



# Clinical Utility of Systemic Immune-inflammatory Index and Systemic Immune Response Index in Symptomatic Patients with Hashimoto's Thyroiditis

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## Abstract

**Aim:** Systemic immune-inflammatory indices have recently been investigated as potential biomarkers in several inflammatory and autoimmune diseases. This study aimed to investigate the symptom-based diagnostic value of the systemic immuno-inflammatory index (SII) and the systemic immunoresponsive index (SIRI) in patients with Hashimoto's thyroiditis (HT).

**Methods:** The medical records of 169 patients who presented to our clinic between January 2023 and June 2023 were retrospectively reviewed. Demographic and laboratory parameters including age, gender, drug use, thyroid-stimulating hormone (TSH), anti-thyroid peroxidase antibody (Anti-TPO), Anti-Tg, platelet (PLT), neutrophil, lymphocyte, monocyte, SIRI, and SII values were analyzed. SII and SIRI indices were calculated using standard formulas based on complete blood count parameters. The association between inflammatory indices and symptom status was evaluated using correlation and logistic regression analyses.

**Results:** Spearman's rho correlation analysis showed that the correlation between symptom positivity and Anti-TPO was significant ( $r=0.203$ ;  $p<0.01$ ). The correlation of symptom positivity with age, gender, drug usage, TSH, anti-Tg, PLT, neutrophil, lymphocyte, monocyte, SIRI, and SII was not statistically significant. Binary logistic regression analysis showed that the effects of gender, drug usage, age, SIRI, and SII on symptom positivity were not statistically significant. Although the effects of SIRI and SII on symptom positivity were not significant, the effect of Anti-TPO was significant ( $B=0.002$ ;  $p<0.01$ ).

**Conclusion:** Neither SIRI nor SII had diagnostic value in patients with HT based on symptoms. Therefore, clinical evaluations based on the SIRI and SII indicators for monitoring disease progression and morbidity in cases of HT may not provide reliable information for symptom-based clinical evaluation.

**Keywords:** Hashimoto's thyroiditis, systemic immune-inflammatory index, systemic immune response index, thyroid

## Introduction

Hashimoto's thyroiditis (HT) is one of the most common autoimmune thyroid diseases and is a leading cause of hypothyroidism in iodine-poor regions (1). Hashimoto's thyroiditis has been associated with acquired hypothyroidism in children, adults, and adolescents (2). Hashimoto's thyroiditis is classified into four forms: juvenile form, fibrous form, painless thyroid, and fibrous variant (3). Risk factors include demographic characteristics such as genetics, gender, and age, as well as daily life

factors such as environment and nutrition (4). Although there are no definitively distinct symptoms, weight gain, constipation, and excessive weakness and fatigue are prominent (5,6). While treatment is easier with early diagnosis, in advanced stages it can lead to many health problems ranging from mental health issues to diabetes, cholesterol problems, circulatory system problems, and cancer (7). Therefore, early diagnosis and treatment of the disease are important to prevent other comorbidities that it may cause. Therefore, both biomarker monitoring and symptom monitoring are important for early diagnosis.

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Systemic immune-inflammatory index (SII) and systemic immune response index (SIRI) are two important biomarkers that have been the subject of recent studies. They are easily obtainable biomarkers that reflect systemic inflammatory status and have been investigated in various diseases (8). Studies on SIRI and SII mostly highlight circulatory tract diseases (9,10).

Since cardiovascular diseases have been reported as comorbidities in patients with HT (5-7), SIRI and SII biomarkers may have value in the symptomatic evaluation of HT. To investigate this, we hypothesized that SII and SIRI values have symptomatic diagnostic value in patients with HT.

## Materials and Methods

### Compliance with Ethical Standards

Ethical approval was obtained for the study from the Demiroglu Science University Clinical Trials Ethical Committee (approval number: 2023-25-01, date: 05.12.2023). Informed patient consent was not applicable because of the retrospective nature of the study. The Declaration of Helsinki and Good Clinical Practice guidelines were followed in the research.

### Study Design

This study was designed as a retrospective cross-sectional study. Clinical and laboratory data, including SIRI and SII indices, were obtained from the medical records of patients who presented to our clinic. The association between these indices and symptom status was evaluated using appropriate statistical analyses.

### Research Data

In this study, the medical records of 168 patients who presented to our clinic between January and June 2023 were retrospectively reviewed. The patients' ages, gender, drug use, thyroid-stimulating hormone (TSH), anti-thyroid peroxidase antibody (Anti-TPO), Anti-Tg, platelet (PLT), neutrophil, lymphocyte, monocyte, SIRI, and SII were analyzed. Since our study was retrospective, the symptoms were based on the statements in the epicrisis. In our study, we performed SII and SIRI calculations as follows:

$SII = (\text{Platelet count} \times \text{neutrophil count}) / \text{lymphocyte count}$

$SIRI = (\text{Neutrophil count} \times \text{monocyte count}) / \text{lymphocyte count}$

### Sample Size

We did not find sufficient research examining the symptoms and the diagnostic value of SIRI and SII in HT. Sample size calculation was performed using G\*Power software (version 3.1). Assuming an effect size of 0.50,

$\alpha=0.05$ , and power of 95%, the minimum required sample size was calculated as 45 participants.

### Inclusion and Exclusion Criteria

Being over 18 and under 75 years of age,  
Having been diagnosed with HT,  
Having complete data in their file,  
Having no inconsistencies in their file data,  
Having no comorbidities or medication use that could affect the research results,

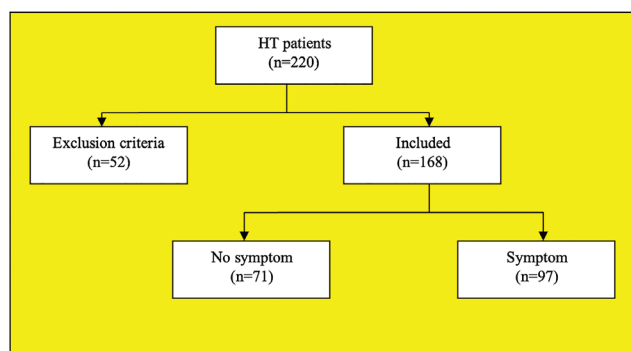
71 patients without symptoms and 97 patients with symptoms were included in the study (Figure 1).

### Statistical Analysis

Descriptive statistics were used to summarize the study variables. Continuous variables were expressed as mean  $\pm$  standard deviation, median, and range, while categorical variables were presented as frequencies and percentages. The Kolmogorov-Smirnov test was used to assess the normality of the distribution of continuous variables. Since several variables did not meet the assumption of normal distribution, non-parametric methods were preferred. Spearman's rho correlation analysis was performed to evaluate the relationship between symptom status (coded as a dummy variable) and the study parameters. To determine the independent effects of clinical and inflammatory indices on symptom positivity, a generalized linear model with logit link function (binary logistic regression) was applied. Statistical analyses were conducted using SPSS version 25.0 (IBM Inc., Armonk, NY, USA), and a p-value of  $<0.05$  was considered statistically significant. To determine the independent effects of clinical and inflammatory indices on symptom positivity, a generalized linear model with logit link function (binary logistic regression) was applied (11).

## Results

The mean age of the symptom-negative group was  $43 \pm 10$  years (range: 18-74), while the mean age of the symptom-positive group was also  $43 \pm 10$  years (range: 18-



**Figure 1.** Research flowchart  
HT: Hashimoto's thyroiditis

**Table 1. Baseline characteristics of patient groups with difference analysis results**

	Symptom		p-value
	No (n=71)	Yes (n=97)	
Age, mean ± SD Median (min-max)	43±10 42 (18-74)	43±10 42 (18-70)	0.928 <sup>a</sup>
Gender, n (%)			0.116 <sup>b</sup>
Female	61 (85.9)	90 (92.8)	
Male	10 (14.1)	7 (7.2)	
Drug usage, n (%)	48 (66.7)	58 (59.8)	0.226 <sup>b</sup>
TSH, mean ± SD Median (min-max)	2.35±4.72 1.44 (0.06-39.00)	2.38±3.06 1.50 (0.30-26.00)	0.220 <sup>a</sup>
Anti-TPO, mean ± SD Median (min-max)	71.00±153.74 2.79 (0.12-857.14)	<b>303.36±789.33</b> <b>49.45 (0.02-6851.18)</b>	0.009 <sup>a</sup>
Anti-Tg, mean ± SD Median (min-max)	28.85±79.89 2.44 (0.20-511.00)	67.85±245.85 5.99 (0.10-2276.15)	0.070 <sup>a</sup>
PLT, mean ± SD Median (min-max)	247.54±51.93 242.00 (163.00-384.00)	261.09±59.37 253.00 (149.00-447.00)	0.122 <sup>a</sup>
Neutrophil, mean ± SD Median (min-max)	3.66±1.12 3.65 (2.10-6.35)	3.78±1.34 3.60 (1.30-7.76)	0.777 <sup>a</sup>
Lymphocyte, mean ± SD Median (min-max)	2.16±0.65 2.00 (0.60-4.91)	2.11±0.64 2.10 (0.61-5.04)	0.561 <sup>a</sup>
Monocyte, mean ± SD Median (min-max)	0.50±0.14 0.50 (0.20-0.90)	0.55±0.72 0.50 (0.20-7.50)	0.445 <sup>a</sup>
SIRI, mean ± SD Median (min-max)	0.90±0.46 0.80 (0.36-2.54)	1.05±1.15 0.85 (0.19-10.63)	0.736 <sup>a</sup>
SII, mean ± SD Median (min-max)	441.32±184.17 380.80 (216.67-1076.67)	494.96±236.67 447.72 (173.91-1475.34)	0.170 <sup>a</sup>

<sup>a</sup>Mann-Whitney U test, <sup>b</sup>Fisher's exact test

SD: Standard deviation, TSH: Thyroid-stimulating hormone, Anti-TPO: Anti-thyroid peroxidase antibody, Anti-Tg: Anti-thyroglobulin antibodies, PLT: Platelet, SIRI: Systemic immune response index, SII: Systemic immuno-inflammatory index

70). Female patients constituted 85.9% of the symptom-negative group and 92.8% of the symptom-positive group. 66.7% of the negative-symptom group and 59.8% of the positive-symptom group used drugs. The mean Anti-TPO level was significantly higher in the positive-symptom group. Differences in age, gender, drug usage, TSH, anti-Tg, PLT, neutrophil, lymphocyte, monocyte, SIRI and SII parameters between symptom groups were not statistically significant (Table 1).

Spearman's rho correlation analysis results showed that correlation of symptom positivity with Anti-TPO was significant ( $r=0.203$ ;  $p<0.01$ ). Correlations of symptom positivity with age, gender, drug usage, TSH, Anti-Tg, PLT, neutrophil, lymphocyte, monocyte, SIRI, and SII parameters were not statistically significant (Table 2).

Results of binary logistic regression analysis showed that the effects of gender, drug usage, age, SIRI, and SII on symptom positivity were statistically insignificant (Table 3).

Although the effects of SIRI and SII on symptom positivity were not significant, the effect of Anti-TPO was significant ( $B=0.002$ ;  $p<0.01$ ) (Table 4).

**Table 2. Spearman's rho correlation analysis between symptom variable (dummy) and research parameters**

Symptom	r	p
Gender	-0.112	0.147
Drug	-0.070	0.364
Age	0.007	0.928
TSH	0.095	0.221
Anti-TPO	0.203**	0.008
Anti-Tg	0.140	0.070
PLT	0.119	0.122
Neutrophil	0.022	0.778
Lymphocyte	-0.045	0.563
Monocyte	-0.059	0.447
SIRI	0.026	0.740
SII	0.106	0.171

\*\* $p<0.01$ , TSH: Thyroid-stimulating hormone, Anti-TPO: Anti-thyroid peroxidase antibody, Anti-Tg: Anti-thyroglobulin antibodies, PLT: Platelet, SIRI: Systemic immune response index, SII: Systemic immuno-inflammatory index

**Table 3. Binary logistic regression analysis for effects of SIRI, SII and baseline characteristics on symptom positivity**

	B	S.E.	Wald	df	p	OR	95% CI for OR	
							Lower	Upper
Gender	-0.746	0.534	1.949	1	0.163	0.474	0.166	1.352
Drug	-0.334	0.338	0.976	1	0.323	0.716	0.369	1.389
Age	0.001	0.016	0.000	1	0.990	1.000	0.969	1.033
SIRI	0.087	0.236	0.137	1	0.712	1.091	0.687	1.731
SII	0.001	0.001	1.041	1	0.308	1.001	0.999	1.003
Constant	0.815	1.062	0.589	1	0.443	2.259		

SIRI: Systemic immune response index, SII: Systemic immuno-inflammatory index, CI: Confidence interval, OR: Odds ratio

**Table 4. Binary logistic regression analysis for effects of SIRI, SII and Anti-TPO on symptom positivity**

	B	S.E.	Wald	df	p	OR	95% C.I.for OR	
							Lower	Upper
SIRI	0.037	0.214	0.030	1	0.862	1.038	0.682	1.580
SII	0.001	0.001	1.604	1	0.205	1.001	0.999	1.003
Anti-TPO	0.002	0.001	7.346	1	0.007	1.002	1.001	1.004
Constant	-0.591	0.407	2.105	1	0.147	0.554		

Anti-TPO: Anti-thyroid peroxidase antibody, SIRI: Systemic immune response index, SII: Systemic immuno-inflammatory index, CI: Confidence interval, OR: Odds ratio

Although the mean SIRI was higher in the symptom-positive group, this difference was not statistically significant. One patient had the highest SIRI value in the symptom-positive group, and we reanalyzed the data after removing this patient. However, the difference remained non-significant (Figure 2).

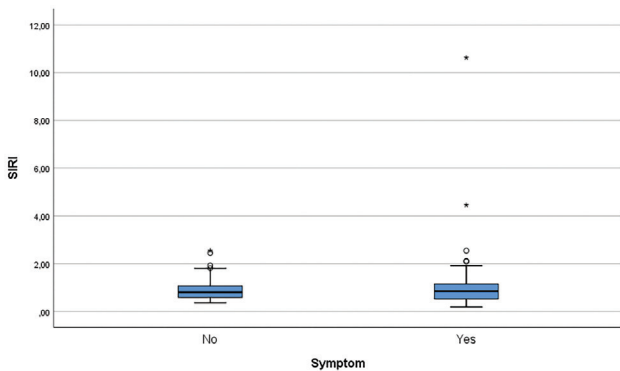
Unlike SIRI means, SII mean differences were closer and distributions were more similar between patient groups; the differences were not statistically significant (Figure 3).

**Discussion**

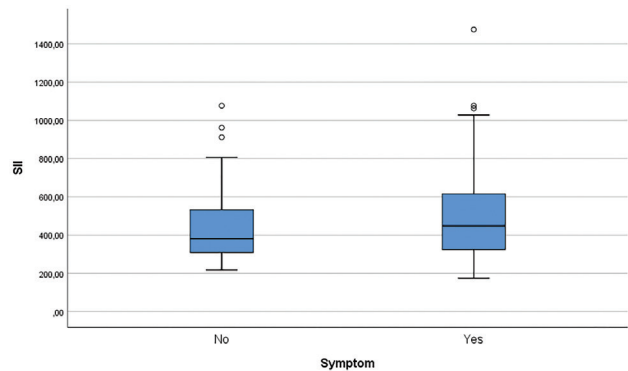
This study aimed to evaluate the diagnostic value of the SII and SIR) for symptoms in patients with HT. Data

from 169 patients who presented to our clinic were retrospectively analyzed. Our findings showed that neither SIRI nor SII had diagnostic value for symptoms in patients with HT.

Hashimoto's thyroiditis is one of the most common autoimmune thyroid disorders and represents a major cause of acquired hypothyroidism across all age groups (12-15). Because HT risk factors are similar to other disease risk factors (4-6) and its symptoms are limited, more biomarkers and parameters are needed for early diagnosis. The emergence of comorbidities and especially circulatory problems in advanced stages of HT (5-7) suggests that symptomatic circulatory indicators may also



**Figure 2.** SIRI means and distributions according to symptom positivity  
SIRI: Systemic immune response index



**Figure 3.** SII means and distributions according to symptom positivity  
SII: Systemic immuno-inflammatory index

have diagnostic value for HT. Two commonly reported biomarkers of circulatory diseases are SIRI and SII (16-18). Based on this, in our study, we investigated the relationship between HT symptoms and SIRI and SII.

Studies on SIRI and SII biomarkers in thyroid diseases are limited. Among these, Wang et al. (19) reported that SIRI and SII parameters may have diagnostic value for treatment progression in thyroid cancer cases. Gu et al. (20) reported that the SII index may have diagnostic value in terms of lymph node positivity in elderly patients with papillary thyroid carcinoma. Yang and Yang (21) reported that SIRI and SII values were significantly higher in patients with differentiated thyroid carcinoma. Zhai et al. (22) examined the relationship between SIRI and thyroid function level and reported that inflammatory diseases and the SIRI index may be markers related to progression, but more evidence is needed. Although these studies suggest a potential relationship between thyroid-related diseases and SIRI and SII, available evidence remains limited.

In our study, neither SIRI nor SII had diagnostic value in patients with symptomatic HT. Although we designed our research to account for patients' cardiovascular disease or anti-inflammatory drug use, the evidence shows that the SIRI and SII indices do not have sufficient discriminatory power to detect HT at the symptom level.

Although HT is a significant health problem, early diagnosis may not be possible through routine blood tests. Early diagnosis significantly affects both the treatment process and disease progression. Our findings reveal that SIRI and SII do not have a value for symptom differentiation. Therefore, our findings suggest that HT patients may have pathophysiologies beyond those indicated by symptomatic blood values.

### Study Limitations

The most significant limitation of the study is that it is a single-center study. Due to its single-center nature, the influence of environmental factors and differing demographic, social, and economic contexts on the research results was not sufficiently assessed. Therefore, multicenter studies and cross-comparisons are needed in future research. Another limitation is the absence of prospective clinical assessment of symptoms, as symptom status was determined retrospectively from medical records. The retrospective design also does not allow adequate inclusion of potential confounders in the study. For this reason, further prospective trials, especially those including other confounders who may be related to Anti-TPO, could be considered. Another significant limitation of the study is the small number of patients and the paucity of literature on symptoms specific to HT. Although our sample size (n=169) exceeds the required number by the

power analysis, more comprehensive data on symptom diversity could be obtained with larger samples. Our study is retrospective, and the derivation of symptoms from statements in the medical records is another significant limitation.

Studies indicate that SIRI and SII have significant value. However, a substantial gap exists in the literature regarding symptoms of HT, necessitating the identification of meaningful indicators and further research. In this respect, the research is important because it examines the relationship between SIRI, SII, and symptoms of HT, which is one of the first questions that comes to mind in the literature. This research contributes to clinical practice by helping to prevent potential misassessments and misinterpretations in treatment through demonstrating that the potential effects of SIRI and SII indices are not applicable to HT. Our sample is not sufficient to definitively conclude that there is no relationship of SIRI and SII with HT, but it is important because it shows that these indicators are unreliable and may even yield misleading results.

### Conclusion

Although some studies report the indicator value of SIRI and SII, our findings indicate that neither SIRI nor SII has diagnostic value in patients with HT when diagnosis is based on symptoms. Therefore, clinical evaluations based on SIRI and SII indicators for monitoring disease progression and morbidity in HT cases may not provide reliable information for symptom-based clinical evaluation. To improve the generalizability of the results obtained in our study, the research sample could be increased by enlarging the sample size and conducting multicenter studies.

### Ethics

**Ethics Committee Approval:** Ethical approval was obtained for the study from the Demiroglu Science University Clinical Trials Ethical Committee (approval number: 2023-25-01, date: 05.12.2023).

**Informed Consent:** Informed patient consent was not applicable because of the retrospective nature of the study.

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### Footnotes

#### Authorship Contributions

Concept: A.G., Design: A.G., Data Collection or Processing: A.G., M.E., Analysis or Interpretation: A.G., M.E., Literature Search: A.G., M.E., Writing: A.G.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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