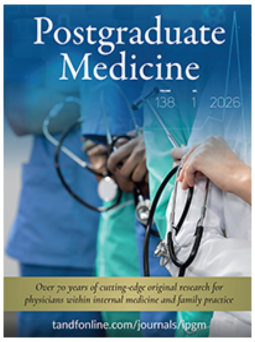

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Postgraduate Medicine

ISSN: 0032-5481 (Print) 1941-9260 (Online) Journal homepage: www.tandfonline.com/journals/ipgm20

Association between Hashimoto’s thyroiditis and hemoglobin-albumin-lymphocyte-platelet score and systemic inflammatory index: a nationwide cohort study

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POSTGRADUATE MEDICINE
2026, VOL. 138, NO. 1, 63–70
https://doi.org/10.1080/00325481.2026.2621575

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ORIGINAL RESEARCH

Association between Hashimoto's thyroiditis and hemoglobin-albumin-lymphocyte-platelet score and systemic inflammatory index: a nationwide cohort study

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ABSTRACT

Objectives: Hashimoto's thyroiditis (HT) is a T-cell mediated autoimmune disease characterized by the progressive destruction of thyroid gland. Hemoglobin-Albumin-Lymphocyte-Platelet (HALP) score and systemic inflammatory index (SII) are novel markers of inflammation. We aimed to compare HALP score and SII values of patients with HT to those in healthy control subjects in the present study.
Methods: Patients diagnosed with HT and healthy volunteers (as controls) were included in the study. The SII and HALP score were calculated using the following formulas: SII = (Platelet count×Neutrophil count)/Lymphocyte count. HALP score = (Hemoglobin×Serum Albumin×Lymphocyte count)/Platelet count. SII and HALP score of patients with HT and healthy controls were compared.
Results: Median SII of the patients with HT (510 (140–3646)) was significantly higher than that of the control subjects (422 (102–2173)) ($p < 0.001$). Median HALP score of the HT group (47 (7–149)) was significantly lower than that of the control group (54 (10–160)) ($p < 0.001$). The sensitivity and specificity of SII (when higher than 452%) in detecting HT were 61% and 62%, respectively (AUC: 0.64, $p < 0.001$, 95%CI: 0.61–0.67). A HALP score lower than 49.5% threshold had 64% sensitivity and 57% specificity in detecting HT (AUC: 0.61, $p < 0.001$, 95%CI: 0.57–0.64). In logistic regression analysis (considering age, gender, eGFR, TSH, CRP, ESR, BMI), a unit increase in SII increased the risk of HT by 0.3% ($p < 0.001$, OR: 1.003, 95%CI: 1.002–1.004). HALP score was also an independent risk factor for HT. A unit increase in HALP score decreased the risk of HT by 2% ($p < 0.001$, OR: 0.977, 95%CI: 0.968–0.985).
Conclusion: We recommend that, due to their inexpensive and easily assessable nature, SII and HALP score could serve as additional diagnostic tools in HT.

ARTICLE HISTORY
Received 28 August 2025
Accepted 14 January 2026

KEYWORDS
Hashimoto's thyroiditis; inflammation; hemoglobin-Albumin-Lymphocyte-Platelet score; systemic inflammatory index; diagnosis

Introduction

Hashimoto's thyroiditis (HT), also known as chronic autoimmune thyroiditis or chronic lymphocytic thyroiditis, is a T-cell mediated autoimmune disease characterized by the progressive destruction of thyroid follicular cells via both cellular and antibody-mediated immune mechanisms. The disease was described in 1912 as 'struma lymphomatosa' by Haruto Hashimoto, and in 1956, it was recognized as having an autoimmune origin [1]. Currently, HT stands as the most common cause of hypothyroidism in iodine-sufficient, developed regions [2]. The prevalence of HT in adults ranges between 5% and 10%, though some territories report rates above 20% or below 0.5% [3]. A recent meta-analysis estimated an average prevalence of 7.5%, with 17.5% in women versus 6% in men [4]. The disease disproportionately affects women, with a female-to-male ratio ranging from 7/1 up to 10/1 [5]. HT usually presents between ages 30–50 or 45–55, but can occur at any age. Environmental and epigenetic factors, such as iodine intake, hygiene hypothesis, microbiome composition, and X-chromosome inactivation, interact with genetic susceptibility in the pathogenesis of HT [5,6]. Immunologically, the disease involves both humoral and cellular processes. Key features include, lymphocytic infiltration of the thyroid gland, production of autoantibodies; notably anti-thyroid peroxidase (TPO) and anti-thyroglobulin (Tg) antibodies, seen in most patients [3], and an imbalance in T-cell subsets, including Th17 upregulation and Treg dysfunction, with increased cytokine-mediated inflammation leading to tissue destruction and fibrosis [7]. Patients may be euthyroid, exhibit subclinical hypothyroidism, or progress to overt hypothyroidism. A transient hyperthyroid phase (Hashitoxicosis) may occur, often early in the course [8]. Histologically, the gland shows lymphocytic infiltration, follicular destruction, possible Hurthle cell change, and progressive fibrosis [2].

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The Hemoglobin, Albumin, Lymphocyte, Platelet(HALP) score is a composite immunonutritional biomarker derived from four routinely assessed laboratory indices. It was originally introduced in 2015 for evaluating prognosis in gastric carcinoma patients [9]. Patients with high HALP score had low mortality and recurrent stroke risk according to Tian et al.'s study [10]. Moreover, decreased levels of HALP score have been linked to increased risk of cardiovascular and all-cause mortality [11]. It is also linked to infectious conditions. For instance, HALP score has been reported to be associated with mortality in patients with sepsis [12]. All of these conditions are characterized with some degree of inflammatory burden, as HT is.

Another novel inflammation marker is systemic immune inflammation index (SII) which has been reported to be associated with various inflammatory conditions such as cancer [13], cerebrovascular disease [14], and type 2 diabetes mellitus [15]. Alike HT, these conditions are characterized with chronic inflammation.

Associations between HT and inflammatory markers have been reported in recent years. Elevated neutrophil-to-lymphocyte ratio [16], pan-immune inflammation index [17], C-reactive protein [18], DeRitis score [19], erythrocyte distribution width [20], and reactive oxygen metabolites [21] are among those inflammatory markers that associated with HT.

To the best of our knowledge, HALP score and SII have not been studied together in patients with HT. Thus, in present multi-center study, we aimed to compare SII and HALP score levels of the patients with HT to those in healthy controls.

Materials and methods

Design, setting and study population

The present retrospective, observational study included patients with HT diagnosed between January 2024 and January 2025 in the internal medicine outpatient clinics of 11 centers, including Bolu Abant Izzet Baysal University, Hacettepe University, Istanbul University Cerrahpasa, Balikesir University, Adnan Menderes University, Kayseri City Hospital, Osmangazi University, Samsun University, Yuzuncu Yil University, Bilkent City Hospital, and Ankara University. All of the centers participated in this work are tertiary referral hospitals. Study protocol was approved by Abant Izzet Baysal University Ethics Committee (date: 6^{th} of February, 2024; approval no: 2024/13). Written informed consent was obtained from all participants. 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 excluded from the study. Patients with active or recent (within 30 days) infectious or inflammatory conditions were not included. Diagnosis of HT was established based on clinical, laboratory and imaging characteristics of the subjects. The control group consisted of patients who presented to our clinics for routine checkups between January 2024 and January 2025 and were determined to be healthy based on the evaluation.

Laboratory analyses

Data such as age, gender, height, body weight, systolic and diastolic blood pressures, leukocyte count (WBC), neutrophil count (neu), lymphocyte count (lym), hemoglobin (Hb), hematocrit (Htc), platelet count (Plt), aspartate (AST) and alanine (ALT) transaminases, blood urea, serum creatinine, estimated glomerular filtration rate (eGFR), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), total serum protein, serum albumin, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, thyroid stimulant hormone (TSH), and free thyroxine (FT4) levels were recorded from the patients' files. Body mass index (BMI) was calculated with division of body weight in kg by the square of height in meters. The SII was calculated using the formula: (Platelet count×Neutrophil count)/Lymphocyte count. The HALP score was determined using the formula: (Hemoglobin×Serum Albumin×Lymphocyte count)/Platelet count. Data of the patients with HT and control subjects were compared.

Statistical analyses

The data were analyzed using the SPSS statistical software (SPSS 16.0 for Windows, IBM Inc., Chicago, Illinois, U.S.A.). The Kolmogorov–Smirnov test was used to assess whether variables fit into normal distribution. Categorical variables were compared using the chi-square test and expressed as n, %. 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 ROC (Receiver Operating Characteristic) curve analysis. Binary logistic regression analysis was used to find out whether SII and HALP score were independent risk factor for HT (adjusted for age, gender, eGFR, TSH, CRP, ESR, BMI). A p-value of <0.05 was considered statistically significant.

Results

A total of 1549 individuals; 1269 patients with HT and 280 control subjects were enrolled to the study. Median ages of the HT and control groups were 43 (18–95) years and 39 (20–59) years, respectively ($p < 0.001$). 919 (72%) of HT group and 220 (79%) of control subjects were women ($p = 0.04$). Table 1 shows general characteristics and anthropometric measures of HT and control subjects.

Median WBC ($p = 0.32$), neu ($p = 0.11$), lym ($p = 0.81$), AST ($p = 0.62$), ALT ($p = 0.1$), blood urea ($p = 0.42$), HDL-cholesterol ($p = 0.95$), systolic ($p = 0.42$), and diastolic ($p = 0.053$) blood pressures were not statistically different between HT and control groups. Median Hb ($p < 0.001$), Htc ($p < 0.001$), Plt ($p < 0.001$), serum creatinine ($p < 0.001$), eGFR ($p = 0.002$), CRP ($p < 0.001$), ESR ($p < 0.001$), serum albumin ($p < 0.001$), triglyceride ($p < 0.001$), total cholesterol ($p < 0.001$), LDL-cholesterol ($p < 0.001$), height ($p < 0.001$), body weight ($p < 0.001$), BMI

Table 1. General characteristics and anthropometric measures of HT and control groups.

		HT group	Control group	p
Gender	Men (n,%)	350 (28%)	60 (21%)	0.04
	Women (n,%)	919 (72%)	220 (79%)	
		Median (min.-max.)		
Age (years)		43 (18–95)	39 (20–59)	<0.001
Height (m)		1.63 (1.2–1.9)	1.65 (1.4–1.95)	<0.001
Body weight (kg)		78 (38–150)	70 (43–115)	<0.001
BMI (kg/m^2)		29.3 (14.2–51.3)	25.5 (16.3–44.9)	<0.001
Systolic blood pressure (mm Hg)		120 (80–200)	120 (90–140)	0.42
Diastolic blood pressure (mm Hg)		75 (45–108)	80 (50–90)	0.053

Table 2. Laboratory data of HT and control groups.

	HT group	Control group	p
	Median (min.-max.)		
WBC (k/mm^3)	7 (3.28–10.6)	7.1 (4.3–10.7)	0.32
Neu (k/mm^3)	4 (2.1–9.5)	3.8 (1.7–7.4)	0.11
Lym (k/mm^3)	2.2 (0.46–5)	2.2 (0.7–4.7)	0.81
Hb (g/dL)	13.3 (8–17.8)	13.8 (12.1–18.9)	<0.001
Htc (%)	40.1 (27–53)	41.2 (36–55)	<0.001
Plt (k/mm^3)	273 (117–583)	245 (153–503)	<0.001
AST (U/L)	19 (16–161)	17 (16–57)	0.62
ALT (U/L)	17 (12–100)	19 (16–51)	0.1
Blood urea (mg/dL)	20 (2–109)	22 (11–64)	0.42
Serum Creatinine (mg/dL)	0.71 (0.3–6)	0.67 (0.21–1.1)	<0.001
eGFR (%)	94 (7–1459	99 (65–126)	0.002
CRP (mg/L)	3.5 (0.1–125)	0.4 (0.1–34)	<0.001
ESR (mm/h)	19 (1–71)	14 (4–25)	<0.001
Serum albumin (g/dL)	4.6 (2.1–5.4)	4.8 (4.1–5.6)	<0.001
Triglyceride (mg/dL)	133 (12–926)	95 (31–455)	<0.001
Total cholesterol (mg/dL)	194 (24–421)	179 (113–324)	<0.001
LDL-cholesterol (mg/dL)	118 (14–278)	107 (40–242)	<0.001
HDL-cholesterol (mg/dL)	53 (13–190)	51 (28–103)	0.95
TSH (uIU/mL)	3.21 (0.1–128)	1.35 (0.4–4.1)	<0.001
FT4 (ng/dL)	1.1 (0.2–9.9)	0.97 (0.7–1.7)	<0.001
SII (%)	510 (140–3646)	422 (102–2173)	<0.001
HALP (%)	47 (7–149)	54 (10–160)	<0.001

($p < 0.001$), TSH ($p < 0.001$), and FT4 ($p < 0.001$) levels were significantly different among HT and control groups. Table 2 summarizes the laboratory data of the HT and control cohorts.

Median SII of the patients with HT (510 (140–3646)%) was significantly higher than that of the control subjects (422 (-102–2173)%) ($p < 0.001$). Median HALP score of the HT group (47 (7–149)%) was significantly lower than that of the control group (54 (10–160)%) ($p < 0.001$).

Correlation analyses revealed that SII was positively correlated with TSH (r: 0.12, $p < 0.001$), CRP (r: 0.12, $p < 0.001$), BMI, (r: 0.1, $p < 0.001$), and eGFR (r: 0.1, $p = 0.01$). HALP score was inversely correlated with TSH (r: −0.1, $p = 0.003$), and CRP (r: −0.1, $p = 0.04$). Moreover, there was a strong inverse correlation between SII and HALP score (r: −0.59, $p < 0.001$). In addition, there was a weak inverse correlation between HALP score and anti-TPO levels in subjects with HT ($r = -0.1$, $p = 0.01$).

The sensitivity and specificity of SII (when higher than 452%) in detecting HT were 61% and 62%, respectively (AUC: 0.64, $p < 0.001$, 95%CI: 0.61–0.67). Figure 1 shows the ROC curve of SII. A HALP score lower than 49.5% threshold had 64% sensitivity and 57% specificity in detecting HT (AUC: 0.61, $p < 0.001$, 95%CI: 0.57–0.64). Figure 2 shows the ROC curve of HALP score.

In logistic regression analysis (considering age, gender, eGFR, TSH, CRP, ESR, BMI), a unit increase in SII increased the risk of HT by 0.3% ($p < 0.001$, OR: 1.003, 95%CI: 1.002–1.004). HALP score was also an independent risk factor for HT. A unit increase in HALP score decreased the risk of HT by 2% ($p < 0.001$, OR: 0.977, 95%CI: 0.968–0.985).

Discussion

Striking findings of the present work include the following: (a) elevated SII and decreased HALP score were associated with HT; (b) despite weak, there was positive correlations between SII and TSH, eGFR, CRP and BMI in the study cohort. Moreover, HALP score was inversely correlated with TSH and CRP; (c) both SII and HALP score had low sensitivity and specificity in detecting HT; (d) both SII and HALP score were independent risk factors for HT.

Present study showed significant association between HT and SII values. Similarly, SII has been reported to be linked to other inflammatory conditions. For example, authors studied 320 subjects and reported that SII was associated with the severity of pneumonia in the study cohort [22]. Another study observed 232 patients with ischemic stroke and found that SII was an independent risk factor for mortality in those patients [23]. In 2024, Ma et al. reported that elevated SII levels were independent risk factor for development of hypertension in 6003 subjects of study cohort [24]. Interestingly, SII was also

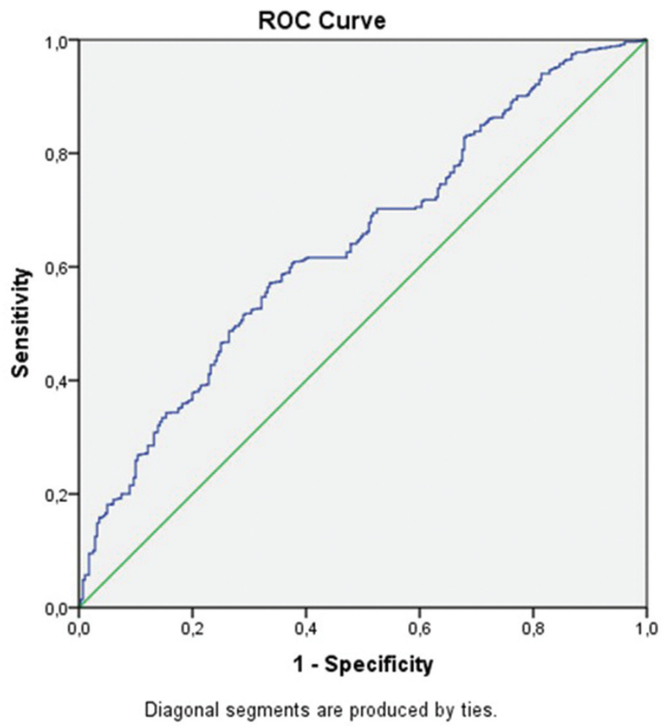

Figure 1. ROC curve of SII in detecting HT.

(SII (when higher than 452%) had 61% sensitivity and 62% specificity in detecting HT (AUC: 0.64, $p < 0.001$, 95%CI: 0.61–0.67)).

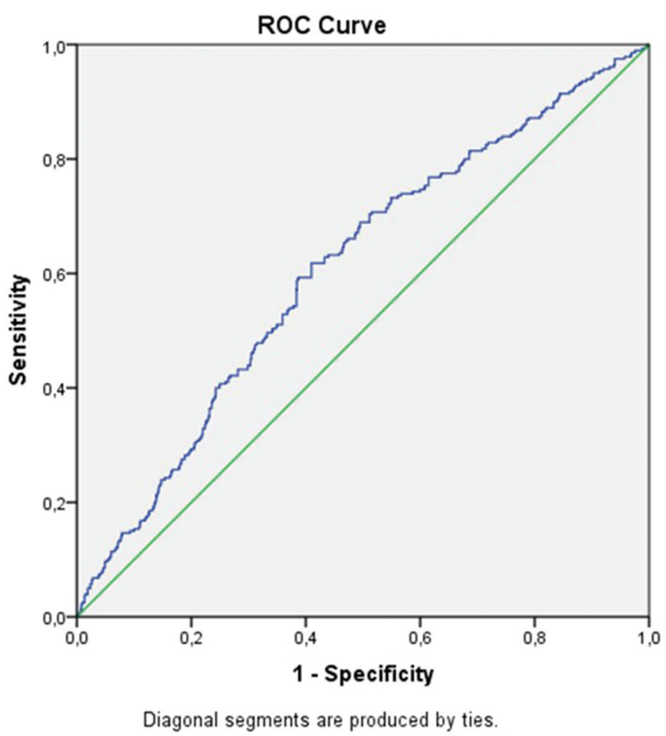

Figure 2. ROC curve of HALP score in detecting HT.

(HALP score (when lower than 49.5% cutoff value) had 64% sensitivity and 57% specificity in detecting HT (AUC: 0.61, $p < 0.001$, 95%CI: 0.57–0.64).

associated with diabetic kidney disease in patients with type 2 diabetes mellitus as reported in a study by Taslamacioglu Duman et al. [25]. All of type 2 diabetes mellitus, hypertension, ischemic stroke and pneumonia produce significant amount of inflammatory burden as HT does. Hence, association between SII and HT was not surprising.

Authors studied the association between HALP score and diabetic kidney injury in diabetes cohort and reported that decreased HALP score was linked to the development of diabetic kidney injury [26]. Another work included 2968 sepsis patients whom analyzed for the predictive value of HALP score in the participants in association with mortality and revealed that HALP score was independently predicted 28 day mortality in patients with sepsis [12]. A Chinese study analyzed HALP score in patients with IGA nephropathy and reported that HALP score was an independent risk factor for renal prognosis in those patients [27]. Moreover, Pan et al. found that elevated HALP score levels were associated with low risk of all cause and cardiovascular mortality in a cohort of 21,578 subjects [11]. In contrast, some other studies found no association between inflammation and HALP score. For instance, a retrospective observational cohort study reported that HALP score was not associated with mortality in patients with pulmonary thromboembolism [28]. HT is also characterized with inflammation as IgA nephropathy, diabetic kidney injury, sepsis and cardiovascular conditions. Accordingly, we reported decreased HALP score levels in patients with HT in the present study.

A study using NHANES data found significant links between SII and multiple thyroid parameters, specifically negative correlation with FT_3 and FT_3/FT_4, and positive with total T_4 [29]. Though TSH wasn't directly reported, this points to a broader inflammatory – thyroid axis. In line with literature, we reported significant positive correlation between TSH and SII levels while HALP score was negatively correlated with TS.

In type 2 diabetes mellitus patients, higher SII was associated with diabetic kidney disease, regardless of eGFR, suggesting SII may flag kidney involvement independent of glomerular filtration rate [30]. Moreover, in diabetic nephropathy, higher SII predicted elevated all-cause and cardiovascular mortality [31]. Accordingly, SII was positively correlated with estimated glomerular filtration rate in the present study.

While not always directly assessed together, inflammation markers like SII often correlate with obesity metrics. NHANES data on SIRI and SII found generally minimal correlation with baseline characteristics ($r < 0.15$) [32]. Similarly, we reported significant positive correlation between BMI, a widely used marker of obesity, and SII levels.

Less direct evidence exists linking HALP with TSH or CRP though a study noted that a one-unit increase in CRP was accompanied by a modest decline in HALP score [33]. The same study indicated that higher BMI corresponded with a decrease in HALP as well (0.1 unit drop per BMI increment) [33]. In addition, a study on HALP and diabetic nephropathy reported a slight positive correlation between HALP and eGFR [34]. Accordingly, HALP score was inversely correlated with TSH and CRP levels in the present study.

We also showed that there was a strong negative correlation between SII and HALP score. Direct studies exploring the inverse relationship between SII and HALP aren't evident in recent literature. However, mechanistically, SII and HALP represent opposing concepts; SII emphasizes inflammation (neutrophils, platelets, lymphocytes), while HALP adds nutritional and immunological context (hemoglobin, albumin, lymphocytes, platelets). It is plausible that higher systemic inflammation (SII) aligns with poorer nutritional/immunological status (lower HALP).

The positive SII – CRP and inverse HALP – CRP trends align with expectations from their construct. SII rises with inflammation and HALP drops. Relationships of SII with renal disease and mortality are well supported. BMI's gentle correlation with both markers reflects the inflammatory nature of obesity.

Recent thyroid studies showed that SII was elevated in patients with thyroid pathology and could discriminate disease subgroups with AUCs in the 0.64–0.75 range depending on population and endpoint (such as, distinguishing benign vs malignant thyroid disease or detecting inflammatory thyroid conditions). This places the SII's AUC (0.64) in present work squarely within published ranges; consistent but not exceptional performance [29,35]. HALP score has been reported and used across several clinical contexts including cancer, cerebrovascular disease, and nutritional disorders. Population studies identified a median HALP about 49% in broad samples and studies often find HALP thresholds around the high-40s to low-50s gave the best tradeoff between sensitivity and specificity for non-oncologic outcomes. That makes the HALP score cutoff (49.5%) in present work biologically and statistically plausible, and the AUC about 0.61 was consistent with HALP score acting as a weak-to-moderate discriminator in non-tumor settings [33,36].

Classic HT diagnostics (TPOAb, TgAb, ultrasound features) generally give AUCs and test characteristics that depend heavily on the population and gold standard used. For example, antibody tests and composite ultrasound/antibody scoring systems can reach AUCs ~0.65–0.72 in some cohorts. Scoring systems combining multiple features can boost specificity (sometimes at cost of sensitivity). The SII and HALP AUCs in the present study were comparable to single lab/ultrasound features reported in the literature, but do not outperform combined clinical/serologic/US models [37,38].

SII and HALP are calculated from routine hemogram and albumin/hemoglobin. These are cheap and widely available, so they are attractive as screening adjuncts in primary care or large cohorts where antibody testing/ultrasound for everyone is impractical. Moreover, SII captures systemic inflammation (by the counts of neutrophils, platelets, lymphocytes); HALP blends immune + nutritional status (hemoglobin, albumin, lymphocytes, platelets). Their different biology suggests they could be combined to improve discrimination, as we reported a strong inverse correlation between SII and HALP. This is consistent with opposing constructs. Furthermore, with sensitivities around 61–64%, these markers could select patients for further workup (antibodies, ultrasound) but probably would miss about 35–40% if used as single tests. We should note that, despite biological and statistical associations with HT, the diagnostic utility of SII and HALP is weak when used alone.

The AUCs of SII and HALP score in detecting HT was limited in the present work. So, many false positives and false negatives would occur if they used alone. Additionally, cutoff points are sample-dependent. Optimal threshold values vary with prevalence, lab methods, and patient mix (age, comorbidity, medications). The cutoffs of SII (452%) and HALP score (49.5%) may not be generalized to other centers without external validation [33,35]. Sensitivity and specificity of these parameters were stable, but positive and negative predictive values would change with HT prevalence in the tested population. Moreover, SII and HALP are influenced by infections, other autoimmune diseases, malignancy, nutritional status, anemia, CKD, and medications (steroids, immunosuppressants). Adjusting for these confounders is important before claiming disease specificity [39,40]. Accordingly, we excluded patients with cancer, end-stage renal failure, cirrhosis, infections, inflammatory conditions, or hematological malignancies, as well as those using medications that could affect hemogram parameters (e.g. corticosteroids). Moreover, we adjusted logistic regression analysis for age, gender, eGFR, BMI, CRP, ESR and TSH to prevent selection bias.

The thresholds for SII and HALP score in the present study produce modest but meaningful diagnostic performance. These findings align with recent literature data showing SII and HALP can discriminate disease states at a similar level, but they shouldn't replace antibody testing or ultrasound [19,29,33,37]. Their biggest value is likely as inexpensive screening/triage markers or as components of a combined diagnostic model.

Most studies on SII focus on mean differences or ROC performance rather than regression-based risk. For example, one study confirmed higher SII in HT patients but did not quantify the effect via logistic regression [41]. Cao et al. studied the association between SII and thyroid nodules in patients with diabetes mellitus and found that SII was an independent risk factor for thyroid nodules [40]. Another NHANES-based analysis explored continuous associations between SII and thyroid function parameters using linear regression, not logistic models [29]. Thus, our finding showing SII as an independent risk factor in a multivariable logistic model is novel and adds valuable data to the current medical literature.

HALP score has primarily been studied as a prognostic marker in cancer patients, not in autoimmune thyroid disease, and not in multivariable logistic models predicting HT. So our report has the novelty. SII is an independent risk factor for HT, even after adjusting for inflammation (CRP, ESR), thyroid function (TSH), renal function, and BMI. Moreover, HALP score has an independent protective association, for example, higher HALP score was associated with lower HT odds, again adjusting for key confounders. Despite ORs are close to 1, because SII and HALP are continuous measures, even small unit changes may accumulate. This finding suggests subtle but statistically robust associations between these markers and HT.

SII reflects immune activation/inflammation; its independent predictive value signals an inflammatory component to HT beyond just CRP/ESR. On the other hand, HALP score reflects nutritional and immune status, and might inversely capture the protective role of well general health or lower immune dysregulation. Thus, we emphasize that our findings in present study are among the first to quantify SII and HALP score's independent associations with HT via adjusted logistic regression.

We demonstrated several statistically significant but overall weak associations between inflammatory indices, thyroid function parameters, and systemic markers. SII showed a positive correlation with TSH, CRP, BMI, and eGFR. Although the correlation coefficients were small, these findings are biologically plausible and support the concept that SII reflects low-grade systemic inflammation rather than a disease-specific process. The positive association between SII and CRP reinforces its role as an inflammatory marker, while the correlation with BMI is consistent with the well-established link between adiposity and chronic low-grade inflammation. The weak positive correlation with TSH may reflect the inflammatory milieu accompanying autoimmune thyroid dysfunction, though it is unlikely to have independent clinical significance given the small effect size. Conversely, the HALP score demonstrated inverse correlations with TSH and CRP, suggesting that lower HALP values are associated with both heightened inflammatory status and greater thyroid dysfunction. Since HALP integrates hemoglobin, albumin, lymphocyte count, and platelet count, a lower score may reflect the combined effects of inflammation, immune dysregulation, and nutritional or metabolic alterations, all of which can be present in autoimmune conditions such as HT. The inverse relationship with CRP further supports the sensitivity of HALP score to systemic inflammatory burden. Additionally, the weak inverse correlation between HALP score and anti-TPO levels in patients with HT suggests a potential link between autoimmune activity and declining immunonutritional status. However, the modest correlation coefficient indicates that HALP is only minimally influenced by thyroid-specific autoimmunity and is more reflective of generalized systemic processes. This supports the notion that HALP, similar to SII, should not be interpreted as a direct surrogate of autoimmune antibody burden. Overall, these correlations are statistically significant, but their weak magnitude highlights an important limitation. SII and HALP are nonspecific markers that reflect systemic inflammation and immune – nutritional status rather than robust indicators of HT severity or autoimmunity. These findings reinforce that such indices may provide complementary information within a broader clinical and biochemical context but lack sufficient strength to serve as independent or disease-specific diagnostic or prognostic tools alone.

Indeed, in routine clinical settings, HT can often be diagnosed with high sensitivity and specificity using standard serological tests, which are relatively inexpensive and widely available. However, the rationale of our study was not to replace established diagnostic methods but to explore a potential adjunctive marker that may provide additional clinical value in specific situations. These include patients with early or atypical disease, seronegative HT, or cases with discordant clinical, biochemical, and ultrasonographic findings, in which diagnosis may still be challenging. In such scenarios, supplementary parameters may contribute to improved diagnostic confidence. Moreover, blood-based diagnostic costs and accessibility can vary across healthcare systems and regions. Identifying additional, easily obtainable, and low-cost parameters derived from routine laboratory tests may still have practical significance, particularly in large-scale screening settings or resource-limited environments. Both SII and HALP scores can be obtained by a drawing a tube of blood, too.

Retrospective and observational design of the present work is another limitation preventing expression of causal relationships instead of simple associations. Relying primarily on comparative analyses is another limitation, so causal inferences cannot be drawn from the current design. Therefore, study findings should be interpreted cautiously. Lack of comparison of thyroid antibody across study groups was another limitation of this work. Antibody data were available for patients with HT but control subjects had no such data. So we couldn't compare them between study and control groups. As a final limitation, we have to state that the diagnostic benefit of HALP and SII were only modest. However, the large cohort from multiple medical centers makes our findings important and valuable for the current literature.

Conclusion

In conclusion, due to their inexpensive and easily assessable nature, SII and HALP score could serve as adjunctive diagnostic tools in HT. Yet, prospective studies are needed to confirm their causal relationship with HT.

Declaration of financial/other relationships

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. No writing assistance was utilized in the production of this manuscript. Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Acknowledgments

Burcin Meryem Atak Tel–design, data curation, literature research, writing first draft. All authors agree to the final form of the manuscript. Irem Biçer-design, data curation, literature research. Isil Bavunoglu–design, data curation, methodology. Nur Duzen Oflas–design, data curation, methodology. Melisa Sahin Tekin–design, data curation, literature research. Hacer Sen–design, data curation, methodology. Ali Can Kurtipek–design, data curation, methodology. Gulali Aktas –design, methodology, statistical analyses, supervision, critical review of the manuscript. Oguz Abdullah Uyaroglu–design, data curation, methodology. Oguzhan Sitki Dizdar–design, data curation, methodology. Elif Duygu Topan–design, data curation, literature research. Pinar Yildiz–design, data curation, literature research. Ugur Kimyon–design, data curation, literature research. Ayse Kevser Demir–design, data curation, methodology. Hilal Bektas Uysal–design, data curation, methodology. Gulay Sain Guven–design, data curation, methodology, supervision. Sevil Uygun Ilikhan–design, data curation, methodology. Tuba Taslamacioglu Duman- design, data curation, writing first draft, Murat Ozdede–design, data curation, literature research. Ali Kirik–design, data curation, literature research. Selma Karaahmetoglu–design, data curation, methodology.

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Funding

No funding was received.

Data availability statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request. The study was a retrospective review of the medical records.

Ethics statement

This study was carried out in line with research regulations, including approval by the Abant Izzet Baysal University ethical committee (approval date: 6 February 2024, approval number: 2024/13). This study is in accordance to the principles of the 'World Medical Association Helsinki Declaration.'
Informed consent received from all participants in the study.

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References

1. Weetman AP. The immunopathogenesis of chronic autoimmune thyroiditis one century after hashimoto. Eur Thyroid J. 2013 Jan;1(4):243–250.
2. Ragusa F, Fallahi P, Elia G, et al. Hashimotos' thyroiditis: epidemiology, pathogenesis, clinic and therapy. Best Pract Res Clin Endocrinol Metab. 2019;33(6):101367. doi: 10.1016/j.beem.2019.101367
3. Vargas-Uricoechea H, Castellanos-Pinedo A, Urrego-Noguera K, et al. A scoping review on the prevalence of Hashimoto's thyroiditis and the possible associated factors. Med Sci (Basel). 2025;13(2):43. doi: 10.3390/medsci13020043
4. Hu X, Chen Y, Shen Y, et al. Global prevalence and epidemiological trends of Hashimoto's thyroiditis in adults: a systematic review and meta-analysis. Front Public Health. 2022;10:1020709. doi: 10.3389/fpubh.2022.1020709
5. Klubo-Gwiezdzinska J, Wartofsky L. Hashimoto thyroiditis: an evidence-based guide to etiology, diagnosis and treatment. Pol Arch Intern Med. 2022;132(3):16222.
6. Ajjan RA, Weetman AP. The pathogenesis of Hashimoto's thyroiditis: further developments in our understanding. Horm Metab Res. 2015;47(10):702–710. doi: 10.1055/s-0035-1548832
7. Pyzik A, Grywalska E, Matyjaszek-Matuszek B, et al. Immune disorders in Hashimoto's thyroiditis: what do we know so far? J Immunol Res. 2015;2015:1–8. doi: 10.1155/2015/979167
8. Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: clinical and diagnostic criteria. Autoimmun Rev. 2014;13(4–5):391–397. doi: 10.1016/j.autrev.2014.01.007
9. Chen XL, Xue L, Wang W, et al. Prognostic significance of the combination of preoperative hemoglobin, albumin, lymphocyte and platelet in patients with gastric carcinoma: a retrospective cohort study. Oncotarget. 2015;6(38):41370–41382. doi: 10.18632/oncotarget.5629
10. 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. doi: 10.3389/fneur.2020.610318
11. Pan H, Lin S. Association of hemoglobin, albumin, lymphocyte, and platelet score with risk of cerebrovascular, cardiovascular, and all-cause mortality in the general population: results from the NHANES 1999–2018. Front Endocrinol (Lausanne). 2023;14:1173399. doi: 10.3389/fendo.2023.1173399
12. Li H, Zhou Y, Zhang X, et al. The relationship between hemoglobin, albumin, lymphocyte, and platelet (HALP) score and 28-day mortality in patients with sepsis: a retrospective analysis of the MIMIC-IV database. BMC Infect Dis. 2025;25(1):333. doi: 10.1186/s12879-025-10739-3
13. Menyhart O, Fekete JT, Győrffy B. Inflammation and colorectal cancer: a meta-analysis of the prognostic significance of the systemic immune-inflammation index (SII) and the systemic inflammation response index (SIRI). Int J Mol Sci. 2024;25(15):8441. doi: 10.3390/ijms25158441
14. 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. Front Immunol. 2022;13:1090305. doi: 10.3389/fimmu.2022.1090305
15. Wang S, Pan X, Jia B, et al. Exploring the correlation between the systemic immune inflammation index (SII), systemic inflammatory response index (SIRI), and type 2 diabetic retinopathy. Diabetes Metab Syndr Obes. 2023;16:3827–3836. doi: 10.2147/DMSO.S437580
16. Aktas G, Sit M, Dikbas O, et al. Elevated neutrophil-to-lymphocyte ratio in the diagnosis of Hashimoto's thyroiditis. Rev Assoc Med Bras (1992). 2017;63(12):1065–1068.
17. Bozdag A, Gundogan Bozdag P. Evaluation of systemic inflammation markers in patients with Hashimoto's thyroiditis. J Int Med Res. 2024;52(9):3000605241280049. doi: 10.1177/03000605241280049
18. Demirkol ME, Aktas G. C-reactive protein to LymphocytE count ratio could be a reliable mArker of thyroiditis; the CLEAR-T study. Precis Med Sci. 2022;11(1):31–34. doi: 10.1002/prm2.12065
19. Duman TT, Erge E, Tel BMA, et al. De Ritis score as an inflammatory marker in Hashimoto's thyroiditis. Precis Med Sci. 2023;12(4):242–246. doi: 10.1002/prm2.12114

20. Aktas G, Sit M, Dikbas O, et al. Could red cell distribution width be a marker in Hashimoto's thyroiditis? Exp Clin Endocrinol Diabetes. 2014;122(10):572–574. doi: 10.1055/s-0034-1383564
21. Ruggeri RM, Vicchio TM, Cristani M, et al. Oxidative stress and advanced glycation end products in Hashimoto's thyroiditis. Thyroid. 2016;26(4):504–511. doi: 10.1089/thy.2015.0592
22. Wang RH, Wen WX, Jiang ZP, et al. The clinical value of neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII), platelet-to-lymphocyte ratio (PLR) and systemic inflammation response index (SIRI) for predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Front Immunol. 2023;14:1115031. doi: 10.3389/fimmu.2023.1115031
23. Ma F, Li L, Xu L, et al. The relationship between systemic inflammation index, systemic immune-inflammatory index, and inflammatory prognostic index and 90-day outcomes in acute ischemic stroke patients treated with intravenous thrombolysis. J Neuroinflammation. 2023;20(1):220. doi: 10.1186/s12974-023-02890-y
24. Ma LL, Xiao HB, Zhang J, et al. Association between systemic immune inflammatory/inflammatory response index and hypertension: a cohort study of functional community. Nutr Metab Cardiovasc Dis. 2024;34(2):334–342. doi: 10.1016/j.numecd.2023.09.025
25. 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). doi: 10.3390/diagnostics13122063
26. Tel BMA, Tel MR, Bilgin S, et al. Diagnostic value of HALP score in detecting diabetic nephropathy in patients with type 2 diabetes mellitus. Ibnosina J Med Biomed Sci. 2024;16(3):116–122. doi: 10.1055/s-0044-1787998
27. Yuan Y, Liang X, He M, et al. Haemoglobin, albumin, lymphocyte, and platelet score as an independent predictor for renal prognosis in IgA nephropathy. Front Endocrinol (Lausanne). 2024;15:1339921. doi: 10.3389/fendo.2024.1339921
28. Yaman M, Orak M, Durgun HM, et al. The prognostic value of HALP score and sPESI in predicting in-hospital mortality in patients with pulmonary thromboembolism. Postgrad Med J. 2024;101(1191):60–65. doi: 10.1093/postmj/qgae124
29. Hu XY, Liang YC, Zhang HH, et al. Association between the systemic immune-inflammation index and thyroid function in U.S. Adults. Mediators Inflamm. 2023;2023:1–12. doi: 10.1155/2023/5831858
30. Guo W, Song Y, Sun Y, et al. Systemic immune-inflammation index is associated with diabetic kidney disease in Type 2 diabetes mellitus patients: evidence from NHANES 2011–2018. Front Endocrinol (Lausanne). 2022;13:1071465. doi: 10.3389/fendo.2022.1071465
31. Zhang F, Han Y, Mao Y, et al. The systemic immune-inflammation index and systemic inflammation response index are useful for predicting mortality in patients with diabetic nephropathy. Diabetol Metab Syndr. 2024;16(1):282. doi: 10.1186/s13098-024-01536-0
32. Kong F, Huang J, Xu C, et al. System inflammation response index: a novel inflammatory indicator to predict all-cause and cardiovascular disease mortality in the obese population. Diabetol Metab Syndr. 2023 Oct 11;15(1):195. doi: 10.1186/s13098-023-01178-8
33. Antar R, Farag C, Xu V, et al. 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. doi: 10.3389/fnut.2023.1206958
34. Xing L, Xie F, Zuorong Z, et al. Hemoglobin, albumin, lymphocyte, and platelet (HALP) score: a risk prediction tool for incidence and mortality in diabetic kidney disease patients with type 2 diabetes, 1. Researchsquare. 2024;PREPRINT (Version 1):1–17. doi: 10.21203/rs.3.rs-5373438/v1
35. Vural S, Muhtaroğlu A, Güngör M. Systemic immune-inflammation index: a new marker in differentiation of different thyroid diseases. Medicine (Baltimore). 2023;102(31):e34596. doi: 10.1097/MD.0000000000034596
36. Xu M, Chen L, Hu Y, et al. The HALP (hemoglobin, albumin, lymphocyte, and platelet) score is associated with early-onset post-stroke cognitive impairment. Neurol Sci. 2023;44(1):237–245. doi: 10.1007/s10072-022-06414-z
37. Grani G, Carbotta G, Nesca A, et al. A comprehensive score to diagnose Hashimoto's thyroiditis: a proposal. Endocrine. 2015;49(2):361–365.
38. Angelopoulos N, Goulis DG, Chrisogonidis I, et al. Ultrasound characteristics of Hashimoto's thyroiditis in the subclinical stages of the disease. WFUMB Ultrasound Open. 2023;1(2):100022. doi: 10.1016/j.wfumbo.2023.100022
39. Zhao MQ, Zhang Y, Huang X, et al. Systemic inflammatory index as a predictive marker for the severity of coronary artery disease in individuals with chronic kidney disease. J Geriatr Cardiol. 2024;21(10):962–971.
40. Cao C, Li C, Li X, et al. Association of systemic immune-inflammation index (SII) and aggregate index of systemic inflammation (AISI) with thyroid nodules in patients with type 2 diabetes mellitus: a retrospective study. BMC Endocr Disord. 2023;23(1):251. doi: 10.1186/s12902-023-01509-w
41. Erinc O, Yesilyurt S, Senat A. A comprehensive evaluation of hemogram-derived inflammatory indices in hashimoto thyroiditis and non-immunogenic hypothyroidism. Acta Endocrinol (Buchar). 2023;19(4):435–440.