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Assessing the role of inflammatory and nutritional biomarkers in the diagnosis of celiac disease

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ABSTRACT

Aims: Celiac disease (CeD) is an immune-mediated enteropathy with multisystem involvement that is often underdiagnosed due to variable clinical manifestations. Identifying reliable, accessible, and noninvasive biomarkers is essential for timely diagnosis, particularly in resource-limited settings. This study aims to evaluate the diagnostic utility of inflammation and nutrition-related indices and scores calculated from routine laboratory tests in predicting CeD.

Methods: This retrospective cross-sectional study included 79 biopsy-confirmed celiac patients and 60 healthy controls. Demographic, hematological, and biochemical data were collected. The platelet-to-lymphocyte ratio (PLR), triglyceride-glucose index (TyG), hemoglobin, albumin, lymphocyte, and platelet (HALP) score, and other inflammation-related indices were calculated via validated formulas. Logistic regression analysis was performed to identify independent predictors of CeD. Receiver operating characteristic (ROC) curves were used to assess diagnostic performance.

Results: Compared with controls, patients with CeD had significantly greater PLRs and lower TyG indices and HALP scores ($p<0.05$ for all). In logistic regression analysis, both the TyG index (OR: 0.248, 95% CI [0.090, 0.685]) and the HALP score (OR: 0.013, 95% CI [0.001, 0.108]) were identified as independent risk factors for CeD. ROC analysis demonstrated that the PLR (AUC: 0.641), TyG score (AUC: 0.643), and HALP score (AUC: 0.697) could distinguish celiac patients from healthy individuals. The optimal cut-off values were 138 for PLR, 8.21 for TyG, and 0.47 for HALP, with corresponding sensitivities and specificities ranging from 53% to 68%.

Conclusion: The TyG index and HALP score are independent predictors of CeD and, may serve as useful noninvasive markers for risk stratification.

Keywords: Celiac disease, PLR, TyG index, HALP score, biomarkers, inflammation, nutrition

INTRODUCTION

Celiac disease (CeD) is a chronic autoimmune enteropathy characterized by small intestinal villous atrophy, crypt hyperplasia, and increased intraepithelial lymphocytes triggered by the ingestion of gluten—a protein found in wheat, barley, and rye—in genetically predisposed individuals.[1,2] The global prevalence of CeD is estimated to be approximately 1–2%, varying by geographic region; however, many cases remain undiagnosed owing to its heterogeneous clinical presentation, despite growing awareness.[1,3-5] Early diagnosis is critical to prevent long-term complications such as anaemia, osteoporosis, and intestinal lymphoma.[2,6]

The standard diagnostic approach for CeD relies on serologic markers such as anti-tissue transglutaminase (anti-tTG) and endomysial antibodies (EMAs), which are typically confirmed via duodenal biopsy.[7] However, serological tests may yield false-negative results in cases of IgA deficiency or early disease, and histological examination remains invasive and resource intensive.[4,8] Given the invasive nature of endoscopy and the variability in clinical presentation, there is a growing need for reliable, noninvasive biomarkers to aid in the early detection and monitoring of disease activity.[4] In this context, increasing attention is being given to the identification of accessible and cost-effective biomarkers that can support CeD diagnosis or risk stratification, particularly in low-resource or primary care settings.[9]

Recent studies have explored the utility of hematological indices derived from complete blood count (CBC) and basic metabolic panels in the context of inflammatory

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and autoimmune disorders.[10-12] Among these indices, the platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are considered indicators of systemic inflammatory burden, whereas the systemic immune-inflammation index (SII) has been associated with immune dysregulation in autoimmune diseases.[13,14]

The triglyceride-glucose (TyG) index, a surrogate marker of insulin resistance, has received increasing attention in studies of metabolic dysfunction and cardiometabolic risk.[15] Untreated patients with CeD often exhibit altered lipid profiles and a lower body-mass index (BMI), suggesting that TyG levels may reflect disease-related metabolic alterations.[16] Additionally, the haemoglobin–albumin–lymphocyte–platelet (HALP) score—initially proposed as a prognostic marker in oncology—integrates nutritional and inflammatory parameters and may be valuable in conditions such as CeD, which involves both immune and nutritional dysregulation.[13] These indices, which are derived from routine laboratory parameters, may offer a cost-effective and accessible means of evaluating systemic inflammation and nutritional status.

To date, previous studies have focused primarily on the predictive role of noninvasive markers in plasma or stool samples in patients with CeD.[17-19] However, many of these biomarkers are neither widely available nor inexpensive. Therefore, this study aimed to investigate the relationship between various indices—such as the PLR, TyG index, and HALP score—and the presence of biopsy-confirmed CeD, and to assess their potential usefulness as noninvasive, low-cost tools to aid early detection and risk stratification.

METHODS

Ethics

All procedures were conducted in accordance with the ethical standards of the institutional research committee and the principles of the Declaration of Helsinki. Owing to the retrospective nature of the study and the use of anonymized data, informed consent was not needed. Before data collection, ethical approval was obtained from the Batman Training and Research Hospital Scientific Researches ethics committee (Date: 25.06.2025, Decision No: 431).

Study Design and Population

This retrospective cross-sectional, observational study included 79 patients with biopsy-confirmed CeD and 60 age- and sex-matched healthy controls who were evaluated in the endocrinology and internal medicine outpatient clinics of a tertiary training and research hospital between January 2019 and October 2024. CeD diagnosis was based on serological tests (positive anti-tTG IgA antibodies) and confirmatory duodenal biopsy consistent with Marsh 2 or 3 lesions.[6] Fasting blood samples collected at the time of diagnosis were used to evaluate routine laboratory parameters in the celiac group. The control group consisted of individuals who presented for routine health check-ups. These participants had no known chronic diseases, medication use, or symptoms suggestive of CeD, and they were confirmed to be healthy following a comprehensive clinical assessment and standard laboratory investigations. herefore, as the study was retrospective and relied on data from routine health screenings, specific testing for anti-tTG or EMA was not performed in asymptomatic individuals.

Both in the patient and control groups, individuals with conditions or treatments known to significantly influence inflammatory or nutritional markers were excluded. These included: active infections (particularly gastrointestinal), chronic inflammatory or autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus), hematological or solid malignancies, recent blood transfusions or surgeries (within 3 months), pregnancy or lactation, severe malnutrition due to non-celiac causes, and the use of medications such as anti-inflammatory drugs, antibiotics, statins, antidiabetic agents, or intravenous iron therapy. Patients who were already on a gluten-free diet were also excluded, as all laboratory tests were conducted at the time of initial diagnosis. Additionally, any non-celiac causes of anemia, vitamin deficiencies, or malabsorption were carefully excluded based on clinical evaluation and laboratory findings. Thus, both groups were rigorously screened to minimize confounding factors that might affect PLR, TyG, or HALP values.

Data Collection and Calculation Indices and Scoring Systems

Demographic data (age, sex) and laboratory parameters were retrospectively extracted from the hospital electronic database. All laboratory analyses were conducted in the hospital's central biochemistry and hematology laboratories using the same standardized autoanalyzer systems throughout the study period (2019–2024), ensuring consistency in measurement. Hematological parameters were analyzed using the Sysmex XN-1000 (Sysmex Co., Kobe, Japan) automated hematology analyzer. Serum total cholesterol, triglycerides, HDL-C, and LDL-C levels were measured using a photometric method on the Abbott Architect c16000 autoanalyzer (Abbott Laboratories, IL, USA). Other biochemical parameters were assessed using a chemiluminescent spectrophotometric technique with a Beckman Coulter analyzer (Brea, CA, USA). Internal and external quality control procedures were routinely implemented to ensure analytical reliability and comparability across time.

The hematological and metabolic indices and scores included in the study were calculated via the following established formulas taken from the literature.[13,20-22]

1. Platelet–lymphocyte ratio (PLR): A marker of subclinical inflammation; a high PLR has been associated with autoimmune and inflammatory disorders.

PLR=Platelet count ($\times10^3$/μL)/lymphocyte count ($\times10^3$/μL)

2. The neutrophil–lymphocyte ratio (NLR): The NLR reflects systemic inflammation and has been used to assess disease activity in various autoimmune conditions.

NLR=Neutrophil count ($\times10^3$/μL)/lymphocyte count ($\times10^3$/μL)

3. Systemic immuno-inflammation index (SII): A composite index representing the immune-inflammation status.

SII=(neutrophil count (×10³/μL)×platelet count (×10³/μL))/ lymphocyte count (×10³/μL)

4. Triglyceride–glucose (TyG) index: TyG is a reliable proxy for insulin resistance and metabolic dysfunction.

TyG= Ln [fasting triglycerides (mg/dl)×fasting plasma glucose (mg (dl)/2)].

5. Hemoglobin-albumin-lymphocyte-platelet (HALP) score: Originally developed to assess prognosis in oncology, HALP also reflects nutritional and immunological status.

HALP=[Hemoglobin (g/L)×albumin (g/L)×lymphocyte count (×10³/μL)]/platelet count (×10³/μL).

6. Prognostic Nutrition Index (PNI): A well-established indicator of nutritional and immune status used in chronic diseases.

PNI=albumin (g/L)+5×lymphocyte count (×10³/μL)

7. The glucose–lymphocyte ratio (GLR): The GLR has been investigated as a marker of metabolic–inflammatory interactions.

GLR=Fasting glucose (mg/dl) lymphocyte count (×10³/μL).

8. Atherogenic index of plasma (AIP): The AIP reflects atherogenic lipid profiles and cardiovascular risk.

AIP=log(Triglycerides (mg/dl)/HDL cholesterol (mg/dl)).

Statistical Analysis

All the data analyses were performed via the IBM Statistical Package for the Social Sciences (SPSS), version 22. A normality assessment was conducted by evaluating the skewness and kurtosis values of all the variables, ensuring that they were within the acceptable range of -2--+2, thereby meeting the assumption of a normal distribution.[23] The data are presented as the means±standard deviations (SDs), frequencies, and percentages, as appropriate.

Comparisons between categorical variables were performed via the Chi-square test. For comparisons between two independent groups, the independent samples t test was used, as the normality assumption was satisfied. The relationships between continuous variables were assessed via Pearson correlation analysis. In multivariate analysis, potential risk factors identified in prior univariate tests were included in a logistic regression model (Backwards Conditional Model) to determine independent predictors of group membership. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of continuous variables and to determine optimal cut-off values. A p value <0.05 was considered to indicate statistical significance.

A post-hoc power analysis was conducted using G*power version 3.1.9.7 (Heinrich-Heine-University Düsseldorf, Germany). Based on the difference in HALP scores between the celiac (mean±SD: 0.408±0.216) and control (0.560±0.231) groups, the calculated effect size (Cohen's d) was 0.683. With a sample size of 79 and 60 for the respective groups, the post-hoc statistical power (1–β) was 97.7% (α = 0.05, two-tailed), indicating sufficient power to detect the observed effect.

RESULTS

A total of 139 participants were included in the study, comprising 79 patients and 60 healthy controls. Among the patients, 55 (69.6%) were female, whereas 42 (70%) of the controls were female. There was no significant difference in sex distribution between the patient and control groups (p>0.05). Comparative results of the demographic characteristics, laboratory parameters, and calculated indices and scores for the patient and control groups are presented in **Table 1**. There was no statistically significant difference between the groups in terms of age (p=0.413), fasting glucose level (p=0.081), serum albumin level (p=0.726), neutrophil count (p=0.173), lymphocyte count (p=0.264), TSH level (p=0.545), glucose–lymphocyte ratio (GLR; p=0.065), atherogenic index of plasma (AIP; p=0.244), neutrophil–lymphocyte ratio (NLR; p=0.763), prognostic nutritional index (PNI; p=0.315), or systemic immune–inflammation index (SII; p=0.103).

Table 1. Comparison of age and blood parameters between celiac patients and control groups

	Patient group n=79	Control group n=60		
	Mean±SD	Mean±SD	t	p
Age (year)	33.95±10	32.62±8.7	-0.822	0.413
Glucose (mg/dl)	91.51±7.86	89.15±7.80	-1.756	0.081
Albumin (g/dl)	4.26±0.42	4.25±0.40	0.351	0.726
Triglyceride (mg/dl)	76.35±31.31	92.67±32.61	2.998	0.003
HDL cholesterol (mg/dl)	49.24±12.15	55.10±15.16	2.529	0.013
Hemoglobin (g/dl)	11.6±2.4	13.69±1.59	6.126	<0.001
Hematocrit (%)	36.76±6.3	41.12±4.2	4.903	<0.001
Neutrophil (×10³/μL)	4070±1241	4368±1308	1.369	0.173
Lymphocyte (×10³/μL)	2233±664	2361±673	1.121	0.264
Platelet (×10³/μL)	304.53±95.34	262.08±60.25	-3.204	0.002
Folic asit (ng/ml)	5.18±2.69	7.71±2.27	5.845	<0.001
Vitamin B12 (pg/ml)	262.24±92.38	391.63±103.81	7.752	<0.001
TSH (mIU/L)	1.95±1.22	1.83±0.90	-0.607	0.545
GLR	89.27±7.81	86.79±7.75	-1.862	0.065
AIP	0.17±0.21	0.21±0.22	1169	0.244
NLR	1.92±0.68	1.96±0.77	0.302	0.763
PLR	145.19±56.67	117.68±37.44	-3.438	0.001
PNI	53.73±5.0	54.62±5.3	1.009	0.315
SII	577.34±254.36	509.88±219.63	-1.641	0.103
TyG	8.08±0.40	8.26±0.36	2.785	0.006
HALP	0.408±0.216	0.560±0.231	3.957	<0.001

Data are presented as the mean±standard deviation (SD). Statistical comparisons were performed via independent samples t tests. p<0.05 was considered statistically significant. Abbreviations: HDL: High-density lipoprotein, TSH: Thyroid-stimulating hormone, GLR: Glucose–lymphocyte ratio, AIP: Atherogenic index of plasma, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet–lymphocyte ratio, PNI: Prognostic nutritional index, SII: Systemic immune–inflammation index, TyG: Triglyceride–glucose index, HALP: Hemoglobin, albumin, lymphocyte, and platelet scores

Compared with controls, celiac patients had significantly lower levels of triglycerides (p=0.003), HDL cholesterol (p=0.013), hemoglobin (p<0.001), hematocrit (p<0.001), triglyceride–glucose index (TyG) (p=0.006), and HALP score (p<0.001). Additionally, as expected, they presented significantly lower levels of folic acid (p<0.001) and vitamin B12 (p<0.001). In contrast, the PLT (p=0.002) and PLR

(p=0.001) were significantly greater in the celiac group than in the control group.

A sex-based comparison was conducted within the patient group (**Table 2**). Although certain parameters were similar between male and female patients, significant differences were observed among the other patients. Among the celiac patients (n=79), 24 were male and 55 were female. There was no significant difference in age between the sexes (p=0.966). However, several biochemical parameters exhibited statistically significant sex-related differences.

Table 2. Relationships between blood parameters and sex in the patient groups

	Male n=24	Female n=55	t	p
	Mean±SD	Mean±SD		
Age (year)	33.88±10.5	33.98±9.85	-0.043	0.966
Glucose (mg/dl)	88.75±8.40	92.71±7.37	-2.103	0.039
Albumin (g/dl)	4.41±0.38	4.19±0.42	2.221	0.029
Triglyceride (mg/dl)	83.8±34.77	73.1±29.42	1.403	0.165
HDL cholesterol (mg/dl)	43.33±11.58	51.82±11.57	-2.997	0.004
Hemoglobin (g/dl)	13.8±2.5	10.6±1.65	6.649	<0.001
Hematocrite (%)	42.68±6.1	34.18±4.4	7006	<0.001
Neutrophil ($\times10^3$/μL)	4275±1251	3980±1239	0.973	0.334
Lymphocyte ($\times10^3$/μL)	2446±809	2140±574	1.678	0.103
Platelet ($\times10^3$/μL)	271.58±93.39	318.91±93.39	-2.071	0.042
Folic asit (ng/ml)	5.12±2.99	5.21±2.58	-0.144	0.886
Vitamin B12 (pg/ml)	254.92±101.15	265.44±89.07	-0.463	0.645
TSH (mIU/L)	2.31±0.94	1.8±1.3	1.756	0.083
GLR	86.30±8.45	90.56±7.22	-2.290	0.025
AIP	0.27±0.19	0.13±0.21	2894	0.006
NLR	1.81±0.39	1.97±0.78	-1.207	0.231
PLR	116.05±36.51	157.90±59.40	-3.192	0.002
PNI	56.35±5.0	52.59±4.6	3.116	0.003
SII	484.46±174.45	617.87±273.83	-2.196	0.031
TyG	8.15±0.40	8.05±0.39	0.980	0.330
HALP	0.588±0.23	0.329±0.155	4.992	<0.001

Data are presented as the mean±standard deviation (SD). Comparisons between sexes were made via independent samples t tests. p<0.05 was considered statistically significant. Abbreviations: HDL: High-density lipoprotein, TSH: Thyroid-stimulating hormone, GLR: Glucose–lymphocyte ratio, AIP: Atherogenic index of plasma, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, PNI: Prognostic nutritional index, SII: Systemic immune-inflammation index, TyG: Triglyceride-glucose index, HALP: Hemoglobin, albumin, lymphocyte, and platelet scores

Compared with males, females had significantly higher levels of glucose (p=0.039), high-density lipoprotein (HDL) cholesterol (p=0.004), and platelet count (p=0.042) but lower levels of albumin (p=0.029), hemoglobin (p<0.001), and hematocrit (p<0.001).

Additionally, females had higher GLRs (p=0.025), PLRs (p=0.002), and SIIs (p=0.031), indicating enhanced systemic inflammatory responses. Conversely, males had higher HALP scores (p<0.001) and PNI values (p=0.003), reflecting better nutritional-inflammatory status.

Other parameters, including triglycerides, lymphocyte and neutrophil counts, folic acid, vitamin B12, TSH, the NLR, TyG, and the AIP, showed no significant sex-related differences (p>0.05).

In the patient group, age was moderately positively correlated with glucose (r=0.270, p=0.016), triglycerides (r=0.242, p=0.032), and the TyG index (r=0.254, p=0.022) and moderately negatively correlated with albumin (r=-0.248, p=0.028). No significant correlations were found between age and the PAI, PLR, NLR, SII, PINI, or HALP score (p>0.05).

Risk factors for CeD among the participants were evaluated using logistic regression analysis (Backward Conditional Model). In the model, CeD was defined as the dependent variable, while age, sex, TyG index, and HALP score were included as independent variables. Due to a strong correlation between the HALP score and the PLR, PLR was excluded from the model to avoid multicollinearity. According to the analysis, sex (OR: 0.271, 95% CI [0.098, 0.751]), TyG index (OR: 0.248, 95% CI [0.090, 0.685]), and HALP score (OR: 0.013, 95% CI [0.001, 0.108]) were identified as significant risk factors for CeD (**Table 3**).

To further assess the diagnostic utility of the PLR, TyG index, and HALP score in predicting CeD, ROC analysis was conducted. The results indicated that the PLR (AUC±SE: 0.641±0.047; 95% CI: 0.550–0.733), TyG score (AUC±SE: 0.643±0.047; 95% CI: 0.551–0.736), and HALP score (AUC±SE: 0.697±0.044; 95% CI: 0.611–0.783) had moderate discriminatory power for predicting CeD. A higher PLR and lower TyG and HALP scores were associated with an increased likelihood of CeD. The optimal cut-off values for predicting CeD were 138 for the PLR (sensitivity: 53.2%, specificity: 76.7%), 8.21 for TyG (sensitivity: 68.4%, specificity: 63.3%), and 0.47 for the HALP score (sensitivity: 67.1%, specificity: 63.3%) (**Table 4, Figure**).

DISCUSSION

In this study, we investigated the associations between several hematological and metabolic indices and the presence of CeD. Our findings demonstrate that TyG and HALP are independently associated with CeD and may serve as predictive markers in clinical practice.

Logistic regression analysis revealed that a lower TyG index and lower HALP score were independent risk factors for CeD. These findings are particularly notable given the emerging role of TyG as a surrogate marker for insulin resistance and metabolic dysfunction. Given that untreated CeD is often associated with malabsorption and reduced BMI, a lower prevalence of insulin resistance may be expected, which could partially explain the inverse association observed in our study.

The HALP score, a composite index reflecting both nutritional and inflammatory status, was also significantly lower in celiac patients. This finding aligns with well-established features of CeD, including chronic inflammation, anaemia, hypoalbuminemia, and lymphocytic activation due to autoimmune mucosal injury.[24] Our data support the clinical relevance of HALP as a noninvasive marker reflecting both systemic inflammation and nutritional compromise in untreated patients with CeD.

Table 3. Risk factors for celiac disease—logistic regression (backwards conditional model)

Risk factors		B	S.E.	p	Exp (B)	95% C.I.for EXP (B)	
						Lower	Upper
Step1[a]	Age	0.032	0.021	0.140	1.032	0.990	1.077
	Gender (1)	-1.321	0.528	0.012	0.267	0.095	0.751
	TyG	-1.614	0.550	0.003	0.199	0.068	0.585
	HALP	-4.451	1.112	0.000	0.012	0.001	0.103
	Constant	14.817	4.473	0.001	2721191.30		
Step 2[a]	Gender (1)	-1.305	0.520	0.012	0.271	0.098	0.751
	TyG	-1.395	0.519	0.007	0.248	0.090	0.685
	HALP	-4.381	1.099	0.000	0.013	0.001	0.108
	Constant	11.599	4.110	0.005	108934.68		

p<0.05: statistical significance level; Gender (1): Female. TyG: Triglyceride–glucose index, HALP score: Haemoglobin albumin/platelet score; B: Regression coefficient, S.E.: Standard error, Exp (B): Odds ratio, 95% CI for Exp (B): 95% confidence interval for the odds ratio, Step 1a: Initial model including all candidate variables identified for inclusion in the logistic regression, Step 2a: Final model retained after backwards elimination of nonsignificant variables on the basis of likelihood ratio tests

Table 4. Area under the curve

Test result variable (s)		Area	Std. error[a]	Asymptotic Sig.[b]	Asymptotic 95% confidence interval	
					Lower bound	Upper bound
Patient group-control group	PLR	0.641	0.047	0.004	0.550	0.733
	TyG	0.643	0.047	0.004	0.551	0.736
	HALP	0.697	0.044	0.000	0.611	0.783

p<0.05: statistical significance level, a. Under the nonparametric assumption, b. Null hypothesis: true area =0.5. Abbreviations: PLR: Platelet–lymphocyte ratio, TyG: Triglyceride–glucose index, HALP:Hemoglobin, albumin, lymphocyte, and platelet score

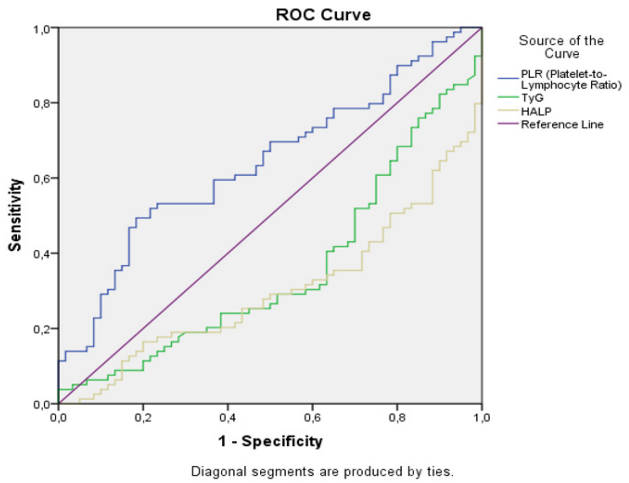

Figure. ROC curve analysis for the PLR, TyG score and HALP score (patient group-control group) PLR (cut-off value 138, sensitivity 53.2%, specificity 76.7%); TyG (cut-off value 8.21, sensitivity 68.4%, specificity 63.3%); HALP score (cut-off value 0.47, sensitivity 67.1%, specificity 63.3%).

PLR: Platelet-to-lymphocyte ratio, TyG: Triglyceride–glucose index, HALP: Hemoglobin, albumin, lymphocyte, and platelet score

The PLR was greater in celiac patients, which is consistent with prior reports suggesting that platelet activation and relative lymphopenia reflect systemic immune dysregulation in autoimmune diseases.[25-28] Although the PLR was not identified as an independent risk factor in the multivariate analysis, its moderate AUC (0.641) in the ROC analysis indicates potential utility in combination with other markers.

ROC analysis further validated the predictive capacity of all three indices. The HALP score demonstrated the highest discriminative ability (AUC: 0.697), followed by TyG (AUC: 0.643) and PLR (AUC: 0.641). These findings suggest that while no single index achieves high diagnostic accuracy, a panel approach that integrates these metrics may enhance the early identification of CeD in at-risk populations. Notably, the HALP cut-off value of 0.47 showed moderate sensitivity (67.1%) and specificity (63.3%), supporting its clinical applicability as a screening tool, particularly in settings with limited access to serologic or endoscopic resources.

Interestingly, our results also highlight sex-based differences in several of these indices within the celiac group, with females exhibiting higher PLRs and SIIs and lower HALP scores. These differences may reflect both hormonal influences on the immune response and differential disease manifestations between sexes. As is well established in the literature, CeD exhibits a female predominance, with a significantly higher prevalence observed in women than in men.[29,30] Further investigations are warranted to explore whether sex-specific cut-off values improve diagnostic performance.

Although our findings suggest that the TyG index, and HALP score may serve as adjunctive tools in identifying patients with CeD, their clinical applicability warrants cautious interpretation. The cut-off values identified in this study (e.g., HALP<0.47, TyG<8.21, PLR>138) showed only moderate sensitivity and specificity, which limits their standalone diagnostic value. Moreover, these scores can be influenced by various modifying factors—including acute infections, comorbid inflammatory or metabolic conditions, and

medication use—which may complicate their interpretation in heterogeneous clinical populations.

Compared with current diagnostic standards such as anti-tTG and EMA serology combined with duodenal biopsy, these indices lack disease specificity and cannot replace established methods. However, their noninvasive, cost-effective nature and wide availability make them attractive candidates for use in resource-limited settings or as preliminary screening tools before more invasive or costly testing is pursued.

In clinical decision-making, such indices should not be used in isolation but rather as part of an integrated assessment that considers patient history, symptoms, and standard serologic testing. Our study is cross-sectional in design, limiting causal inference. Additionally, all patients were evaluated at the time of initial diagnosis and had not yet initiated a gluten-free diet; therefore, the potential modifying effect of dietary adherence was not relevant in our cohort. However, future longitudinal studies are warranted to investigate whether these indices change in response to gluten-free diet adherence and whether they correlate with disease duration or treatment response over time. Such studies will be essential in determining whether these indices can meaningfully support clinical decisions in real-world practice.

Limitations

Another limitation of our study is the absence of BMI data, which were not consistently available in the electronic medical records due to the retrospective design. As BMI is known to influence metabolic and inflammatory parameters, its omission may have introduced residual confounding, particularly in the interpretation of the TyG index and HALP score. Future studies with comprehensive anthropometric data are warranted to confirm these associations.

CONCLUSION

As a result, this study identified low TyG and HALP scores as independent risk factors for CeD and supported the utility of the TyG and HALP as potential adjunctive tools for disease prediction. These noninvasive, inexpensive, and easily obtainable indices may offer valuable support for early diagnosis and risk stratification, particularly in resource-limited settings.

ETHICAL DECLARATIONS

Ethics Committee Approval

Before data collection, ethical approval was obtained from the Batman Training and Research Hospital Scientific Researches ethics committee (Date: 25.06.2025, Decision No: 431).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

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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