Systemic Immune-Inflammation Index in Assessing Disease Activity and Extraglandular Involvements in Primary Sjogren's Syndrome

Ozlem Kilic, Mehmet Nur Kaya, Duygu Tecer and Sedat Yilmaz

Department of Rheumatology, University of Health Sciences, Gulhane Training and Research Hospital, Ankara, Turkiye

ABSTRACT

Objective: To evaluate if the systemic immune inflammation index (SII) predicts extraglandular involvement and disease activity in primary Sjogren's Syndrome (pSS).

Study Design: Cross-sectional, observational study.

Place and Duration of the Study: Department of Rheumatology, University of Health Sciences, Gulhane Training and Research Hospital, Ankara, Turkiye, from July 2022 to January 2023.

Methodology: This study included 102 healthy controls (HCs) and 128 pSS patients, matched for gender and age. SII, monocyte/lymphocyte ratio (MLR), plateletcrit (PCT), neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) were calculated. The EULAR Sjogren's syndrome patient-reported index (ESSPRI) and the EULAR Sjogren's Syndrome disease activity index (ESSDAI) were used to measure disease activity. Logistic regression identified predictors of disease activity and extraglandular involvement. SII's diagnostic performance was evaluated *via* receiver operating characteristic curve analysis.

Results: Primary Sjogren's syndrome had higher NLR, MLR, SII, PLR, and PCT than HCs (all $p < 0.001$). According to the ESSDAI, the SII was higher in moderate-to-severe disease activity ($p < 0.001$). SII, with a moderate positive correlation between ESSDAI and ESSPRI, showed diagnostic performance when disease activity was assessed by both ESSDAI and ESSPRI (area under the curve: 0.930, 0.983, respectively, $p < 0.001$). SII was associated with moderate-to-severe disease activity as well as pulmonary and neurological involvement. PLR was associated with skin involvement. The cut-off value of SII for predicting moderate-to-severe disease activity was 660.2 x 10^3 cells/μL.

Conclusion: Haematological indices such as MLR, NLR, PLR, and PCT, especially SII, which are economical and practical, can be effective clinical assessment tools to monitor extraglandular involvement and disease activity.

Key Words: *Systemic immune-inflammation index, Primary Sjogren's syndrome, Blood cell count, Pulmonary, Neurological involvement.*

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INTRODUCTION

Extraglandular symptoms are seen in primary Sjogren's syndrome (pSS), a systemic, chronic autoimmune disease. Lymphocyte infiltration of the exocrine glands is characteristic of its pathology.[1] The reported incidence of pSS is between 3.9 and 5.3 per 100,000 patients per year.[2] The global prevalence of pSS is estimated to be between 0.03 and 2.7% of the population.[2] Dryness due to exocrine gland involvement is the main presenting symptom. Fever, fatigue, weight loss, weakness, malaise, pyrexia, and arthralgia are common symptoms.[1]

Correspondence to: Dr. Ozlem Kilic, Department of Rheumatology, University of Health Sciences, Gulhane Training and Research Hospital, Ankara, Turkiye
E-mail: ozlemk.kara@gmail.com

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The most important step in preventing mortality and morbidity from rheumatic diseases is early diagnosis and treatment. Assessment of disease activity is crucial for both treatment and monitoring strategies.[3] Disease activity is difficult to measure because pSS is a multisystem disease and involvement of different organs can occur over time, even in the same patient. No single parameter fully defines disease activation in pSS. The Sjogren's syndrome patient-reported index (ESSPRI) and disease activity index (ESSDAI) of the European League Against Rheumatism have been developed to assess systemic involvement and disease severity in pSS, but can be time-consuming to use in clinical practice.[4,5] The most commonly used indicators of inflammation in clinical practice include C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). However, due to their non-specificity and unsatisfactory specificity and sensitivity, efforts to find new specific biomarkers in the field of rheumatology have been and continue to be the focus of interest in the literature.[6]

In numerous inflammatory rheumatic diseases, including pSS, plateletcrit (PCT), mean platelet volume (MPV), platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio

(NLR), which can be readily determined from complete blood count parameters, are reliable markers for predicting disease activity and systemic inflammation.[7-12] The MLR, PLR, and NLR were calculated by dividing the number of monocytes, platelets, and neutrophils by the total number of lymphocytes. PCT represents the volume occupied by platelets as a percentage of the blood and was calculated using the formula: (Platelet count × MPV)/10,000.[3,9]

A novel haematological index, called the systemic immune inflammation index (SII), is more sensitive than either the PLR or NLR alone in predicting systemic inflammation and disease activity. First reported in 2014, it was associated with an unfavourable prognosis in a group of people with hepatocellular carcinoma.[9] Since then, it has been shown to be useful in various conditions, including inflammatory rheumatic diseases. The SII was calculated using the formula: (Neutrophil count x Platelet count)/lymphocyte count.[3,6,13]

There is little information in the literature on the relationship between SII and pSS. A recent study reported a correlation between haematological parameters (NLR, SII, and PLR) and developing dry eye in pSS.[14] Due to the limited data in the literature, the primary aim of this study was to evaluate the efficacy of SII in terms of extraglandular involvement and disease activity in patients with pSS. Secondary objectives were to evaluate the efficacy of NLR, PCT MLR, and PLR indices in terms of extraglandular involvement and disease activity in patients with pSS.

METHODOLOGY

This study used a cross-sectional research design. During the six-month study period (from July 2022 to January 2023), a total of 8,656 patients visited the outpatient clinics of the Department of Rheumatology, University of Health Sciences, Gulhane Training and Research Hospital, Ankara, Turkiye. Among these patients, a total of 156 patients had a diagnosis of pSS. Twenty-eight of these pSS patients were excluded from the study as per exclusion criteria. A total of 230 people (128 patients and 102 healthy participants) who met the inclusion criteria were included in the study. The project was approved by the local Ethics Committee of the University of Health Sciences. Written informed consent was obtained from patients before participation in the study. The tenets of the Declaration of Helsinki were followed in this study.

Patients with pSS who met the 2016 American College of Rheumatology (ACR) and the EULAR diagnostic criteria and who had not changed their treatment regimen in the previous three months were eligible for inclusion. The 2016 ACR/EULAR classification criteria after application of exclusion criteria including head/neck irradiation, HIV/AIDS, sarcoidosis, active hepatitis C virus infection, amyloidosis, graft-*versus*-host disease, IgG4-related disease in patients with dry eyes and/or mouth for at least three months, Schirmer test <5mm/5 minutes (1 point), positive anti-SSA/Ro and/or anti-SSB/La (3 points), minor salivary gland biopsy suggestive of focal lymphocytic sialoadenitis-focus score ≥1/4mm^2 (3 points), ocular surface staining score >5 (1 point), and unstimulated salivary flow <0.1 ml/minute (1 point) were diagnosed with a total score ≥4 points of the criteria.[15] Patients were included in this study according to the Schirmer test, salivary gland biopsy, and anti-SSA/Ro and/or anti-SSB/La results.

The control group consisted of volunteer participants with demographic characteristics similar to the patient group in terms of age and gender. Exclusion criteria for patients and participants were history of any surgery within three months, current corticosteroid therapy, smoking and alcohol use, haematological or solid malignancies, anti-cholinergic and antidepressant medicines use, systemic diseases such as hypertension and diabetes mellitus, chronic or active infections, liver/kidney disease, breastfeeding or pregnancy, and any rheumatic disease except pSS.

Treatment, demographic, laboratory, and clinical data were collected from medical records. Demographic data included gender and age. Results of routine laboratory tests of patients and HCs were recorded. These included ESR (0-20 mm/h), CRP (0-5 mg/L), immunoglobulins, and a complete blood count including neutrophils (1.82-7.42 103 cells/μL), platelets (171-388 103 cells/μL), monocytes (0. 25-0.84 103 cells/μL), white blood cells (WBC) (4-10.5 103 cells/μL), MPV (7.5-11.2 fL), and lymphocytes (1.26-3.35 103 cells/μL). Anti-SSA/Ro and anti-SSB/La results were obtained from medical records.

MLR, PLR, PCT, SII, and NLR were calculated using formulae mentioned in the introduction. In 2009, the ESSDAI was developed by the EULAR to assess disease severity and systemic involvement in pSS. The ESSDAI includes 12 domains (constitutional (night sweats, fever, weight loss), glandular (lacrimal glands and/or swelling of salivary and/or), articular, pulmonary, lymphadenopathy and/or lymphoma, cutaneous, muscular, peripheral nervous system, renal, central nervous system, biological (cryoglobulins, complement, hypergammaglobulinaemia), and haematological. Each characteristic is assigned a number from 0 to 3 based on the level of activity and from 1 to 6 based on the weight of each characteristic. Each characteristic is multiplied by 19 for these two values. The activity index is finally derived by aggregating the numbers obtained from each domain. It is scored and ranges from 0 to 123. Based on the total score, disease activity is categorised as moderate (5≤ ESSDAI ≤13), severe (ESSDAI ≥14), and low (ESSDAI <5).[3] It covers disease activity in a way that assesses all systemic involvement, is suitable for use in trials and daily practice, and has high validity. In this study, extraglandular involvement of pSS was defined according to the ESSDAI.[4]

ESSPRI evaluates the patient's fatigue, dryness, and pain scores according to VAS 10 for each domain. The total score is the average of the 3 domains. The total score is divided into two categories: Low disease activity (ESSPRI <5) and severe disease activity (ESSPRI ≥5).[5]

Statistical software (Statistical Package for the Social Sciences- 26) was used to analyse each piece of the data. Using

Kolmogorov-Smirnov or Shapiro-Wilk's test, the distribution of numerical variables was detected. For the analysis of numerical data having a normal distribution, the student's t-test was employed. Results were shown, including the mean and standard deviation. The median (interquartile range) was presented as the result of the Mann-Whitney U test analysis for non-normally distributed numerical data. The x2 or Fischer's exact x2 test was used for the analysis of qualitative data, and results were expressed as frequencies (percentages). The patients were split into two subgroups based on the ESSDAI cut-off value of 5. Spearman's correlation analysis was performed between ESSDAI, ESSPRI scores, NLR, PLR, SII, MLR, PCT indices, and CRP and ESR levels. The correlations fell into the following categories: Correlation coefficient: 0.90 to 1.00 indicated a very strong correlation; 0.70 to 0.89 indicated a strong correlation; 0.40 to 0.69 indicated a moderate correlation; 0.10 to 0.39 indicated a weak correlation; and <0.10 indicated absolutely no association. Univariate and multivariate analyses were used to identify the most independently associated markers among PLR, NLR, SII, MLR, and PCT markers that were found to influence disease activity and extraglandular involvement in pSS. Model fit was assessed using the Hosmer-Lemeshow test. In addition, the ability of these haematological markers to discriminate between moderate and severe disease activity was evaluated using receiver operating characteristic (ROC) analysis. Youden's index was used to determine the performance of these cut-off values (specificity, sensitivity, negative, positive predictive values, and negative and positive likelihood ratios). A criterion of p <0.05 was established for statistical significance.

RESULTS

The groups' differences in age and gender did not reach statistical significance (p >0.05). The median age of the HCs group was 53 years, with 88.2% of them being female. The median age of the individuals in the pSS group was 54 years, with 94.5% of them being female. The values of NLR, PLR, SII, MLR, and PCT were notably greater in the pSS compared to the HCs (p <0.001 for all). CRP, ESR, and platelet count were all considerably higher in pSS patients than in HCs (p <0.05 in all cases). The levels of WBC, monocytes, and lymphocytes were seen to be lower than those of the control group (all, p <0.05).

According to the ESSDAI scores, there were 51 pSS patients with moderate-to-severe disease activity and 77 patients with low disease activity. The two groups did not differ significantly in terms of disease diagnoses or duration (p >0.05). When comparing the two groups, NLR, SII, MLR, PLR, and PCT levels were greater in the moderate-severe disease activity group (for all, p <0.001, Table I).

The area under the curve (AUC) values of NLR, PLR, SII, MLR, PCT, ESR, and CRP were 0.930, 0.928, 0.864, 0.824, 0.722, and 0.701, respectively, when disease activity was determined by ESSDAI (Figure 1C). The AUC values of SII, NLR, PLR, MLR, PCT, ESR, and CRP were 0.883, 0.870, 0.814, 0.796, 0.705, 0.705, and 0.653, respectively, when disease activity was determined by ESSPRI. SII exhibited the greatest AUC, sensitivity, and specificity when ESSDAI and ESSPRI were used to evaluate disease activity. According to ESSDAI, the most appropriate cut-off values for moderate-to-severe disease activity were as follows: SII, 660.2; N LR, 2.44; PLR, 176.9; MLR, 0.29; PCT, 0.27; ESR: 40.5, and CRP, 4.45 (Table II, Figure 1D).

A moderate positive correlation was found between ESSDAI and NLR, SII, PLR, MLR, and ESR; (r = 0.690, 0.667, 0.583, 0.543, and 0.404, respectively, p <0.001). For SII (Figure 1A, B), a moderate positive correlation was also observed between ESSPRI and NLR, PLR, and MLR (r = 0. 546, 0.535 0.466, and 0.411, respectively).

There was a strong positive correlation between ESSDAI and ESSPRI. SII and NLR showed the best correlation among these haematologic indices (r = 0.787, p <0.001). In multivariate analysis of these haematologic indices, SII was independently associated with moderate-to-severe disease activity, pulmonary and neurologic involvement (p = 0.010, <0.001, 0.003, respectively), whereas PLR was associated with skin involvement (p = 0.002, Table III).

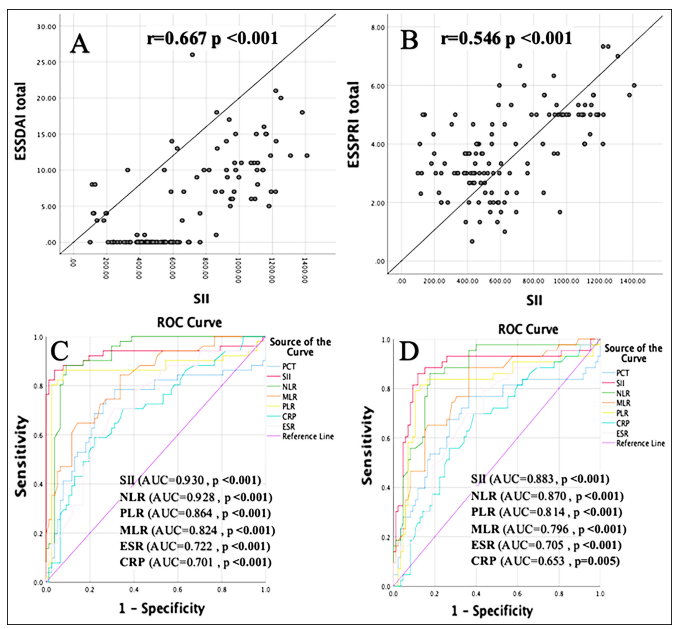

Figure 1: (A) The correlation of ESSDAI and (B) ESSPRI with SII and ROC curve analyses. (C) According to the ESSDAI score AUC values. (D) According to the ESSPRI AUC values in pSS for moderate-high disease activity.

ESSPRI: European League Against Rheumatism Sjogren's syndrome patient-reported index, SII: Systemic immune-inflammation index, ESSDAI: European League Against Rheumatism Sjogren's syndrome disease activity index, PLR: Platelet-to-lymphocyte ratio, MLR: Monocyte-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, ESR: Erythrocytic sedimentation rate, CRP: C-reactive protein, PCT: Plateletcrit, pSS: Primary Sjogren's syndrome.

Table I: Comparison of clinical and demographic traits among pSS patient groups based on ESSDAI score.

Parameters	Low disease activity (n = 77)	Moderate-severe disease activity (n = 51)	p-value
Gender (F/M), n (%)	77/0 (100/0)	44/7 (86.3/13.7)	**0.001**[b]
Age (years)[a]	53 (15)	55 (16)	0.750[c]
Disease duration (months)[a]	23.8 (37.65)	24.43 (37.33)	0.316[c]
Diagnosis duration (months)[a]	15.6 (30.88)	23.3 (40.53)	0.099[c]
ESR (mm/h)[a]	31 (27.5)	46 (28)	**<0.001**[c]
CRP (mg/L)[a]	3.5 (4.5)	7.8 (9.6)	**<0.001**[c]
WBC ($\times10^3$ cells/µL)[a]	6.6 (2.4)	5.7 (1.25)	**0.003**[c]
Lymphocyte ($\times10^3$ cells/µL)[a]	2.1 (1.0)	1.2 (0.3)	**<0.001**[c]
Monocyte ($\times10^3$ cells/µL)[a]	0.5 (0.2)	0.48 (0.3)	0.895[c]
Neutrophil ($\times10^3$ cells/µL)[a]	3.73 (1.6)	3.6 (0.9)	0.981[c]
Platelet ($\times10^3$ cells/µL)[a]	266 (83)	348 (52)	**0.001**[c]
SII ($\times10^3$ cells/µL)[a]	451.37 (171.68)	978.7 (285.5)	**<0.001**[c]
PLR[a]	123.78 (51.6)	290 (63.5)	**<0.001**[c]
NLR[a]	1.76 (0.66)	2.91 (0.76)	**<0.001**[c]
MLR[a]	0.23 (0.11)	0.38 (0.32)	**<0.001**[c]
PCT (%) [a]	0.25 (0.08)	0.31 (0.08)	**<0.001**[c]
Hypergammaglobulinaemia, n (%)	12 (15.6)	43 (84.3)	**<0.001**[b]
Anti-Ro/SSA positive, n (%)	39 (50.6)	40 (78.4)	***0.002***[b]
Anti-La/SSB positive, n (%)	19 (24.7)	23 (45.1)	***0.016***[b]
Pulmonary involvement[d], n (%)	2 (2.6)	17 (33.3)	***<0.001***[b]
Neurological involvement[e], n (%)	0 (0)	8 (15.7)	***<0.001***[b]
Haematological involvement, n (%)	8 (10.4)	8 (15.7)	0.420[b]
Skin involvement, n (%)	0 (0)	10 (19.7)	***<0.001***[b]
ESSDAI[a]	0 (0)	10 (7)	***<0.001***[c]
ESSPRI total[a]	3 (1.36)	5 (0.67)	***<0.001***[c]
ESSPRI dryness[a]	4 (2)	5 (2)	***<0.001***[c]
ESSPRI fatigue[a]	2 (2)	5 (2)	***<0.001***[c]
ESSPRI pain[a]	2 (2)	5 (1)	***<0.001***[c]
AECG score[a]	6 (2.5)	6 (3)	0.258[c]

[a]Median (interquartile range (IQR), [b]Chi-square, [c]Mann-Whitney U, [d]Non-specific interstitial pneumonia (n = 14), Usual interstitial pneumonia (n = 3), Lenfositik interstisyel pnomoni (n = 2), [e]axonal sensory polyneuropathy (n = 3), axonal sensorimotor polyneuropathy (n = 3), central nervous system involvement (n = 2), pSS: Primary Sjogren's syndrome, median (interquartile range (IQR), ESSDAI: European league against rheumatism Sjogren's syndrome disease activity index, ESR: Erythrocytic sedimentation rate, WBC: White blood cell, PLR: Platelet-to-lymphocyte ratio, CRP: C-reactive protein, SII: Systemic immune-inflammation index, MLR: Monocyte-to-lymphocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, PCT: Plateletcrit, RF: Rheumatoid factor, ESSPRI: European league against rheumatism Sjogren's syndrome patient-reported index, AECG: American European consensus criteria for Sjogren's syndrome. Statistical significance is shown by bold values, F/M: Female/Male, <0.05 = statistically significant.

Table II: SII, NLR, PLR, MLR, PCT indices, ESR, and CRP performance and ideal cut-off values in relation to active disease in pSS patients.

Parameters	AUC	SE	95% CI	Cut-off	Sensitivity	Specificity	p-value	PPV	NPV
SII ($\times10^3$ cells/µL)	0.930	0.031	0.870-0.991	660.2	88.24%	92.21%	**<0.001**	88.24%	92.21%
NLR	0.928	0.024	0.882-0.974	2.44	88.24%	90.91%	**<0.001**	86.54%	92.11%
PLR	0.864	0.042	0.781-0.947	176.9	86.27%	92.21%	**<0.001**	88%	91.03%
MLR	0.824	0.037	0.752-0.896	0.29	72.55%	75.32%	**<0.001**	66.07%	80.56%
PCT (%)	0.723	0.051	0.623-0.823	0.27	78.43%	68.83%	**<0.001**	62.50%	82.81%
ESR (mm/h)	0.722	0.046	0.631-0.813	40.5	70.59%	68.83%	**<0.001**	60%	77.94%
CRP (mg/L)	0.701	0.048	0.608-0.795	4.45	70.59%	64.94%	**<0.001**	57.14%	76.92%

pSS: Primary Sjogren's syndrome, AUC: Area under curve, CI: Confidence interval, SE: Standard error, PPV: Positive predictive value, NPV: Negative predictive value, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index, PCT: Plateletcrit, ESR: Erythrocytic sedimentation rate, MLR: Monocyte-to-lymphocyte ratio, CRP: C-reactive protein. Statistical significance is shown by bold values. p <0.05 = statistically significant.

Table III: Multivariate and univariate logistic regression analyses to examine factors associated with neurological, pulmonary, and skin involvement and moderate-to-severe disease activity in pSS patients.

Parameters	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
For moderate-high disease activity	-					
SII ($\times10^3$ cells/µL)	1.009	1.006-1.012	**<0.001**	1.009	1.002-1.015	0.010
PLR	1.021	1.014-1.028	**<0.001**			
NLR	18.244	6.803-48.929	**<0.001**			
MLR	11260.897	293.429-432157.941	**<0.001**			
PCT (%)	341.049	3.107-37438.863	**0.015**			
For pulmonary involvement						
SII ($\times10^3$ cells/µL)	1.003	1.002-1.005	**<0.001**	1.003	1.002-1.005	<0.001
PLR	1.09	1.004-1.015	**0.001**			
NLR	1.110	0.917-1.344	0.284			
MLR	10.261	1.391-75.688	**0.022**			
PCT (%)	2181.762	1.639-2904251.23	**0.036**			
For skin involvement						
SII ($\times10^3$ cells/µL)	0.996	0.994-0.999	**0.003**			
PLR	0.988	0.980-0.995	**0.002**	0.988	0.980-0.995	0.002
NLR	0.932	0.726-1.197	0.584			
MLR	0.872	0.047-16.193	0.927			
PCT (%)	0.000	0.000-2.317	0.073			
For neurological involvement						
SII ($\times10^3$ cells/µL)	1.004	1.002-1.007	**0.003**	1.004	1.002-1.007	0.003
PLR	1.013	1.004-1.022	**0.003**			
NLR	1.070	0.813-1.409	0.628			
MLR	0.707	0.018-27.20	0.852			
PCT (%)	10593.349	0.93-580438087	0.096			

CI: Confidence interval, pSS: Primary Sjogren's syndrome, OR: Odds ratio, NLR: Neutrophil-to-lymphocyte ratio, PCT: Plateletcrit, MLR: Monocyte-to-lymphocyte ratio, SII: Systemic immune-inflammation index, PLR: Platelet-to-lymphocyte ratio. Statistical significance is shown by bold values. p <0.05 = statistically significant.

DISCUSSION

Although sicca symptoms are a common manifestation of pSS, approximately 40% of patients have systemic involvement.[16] In the literature, there is limited information about haematological parameters and especially SII in pSS. The relationship between haematological parameters, including SII and systemic involvement, especially pulmonary and neurological involvement, remains unclear. In this study, patients with pSS were shown to have a higher SII compared to HCs. Furthermore, a higher SII was associated with neurological, pulmonary and increased disease activity. There was a positive correlation between SII, ESSDAI, and ESSPRI. Finally, when disease activity was calculated according to ESSDAI, and ESSPRI, this study showed that SII had the best diagnostic value in differentiating disease activity.

Lymphocytes are an important factor in the development of autoimmune diseases. They play a role in the formation of auto-antibodies in pSS, and prolonged activation of lymphocytes by antigens may even increase the risk of lymphoma formation. Mihai *et al*. reported that haematological parameters such as MLR, PLR, and NLR were predictors of cutaneous vasculitis in their study of pSS patients.[10] Another retrospective study reported red cell distribution width and NLR as markers associated with disease activity.[11] Yildiz *et al*. showed that NLR, PCT, and PLR were associated with disease activity in pSS, which is consistent with the findings of this study.[17] In addition, unlike this study, they reported MPV as an indicator of disease activity and PLR as an indicator of neurological involvement. In this study, the authors found that the lymphocyte count was significantly lower in pSS patients, especially in the group with moderate-to-severe disease activity. As a natural consequence of the low lymphocyte count, higher MLR, PLR, and NLR were found in the pSS group, in line with literature data. In addition, the cut-off values for disease activity were calculated differently in this study than in the literature.[10,11,17,18]

The relatively new SII index is based on the total number of lymphocytes, platelets, and neutrophils in peripheral blood. It is inexpensive and efficient because it can be easily determined using the standard haemogram panel. A few rheumatology studies have been published in the literature showing an association between SII and the following conditions: Psoriatic arthritis (PsA), adult-onset still's disease (AOSD), Behcet's disease (BD), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), spondyloarthropathy (SpA), immunoglobulin G4-related disease (IgG4-RD), and RA.[3,6,12,19-25]

In studies conducted on some rheumatological diseases in the literature, SII was found to be related to disease activity. Different cut-off values have been reported for each disease.[3,6,21-24] Uzeli *et al*. found a strong positive correlation between SII and pSS disease activity in their study of 28 pSS patients and 28 controls.[14] They also found a negative correlation between SII and Schirmer's test. In conclusion, it was reported that NLR, SII, and PLR were correlated with the development of dry eye in pSS. They reported that these markers showed statistically significant changes in pSS patients. In this study, SII was shown to be associated with high disease activity with a cut-off value of $660.2x10^3$ cells/μL. SII has also been associated with neurological and pulmonary involvement.

This study has several limitations. Firstly, due to the nature of cross-sectional observational studies, the generalisability of the results is limited. Secondly, as this was a single-centre study, the sample size limits the generalisability of the results. Regarding the strengths of the study, firstly, at the end of the comparative evaluation of patients diagnosed with SII and pSS, some haematological-based inflammatory indices were analysed in detail. Secondly, this study adds new information to the literature, as it is the first study to investigate the relationship between SII and pSS, with the largest number of patients and controls, and to give the cut-off value in terms of the markers mentioned, and also to investigate the relationship with some common extraglandular involvements.

CONCLUSION

According to the results of this study, NLR, SII, PLR, MLR, and PCT were found to be associated with disease activity in pSS patients. In particular, SII, with its high capacity for association with moderate-to-severe disease activity, showed that it can be used as a promising parameter for follow-up. Furthermore, SII was the only marker associated with pulmonary and neurological involvement compared to the other markers mentioned. This study highlights the importance of including SII and other assessed indices in routine practice for better management and follow-up of pSS patients. Further studies with larger samples are needed to confirm the findings regarding the correlation between SII and pSS.

ETHICAL APPROVAL:
The University of Health Sciences Gulhane Clinical Research Ethics Committee granted the study approval in compliance with the Helsinki Declaration (No: 2022/71; Date: 01.06.2022).

PATIENTS' CONSENT:
An informed consent was obtained from all the patients included in the study.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
OK, MNK: Analysis and data collection.
OK, DT: Design and concept.
OK, SY: Drafting and revision.
DT, SY: General oversight, analysis of the information, and final manuscript review.
All authors approved the final version of the manuscript to be published.

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