin, a protein synthesized in the liver, is essential for binding and transporting various substances , including fatty acids, hormones, bilirubin, metal ions, and drugs [13]. Additionally, albumin has well-documented physiological functions, including antioxidant, anti-inflammatory, antiplatelet, and anticoagulant activities, as well as roles in immune regulation, endothelial cell protection, and neuronal defense against ischemia and reperfusion injury [14].

A study has shown a significant inverse relationship between serum albumin level and the risk of DPN, with this association being more substantial in patients with a higher body mass index (BMI ≥ 24 kg/m^2) [15]. In our study, the two groups detected no significant difference in albumin levels.

HALP score has recently been reported as a prognostic indicator, especially in patients with malignancy and ischemic stroke [16]. This score reflects the patient's nutritional status and systemic inflammation [17]. In oncology, a high HALP score is linked to better long-term survival. In contrast, a study of patients with myelodysplastic syndrome found that a high HALP score was associated with poor prognosis, especially in cases of severe thrombocytopenia [18]. A study of 1,337 ischemic stroke patients found that high HALP scores were strongly associated with a reduced risk of recurrent stroke and death within 90 days and one year [19].

In relation to diabetic microvascular complications, research related to diabetic retinopathy (DR) has shown that patients who have a high HALP score (≥49.2) tend to have a lower rate of retinopathy compared to those with lower HALP scores [20].

Another study involving 674 patients found a negative relationship between HALP score and DR incidence, suggesting that the HALP score may be more sensitive in men [21]. In research focused on diabetic nephropathy, a HALP score below 45.9 demonstrated a sensitivity of 73% and a specificity of 52% in detecting diabetic nephropathy [7].

Comorbidities, prior treatments, and demographic factors can influence the HALP score. Additionally, the sample size in our study was smaller than in many published studies, and factors such as the duration of diabetes, blood glucose control, and medication effects were not recorded. One of the limitations of our study was the lack of a classification of the type and severity of diabetic neuropathy and data on the duration of diabetic neuropathy symptoms.

HALP score is known as a prognostic indicator especially in patients with malignancy and ischemic stroke. In this study, no statistically significant difference was found between the patient groups with diabetic polyneuropathy and those without diabetic polyneuropathy in terms of HALP scores. Comprehensive and more detailed studies are needed to investigate the potential of the HALP score to predict the development of diabetic neuropathy.

Ethical approval

The study was approved by the Kastamonu Training and Research Hospital Clinical Research Ethics Committee (date: 10/12/2024 and approval number: 2024-KAEK-123).

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Conflict of interest

The authors declare that there is no conflict of interest.

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