Journal of Endocrine Systems Research

https://jesr.cultechpub.com/

Cultech Publishing

Article

The Relationship between Frailty, Hemoglobin-Albumin-lymphocyte-Platelet (HALP) Score, and Systemic Inflammatory Index (SII) in Elderly Type 2 Diabetic Patients

Gulali Aktas[1,*], Murat Pehlivan[2], Burcin Meryem Atak Tel[1], Satilmis Bilgin[1], Elif Basaran[3], Atiqa Khalid[4], Emre Cimenden[1], Tuba Taslamacioglu Duman[1]

[1]Abant Izzet Baysal University Hospital, Department of Internal Medicine, Bolu, Turkey

[2]Hacettepe University Hospital, Department of Geriatrics, Ankara, Turkey

[3]Ankara Liv Hospital, Department of Internal Medicine, Ankara, Turkey

[4]Woman Medical Officer, Gynaecology and Obstetrics Department, Tehsil Headquarter Hospital, Jahanian, Pakistan

[*]Corresponding author: Gulali Aktas, draliaktas@yahoo.com

Abstract

Aim**:** Frailty, a clinical syndrome of reduced physiological reserves and increased vulnerability, is a key concern in managing type 2 diabetes mellitus (T2DM). Biomarkers like the systemic inflammatory index (SII) and the hemoglobin-albumin-lymphocyte-platelet (HALP) score have shown promise in understanding the inflammatory and nutritional factors underlying frailty. Present study explored the relationship between frailty, HALP, and SII in elderly diabetic patients.

Method: We included diabetic patients aged 65 years and older who visited the institutional outpatient clinics. Participants were classified as frail or non-frail using the Edmonton Frail Scale. The SII and HALP score of the frail and non-frail diabetic subjects were compared.

Results: There were 112 and 189 subjects in frail and non-frail groups, respectively. Mean SII level of the frail patients was significantly higher than that of the non-frail diabetic subjects (911 ± 322 vs 568 ± 286), ($p<0.001$). Median HALP score of the frail group (35 [7-142]) was significantly lower than the HALP score of the non-frail group (54 [6-143]), ($p<0.001$). According to the ROC analyses, the sensitivity and specificity of HALP score (when lower than 38.7) in detecting frailty in diabetic patients were 76% and 59%, respectively. The sensitivity and specificity of SII (when higher than 652) in detecting frailty were 60% and 73%, respectively. Multivariate analyses revealed that both SII and HALP score were independent risk factors for frailty.

Conclusion: HALP and SII may serve as potential screening markers and warrant validation in larger longitudinal studies. We suggest that elevated SII and decreased HALP score in patients with T2DM should alert physicians for possible frailty.

Keywords

Frailty, HALP score, Inflammation, SII, Type 2 diabetes mellitus, Elderly

Article History

Received: 23 September 2025
Revised: 23 October 2025
Accepted: 30 October 2025
Available Online: 20 November 2025

1. Introduction

Type 2 diabetes mellitus (T2DM) is one of the most common chronic diseases worldwide. Effective management of type 2 diabetes, which is associated with significant morbidity and mortality, has been linked to a reduction in diabetic complications. Frailty is a clinical syndrome characterized by reduced physiological reserves and increased vulnerability to adverse health outcomes, especially in older adults [1]. Identifying and managing frailty is crucial in mitigating risks such as falls, hospitalization, and mortality. Frailty is particularly important in diabetic subjects, for instance, poor glycemic control has been linked with an increased risk of frailty [2]. Frailty is reported to be linked with thyroid dysfunction [3]. Moreover, frail diabetic elderly individuals have been shown to have a higher rate of poor diabetes control [4]. This is because sarcopenia being an important determinant of frailty. Glucose utilization is decreased and blood glucose is increased due to decreased muscle mass in frail subjects.

The systemic inflammatory index (SII), a biomarker derived from platelet, neutrophil, and lymphocyte counts, has emerged as a promising tool in understanding frailty. Reflecting the balance between immune and inflammatory responses, SII offers insights into the biological underpinnings of frailty, including chronic inflammation, immune dysfunction, and hematological changes [5]. On the other hand, the Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) score is an emerging biomarker that integrates nutritional and inflammatory status into a single index [6]. Given the significant roles of anemia, hypoalbuminemia, immune imbalance, and inflammation in the pathophysiology of frailty, the HALP score offers a comprehensive and practical approach to assessing this complex condition.

Both T2DM [7], and frailty [8] have been found to be associated with elevated levels of certain inflammatory markers in the blood. Moreover, the hemoglobin-albumin-lymphocyte-platelet score and systemic inflammatory index have been reported to correlate with various inflammatory conditions. Chronic conditions characterized by inflammation, such as diabetic nephropathy [9], and autoimmune hepatitis [10] have been reported to be associated with SII and HALP score values, respectively.

In present study, we aimed to investigate whether frailty has relationship with HALP and SII values in elderly diabetic patients who presented to the internal medicine clinic of Abant Izzet Baysal University Hospital.

2. Methods

2.1. Study Population

The study included diabetic patients aged 65 and older who presented to the internal medicine outpatient clinics of Bolu Abant Izzet Baysal University Hospital between January and August 2024. Data collected from patients' files and computerized database of our institution. Study protocol was approved by Abant Izzet Baysal University Ethics Committee (date: 24th of September, 2024; approval no: 2024/237). The subjects with cancer, end-stage renal failure, cirrhosis, or hematological malignancies, as well as those using medications that could affect hemogram parameters (e.g., corticosteroids) were not included to the study. Patients with active or recent (within 30 days) infectious or inflammatory conditions were also excluded. We enrolled 319 subjects to the study initially. 18 of them excluded according to the exclusion criteria and data of remaining 301 patients were included to the final analysis. According to the Edmonton Frail Scale [11], patients were divided into two groups: frail and non-frail.

2.2. Laboratory Analyses

Data such as age, gender, body mass index (BMI), comorbidities, duration of illnesses, and diabetes duration were recorded from the patients' files. Additionally, routinely assessed laboratory values, including hemogram, kidney and liver function tests, serum lipids, albumin levels, glycated hemoglobin (HbA1c), fasting glucose, and C-reactive protein (CRP), were retrospectively obtained and recorded. The systemic inflammatory index (SII) was calculated using the formula SII=(Platelet count × Neutrophil count) / Lymphocyte count. The HALP score was determined using the formula HALP=(Hemoglobin × Serum Albumin × Lymphocyte count) / Platelet count. The data of frail and non-frail patients were compared.

2.3 Statistical Analyses

The data were analyzed using the SPSS statistical software (SPSS 20.0 for Windows, IBM Inc., Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to assess normal distribution. Categorical variables were compared using the chi-square test. Data following a normal distribution were compared between groups using the t-test and expressed as mean ± standard deviation. Data not following a normal distribution were compared using the Mann-Whitney U test and expressed as median (min.–max.). The correlation between study variables was analyzed using the Pearson correlation test. The sensitivity and specificity of SII and HALP values in detecting frailty were evaluated using receiver operating characteristic (ROC) curve analysis. A p-value of <0.05 was considered statistically significant.

3. Results

Study cohort consisted of 301 patients with T2DM. Of them, 112 were in frail group and 189 were in non-frail group. Mean age of the frail and non-frail groups were 69.7 ± 8.6 years and 66.2 ± 7.7 years, respectively (p<0.001). 48% of the frail subjects were men and 52% of them were women while 60% of the non-frail subjects were men and 40% of them were women. Gender distribution of the frail and non-frail groups was significantly different (p=0.041). Median Edmonton scores of the frail and non-frail groups were 9 (7-15) and 4 (0-6), respectively (p<0.001).

Mean Hb, Htc, and low density lipoprotein (LDL)-cholesterol values of the frail and non-frail groups were not statistically different. Moreover, median height, weight, waist circumference, body mass index (BMI), duration of diabetes, systolic and diastolic blood pressures, leukocyte count, neutrophil count, lymphocyte count, platelet count, fasting plasma glucose, blood urea, serum creatinine, estimated glomerular filtration rate, plasma sodium, potassium, aspartate transaminase, total cholesterol, high density lipoprotein (HDL)-cholesterol, serum uric acid, and spot urine protein to creatinine ratio levels of the frail and non-frail patients were not statistically different (p>0.05 for all).

Median HbA1c (p=0.018), and CRP (p=0.022) levels of the frail subjects were significantly higher than those of the non-frail group. In contrast, alanine transaminase (p<0.001), triglyceride (p=0.002), and serum albumin (p=0.002) levels of the frail patients were lower than those of the non-frail subjects. Table 1 shows general characteristics and laboratory data of the frail and non-frail diabetic subjects.

Table 1. General characteristics and laboratory data of the frail and non-frail groups.

		Frail diabetic patients	**Non-frail diabetic patients**	**p**
Sex	Men (n,%)	54 (48%)	114 (60%)	**0.041***
	Women (n,%)	58 (52%)	75 (40%)	
		*Mean ± SD***		
Age (years)		69.7 ± 8.6	66.2 ± 7.7	**<0.001**
Hb (g/dL)		12.4 ± 1.8	13 ± 1.9	0.109
Htc (%)		38.2 ± 5.5	40 ± 5.5	0.123
LDL (mg/dL)		99 ± 36.7	103 ± 37	0.406
SII (%)		911 ± 322	568 ± 286	**<0.001**
		*Median (min-max)****		
HALP (%)		35 (7-142)	54 (6-143)	**<0.001**
Height (m)		1.64 (1.4-1.82)	1.65 (1.38-1.9)	0.106
Weight (kg)		79 (56-132)	80 (57-125)	0.108
Waist circumference (cm)		106 (80-136)	104 (72-149)	0.762
BMI (kg/m^2)		29.4 (19.6-48.3)	30 (20.5-55.6)	0.742
Diabetes duration (years)		10 (1-40)	10 (1-40)	0.637
Edmonton score		9 (7-15)	4 (0-6)	**<0.001**
SBP (mm Hg)		126 (90-180)	120 (100-170)	0.598
DBP (mm Hg)		73 (60-100)	71 (50-100)	0.683
Leukocyte count (k/mm^3)		7.5 (3.8-11)	7.6 (4-11.4)	0.677
Neu (k/mm^3)		4.6 (2.1-9.7)	4.5 (2-8.2)	0.855
Lym (k/mm^3)		1.9 (1-4.9)	2 (1.5-4.6)	0.056
Plt (k/mm^3)		242 (110-480)	245 (122-465)	0.787
HbA1c (%)		8.2 (4.9-15.3)	7.6 (5.4-17.6)	0.018
FPG (mg/dL)		150 (50-511)	150 (65-560)	0.597
Creatinine (mg /dL)		0.9 (0.6-1.9)	0.9 (0.4-2.2)	0.566
Urea (mg/dL)		39 (17-78)	36 (13-74)	0.273
GFR (%)		73 (30-105)	77 (28-102)	0.155
Na (meq/L)		139 (128-147)	139 (126-146)	0.571
K (meq/L)		4.5 (3.1-6.1)	4.5 (3.2-6)	0.254
AST (U/L)		17 (9-55)	18 (8-64)	0.071
ALT (U/L)		16 (6-95)	20 (6-132)	**<0.001**
Total cholesterol (mg/dL)		169 (67-293)	177 (65-326)	0.149
HDL (mg/dL)		46 (19-110)	43 (20-114)	0.243
Triglyceride (mg/dL)		131 (36-588)	162 (39-540)	**0.002**
Albumin (g/dL)		4 (2.3-5.1)	4.2 (2.4-5.7)	**0.002**
CRP (mg/L)		6.5 (0.1-14)	4.1 (0.1-15)	**0.022**
Uric acid (mg/dL)		5.7 (2.6-15.7)	5.7 (1.8-16)	0.967
Spot urine prot/crea (%)		40 (0.3-3266)	22 (0.4-4490)	0.091

* Chi-square test; ** independent samples t test; *** Mann-Whitney U test.

Abbreviations. Hb: Hemoglobin; Htc: hematocrit; LDL: Low density lipoprotein; SII: systemic inflammatory index; HALP: hemoglobin-albumin-lymphocyte-platelet score; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure;

Neu: neutrophil count; Lym: lymphocyte count; Plt: platelet count; HbA1c: glycated hemoglobin; FPG: fasting plasma glucose; GFR: glomerular filtration rate; Na: sodium; K: potassium; AST: aspartate transaminase; ALT: alanine transaminase; HDL: high density lipoprotein; CRP: C-reactive protein

Mean SII level of the frail patients was significantly higher than that of the non-frail diabetic subjects (911 ± 322% vs 568 ± 286%), (p<0.001). Median HALP score of the frail group (35 [7-142]%) was significantly lower than the HALP score of the non-frail group (54 [6-143]%), (p<0.001).

Presence of comorbidities was similar in frail and non-frail groups; 82% of frail and 81.5% of the non-frail subjects had additional diseases (p=0.886). Control level of the diabetes was not significantly different between frail and non-frail groups. Thirty percent of the frail group and fort one percent of the non-frail groups had well controlled diabetes mellitus (p=0.058).

The HALP score was significantly and positively correlated with serum albumin (r=0.181, p=0.002). HALP score was inversely correlated with SII (r=-0.351, p<0.001), age (r=-0.193, p=0.001), and Edmonton score (r=-0.405, p<0.001). In addition, correlation analyses revealed that SII was significantly and positively correlated with age (r=0.250, p<0.001), Edmonton score (r=0.276, p<0.001), and CRP (r=0.226, p<0.001), while it was inversely correlated with serum albumin (r=-0.275, p<0.001), and triglyceride (r=-0.114, p=0.049) levels. Table 2 shows correlations between study variables.

Table 2. Correlations between study variables.

	SII	**HALP**	**Age**	**Edm. score**	**Triglyceride**	**Albumin**	**CRP**
SII	-	r=-0.351 p<0.001	r=0.250 p<0.001	r=0.276 p<0.001	r=-0.114 p=0.049	r=-0.275 p<0.001	r=0.226 p<0.001
HALP	r=-0.351 p<0.001	-	r=-0.193 p=0.001	r=-0.405 p<0.001	-	r=0.181 p=0.002	-

* Pearson's Correlation analysis test.

Abbreviations. SII: systemic inflammatory index; HALP: hemoglobin-albumin-lymphocyte-platelet score; Edm. score: Edmonton score; CRP: C-reactive protein.

According to the ROC analyses, the sensitivity and specificity of HALP score (when lower than 38.7) in detecting frailty in diabetic patients were 76% and 59%, respectively (AUC: 0.761, p<0.001, 95%CI: 0.707-0.816). Figure 1 shows the ROC curve of HALP score in detecting frailty in the study population.

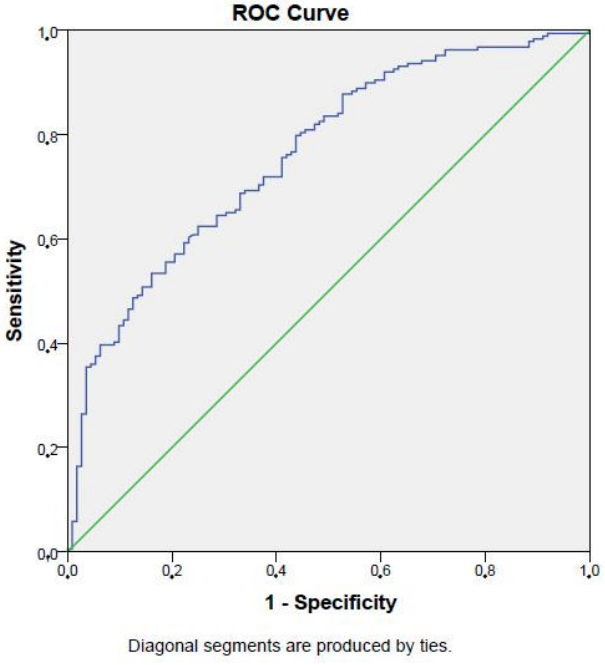

Figure 1. The ROC curve of HALP score in detecting frailty in the study population (n=112 in frail and n=189 in non-frail group).

The sensitivity and specificity of SII (when higher than 652) in detecting frailty were 60% and 73%, respectively (AUC: 0.676, p<0.001, 95%CI: 0.612-0.740). Figure 2 shows the ROC curve of SII in detecting frailty in the study population.

Logistic regression analysis, considering SII, HALP score, age, sex, HbA1c, triglyceride, serum albumin, and CRP, revealed that SII was an independent risk factor of frailty in diabetic patients (p<0.001, OR=1.1, 95%CI: 1.05-1.13). A unit increase in SII increases the frailty risk by 10%. Moreover, multivariate regression analysis which considers HALP score, SII, age, sex, HbA1c, triglyceride, serum albumin, and CRP, revealed that a unit decrease in HALP score increase the risk of frailty by 2% (p=0.04, OR=0.98, 95%CI: 0.97-0.99).

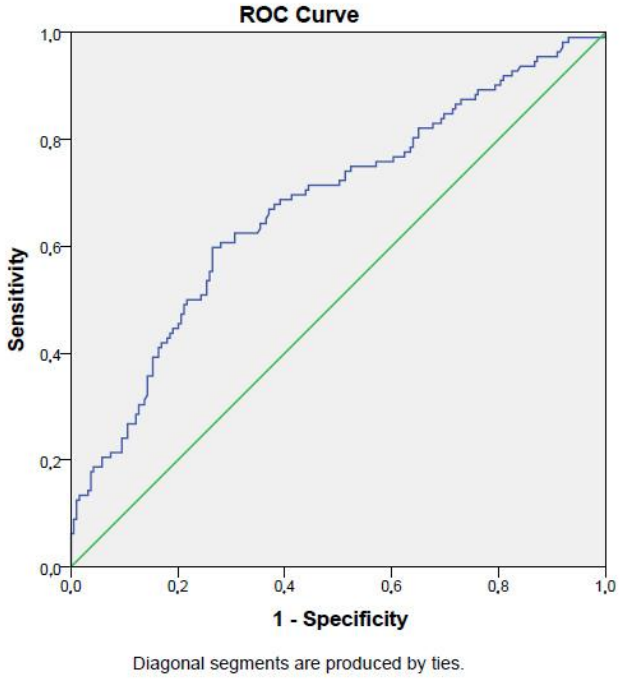

Figure 2. The ROC curve of SII in detecting frailty in the study population (n=112 in frail and n=189 in non-frail group).

4. Discussion

The present study has several striking findings; (a) the HALP score was significantly decreased in frail diabetic subjects compared to non-frail patients with T2DM; (b) the SII was significantly increased in frail subjects compared to non-frail controls; (c) SII was significantly correlated with age, Edmonton score, CRP, serum albumin, and triglyceride levels, while the HALP score was correlated with serum albumin, SII, age, and Edmonton score; (d) the sensitivity and specificity of SII and HALP scores in detecting frailty in diabetic subjects were statistically significant; and (e) both HALP score and SII were independent risk factors for frailty in patients with T2DM.

The results of the present study demonstrated a statistically significant increase in SII levels in frail patients compared to non-frail subjects. Monitoring SII levels may provide insights into the early detection of frailty, allowing for timely interventions to mitigate its progression. Indeed, elevated CRP levels have been reported in frailty [12]. Moreover, a recent meta-analysis showed increased CRP levels in frail patients compared to non-frail individuals [13]. This finding aligns with the understanding that inflammation plays a crucial role in the pathophysiology of frailty [14]. SII is also associated with inflammatory conditions other than frailty, including coronary heart disease [15], stroke [16], and cancer [17]. Thus, the elevated SII observed in frail subjects compared to non-frail individuals is consistent with the existing literature.

The increase in SII values in frail diabetic patients can be explained by several mechanisms. Chronic inflammation in these patients may result from increased oxidative stress, metabolic dysfunction, or immune dysregulation; factors often exacerbated in T2DM [18, 19]. The interplay between hyperglycemia, inflammatory cytokines, and cellular senescence could also contribute to the elevated SII levels in frail diabetic patients [20]. It can be speculated that treatment strategies targeting systemic inflammation may be beneficial for managing frailty in diabetic subjects. Previous studies have reported that the prevalence of frailty was lower in patients with well-controlled T2DM compared to those with poor disease control [21]. Furthermore, another study found that frail diabetic patients had significantly higher HbA1c levels than non-frail diabetic subjects [22].

The HALP score was significantly decreased in frail diabetic patients compared to non-frail subjects in the present study. This finding indicates that frailty is associated with poorer nutritional and immune status, as the HALP score reflects systemic inflammation, nutritional reserves, and overall physiological health [23]. In addition, lower HALP scores in the frail group may imply malnutrition or suboptimal nutritional status, a well-documented contributor to frailty. For example, decreased hemoglobin suggests anemia, which impairs physical capacity and contributes to frailty [24]. Similarly, decreased albumin levels may indicate poor protein reserves, which are common in frailty due to inadequate intake or chronic disease [25]. Immune function is also compromised in frailty. Reduced lymphocyte counts in frail individuals reflect immune dysregulation, increasing susceptibility to infections and slowing recovery from illness [26]. Additionally, platelet abnormalities might indicate underlying inflammation, a hallmark of both frailty and chronic conditions such as T2DM [27].

The reduced HALP score in frail diabetic subjects could be explained by several mechanisms. Frail individuals often experience heightened systemic inflammation and oxidative stress, directly affecting the components of the HALP score [28]. Chronic diseases like T2DM further exacerbate these conditions, compounding their impact on frailty [29]. Another possible mechanism is the catabolic state associated with frailty. Frailty is characterized by a hypercatabolic condition that leads to muscle wasting, low albumin, and anemia, all of which contribute to a declining HALP score [30].

The present study revealed that the HALP score was positively correlated with serum albumin levels. This positive correlation indicates that higher HALP scores are associated with better nutritional status, as albumin is a key marker of protein reserves and overall nutritional health. Consequently, a higher HALP score reflects better systemic health and nutritional adequacy, both of which are protective against frailty [31].

We also found that the HALP score was inversely correlated with the SII value. This moderate inverse correlation suggests that as SII increased, indicating heightened systemic inflammation, the HALP score decreased. This finding aligns with the understanding that inflammation negatively affects nutritional and hematological parameters [32].

Age was also inversely correlated with the HALP score. This reflects the natural decline in nutritional reserves, immune function, and hematological health associated with aging [33]. Although age alone does not determine the HALP score, the decrease in HALP score with advancing age reflects the compounded effects of age-related physiological changes and increased inflammatory activity [34].

The HALP score was negatively correlated with the Edmonton Frailty Score. A recent meta-analysis reported that serum albumin was associated with the degree of frailty in older adults [35]. Since serum albumin is a component of the HALP score, the strong inverse correlation between HALP and the Edmonton Frailty Score suggests that lower HALP scores are associated with higher degrees of frailty, making it a potential biomarker for frailty severity.

The present work also revealed a significant correlation between SII and age. This correlation suggests that SII tends to increase with age, consistent with the known association between aging and heightened systemic inflammation, a phenomenon termed “inflammaging” [36]. Aging is associated with immune system dysregulation, including increased pro-inflammatory cytokines and reduced immune resolution, which elevate SII components such as neutrophils and platelets [37].

Furthermore, the present study showed a moderate positive correlation between SII and the Edmonton Frailty Score, indicating that higher SII levels were associated with greater frailty severity. Frailty is often accompanied by chronic low-grade inflammation, immune dysfunction, and oxidative stress, all of which increase neutrophil and platelet counts, contributing to a higher SII [38].

A positive correlation between CRP and SII was another finding of the present work. SII has been reported to increase in many inflammatory conditions such as diabetic nephropathy [39], metabolic syndrome [40], and chronic obstructive pulmonary disease [41]. These findings suggest that SII could be a reliable marker of inflammatory burden in frail diabetic subjects. Accordingly, both SII and CRP are elevated in response to pro-inflammatory stimuli such as infections, chronic diseases, or tissue damage [42].

SII levels were inversely correlated with serum albumin in the present study. This inverse correlation indicates that higher SII levels are associated with lower serum albumin, a marker of nutritional status, inflammation, and systemic health. Chronic inflammation in frail subjects suppresses albumin synthesis in the liver and increases protein catabolism, resulting in reduced albumin levels [43]. This finding supports the inflammatory nature of elevated SII. The combination of low albumin and high SII could help identify individuals at risk of poor outcomes such as malnutrition, frailty, or complications from chronic diseases, including T2DM.

We also noted an inverse correlation between SII and serum triglyceride levels. Although weak, this correlation suggests a mild association between higher SII levels and lower triglycerides, which may reflect metabolic alterations related to inflammation. The inflammatory burden is known to affect lipid metabolism, potentially reducing triglyceride levels in certain contexts [44].

Our study showed that the HALP score had relatively high sensitivity and moderate specificity for detecting frailty, highlighting its diagnostic utility in diabetic patients. In addition, the AUC of 0.76 indicates good discriminatory power of the HALP score in distinguishing between frail and non-frail diabetic patients. An area under the curve (AUC) value closer to 1.0 represents excellent discrimination, while 0.5 indicates no discrimination [45]. Therefore, the HALP score appears to be a reasonably accurate, non-invasive, and cost-effective tool for identifying frailty in diabetic populations, making it practical for clinical use.

The HALP score’s ability to predict frailty risk makes it a valuable tool in diabetic care, particularly because nutritional and inflammatory markers are modifiable through targeted interventions. The HALP score has also been recognized as an independent risk factor in other inflammatory conditions. Zhou et al. studied the HALP score in patients with hepatocellular carcinoma and found that it was an independent risk factor for overall survival in that population [46]. Similarly, other authors have suggested that the HALP score is an independent prognostic factor in hemodialysis patients [47].

Studies in the literature have evaluated SII and HALP scores together in various conditions. For example, authors found decreased HALP scores and increased SII values in patients with hyperemesis gravidarum [48]. Moreover, decreased HALP scores and elevated SII levels were reported in patients with asthma compared to healthy controls in a study from Turkey [49]. Similarly, we observed high SII and low HALP score values in frail subjects compared to non-frail diabetic patients in the present study. While SII and HALP show potential for frailty detection in elderly T2DM patients, their moderate sensitivity and specificity highlight the need for a multimodal assessment strategy. Their role may be most beneficial as part of a broader screening framework rather than as standalone diagnostic tools.

The present study has several limitations that should be considered when interpreting the findings. First, the retrospective design limits the analysis to simple associations and does not allow for establishing causal relationships. Second, the relatively small cohort size may restrict the generalizability of the results. Nevertheless, this is the first study in the literature to report an association between frailty and SII and HALP scores in elderly diabetic patients.

5. Conclusion

Evaluation of SII and HALP scores in diabetic subjects is recommended for the early diagnosis of frailty. Elevated SII and decreased HALP scores in patients with T2DM should alert clinicians to possible frailty, allowing for timely assessment and intervention.

Abbreviations

HALP: hemoglobin-albumin-lymphocyte-platelet

SII: systemic inflammatory index

T2DM: type 2 diabetes mellitus

HbA1c: glycated hemoglobin

CRP: C-reactive protein

ROC: receiver operating characteristic

BMI: body mass index

LDL: low density lipoprotein

HDL: high density lipoprotein

Author contributions

Conceptualization, T.T.D. and B.M.A.T.; Methodology, M.P., E.B., and G.A.; Software, E.C.; Validation, T.T.D., S.B. and B.M.A.T.; Formal Analysis, A.K. and S.B.; Investigation, E.C. and E.B.; Data Curation, T.T.D., S.B. and B.M.A.T.; Writing – Original Draft Preparation, M.P.; Writing – Review & Editing, A.K. and G.A.; Visualization, E.B.; Supervision, G.A.

Conflicts of interest

The authors have no conflicts of interest.

Ethical approval

The study was approved by the institutional ethics committee of the Abant Izzet Baysal University (date: 24th of September, 2024; approval no: 2024/237).

Consent to participate

All participants have given informed consent to participate in the study.

Consent to publication

Not applicable.

Availability of data and materials

The data used and/or analyzed during the current study are available upon reasonable request to the corresponding author.

Funding

Not applicable.

ORCID

Gulali Aktas https://orcid.org/0000-0001-7306-5233

Generative AI Statement

The authors declare that no Gen AI was used in the creation of this manuscript.

References

[1] Khan KT, Hemati K, Donovan AL. Geriatric Physiology and the Frailty Syndrome. Anesthesiology Clinics, 2019; 37(3), 453-474. DOI: 10.1016/j.anclin.2019.04.006
[2] Keegan GL, Bhardwaj N, Abdelhafiz AH. The outcome of frailty in older people with diabetes as a function of glycaemic control and hypoglycaemic therapy: a review. Expert Review of Endocrinology & Metabolism, 2023, 18(5), 361-375. DOI: 10.1080/17446651.2023.2239907
[3] Lee YJ, Kim MH, Lim DJ, Lee JM, Chang SA, Lee J. Exploring the Association between Thyroid Function and Frailty: Insights from Representative Korean Data. Endocrinology and Metabolism (Seoul, Korea), 2023, 38(6), 729-738. DOI: 10.3803/EnM.2023.1769
[4] Akan S, Aktas G. Relationship between frailty, according to three frail scores, and clinical and laboratory parameters of the geriatric patients with type 2 Diabetes Mellitus. Revista da Associacao Medica Brasileira (1992), 2022, 68(8), 1073-1077. DOI: 10.1590/1806-9282.20220271
[5] Zheng Z, Luo HH, Xue QY. U-shaped association of systemic immune-inflammation index levels with cancer-related and all-cause mortality in middle-aged and older individuals with frailty. Archives of Gerontology and Geriatrics, 2023, 116, 105228. DOI: 10.1016/j.archger.2023.105228
[6] Tian MK, Li YF, Wang X, Tian X, Pei LL, Wang X, et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score Is Associated With Poor Outcome of Acute Ischemic Stroke. Frontiers in Neurology, 2020, 11, 610318. DOI: 10.3389/fneur.2020.610318
[7] Bilgin S, Aktas G, Zahid Kocak M, Atak BM, Kurtkulagi O, Taslamacioglu Duman T, et al. Association between novel inflammatory markers derived from hemogram indices and metabolic parameters in type 2 diabetic men.The Aging Male, 2020, 23(5), 923-927. DOI: 10.1080/13685538.2019.1632283
[8] Bilgin S, Aktas G, Kahveci G, Atak BM, Kurtkulagi O, Taslamacioglu Duman T. Does mean platelet volume/lymphocyte count ratio associate with frailty in type 2 diabetes mellitus? Bratislavske Lekarske Listy, 2021, 122(2), 116-119. DOI: 10.4149/bll_2021_017
[9] Taslamacioglu Duman T, Ozkul FN, Balci B. Could Systemic Inflammatory Index Predict Diabetic Kidney Injury in Type 2 Diabetes Mellitus? Diagnostics (Basel), 2023, 13(12), 2063. DOI: 10.3390/diagnostics13122063
[10] Ustaoglu M, Aktas G, Kucukdemirci O, Goren I, Bas B. Could a reduced hemoglobin, albumin, lymphocyte, and platelet (HALP) score predict autoimmune hepatitis and degree of liver fibrosis? Revista da Associacao Medica Brasileira (1992), 2024, 70(1), e20230905. DOI: 10.1590/1806-9282.20230905
[11] Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. Age and Ageing, 2006, 35(5), 526-529. DOI: 10.1093/ageing/afl041
[12] Puts MT, Visser M, Twisk JW, Deeg DJ, Lips P. Endocrine and inflammatory markers as predictors of frailty. Clinical Endocrinology (Oxf), 2005, 63(4), 403-411. DOI: 10.1111/j.1365-2265.2005.02355.x
[13] Soysal P, Stubbs B, Lucato P, Luchini C, Solmi M, Peluso R, et al. Inflammation and frailty in the elderly: A systematic review and meta-analysis. Ageing Reseach Reviews, 2016, 31, 1-8. DOI: 10.1016/j.arr.2016.08.006
[14] Ferrucci L, Fabbri E. Inflammageing: chronic inflammation in ageing, cardiovascular disease, and frailty. Nature Reviews Cardiology, 2018, 15, 505-522. DOI: 10.1038/s41569-018-0064-2
[15] Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. European Journal of Clinical Investigation, 2020, 50(5), e13230. DOI: 10.1111/eci.13230
[16] Huang YW, Yin XS, Li ZP. Association of the systemic immune-inflammation index (SII) and clinical outcomes in patients with stroke: A systematic review and meta-analysis. Frontiers in Immunology, 2022, 13, 1090305. DOI: 10.3389/fimmu.2022.1090305
[17] Fu HY, Zheng J, Cai JY, Zeng KN, Yao J, Chen L, et al. Systemic Immune-Inflammation Index (SII) is Useful to Predict Survival Outcomes in Patients After Liver Transplantation for Hepatocellular Carcinoma within Hangzhou Criteria. Celularl Physiology and Biochemistry, 2018, 47(1), 293-301. doi:10.1159/000489807
[18] Uchmanowicz I. Oxidative Stress, Frailty and Cardiovascular Diseases: Current Evidence. Advance in Experimental Medicine Biology, 2020, 1216, 65-77. DOI: 10.1007/978-3-030-33330-0_8

[19] Mir R, Jha CK, Khullar N, Maqbool M, Dabla PK, Mathur S, et al. The Role of Inflammatory and Cytokine Biomarkers in the Pathogenesis of Frailty Syndrome. Endocrine Metabolic and Immune Disorders Drug Targets, 2022, 22(14), 1357-1366. DOI: 10.2174/1871530322666220304220522
[20] Wang G, Han BH, Zhang RX, Liu Q, Wang XD, Huang XT, et al. C1q/TNF-Related Protein 9 Attenuates Atherosclerosis by Inhibiting Hyperglycemia-Induced Endothelial Cell Senescence Through the AMPKα/KLF4 Signaling Pathway. Frontiers in Pharmacology, 2021, 12, 758792. DOI: 10.3389/fphar.2021.758792
[21] Bilgin S, Aktas G, Kurtkulagi O, Atak BM, Duman TT, et al. Edmonton frail score is associated with diabetic control in elderly type 2 diabetic subjects. Journal of Diabetes Metabolic Disorders, 2020, 19(1), 511-514. DOI: 10.1007/s40200-020-00542-z
[22] Tel BMA, Bilgin S, Kurtkulagi O, Kahveci G, Duman TT, Sagdic T, et al. Frailty in diabetic subjects during COVID-19 and its association with HbA1c, mean platelet volume and monocyte/lymphocyte ratio. Clinical Diabetology, 2022, 11(2), 119-126. DOI: 10.5603/DK.a2022.0015
[23] Güç ZG, Alacacıoğlu A, Kalender ME, Oflazoğlu U, Ünal S, Yıldız Y, et al. HALP score and GNRI: Simple and easily accessible indexes for predicting prognosis in advanced stage NSCLC patients. The İzmir oncology group (IZOG) study. Frontiers in Nutrition, 2022, 9, 905292. DOI: 10.3389/fnut.2022.905292
[24] Zhang HR, Wei XJ, Chen XT, Sun XD. Mortality from all-cause and cause-specific in the elderly: Joint implications of anemia and frailty. Archives of Gerontology and Geriatrics, 2023, 115, 105213. DOI: 10.1016/j.archger.2023.105213
[25] Yamamoto M, Adachi H, Enomoto M, Fukami A, Nakamura S, Nohara Y, et al. Lower albumin levels are associated with frailty measures, trace elements, and an inflammation marker in a cross-sectional study in Tanushimaru. Environmental Health and Preventive Medicine, 2021, 26(1), 25. DOI: 10.1186/s12199-021-00946-0
[26] Buigues C, Navarro-Martínez R, Sánchez-Martínez V, Serrano-Carrascosa M, Rubio-Briones J, Cauli O. Interleukin-6 and Lymphocyte Count Associated and Predicted the Progression of Frailty Syndrome in Prostate Cancer Patients Undergoing Antiandrogen Therapy. Cancers (Basel), 2020, 12. DOI: 10.3390/cancers12071716
[27] Arauna D, García F, Rodríguez-Mañas L, Marrugat J, Sáez C, Alarcón M, et al. Older adults with frailty syndrome present an altered platelet function and an increased level of circulating oxidative stress and mitochondrial dysfunction biomarker GDF-15. Free Radical Biology & Medicine, 2020, 149: 64-71. DOI: 10.1016/j.freeradbiomed.2020.01.007
[28] Sciacchitano S, Carola V, Nicolais G, Sciacchitano S, Napoli C, Mancini R, et al. To Be Frail or Not to Be Frail: This Is the Question-A Critical Narrative Review of Frailty. Journal of Clinical Medicine, 2024, 13(3). DOI: 10.3390/jcm13030721
[29] Bhatti JS, Sehrawat A, Mishra J, Sidhu IS, Navik U, Khullar N, et al. Oxidative stress in the pathophysiology of type 2 diabetes and related complications: Current therapeutics strategies and future perspectives. Free Radical Biology & Medicine, 2022, 184, 114-134. DOI: 10.1016/j.freeradbiomed.2022.03.019
[30] Thuluvath AJ, Verna EC. Deciphering an expanding array of clinical and research frailty measures. Clinical Liver Disease (Hoboken), 2024, 23(1), e0180. DOI: 10.1097/cld.0000000000000180
[31] Moradell A, Fernández-García ÁI, Navarrete-Villanueva D, Sagarra-Romero L, Gesteiro E, Pérez-Gómez J, et al. Functional Frailty, Dietary Intake, and Risk of Malnutrition. Are Nutrients Involved in Muscle Synthesis the Key for Frailty Prevention? Nutrients, 2021, 13(4). DOI: 10.3390/nu13041231
[32] Eckart A, Struja T, Kutz A, Baumgartner A, Baumgartner T, Zurfluh S, et al. Relationship of Nutritional Status, Inflammation, and Serum Albumin Levels During Acute Illness: A Prospective Study. The American Journal of Medicine, 2020, 133(6), 713-722.e717. DOI: 10.1016/j.amjmed.2019.10.031
[33] Shevyrev D, Tereshchenko V, Berezina TN, Rybtsov S. Hematopoietic Stem Cells and the Immune System in Development and Aging. International Journal of Molecular Sciences, 2023, 24(6). DOI: 10.3390/ijms24065862
[34] Baechle JJ, Chen N, Makhijani P, Winer S, Furman D, Winer DA. Chronic inflammation and the hallmarks of aging. Molecular Metabolish, 2023, 74, 101755. DOI: 10.1016/j.molmet.2023.101755
[35] Zhang LX, Yang PP, Yin FR, Zhang JB, Zhao BL, Zhou JM. Association between frailty and hypoproteinaemia in older patients: meta-analysis and systematic review. BMC Geriatrics, 2024, 24(1), 689. DOI: 10.1186/s12877-024-05275-9
[36] Fulop T, Larbi A, Pawelec G, Khalil A, Cohen AA, Hirokawa K, et al. Immunology of Aging: the Birth of Inflammaging. Clinical Reviews in Allergy & Immunology, 2023, 64(2), 109-122. DOI: 10.1007/s12016-021-08899-6
[37] Lewis ED, Wu DY, Meydani SN. Age-associated alterations in immune function and inflammation. Progress in Neuro-psychopharmacol & Biological Psychiatry, 2022, 118, 110576. DOI: 10.1016/j.pnpbp.2022.110576
[38] Johnson J, Jaggers RM, Gopalkrishna S, Dahdah A, Murphy AJ, Hanssen NMJ, et al. Oxidative Stress in Neutrophils: Implications for Diabetic Cardiovascular Complications. Antioxidants & Redox Signaling, 2022, 36(10-12), 652-666. DOI: 10.1089/ars.2021.0116
[39] Guo WC, Song YC, Sun Y, Du HS, Cai Y,You QQ, et al. Systemic immune-inflammation index is associated with diabetic kidney disease in Type 2 diabetes mellitus patients: Evidence from NHANES 2011-2018. Frontiers in Endocrinology (Lausanne), 2022, 13, 1071465. DOI: 10.3389/fendo.2022.1071465
[40] Zhao Y, Shao WY, Zhu QH, Zhang R, Sun T, Wang BJ, et al. Association between systemic immune-inflammation index and metabolic syndrome and its components: results from the National Health and Nutrition Examination Survey 2011-2016. Journal of Translational Medicine, 2023, 21(1), 691. DOI: 10.1186/s12967-023-04491-y
[41] Ye CL, Yuan L, Wu KL, Shen BZ, Zhu CL. Association between systemic immune-inflammation index and chronic obstructive pulmonary disease: a population-based study. BMC Pulmonary Medicine, 2023, 23(1), 295. DOI: 10.1186/s12890-023-02583-5
[42] Olson ME, Hornick MG, Stefanski A, Albanna HR, Gjoni A, Hall GD, et al. A biofunctional review of C-reactive protein (CRP) as a mediator of inflammatory and immune responses: differentiating pentameric and modified CRP isoform effects. Frontiers in Immunology, 2023, 14, 1264383. DOI: 10.3389/fimmu.2023.1264383
[43] Molinari P, Caldiroli L, Abinti M, Nardelli L, Armelloni S, Cesari M, et al. Frailty Is Associated with Malnutrition-Inflammation Syndrome in Older CKD Patients. Nutrients, 2024, 16(16), 2626. DOI: 10.3390/nu16162626
[44] Chen Y, Yu CY, Deng WM. The role of pro-inflammatory cytokines in lipid metabolism of metabolic diseases. International Reviews of Immunology, 2019, 38(6), 249-266. DOI: 10.1080/08830185.2019.1645138
[45] Jiménez-Valverde A. Threshold-dependence as a desirable attribute for discrimination assessment: implications for the evaluation of species distribution models. Biodiversity and Conservation, 2014, 23, 369-385. DOI: 10.1007/s10531-013-0606-1

[46] Zhou J, Yang DF. Prognostic Significance of Hemoglobin, Albumin, Lymphocyte and Platelet (HALP) Score in Hepatocellular Carcinoma. Journal of Hepatocellular Carcinoma, 2023, 10, 821-831. DOI: 10.2147/jhc.s411521
[47] Zhang FP, Li LH, Shi TT, 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: e33650. doi:10.1097/md.0000000000033650
[48] Bayram F, Ozgen G, Karasın SS, Ozgen L. The predictive value of HALP score and systemic immune inflammation (SII) index in hyperemesis gravidarum. Journal of Obstetrics and Gynaecology Research, 2023, 49(7), 1729-1735. DOI: 10.1111/jog.15666
[49] Günaydın FE. The predictive value of HALP score and systemic immune inflammation (SII) index in patients with asthma. The Annals of Clinical and Analytical Medicine, 2023, 14, S357-360. DOI: 10.4328/ACAM.21945