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Original Article

Relationship of Anti-TPO antibody levels with hematologic inflammation indices in hashimoto's thyroiditis

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Abstract

Aim: This study aimed to evaluate the relationship between anti-thyroid peroxidase antibody (anti-TPO) levels and hematological markers of systemic inflammation — including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII) in treatment-naïve patients with Hashimoto's thyroiditis (HT).
Materials and Methods: This retrospective, cross-sectional study included 416 newly diagnosed, treatment-naïve HT patients. Participants were categorized into low (n=208) and high (n=208) anti-TPO groups based on the median anti-TPO value (208 IU/mL). Thyroid function tests and complete blood count parameters were analyzed, and NLR, PLR, MLR, and SII were calculated. Spearman's correlation and multivariable linear regression analyses were performed.
Results: The high anti-TPO group had significantly higher TSH [5.87 (3.60–10.07) vs. 4.14 (2.62–6.60) µIU/mL; $p<0.001$] and lower fT4 levels [0.75 (0.64–0.86) vs. 0.80 (0.70–0.90) ng/dL; $p=0.001$] compared with the low group. Anti-TPO correlated positively with TSH ($\rho=0.248$; $p<0.001$) and negatively with fT4 ($\rho=-0.185$; $p<0.001$). PLR was significantly lower in the high anti-TPO group [113 (92.3–146) vs. 122 (97–155); $p=0.025$]. However, no significant correlations or independent associations were found between anti-TPO and NLR, MLR, or SII in regression analysis (model $R^2=0.015$; $p=0.190$). Although PLR differed between groups, it was not an independent predictor of anti-TPO after adjustment. The low R2 suggests a biological dissociation between local autoimmunity and systemic inflammation.
Conclusion: Anti-TPO levels were not significantly associated with hematologic inflammatory markers in treatment-naïve HT. These findings suggest that, in early-stage HT, local autoimmune activation may occur independently of systemic inflammation and that hematologic indices may have limited clinical utility for early diagnosis or disease monitoring.

Keywords: Hashimoto's thyroiditis, anti-TPO, systemic inflammation

INTRODUCTION

Hashimoto's thyroiditis (HT) is a common autoimmune endocrine disorder characterized by chronic lymphocytic infiltration and progressive autoimmune destruction of thyroid tissue, resulting from the interplay between genetic predisposition and environmental factors (1). At the core of its pathogenesis lies the loss of immune tolerance to thyroid autoantigens, particularly thyroid peroxidase (TPO) (2). Recent research has demonstrated that this organ-specific autoimmune process may not be confined to a local phenomenon but may also interact with systemic inflammatory pathways (3).

Hematological parameters that serve as easily accessible and reliable indicators of systemic inflammation including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII) have gained increasing recognition as prognostic biomarkers in cardiovascular, metabolic, and neoplastic diseases (6–8). Their strong association with mortality in the general population underscores their potential clinical value in assessing systemic inflammatory status (4-6).

However, the role of these hematologic indices in Hashimoto's thyroiditis remains insufficiently clarified, and the existing literature shows considerable inconsistency. While some studies have reported elevated oxidative stress and systemic

inflammatory activity in HT, reflected by increased NLR and PLR levels (7-9), others have failed to confirm these associations (10). Such discrepancies likely stem from heterogeneity among study populations particularly the inclusion of patients with different thyroid functional stages and treatment histories within the same cohort. Consequently, methodological heterogeneity and conceptual ambiguity in previous studies have hindered a clear understanding of the relationship between anti-TPO–mediated autoimmune activity and hematologic markers of systemic inflammation in early-stage HT.

This study was designed to address these limitations by objectively evaluating this relationship in a homogeneous group of treatment-naïve, newly diagnosed patients representing all functional stages of the disease (euthyroid, subclinical, and overt hypothyroid). To our knowledge, this is one of the first studies to comprehensively investigate the association between anti-TPO levels and hematologic inflammatory indices (NLR, PLR, MLR, and SII) in untreated HT patients, thereby enabling a direct assessment of autoimmune activity and its systemic inflammatory reflections independent of thyroid function or treatment-related variability.

MATERIALS AND METHODS

Study Design and Population

This retrospective, cross-sectional study was conducted at Kahramanmaraş Necip Fazıl City Hospital, Yörükselim Annex Building, between September 1, 2023, and September 1, 2025, and included newly diagnosed, treatment-naïve patients with Hashimoto's thyroiditis (HT). A total of 416 patients were enrolled. The diagnosis of HT was established based on the presence of both of the following criteria:

1. Serum anti-thyroid peroxidase antibody (anti-TPO) level >35 IU/mL, and
2. Documented confirmation of the diagnosis by an internal medicine specialist in the clinical records.

Patients were stratified according to the median anti-TPO value (208 IU/mL) into two categories: a Low Anti-TPO group (n=208) and a High Anti-TPO group (n=208). In the absence of a clinically validated threshold for stratifying anti-TPO titers, the median was utilized as a non-arbitrary, data-driven cutoff to ensure equal group sizes, thereby minimizing potential bias and maximizing the efficiency of the statistical power in detecting intergroup differences.All newly diagnosed individuals were included irrespective of thyroid functional status, encompassing euthyroid, subclinical hypothyroid, and overt hypothyroid cases.

Inclusion and Exclusion Criteria

Participants aged between 18 and 65 years with serum anti-thyroid peroxidase antibody (anti-TPO) levels greater than 35 IU/mL were eligible for inclusion. Only treatment-naïve individuals without any prior use of levothyroxine or immunomodulatory agents were enrolled. Complete laboratory data, including thyroid-stimulating hormone (TSH), free thyroxine (fT4), anti-TPO, and complete blood count (CBC) parameters, obtained within a 15-day interval, were required for study inclusion.

Patients were excluded if they had active infection (white blood cell count >11.000/μL), hematologic disorders, malignancy, or other autoimmune diseases. Additional exclusion criteria included chronic hepatic or renal insufficiency, pregnancy or lactation, and the use of corticosteroids, immunosuppressive agents, or chemotherapeutic drugs within the previous three months.

Data Collection and Variables

Demographic characteristics (age, sex) and laboratory data were retrospectively retrieved from the hospital information management system (HBYS). Laboratory assessments included thyroid function tests (TSH, fT4, and anti-TPO) and complete blood count (CBC) parameters, including white blood cell count, neutrophil, lymphocyte, monocyte, platelet counts, hemoglobin, and mean platelet volume (MPV).

In addition to these conventional hematologic indices, derived hematologic inflammatory markers reflecting systemic immune-inflammatory activity were calculated as follows:

1. Neutrophil-to-Lymphocyte Ratio (NLR) = neutrophil / lymphocyte
2. Platelet-to-Lymphocyte Ratio (PLR) = platelet/lymphocyte
3. Monocyte-to-Lymphocyte Ratio (MLR) = monocyte / lymphocyte
4. Systemic Immune-Inflammation Index (SII) = (neutrophil × platelet) / lymphocyte

All laboratory measurements were performed within the same analytical period (≤15 days apart) using standardized assays in the hospital's central biochemistry laboratory.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki (2013) and Good Clinical Practice (GCP) guidelines. Ethical approval was obtained from the Ethics Committee of Kahramanmaraş Sütçü İmam University University (KSU TAREK) (Protocol No. 289 and date:10.08.2025). All patient data were anonymized prior to analysis, and no additional diagnostic or therapeutic procedures were performed for research purposes.

Statistical Analysis

The normality of continuous variables was assessed using the Shapiro–Wilk test, histograms, and Q–Q plots. Non-normally distributed data were presented as median (interquartile range, IQR), and categorical variables were expressed as number and percentage [n (%)]. Differences between low and high anti-TPO groups were analyzed using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. Correlations between

anti-TPO levels and continuous variables were evaluated using Spearman's rank correlation coefficient.

Anti-TPO levels were used as the dependent variable to serve as a surrogate marker of thyroid-specific autoimmune activity. Anti-TPO levels were log-transformed to approximate normality. Skewed inflammatory markers (PLR, NLR, MLR, SII) were log-transformed, and TSH was normalized using square-root transformation. Variables with a p-value<0.20 in univariate linear regression or considered clinically relevant (age, sex, TSH, fT4) were included in the multivariable model. The final multivariable linear regression model included log(PLR) as the primary predictor and was adjusted for age, sex, √TSH, and fT4. Model assumptions were verified using residual and Q–Q plots, and statistical significance was set at two-tailed p<0.05. All analyses were performed using R software (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 416 treatment-naïve patients with Hashimoto's thyroiditis (HT) were included in this retrospective cross-sectional study. Patients were divided into two groups according to the median serum anti-TPO level (n=208 in each group). The baseline demographic and biochemical characteristics of the study population are summarized in Table 1. The median age of participants was 39 years (IQR: 28–47), and there was no significant difference in age distribution between groups (p=0.070). The majority of patients were female (92.1%), with similar sex distribution across groups (p=0.468).

Table 1. Baseline characteristics of treatment-naïve hashimoto's thyroiditis patients stratified by Anti-TPO levels

Variable	Total (n=416)	Low Anti-TPO (n=208)	High Anti-TPO (n=208)	p-value
Demographic				
Age (years)	39 (28-47)	40 (29-49)	36 (27-46)	0.070
Sex (female, n%)	383 (92.1%)	189 (90.9%)	194 (93.3%)	0.468
Thyroid Function				
TSH (µIU/mL)	5.15 (2.96-8.21)	4.14 (2.62-6.60)	5.87 (3.60-10.07)	<0.001
fT4 (ng/dL)	0.78 (0.67-0.87)	0.80 (0.70-0.90)	0.75 (0.64-0.86)	0.001
Hematologic Parameters				
WBC (×10⁹/L)	7.69 (6.55-8.98)	7.73 (6.71-9.05)	7.52 (6.50-8.86)	0.224
Hemoglobin (g/dL)	13.2 (12.4-14.0)	13.3 (12.5-14.1)	13.2 (12.4-14.0)	0.511
Platelet (×10⁹/L)	278 (242-328)	278 (247-328)	278 (237-328)	0.690
MPV (fL)	10.3 (9.8-10.9)	10.3 (9.7-10.9)	10.4 (9.8-10.9)	0.640
Monocyte (×10⁹/L)	0.56 (0.46-0.68)	0.54 (0.46-0.67)	0.59 (0.47-0.70)	0.159
Neutrophil (×10⁹/L)	4.38 (3.60-5.25)	4.27 (3.52-4.98)	4.45 (3.70-5.44)	0.078
Lymphocyte (×10⁹/L)	2.36 (1.94-2.91)	2.31 (1.87-2.83)	2.45 (2.03-3.00)	0.039
Inflammatory Markers				
NLR	1.78 (1.42-2.33)	1.81 (1.41-2.45)	1.77 (1.43-2.24)	0.686
PLR	117.3 (93.6-148.6)	122.0 (97.0-155.0)	113.0(92.3-146.0)	0.025
MLR	0.23 (0.18-0.30)	0.24 (0.18-0.29)	0.23 (0.19-0.30)	0.577
SII	504.9 (382.0-680.0)	504.0 (381.0-688.0)	505.0 (384.0-669.0)	0.623

TSH, thyroid-stimulating hormone; fT4, free thyroxine; WBC, white blood cell; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index. Bold p-values indicate statistical significance (p<0.05)

Regarding thyroid function tests, patients in the high anti-TPO group had significantly higher TSH levels and lower fT4 levels compared with those in the low anti-TPO group [TSH: 5.87 (3.60–10.07) vs. 4.14 (2.62–6.60) μIU/mL; p<0.001; fT4: 0.75 (0.64–0.86) vs. 0.80 (0.70–0.90) ng/dL; p=0.001]. These findings suggest that anti-TPO levels are associated with biochemical indicators of thyroid dysfunction. In the comparison of hematological parameters and inflammatory markers, lymphocyte count was significantly higher [2.45 (2.03–3.00) vs. 2.31 (1.87–2.83) $\times 10^9$/L; p=0.039], whereas platelet-to-lymphocyte ratio (PLR) was significantly lower [113 (92.3–146) vs. 122 (97–155); p=0.025] in the high anti-TPO group. No significant differences were observed for other inflammatory indices (NLR, MLR, and SII). Spearman correlation analysis revealed a weak positive correlation between anti-TPO and TSH (ρ=0.248; p<0.001) and a weak negative correlation between anti-TPO and fT4 (ρ=−0.185; p<0.001). Although both correlations were statistically significant, the low correlation coefficients indicate that these associations are of weak magnitude and limited clinical relevance. No significant correlations were observed between anti-TPO and inflammatory markers (Table 2 and Table 3).

Table 2. Spearman correlations between Anti-TPO, age, thyroid function, and hematologic inflammatory parameters

Variable	Spearman's ρ	p-value
Thyroid Function		
TSH	+0.248	**<0.001**
fT4	-0.185	**<0.001**
Demographic		
Age	+0.062	0.190
Hematologic Parameters		
WBC	-0.029	0.550
Hemoglobin	-0.020	0.679
Platelet	-0.026	0.600
MPV	-0.031	0.520
Monocyte	-0.035	0.460
Neutrophil	-0.043	0.370
Lymphocyte	+0.041	0.390
Inflammatory Markers		
NLR	-0.052	0.280
PLR	-0.087	0.070
MLR	-0.041	0.400
SII	-0.048	0.320

TSH, thyroid-stimulating hormone; fT4, free thyroxine; WBC, white blood cell; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index. Bold values indicate statistically significant correlations (p<0.05). Correlation strength was interpreted as follows: |ρ|<0.3, weak; 0.3–0.5, moderate; >0.5, strong

Table 3. Univariate linear regression analyses of variables associated with Anti-TPO levels in treatment-naïve patients with hashimoto's thyroiditis

Variable	Total (n=416)	Low Anti-TPO (n=208)	High Anti-TPO (n=208)
Inf. Markers			
log(PLR)	0.113 (-0.035-0.261)	0.135	
log(NLR)	-0.021 (-0.177-0.135)	0.793	(p<0.20)
log(MLR)	0.062 (-0.074-0.199)	0.370	
log(SII)	0.073 (-0.060-0.205)	0.276	
Covariates			
FT4	-0.148 (-0.305-0.009)	0.064	(p<0.20)
Age	-0.003 (-0.008-0.002)	0.282	(clinical)
Sex	0.038 (-0.078-0.154)	0.519	(clinical)
√TSH	0.002 (-0.003-0.006)	0.488	(clinical)

The dependent variable was log-transformed Anti-TPO. All inflammatory markers were log-transformed due to non-normal distribution. TSH was square-root transformed to reduce extreme skewness. Variables with p<0.20 in univariate analysis or of clinical relevance (age, sex, TSH, and fT4) were included in the multivariate model. FT4 showed borderline significance and was therefore retained in the final model. TSH, thyroid-stimulating hormone; FT4, free thyroxine; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; SII, systemic immune-inflammation index; β,regression coefficient; CI: confidence interval

In linear regression analyses, variables showing a p-value <0.20 in univariate analyses (log[PLR], fT4), together with clinically relevant covariates (age, sex, and √TSH), were included in the multivariate model. In the multivariate linear regression (Table 4, Figure 1), none of the variables including log(PLR) (β=0.104; p=0.147) showed a statistically significant independent association with anti-TPO levels. fT4 demonstrated borderline significance (β=−0.156; p=0.053). The overall model statistics (R^2=0.015, adjusted R^2=0.005, F(5,122)=1.50, p=0.190) indicated that the model was not statistically significant and accounted for only 1.5% of the variance in anti-TPO levels. These results suggest that peripheral inflammatory markers do not exhibit significant or independent associations with anti-TPO levels in treatment-naïve patients with Hashimoto's thyroiditis.

Table 4. Multivariate linear regression analyses of variables associated with Anti-TPO levels in treatment-naïve patients with hashimoto's thyroiditis

Variable	β (95% CI)	p-value
Primary Predictor		
log(PLR)	0.104 (-0.037 to 0.245)	0.147
Adjusted Covariates		
Age	-0.002 (-0.007 to 0.003)	0.382
Sex	0.010 (-0.106 to 0.126)	0.862
√TSH	0.002 (-0.003 to 0.006)	0.488
FT4	-0.156 (-0.314 to 0.002)	0.053

Multivariate linear regression analysis with log-transformed Anti-TPO as the dependent variable. The model included log(PLR) (selected based on p<0.20 criterion) and was adjusted for age, sex, √TSH, and FT4. TSH, thyroid-stimulating hormone; FT4, free thyroxine; PLR, platelet-to-lymphocyte ratio; β,regression coefficient; CI: confidence interval

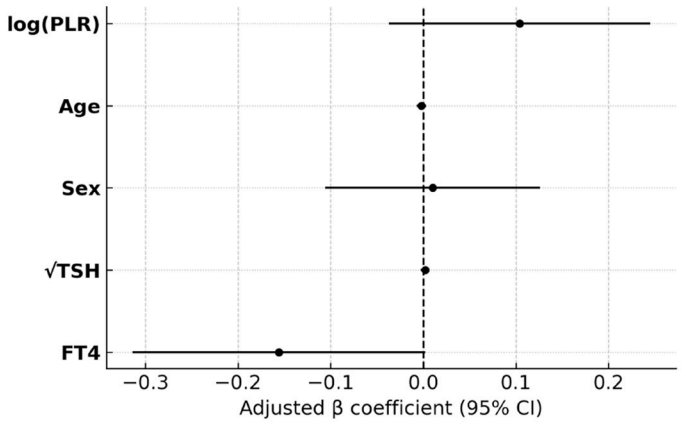

Figure 1. No independent associations between inflammatory markers and Anti-TPO levels after multivariable adjustment in hashimoto's thyroiditis

DISCUSSION

Hashimoto's thyroiditis (HT) is a chronic autoimmune disease characterized by progressive lymphocytic infiltration and destruction of thyroid tissue, arising from the interaction between genetic susceptibility and environmental triggers (1,2). Elucidating the relationship between autoimmune processes and systemic inflammation has become increasingly important for understanding the immunopathogenesis of HT (2,3). Hematologic inflammatory markers — such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII) have emerged as indirect indicators of systemic inflammation in autoimmune and metabolic diseases. However, most existing studies have been conducted in heterogeneous or treatment-exposed populations (3,7,8) Accordingly, the present study is among the first to systematically evaluate the relationship between anti-TPO titers and hematologic inflammatory indices in a homogeneous cohort of treatment-naïve, newly diagnosed patients encompassing all functional stages of the disease (euthyroid, subclinical, and overt hypothyroid). Our findings demonstrated that higher anti-TPO levels paralleled the expected pattern of thyroid dysfunction (elevated TSH and reduced fT4) but showed no significant or independent association with peripheral hematologic inflammatory markers. This observation suggests that, in the early stages of HT, autoimmune activity exhibits a weaker-than-expected correlation with systemic inflammatory response, thereby offering a novel perspective on the early pathophysiology of the disease. The low explanatory power of our multivariable model further suggests a biological dissociation between thyroid-specific autoimmunity and systemic inflammation in the initial stages of Hashimoto's thyroiditis.

Hematologic inflammatory indices have been widely established as markers of systemic inflammation in diverse clinical contexts, including cardiovascular and metabolic diseases (11,4,5). However, in organ-specific autoimmune conditions such as Hashimoto's thyroiditis (HT), their clinical relevance is more complex, with inconsistent results reported in the literature (6-9). In our study, the discrepancy between the significant group difference in PLR and its lack of independent association in the multivariable model likely stems from the confounding influence of thyroid function and individual lymphocyte counts, which are closely linked to the autoimmune process.

These inconsistencies are most likely attributable to heterogeneity within study populations and the inability to control for treatment-related confounders; however, the underlying immunological complexity of HT should not be overlooked. Kristensen et al. (10) characterized regulatory B cells in Graves' disease and Hashimoto's thyroiditis, revealing the dynamic and disease-specific nature of immune regulatory mechanisms in these disorders. Similarly, Ferrari et al. (12), through comprehensive analyses of coexisting autoimmune diseases in patients with autoimmune thyroiditis, demonstrated that HT develops within a broader context of autoimmune susceptibility, underscoring the multilayered nature of its pathogenesis. The contemporary pathogenic framework proposed by Weetman (13) further emphasizes that the dynamic interplay between local and systemic immune responses plays a pivotal role in disease evolution.

Within this methodological and immunological context, our study was designed to minimize the limitations of previous research and to assess this multilayered structure in a more controlled and simplified setting. By focusing on a completely treatment-naïve, newly diagnosed, and homogeneous patient cohort, we directly examined the relationship between anti-TPO–mediated autoimmune response and hematologic markers of systemic inflammation. We believe this approach minimizes the influence of secondary immune variability related to pharmacologic therapy or chronic disease progression, thereby allowing a clearer evaluation of early immunologic mechanisms specific to HT. Our findings suggest that, in the initial stages of the disease, the association between local autoimmune activity and systemic inflammatory markers may be weaker than anticipated, highlighting the need to reassess the early-phase dynamics of HT pathogenesis.

The underlying mechanisms behind this finding are likely related to the unique immune dynamics of early-stage Hashimoto's thyroiditis. The absence of a significant association between anti-TPO levels and hematologic inflammatory markers in our study provides important pathophysiological insights into the early disease process of HT. One plausible explanation lies in the thyroid gland's status as an immune-privileged site (14). In the early phase of HT, the autoimmune response may remain largely organ-specific, with limited release of inflammatory mediators into the systemic circulation, thereby preventing detectable alterations in peripheral hematologic parameters.

An alternative mechanism may involve compensatory changes in lymphocyte subpopulations. Despite the pronounced T- and B-cell infiltration within the thyroid tissue, the maintenance of peripheral homeostasis among these cells may obscure expected

variations in ratios such as NLR or PLR (10,12). A third possible explanation is that anti-TPO–mediated autoimmune activity and systemic inflammatory responses proceed through distinct immunopathological pathways (2,13). Indeed, recent experimental data suggest that thyroid-specific autoimmunity in HT primarily arises through T-cell–mediated cellular immunity, whereas systemic inflammation develops via activation of humoral and innate immune mechanisms (1,2,13). Furthermore, given that hematologic inflammatory indices predominantly reflect myeloid-derived inflammation, their limited sensitivity to lymphocytic infiltration which dominates in the early stages of HT may also explain the lack of significant associations (6,10,12). Consistent with these interpretations, the "two-phase pathogenesis" model proposed by Weetman (13) and Caturegli (15) supports the notion that, in the early stage of HT, local autoimmune activation may be dissociated from systemic inflammatory activity.

The findings of our study also carry noteworthy implications for clinical practice. The observation that hematologic inflammatory markers do not reflect anti-TPO levels in the early stages of Hashimoto's thyroiditis suggests that these indices may have limited clinical value in the early diagnosis of the disease or in monitoring the intensity of autoimmune activity. Fröhlich and Wahl likewise emphasized that anti-thyroid antibodies remain the cornerstone for assessing thyroid autoimmunity, while peripheral hematologic markers serve as supportive but secondary parameters (16). Accordingly, clinicians should not expect marked alterations in peripheral hematologic indices during the early phase of HT and should prioritize anti-TPO titers and thyroid function tests when evaluating autoimmune activity. As Brent highlighted, current evidence-based guidelines for autoimmune thyroid diseases place antibody measurement at the center of diagnostic and monitoring strategies (17). Nevertheless, our results also offer important perspectives for future research. The evaluation of biomarkers that may more specifically capture systemic inflammation in early HT such as cytokine profiling, immune cell subset analysis, or inflammatory gene expression panels — could deepen our understanding of the dynamic interplay between local autoimmunity and systemic inflammation. As emphasized by Ajjan and Weetman (18), elucidating the full pathogenesis of Hashimoto's thyroiditis will require the identification of novel, sensitive, and mechanistically targeted biomarkers.

This study has several limitations. Most notably its retrospective and single-center design, which may limit the generalizability of the findings to broader and more diverse clinical settings. Due to this cross-sectional nature, causal inferences between variables cannot be established. Furthermore, potential confounders such as body mass index, smoking status, dietary habits, and socioeconomic factors could not be fully controlled and may have indirectly influenced the results. Additionally, natural biological variability in hematologic parameters may have affected the measurements. Finally, our analysis was restricted to hematologic markers, without including more specific inflammatory indicators such as CRP, IL-6, or TNF-α. Nevertheless, the exclusive inclusion of a completely treatment-naïve and homogeneous patient cohort partially mitigates these limitations and enhances the internal validity of the study.

CONCLUSION

In conclusion, this study demonstrated that there is no significant association between anti-TPO–mediated autoimmune activity and hematologic inflammatory markers in treatment-naïve individuals with Hashimoto's thyroiditis. This "negative" finding in fact offers a valuable insight into the early pathogenesis of the disease: in the initial phase of HT, local thyroidal autoimmunity and systemic inflammatory responses reflected by peripheral hematologic indices may diverge and proceed independently. The strength of our study lies in its homogeneous, treatment-naïve, newly diagnosed cohort, which indicates that this lack of association likely reflects the intrinsic immunologic nature of early disease, rather than confounding effects of long-term disease duration or therapy. Therefore, our findings highlight that routine hematologic inflammatory indices have limited clinical utility in the early diagnosis or monitoring of autoimmune activity in Hashimoto's thyroiditis. Collectively, our findings suggest that the immunopathogenesis of Hashimoto's thyroiditis is more complex and multilayered than previously appreciated. Future research employing longitudinal designs and incorporating more specific inflammatory biomarkers such as cytokine profiling will be crucial to elucidate the temporal dynamics between local autoimmune activation and systemic inflammation.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that there is no financial support.

Ethical Approval
The study protocol received approval from the Kahramanmaraş Sütçü İmam University, TAREK (Protocol No. 289, Date: 10.08.2025).

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