JEIMP
The Journal of European Internal Medicine Professionals

Original Article

Can the HALP Score Be Predictive in Different Clinical Stages of Diabetes?

Author(s)
[1]Yaşar Küçükardalı, [1]Mehmet Akif Öztürk, [1]Adeviye Özsoy, [1]Lidya Aden Çağlar, [2]Ahmet Enes Küçükardalı

J Eur Int Prof. Year; 2025, Volume: 3, Issue: 1
Submitted at: 14.11.2024 Accepted at: 07.01.2025 Published at: 31.01.2025
doi 10.5281/zenodo.14740592

Affiliation(s)
[1]Department of Internal Medicine, Yeditepe University Hospital, Istanbul, Turkiye
[2]Department of Emergency Medicine, Hatay Defne Government Hospital, Hatay, Turkiye

Corresponding Author: Lidya Aden Çağlar, M.D., Department of Internal Medicine, Yeditepe University Hospital, Istanbul, Turkiye.
E-mail: drecet.76@gmail.com

Abstract

Background: The Hemoglobin, Albumin, Lymphocyte, Platelet (HALP) score is a novel biomarker integrating routine laboratory parameters to assess a patient's immune nutritional status. Integrating the HALP score into routine diabetes management could help stratify patients based on their risk of complications and guide treatment strategies accordingly. For example, a patient with a low HALP score presenting to a clinic might be flagged for immediate nutritional support and more frequent monitoring of inflammatory markers. In contrast, those with higher scores could follow standard care protocols. This study investigated the potential of the HALP score as a prognostic biomarker by evaluating its correlation with clinical and laboratory parameters between diabetic patients and healthy controls.

Method: A total of 133 participants, comprising 96 diabetic patients and 37 healthy individuals were included in the study. Participants were divided into four groups: control (n=37), prediabetes (n=37), diabetes (=30), and complicated diabetes (n=29). Comprehensive demographic, clinical, and laboratory data were collected, and the HALP score was calculated as hemoglobin × albumin × lymphocyte count/platelet count. The HALP score was calculated and its relationship with various parameters was analyzed using Spearman correlation and ROC analysis.

Results: The study found significant differences in HALP scores between the groups; the highest score was observed in the prediabetes group at 49 (18-101), while the lowest score was in the complicated diabetes group at 39 (13-101). There was no significant difference in HALP scores between genders. A weak negative correlation was found between age and HALP score. Significant correlations were identified between HALP scores and parameters such as albumin, hemoglobin, lymphocytes, BUN, CRP, and HbA1c. ROC analysis demonstrated high diagnostic accuracy of low HALP scores in identifying complicated diabetes, with AUC> 0.7 ($p< 0.003$). Among comorbidities, only the anemic group had a significantly lower HALP score of 28 compared to 50 in the non-anemic group ($p= 0.026$).

Conclusion: This study underscores the HALP score's potential as a powerful prognostic biomarker for diabetes, offering a cost-effective and readily accessible tool for clinical stratification. Its significant correlations with disease severity, inflammatory markers, and nutritional parameters position it as an indispensable addition to the diagnostic arsenal for diabetes management. Future research, including longitudinal studies, is warranted to validate these findings and establish standardized clinical applications.

Keywords: HALP Score, Diabetes Mellitus, Biological Markers

INTRODUCTION

The hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score is a new and promising biomarker that combines various routine laboratory indicators to assess a patient's immunonutritional status. The HALP score is increasingly gaining attention for its prognostic value in cancer and other diseases. This biomarker is associated with overall survival, progression-free survival, and recurrence-free survival in various clinical settings. For example, the prognostic capability of the HALP score has been extensively examined in several cancers, including stomach, colorectal, bladder, prostate, kidney,

esophagus, pharynx, lung, breast, and cervical cancers (1).

In a study involving patients with metastatic prostate cancer, a low preoperative HALP score was found to be significantly associated with decreased PSA progression-free survival in patients undergoing cytoreductive radical prostatectomy (2). In Hispanic colon cancer patients, a low HALP score was independently associated with shorter overall survival (3). In patients with diffuse large B-cell lymphoma, low HALP scores were associated with worse overall survival and event-free survival (4). Additionally, in patients with esophageal squamous cell carcinoma, the preoperative HALP score was an independent prognostic factor for cancer-specific survival in patients undergoing curative resection (5). In patients with upper urinary tract urothelial carcinoma, low HALP scores were identified as independent risk factors for overall survival and progression-free survival in patients undergoing radical nephroureterectomy (6).

In a retrospective study, involving 158 patients who underwent gastrectomy for gastric adenocarcinoma, highlights the utility of the HALP score in clinical prognostication. The findings reveal significant negative correlations between HALP scores and both T stage and N stage, as well as tumor diameter and metastatic lymph node count.

Beyond cancer, the HALP score has shown promise in non-cancerous conditions, such as acute ischemic stroke and heart failure, where it has been linked to reduced risks of mortality and recurrent events. The prognostic value of the HALP score has also been demonstrated in non-cancer conditions. In patients with acute ischemic stroke, high HALP scores were associated with a reduced risk of recurrent stroke and death within 90 days and 1 year (8). In patients with acute heart failure, the modified HALP (m-HALP) score was identified as a potential independent prognostic index predicting 3-month mortality in patients presenting to the emergency department (9). HALP scores are also significantly associated with various demographic, socioeconomic, and health conditions, such as anemia treatment, age, kidney function, and cancer (10). Low HALP scores are associated with poorer health status and impaired lipid profiles related to dyslipidemia (11), suggesting that the HALP score may aid in cardiovascular risk assessment.

In patients with coronary heart disease, low HALP scores are associated with the risk of all-cause mortality, though the causal relationship between HALP score and mortality needs further investigation (12). Additionally, in hemodialysis patients, high HALP values are associated with reduced risk of cardiovascular disease death and all-cause mortality (13).

Recent studies have begun to explore the HALP score's potential in diabetes management. HALP components, such as albumin and lymphocytes, are known to reflect systemic inflammation and nutritional deficits, which are central to the pathophysiology of diabetes and its complications(14,15). For instance, Wang et al. demonstrated that lower HALP scores are associated with increased risks of diabetic complications, including nephropathy and retinopathy, highlighting its predictive value in identifying high-risk patients (15). Similarly, Ranran Ding et al. revealed a non-linear relationship between HALP scores and diabetic retinopathy risk, suggesting that both extremely high and low scores could signal metabolic imbalances in diabetic patients(17)

HALP score is emerging as a promising prognostic biomarker in various clinical conditions, especially in different types of cancers and acute illnesses. Based on routine laboratory tests, the HALP score offers a cost-effective and accessible option to improve patient care. By contributing to personalized medicine approaches, the HALP score allows for a better understanding of patients' immunonutritional status and guides clinical decisions.

By contributing to personalized medicine, the HALP score bridges the gap between diagnostic markers and actionable treatment strategies. This study aims to evaluate the HALP score's prognostic value in diabetes by correlating it with clinical and laboratory parameters across different stages of diabetes, providing a foundation for its potential integration into routine care.

In this study we aimed to investigate the potential of the HALP score as a prognostic biomarker by evaluating its correlation with clinical and laboratory parameters between control, pre-diabetes, diabetes, and complicated diabetes patients.

METHODS

Study Population and Objective

A total of 96 diabetic patients at different stages were diagnosed after detailed examinations at the Internal Medicine Clinic of Yeditepe University Medical School and 37 healthy individuals were included in the study. In accordance with the Helsinki Declaration and with hospital ethics committee approval, demographic and clinical laboratory data of all participants were documented. Written informed consent was obtained from all participants prior to the study. Peripheral blood samples were collected from participants by specialists. All phases, from obtaining the necessary biological samples for research to conducting the experiments, were carried out in accordance with ethical approval of Yeditepe University Clinical Research Ethics Committee; IRB= 23.06.2022/1626. This research was conducted in patients presenting to the outpatient clinic of the Internal Medicine Department at Yeditepe University Medical School.

Study Groups and Inclusion/Exclusion Criteria
Participants were divided into 4 groups as follows:

1.Control (C) (n=37): Healthy controls with normal glucose tolerance (NGT):
- ○Fasting Plasma Glucose (FPG) < 100 mg/dl
- ○2-hour postprandial glucose <140 mg/dl
- ○HbA1c < 5.7%

2.Pre-diabetes (Pre-DM) (n=37):
- ○**Impaired Fasting Glucose:**
  - FPG 100-126 mg/dl
  - 2-hour postprandial glucose < 140 mg/dl
- ○**Impaired Glucose Tolerance:**
  - FPG < 100 mg/dl
  - 2-hour postprandial glucose 140-200 mg/dl
  - HbA1c 5.7-6.4%

3.Diabetes mellitus (DM) (n=30):
- ○FPG > 126 mg/dl
- ○2-hour postprandial glucose 200 mg/dl
- ○HbA1c > 6.4%

4.Complicated Diabetes Mellitus (CDM) (n=29):
- ○Patients with macrovascular and/or microvascular complications

Inclusion/Exclusion Criteria: Individuals aged 18-80 who accepted the study protocol, regardless of gender, were included. For analysis, only those with complete medical records were considered.

HOMA-IR (Homeostatic Model Assessment of Insulin Resistance) was calculated using the formula (glucose/18 x insulin)/22.5. Correlation between HALP score and various parameters such as glucose, AST, ALT, GGT, uric acid, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, insulin level, creatinine, albumin, hemoglobin, lymphocyte count, and platelet count was assessed.

Additionally, the relationship of HALP score with various parameters such as smoking, weight gain, fatigue, polydipsia, polyuria, polyneuropathy, vision loss, pruritus, chest pain, dyspnea, claudication, macrovascular complications, microvascular complications, hypertension, hyperlipidemia, fatty liver, anemia, hypothyroidism, kidney failure, and heart failure was evaluated.

The HALP score is calculated by hemoglobin (g/L)×albumin (g/L)×lymphocytes (/L)/platelets (/L), where theoretical thresholds of low scores denote poorer immune nutritional status. A clinically relevant universal threshold is yet to be determined.

STATISTICAL ANALYSIS

HALP did not follow a normal distribution and is expressed as median, including the interquartile range (IQR) (25th and 75th percentiles). Differences between variable groups were assessed through Median and Mann-Whitney U non-parametric tests. Non-parametric tests were chosen due to the non-normal distribution of the HALP scores, as determined by the Shapiro-Wilk test. Unlike parametric methods, which assume normality, non-parametric tests are robust against deviations from this assumption. This makes them particularly suitable for clinical datasets where data often include outliers or skewed distributions. These methods are appropriate for analyzing skewed data distributions, providing robust results. Spearman's correlation was performed for correlations between continuous variables and HALP scores. Correlation analysis of non-parametric values was performed using the Spearman correlation coefficient. The diagnostic accuracy of the HALP score was assessed through receiver operating characteristics (ROC) curve formation and calculation of the area under the curve (AUC). All statistical calculations were performed in SPSS software (version 29.0; SPSS Inc., Chicago, IL, USA). All reported p-values were based on two-sided hypotheses, with a p-value of < 0.05 considered statistically significant.

RESULTS

Our total population consisted of 133 participants with a median HALP score of 51 (17.1–48). The highest HALP score was observed in the pre-DM group at 49 (18-101), while the lowest was in the complicated DM group at 39 (13-101) (p=0.000). The number of male patients was 59 (44%) with a median HALP score of 42 (13-75), and the number of female patients was 74 (56%) with a median HALP score of 30 (18-100). There was no significant difference in HALP scores between males and females (p>0.05). A weak negative correlation was found between age and HALP score (r = -0.188, p = 0.03). However, the median HALP score for those under 65 years old was 43 (12-96), and for those over 65 years old, it was 30 (17-86); this difference was not statistically significant (p = 0.07). The clinical and laboratory parameters of our sample are shown in **Table 1**. In the comparison of the median HALP score between groups, there was a significant statistical difference between C-CDM (p=0.004), PreDM-CDM (p=0.001), and DM-CDM (p<0.001) (Post Hoc Tukey Test).

No significant differences were found between groups for total cholesterol, LDL cholesterol, potassium, calcium, and lymphocyte parameters. However, significant differences were observed for other parameters (glucose, AST, ALT, GGT, uric acid, sodium, HDL cholesterol, triglycerides, insulin, creatinine, albumin, hemoglobin, and platelet count) (p<0.05). The median HALP scores for symptoms and comorbidities such as fatigue, polydipsia, polyuria, polyneuropathy, vision loss, pruritis, chest pain, dyspnea, claudication, macrovascular complications, microvascular complications, hypertension, hyperlipidemia, fatty liver, anemia, hypothyroidism, renal failure, and heart failure are shown in **Table 2**.

Table 1. Comparison of general data and laboratory-related indicators in all patients

Variable	Total n=133	Control n=37	PreDM n=37	DM n=30	Complicated DM n=29	P-value
Age (years)	49±12	39±14	42±11	50±14	68±8	0.000
The course of Disease (years)	8±8	-	3±1	6±5	17±8	0.000*
BMI (kg/m2	28±5	23±3	28±4	29±4	31±5	0.000
Waist (cm)	101±13	90±7	100±11	108±11	111±13	0.000
SBP (mmHg)	122±14	114±12	120±15	127±10	132±11	0.000
DBP (mmHg)	77±8	71±7	76±9	80±7	82±6	0.000
Pulse (bpm)	81±12	75±7	81±7	85±9	85±18	0.000
Glucose (mg/dl)	124±45	93±7	102±9	145±49	169±52	0.000
HbA1c (%)	6.3±1.3	5.3±0.3	5.6±0.4	7.1±1.3	7.6±1.3	0.000
Insulin(ul/ml)	13±7	7±1	16±7	20±9	13±6	0.000
T. C (mg/dl)	215±41	217±48	219±39	217±36	207±39	0.668
HDL- C (mg/dl)	53±21	61±27	54±17	50±20	46±17	0.029
LDL-.C (mg/dl)	127±38	127±41	134±37	126±40	119±36	0.498
TG (mg/dl)	160±72	123±54	151±61	191±91	185	0.000
AST(U/L)	24±14	18±5	25±21	25±13	28±12	0.042
ALT (U/L)	25±16	17±6	25±15	23±21	25±13	0.001
GGT (U/L)	33±34	20±8	33±37	40±44	44±35	0.020*
ALB (g/L)	41±4	41±3	42±3	42±3	38±4	0.002
CRP	8±10	3±4	5±6	8±10	20±26	0.000*
BUN (mmol/L)	8±4	12±4	11±4	12±5	26±20	0.000
Cr (mmol /L)	0.8±0.4	0.7±0.2	0.7±0.1	0.8±0.1	1.1±0.7	0.000
UA (mg/dl)	5.4±1.3	4.5±1.0	5.2±1.3	5.6±1.0	6.3±1.2	0.000
Na (mmol/L)	138±3	138±4	139±3	138±3	135±3	0.001
K (mmol/L)	4.5±0.4	4.2±0.4	4.3±0.4	4.3±0.3	4.3±0.3	0.867
Ca(mg/dl)	9.3±1.0	9.2±1.3	9.4±0.4	9.4±1.4	9.1±0.4	0.742
HGB ((g/L)	132±18	131±16	132±16	138±18	120±06	0.000
Leu (109/L)	7.3±2.4	7.0±2.2	6.9±2.4	7.4±2.8	8.0±2.6	0.000
LYM (109/L)	2.2±1.0	2.1±0.5	2.1±0.8	2.3±1.3	2.2±1.7	0.928
PLT(109/L)	251±77	252±66	252±60	251±74	247±100	0.985
HALP score	51(9-48)	49(21-83) a p :0.004	51(18-101) b p: 0.001	47(9-155) c p: 0.000	39(13-101)	0.000

*abnormal disturibution , a: PostHoc Tukey C-CDM, b: PostHoc Tukey PreDM-CDM. c: PostHoc Tukey DM-CDM
SBP; systolic blood pressure, DBP; diastolic blood pressure, BMI; body mass index, HbA1c; glycated hemoglobin, ALB; albumin, AST; aspartate aminotransferase, ALT; alanine transaminase, HGB; hemoglobin, Leu; Leucocyte, LYM; lymphocyte count, PLT; platelet count, Cr; blood creatinine, UA; blood uric acid, BUN; blood urea nitrogen, TC; total cholesterol, TG; triglycerides, HDL-C; high-density lipoprotein cholesterol, LDL-C; low-density lipoprotein cholesterol, HALP score= hemoglobin, albumin, lymphocyte count, platelet count score.

The HALP score for the group with anemia (28 [19-101]) was lower than that of the group without anemia (50 [18-115]), and this difference was statistically significant (p=0.026).

The ROC curve demonstrates a model's ability to balance sensitivity and specificity. The area under the curve (AUC) measures the accuracy of the model, with values closer to 1 indicating higher accuracy. **Table 3** summarizes the HALP scores across the study groups.

The table reports the results of key metrics for each group, including AUC, 95% Confidence Interval, Cut-off Point, Sensitivity, Specificity, and p-value. There was no significant difference in HALP scores between the control and prediabetes or DM groups ($p > 0.05$). However, there was a significant difference in HALP scores between the control, prediabetes, and DM groups compared to the complication DM group. The HALP score was lower in the complication DM group ($p < 0.003$). This indicates that the HALP score serves as a more distinct diagnostic marker, particularly in the complication DM group, compared to other groups. The

Table 2. Comorbidities and other factors

Variable		Median HALP Score	Median Test	Mann-Whitney Test
Sex	M=57	42 (13-75)	0.0671	0.821
	F=72	30 (8 -100)		
Age	<65	43 (12-130)	0.07	0.207
	65+	30 (7- 86)		
Smoking	No=70	48 (12-121)	0.538	0.952
	Yes=33	47 (9-155)		
Fatique	No=41	50 (12-155)	0.422	0.707
	Yes=63	48 (9-121)		
	No=70	49 (9-155)	0.842	0.912
	Yes=34	48 (13-101)		
Chest pain	No=96	48 (9-155)	0.713	0.502
	Yes=8	52(32-101)		
Dyspnea	No=91	52 (9-155)	0.700	0.750
	Yes=13	39 (17-101)		
Claudicatio	No=90	49 (9-155)	0.890	0.478
	Yes=14	49 (13-101)		
Hypertension	No=71	50 (9-101)	0.092	0.480
	Yes=33	40 (13-155)		
Hyperlipidemia	No=62	49 (9-155)	0.842	0.947
	Yes=42	47(13-155)		
Fatty liver	No=60	48 (18-155)	0.843	0.856
	Yes=44	48 (9-155)		
Anemia	No=50	50 (18-155)	0.026	0.009
	Yes=15	28 (9-101)		
Chronic Kidney Failure	No=96	49 (9-155)	0.270	0.327
	Yes=8	45 (13-67)		
Congestive Heart Failure	No=96	49 (9-155)	0.270	0.272
	Yes=8	45 (13-150)		

diagnostic accuracy of the HALP score in these groups is high (AUC values > 0.7), with significant sensitivity and specificity rates. The ROC analyses of the study groups are shown in **Figure 1**.

When examining the correlation of HALP score with laboratory and clinical parameters, it was found that there is a positive correlation with albumin, hemoglobin, lymphocytes, and calcium. Conversely, there is a negative correlation with BUN, CRP, HbA1c, age, polyneuropathy, vision loss, chest pain, claudication, hypertension, macrovascular disease, microvascular disease, chronic kidney failure, and congestive heart failure (**Table 4**).

DISCUSSION

Comparison of HALP Scores Between Groups

Our study revealed that the total population consisted of 133 participants with a median HALP score of 51 (17.1–48). The highest HALP score was observed in the pre-DM group at 49 (18-101), and the lowest in the complicated DM group at 39 (13-101), showing a significant difference (p=0.000). Among the participants, 59 (44%) were male with a median HALP score of 42 (13-75), while 44 (66%) were female with a median HALP score of 30 (18-100). No significant difference in HALP scores was observed between males and females (p<0.05). A weak negative correlation between age and HALP score was found (r -0.188, p 0.03). The median HALP score for participants under 65 years old was 43

Table 3. Summarize of HALP score in study groups

Groups	AUC	CI95%	Cutt off	Sensitivity	Specificity	P. Sig
C -PreDM	0.488	0.353-0.624	45.5	55	56	0.864
C-DM	0.486	0.340-0.632	55.4	66	67	0.845
C-CDM	0.735	0.599-0.870	51.3	92	86	0.002
PreDM- DM	0.487	0.344-0.630	54.6	66	65	0.830
PreDM-CDM	0.744	0.613-0.875	50.4	92	67	0.001
DM-CDM	0.736	0.601-0.871	52.5	88	70	0.003

C; control, Pre-DM; prediabetes mellitus, DM; diabetes mellitus, CDM; diabetes with copmplications

Table 4. Correlation of HALP score between clinical and laboratory parameters

	Age	ALB	BUN	CRP	HGB	PLT	LYM	Ca	HbA1c
r	-0.188	0.337	-0.259	-0.173	0.327	-0.180	0.549	0.299	-0.21
P-value	0.030	0.00	0.003	0.049	0.00	0.030	0.00	0.013	0.043
	PolyNP	**Vision Loss**	**Chst P**	**Claudication**	**Hypert**	**MaVH**	**Anemia**	**ChK F**	**CHF**
r	-0.180	-0.246	-0.226	-0.331	-0.211	-0.383	0.355	-0.206	-0.239
p-value	0.38	0.004	0.009	0.000	0.015	0.000	0.000	0.017	0.006

Normal distribution and linear values (parametric) were analyzed using Pearson correlation, while non-normally distributed and ordinal values (non-parametric) were analyzed using Spearman correlation.

(12-96) and for those over 65 was 30 (17-86), which was not statistically significant (p 0.07).

Clinical and Laboratory Parameters

The comparison of clinical and laboratory parameters among different groups showed significant differences in glucose, AST, ALT, GGT, uric acid, sodium, HDL cholesterol, triglycerides, insulin, creatinine, albumin, hemoglobin, and platelet count ($p<0.05$). However, no significant differences were found in total cholesterol, LDL cholesterol, potassium, calcium, and lymphocyte parameters.

The analysis of comorbidities revealed that only the group with anemia had a significantly lower HALP score (28) compared to the non-anemic group (50) (p=0,026). ROC curve analysis, which evaluates the balance between sensitivity and specificity, indicated that HALP scores had significant diagnostic accuracy, particularly in the complicated DM group with high AUC values (>0.7) and significant sensitivity and specificity.

Correlation with Other Parameters

Correlation analysis showed positive correlations between HALP scores and albumin, hemoglobin, lymphocyte count, and calcium. Negative correlations were found with BUN, CRP, HbA1c, age, polyneuropathy, vision loss, chest pain, claudication, hypertension, macrovascular disease, microvascular disease, chronic kidney disease, and congestive heart failure.

Mechanisms Underlying HALP Score Associations

The HALP score, incorporating hemoglobin, albumin, lymphocyte count, and platelets, reflects both nutritional and inflammatory status, which are pivotal in the pathophysiology of diabetes and its complications. Nutritional deficiencies and chronic inflammation exacerbate oxidative stress and endothelial dysfunction, further promoting the progression of diabetes-related complications (15). Our findings of reduced HALP scores in complicated DM groups align with the hypothesis that systemic inflammation and poor nutritional status significantly impair metabolic homeostasis (17).

Albumin and hemoglobin are critical markers of protein synthesis and oxygen-carrying capacity, respectively, while lymphocytes and platelets are involved in immune response and hemostasis. Their combined reduction, as reflected in lower HALP scores, indicate the combined impact of chronic hyperglycemia, vascular damage, and immune dysregulation (16).

Clinical Applications of HALP Scores

The HALP score's diagnostic and prognostic utility can be leveraged to identify high-risk diabetic patients early, enabling targeted interventions to prevent complications. Monitoring HALP scores in outpatient clinics could aid in stratifying patients based on their risk of developing nephropathy or retinopathy (14). Furthermore, incorporating HALP scores into routine diabetic assessments could improve personalized care by guiding nutritional and anti-inflammatory interventions. Recent studies suggest that the HALP score also correlates with cardiovascular risk, with lower scores indicating higher susceptibility to macrovascular and microvascular diseases (19). In light of our findings, integrating HALP scores with other biomarkers, such as CRP and HbA1c, enhance the prediction and management of diabetes-related cardiovascular complications.

Furthermore, novel research has proposed combining HALP scores with emerging markers such as galectin-3 and soluble ST2 to improve risk stratification in diabetic populations (20). Recent data highlight HALP's potential to integrate into multi-biomarker panels for a more comprehensive risk assessment in clinical practice (21).

Comparison with Existing Literature

Our findings align with multiple studies that emphasize the diagnostic and prognostic value of HALP scores in diabetic patients, particularly those with complications. Zhang et al. (14) highlighted that lower HALP scores are associated with poorer outcomes in patients with diabetic complications, supporting our findings that the complicated DM group had the lowest HALP scores.

In addition, Cheng et al. (15) found that HALP scores correlate with nutritional and inflammatory status in diabetic patients, with higher scores indicating better overall health. This aligns with our observation of positive

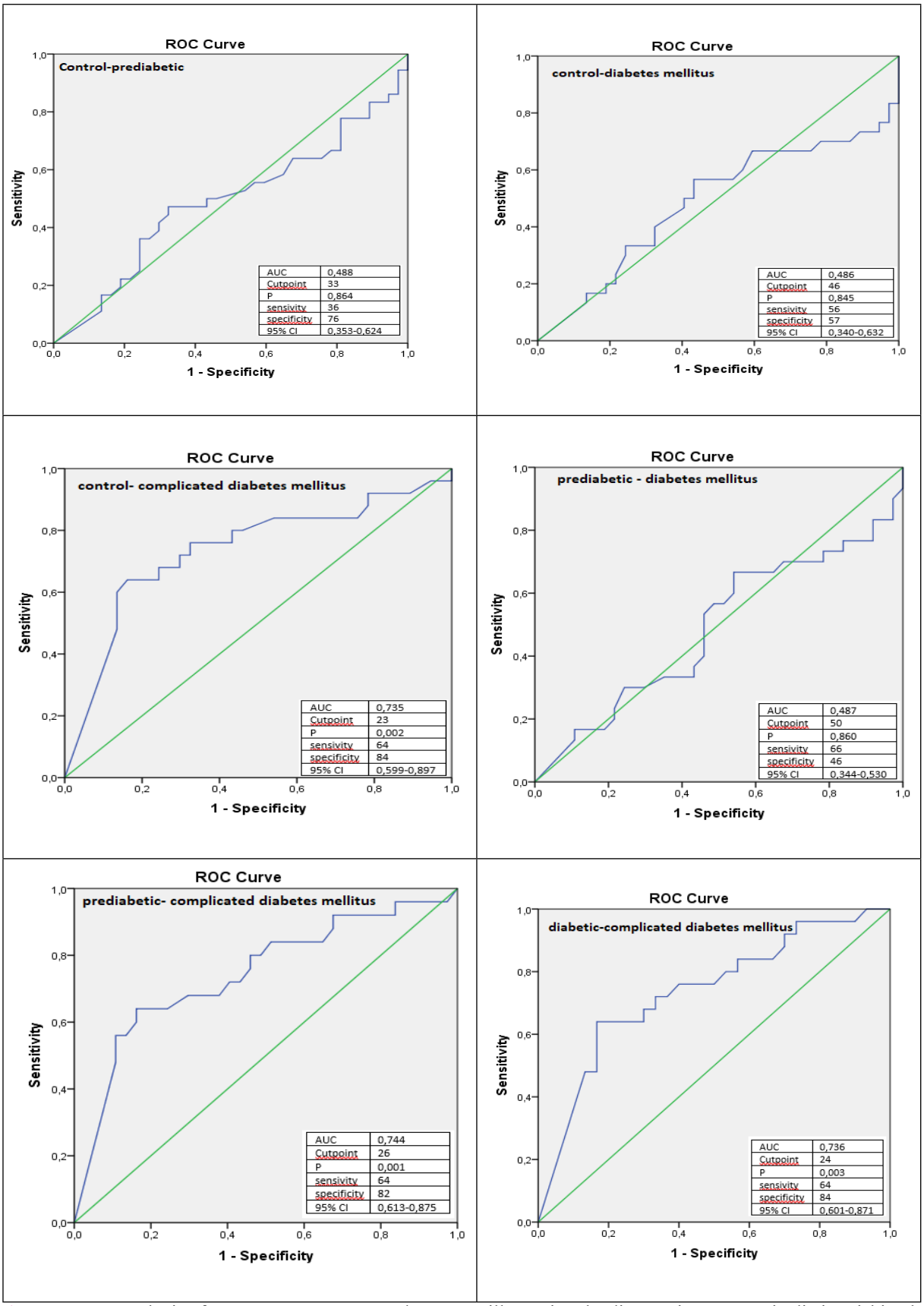

Figure 1. ROC curve analysis of HALP scores across study groups, illustrating the diagnostic accuracy in distinguishing between diabetes stages

correlations between HALP scores and parameters such as albumin, hemoglobin, and lymphocyte count.

Further supporting our results, Wang et al. (16) demonstrated that HALP scores could predict the severity of diabetic complications, including nephropathy and retinopathy. Their study suggested that monitoring HALP scores could help in the early identification and management of these complications, similar to our

findings on the diagnostic accuracy of HALP scores in the complicated DM group.

In a recent study by Ranran Ding et al., (17) the HALP score was examined as a potential predictor of diabetic foot ulcer severity. The findings revealed that lower HALP scores were strongly associated with advanced stages of diabetic foot ulcers and poorer wound healing outcomes. This aligns with the hypothesis that HALP reflects underlying systemic inflammation and nutritional deficits, which are pivotal in diabetic complications. Additionally, the study emphasized the clinical utility of HALP in predicting outcomes and guiding therapeutic strategies in diabetic foot management.

Furthermore, higher HALP scores are associated with a lower risk of diabetic kidney disease (DKD) and decreased all-cause and cardiovascular mortality in type 2 diabetes patients. This underscores the potential of the HALP score in risk stratification and guiding clinical decisions for DKD management (17).

Moreover, a study by Lee et al. (18) indicated that HALP scores are influenced by both inflammatory and nutritional factors, which are critical in the pathophysiology of diabetes and its complications. They observed that lower HALP scores were associated with higher levels of inflammatory markers such as CRP, which is consistent with our results showing negative correlations between HALP scores and CRP.

Lastly, the work of Kim et al. (19) suggested that HALP scores could be a valuable marker for assessing the risk of cardiovascular diseases in diabetic patients. Their findings of lower HALP scores in patients with cardiovascular complications mirror our results where complications such as hypertension, macrovascular, and microvascular diseases showed negative correlations with HALP scores.

These examples underscore the practical utility of HALP scores in tailoring diabetes management. Patients with persistently low HALP scores may benefit from intensified nutritional support, closer monitoring for microvascular complications, or early therapeutic adjustments to mitigate disease progression.

Limitations

This study has several limitations. The cross-sectional design precludes causal inferences about the relationships between HALP scores and diabetes stages. Additionally, the relatively small sample size may limit the generalizability of the findings. Another limitation is the lack of stratification by treatment regimens, which could have provided insight into HALP score variability among different therapeutic approaches. We also acknowledge the absence of multivariable regression analysis, which would have allowed us to better account for confounding factors such as medications and comorbidities. However, the limited sample size and study design restricted our ability to perform this analysis. Future longitudinal studies with larger and more diverse populations are necessary to validate these results. These studies should include diverse ethnic groups, variations in socioeconomic status, and patients with different baseline levels of glycemic control to ensure broader applicability of the findings.

CONCLUSION

Our study confirms the utility of HALP scores as a valuable marker for assessing disease severity and the presence of complications in diabetic patients. The significant correlations between HALP scores and various clinical and laboratory parameters underscore the multifaceted nature of diabetes and its complications. HALP scores could be used in outpatient settings to identify high-risk patients who may benefit from early interventions such as nutritional counseling, anti-inflammatory therapies, or closer monitoring of glycemic control. Routine incorporation of HALP scores in electronic health records could facilitate decision-making, enabling real-time risk assessments during clinic visits. These findings highlight the potential of HALP scores in clinical practice, particularly in monitoring and managing diabetes and its associated complications.

DECLERATIONS

Ethical Issues: This study was conducted in accordance with the Declaration of Helsinki and was approved by the Yeditepe University Clinical Research Ethics Committee 23.06.2022/1626. Informed consent was obtained from all participants involved in this study. As this research involved a retrospective review of existing data, it posed minimal risk to participants, and no additional interventions were performed. There were no ethical issues encountered during the conduct of this study.

Funding and Conflict of Interest: The authors declare that this research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. There are no conflicts of interest to disclose related to this study.

Author Contributions: Conceptualization; Yaşar Küçükardalı, Prof; Mehmet Akif Öztürk, Assoc.Prof/ Methodology; Yaşar Küçükardalı, Prof; Ahmet Enes Küçükardalı, M.D./Formal Analysis: Yaşar Küçükardalı, Prof; Adeviye Özsoy, M.D./Investigation; Yaşar Küçükardalı, Prof; Mehmet Akif Öztürk, Assoc.Prof/ Data Curation; Ahmet Enes Küçükardalı, M.D; Adeviye Özsoy, M.D., /Writing; Yaşar Küçükardalı, Prof; Lidya Aden Çağlar, M.D./Original Draft Preparation; Yaşar Küçükardalı, Prof; Ahmet Enes Küçükardalı, M.D; Adeviye Özsoy, M.D.; Lidya Aden Çağlar, M.D./Review and Editing; Mehmet Akif Öztürk, Assoc.Prof; Lidya Aden Çağlar, M.D./Supervision: Yaşar Küçükardalı, Prof.

AI: We hereby confirm that the content of this article was written entirely by the authors and does not involve the use of artificial intelligence or AI-assisted writing tools. All intellectual contributions, data analysis, and interpretations presented in this manuscript are the result of the authors' original work.

REFERENCES

1. Farag CM, Antar R, Akosman S, Ng M, Whalen MJ. What is hemoglobin, albumin, lymphocyte, platelet (HALP) score? A comprehensive literature review of HALP's prognostic ability in different cancer types. *Oncotarget*. 2023;14:153-172. Published 2023 Feb 25. doi:10.18632/oncotarget.28367
2. Guo Y, Shi D, Zhang J, et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score is a Novel Significant Prognostic Factor for Patients with Metastatic Prostate Cancer Undergoing Cytoreductive Radical Prostatectomy. *J Cancer*. 2019;10(1):81-91. Published 2019 Jan 1. doi:10.7150/jca.27210
3. Guijosa A., Calderillo-Ruiz G., Munoz Montano W. R., et al. HALP index prognostic significance for colon cancer patients in a Hispanic-based population. *Journal of Clinical Oncology*. 2022;40(16) doi: 10.1200/JCO.2022.40.16_suppl.e15521.e15521
4. Vlatka P, Marko L, Stefan M, Dorian L. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score is a novel prognostic factor for patients with diffuse large B-cell lymphoma. *J Cancer Res Ther*. 2022;18(3):725-732. doi:10.4103/jcrt.jcrt_174_21
5. Feng JF, Wang L, Yang X. The preoperative hemoglobin, albumin, lymphocyte and platelet (HALP) score is a useful predictor in patients with resectable esophageal squamous cell carcinoma. *Bosn J Basic Med Sci.* 2021;21(6):773-781. Published 2021 Dec 1. doi:10.17305/bjbms.2021.5666
6. Gao X, Lin B, Lin Q, et al. A HALP score-based prediction model for survival of patients with the upper tract urothelial carcinoma undergoing radical nephroureterectomy. *Bosn J Basic Med Sci*. 2022;22(2):280-290. Published 2022 Apr 1. doi:10.17305/bjbms.2021.6543
7. Akgül, GG. The Relationship Between the HALP Score and Gastric Cancer Prognosis: HALP Score in Gastric Cancer. *J Eur Int Med Prof.* 2023;1(4):156:161. Doi:10.5281/zenodo.10019807
8. Tian M, Li Y, Wang X, et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score Is Associated With Poor Outcome of Acute Ischemic Stroke. *Front Neurol.* 2021;11:610318. Published 2021 Jan 12. doi:10.3389/fneur.2020.610318
9. Kocaoglu S, Alatli T. The Efficiency of the HALP Score and the Modified HALP Score in Predicting Mortality in Patients with Acute Heart Failure Presenting to the Emergency Department. *J Coll Physicians Surg Pak.* 2022;32(6):706-711. doi:10.29271/jcpsp.2022.06.706
10. Antar R, Farag C, Xu V, Drouaud A, Gordon O, Whalen MJ. Evaluating the baseline hemoglobin, albumin, lymphocyte, and platelet (HALP) score in the United States adult population and comorbidities: an analysis of the NHANES. *Front Nutr.* 2023;10:1206958. Published 2023 May 18. doi:10.3389/fnut.2023.1206958
11. Alshuweishi Y, Basudan AM, Alfaifi M, Daghistani H, Alfhili MA. Association of the HALP Score with Dyslipidemia: A Large, Nationwide Retrospective Study. *Medicina (Kaunas)*. 2023;59(11):2002. Published 2023 Nov 14. doi:10.3390/medicina59112002
12. Zheng Y, Huang Y, Li H. Hemoglobin albumin lymphocyte and platelet score and all-cause mortality in coronary heart disease: a retrospective cohort study of NHANES database. *Front Cardiovasc Med.* 2023;10:1241217. Published 2023 Nov 13. doi:10.3389/fcvm.2023.1241217
13. Zhang F, Li L, Shi T, Liu Y, Xie J, Yu L. The hemoglobin, albumin, lymphocyte, and platelet (HALP) is a potent indicator for the prognosis in hemodialysis patients. *Medicine (Baltimore).* 2023;102(19):e33650. doi:10.1097/MD.0000000000033650
14. Zhang X, et al. Prognostic value of HALP score in patients with diabetic complications. *J Diabetes Res*. 2023.
15. Cheng H, et al. Correlation of HALP score with nutritional and inflammatory status in diabetic patients. *Clin Diabetes Endocrinol.* 2022;8(1):12-19.
16. Wang Y, et al. Predictive value of HALP score for diabetic complications. *Diabetes Metab.* 2021;47(2):101-11.
17. Ding R, Zeng Y, Wei Z, et al. The L-shape relationship between hemoglobin, albumin, lymphocyte, platelet score and the risk of diabetic retinopathy in the US population. *Front Endocrinol (Lausanne).* 2024;15:1356929. Published 2024 May 10. doi:10.3389/fendo.2024.1356929
18. Lee J, et al. Influence of inflammatory and nutritional factors on HALP scores in diabetic patients. *J Clin Endocrinol Metab.* 2020;105(6):1772-1780.
19. Kim S, et al. HALP scores and cardiovascular risk in diabetic patients. *Cardiovasc Diabetol.* 2019;18(1):45-53.
20. Miller B, Chen L, Santos A. Emerging biomarkers combined with HALP scores for enhanced risk prediction in diabetes. *J Diabetes Sci Technol.* 2022;16(2):284-295. doi:10.1177/19322968221080928.
21. Taylor M, Nguyen A, Blake R. Multi-biomarker strategies incorporating HALP scores for diabetes risk stratification. *Endocr Res.* 2023;48(1):77-89. doi:10.1080/074358023.