Original Paper

Systemic Immune-Inflammation Index (SII) Predicts Increased Severity in Psoriasis and Psoriatic Arthritis

AHU YORULMAZ[1], YILDIZ HAYRAN[1], UMIT AKPINAR[1], BASAK YALCIN[1]

[1]Ankara Bilkent City Hospital

ABSTRACT: Background: Psoriasis is a common chronic inflammatory dermatosis. Systemic immune inflammation index (SII) is an inflammation-based biomarker, which has been shown to be an effective prognostic factor in diseases with an inflammation-related etiology. Objectives: The aim of the present study was to investigate the potential efficacy of SII as a prognostic factor in patients with psoriasis and psoriatic arthritis. Materials and methods: This is a study developed based on the analysis of the medical records of patients with psoriasis. The study retrospectively evaluated the records of the participants for complete blood count results. The SII was calculated by the formula: neutrophil x platelet/lymphocyte. Neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR) and platelet-lymphocyte ratio (PLR) were determined. Results: SII was significantly higher in patients with psoriasis than in controls (578.1 vs. 396, p<0.001). The differences between the median NLR (2.2 vs. 1.5, p<0.001), MLR (0.25 vs. 0.21, p<0.001) and the mean red cell distribution width coefficient of variation (13.8 vs. 12.8, p<0.001) values of patient and control group were significant. SII was higher in patients with moderate/severe psoriasis than patients with mild psoriasis (687.3 vs. 506.6, p=0.034). A positive correlation was observed between SII and PASI (p<0.001; r=0.37). SII was higher in patients with arthritis than patients without (672.1 vs. 548.2, p=0.018). Conclusion: This is the first study to prove that SII might serve as an independent prognostic indicator for patients with psoriasis and psoriatic arthritis.

KEYWORDS: *Psoriasis, psoriatic arthritis, systemic immune-inflammation index, severity, prognosis.*

Introduction

Psoriasis is a common chronic inflammatory dermatosis, characterized by well-defined erythematous plaques with silvery scales.

Recent years have witnessed an evolution in our understanding the pathogenic pathways of psoriasis.

Currently, it is universally accepted that psoriasis is an immune-mediated inflammatory disease, of which etiology is mainly dominated by an aberrant immune response in the skin, shaped by intrinsic and extrinsic factors [1-3].

Systemic immune inflammation index (SII) is an inflammation-based biomarker, which has been shown to be an effective prognostic factor in diseases with an inflammation-related etiology [4].

To the best of our knowledge, there is no evidence in the literature on the assessment of efficiency of SII in determining activity of psoriasis.

The aim of this study was to investigate the prognostic role of SII in patients with psoriasis and psoriatic arthritis.

Materials and Methods

A retrospective study was conducted in patients with psoriasis admitted to the Dermatology Department of Ankara Bilkent City Hospital, Turkey, between May 2019 and May 2020.

The study was approved by the local medical ethical committee.

Patients with a diagnosis of psoriasis vulgaris were included.

Each patient provided a written informed consent prior to study inclusion.

The inclusion criteria of the study were being 18 years old or above and not receiving any systemic treatment for psoriasis at the time of hospital application. 171 medical records were obtained through the hospital information system. 171 healthy controls, who had applied for cosmetic procedures, were selected from the medical electronic database of the department.

The following demographic and clinical characteristics of the patients were obtained from the records: age, sex, family history, disease duration, age of disease onset, psoriasis severity, Psoriasis Area Severity Index (PASI) value, accompanying arthritis, nail involvement and complete blood count (CBC) results.

Other than demographic parameters CBC results were evaluated for the control group. Patients were classified into 2 groups according

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to psoriasis severity: PASI<10 (mild psoriasis), PASI>10 (moderate/severe psoriasis).

The following parameters retrieved from the CBC reports: white blood cell (WBC), neutrophil, lymphocyte, platelet and monocyte counts, mean corpuscular volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), platelet distribution width (PDW) and red cell distribution width coefficient of variation (RDW-CV).

SII was calculated by the formula: neutrophil (N) x platelet (P)/lymphocyte (L) (SII=N x P/L ratio).

Neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR) and platelet-lymphocyte ratio (PLR) were determined.

Statistical analysis was performed using SPSS software, Version 25 (SPSS Inc., Chicago IL, USA).

Descriptive frequencies were calculated for demographic and clinical variables.

Categorical variables were expressed as frequencies and percentages and continuous variables were described as mean, median, and interquartile range (IQR).

Categorical variables were examined using Chi-Square test, while continuous variables were explored using Mann-Whitney U test/ Student t test.

Receiver operating characteristic (ROC) curve analysis was performed to analyse the area under the ROC curve (AUC). A p-value of<0.05 was considered statistically significant.

Results

A total of 171 patients [69 women (40.4%) and 102 (59.6%) men; mean age, 43.6±13.6 years (range: 18-78)] and 171 controls were enrolled in the present study.

Demographic data of the patient group

The median PASI was 6.5 (range: 2.9-13.1). 63.3% of the patients (n=100) had mild psoriasis, 36.7% (n=58) had moderate/severe psoriasis.

Table 1 illustrates disease duration, age of disease onset, family history and frequencies of nail involvement and accompanying arthritis in the patient population (Table 1).

Table 1. Clinical and demographical characteristics of the patients.

Characteristic	*n (%)*
Age, years*	43.6 (13.6)
Sex	
Female	69 (40.4)
Male	102 (59.6)
PASI**	6.5 (2.9-13.1)
Psoriasis severity	
Mild	100 (63.3)
Moderate/severe	58 (36.7)
Arthritis	
Present	21 (27.3)
Absent	56 (72.7)
Nail involvement	
Present	66 (40.5)
Absent	97 (59.5)
Family history of psoriasis	
Present	58 (37.2)
Absent	98 (62.8)
Duration of psoriasis, years**	9.5 (3-15)
Age of onset**	30 (22-43.5)

PASI: Psoriasis Area and Severity Index,
*mean (standard deviation),
**median (interquartile range, IQR)

Analysis of SII values and other laboratory parameters in the study group

The median SII was 578.1 (IQR: 431.1-834.6) in patients with psoriasis, while it was 396 (IQR: 284.1-542.2) in the control group. SII was significantly higher in patients with psoriasis than in controls (p<0.001) (Figure 1).

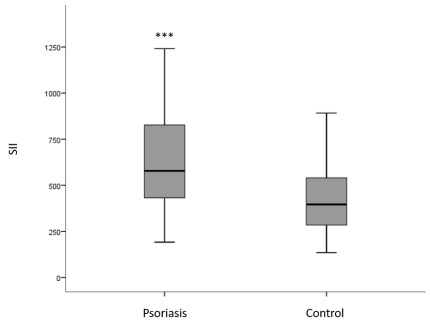

Figure 1. Comparison of SII values between patient and control groups (: p<0.001).***

White blood cell (WBC) and neutrophil counts and RDW-CV, NLR, MLR and PLR were higher in patients than in controls (p=0.042, p<0.001, p<0.001, p<0.001, p<0.001, p<0.001, respectively).

On the other hand, lymphocyte count was lower in patients when compared with controls (p<0.001).

Table 2 shows the comparison of laboratory parameters within the study group (Table 2).

Table 2. Comparison of demographic and laboratory findings between the patient and control group.

	Psoriasis patients (n=171)	Control group (n=171)	P-value
Age*	43.6 (13.6)	43.2 (14.4)	0.67
Gender (Male/Female)	102/69	102/69	> 0.99
WBC (10^9/L)*	7.8 (2.1)	7.1 (1.7)	**0.042**
Neutrophil (10^9/L)**	4.6 (3.7-5.7)	3.8 (3.1-4.5)	**< 0.001**
Lymphocyte (10^9/L)**	2.1 (1.7-2.6)	2.6 (2.1-3)	**< 0.001**
Monocyte (10^9/L)**	0.6 (0.4-0.7)	0.5 (0.4-0.6)	0.051
MCV (fL)*	86.8 (5.8)	86.5 (4.6)	0.46
MCH (pg)*	28.4 (2.7)	28.6 (1.9)	0.69
MCHC (g/dl)*	33.1 (1.3)	33.1 (1.2)	0.58
Platelet (10^9/L)**	262 (224.7-309.5)	276 (219-326.5)	0.39
PDW (%)*	12.2 (1.8)	12.1 (2.3)	0.67
RDW-CV (%)*	13.8 (1.9)	12.8 (0.6)	**< 0.001**
SII**	578.1 (431.1-834.6)	396 (284.1-542.2)	**< 0.001**
NLR**	2.2 (1.7-2.9)	1.5 (1.2-1.8)	**< 0.001**
MLR**	0.25 (0.21-0.32)	0.21 (0.17-0.25)	**< 0.001**
PLR**	128.9 (100.7-169.1)	103.7 (83.6-132)	< 0.001

MCV: mean corpuscular volume; MCH: mean cell hemoglobin; MCHC: mean cell hemoglobin concentration; NLR: neutrophil-lymphocyte ratio; MLR: monocyte-lymphocyte ratio; PLR: platelet-lymphocyte ratio; WBC: white blood cell; P: significance level; PDW: platelet distribution width; RDW-CV: red cell distribution width coefficient of variation; SII: systemic immune inflammatory index, *mean (standard deviation), **median (interquartile range, IQR)

Correlation between SII and clinical characteristics of the patients

The median SII was 560.6 (IQR: 425.9-721.5) in patients with mild psoriasis, whereas it was 687.3 (IQR: 468.5-980) in patients with moderate/severe psoriasis.

SII was significantly higher in patients with moderate/severe psoriasis than in patients with mild psoriasis (p=0.034) (Figure 2).

A positive correlation was observed between SII and PASI (p<0.001; r=0.37) (Figure 3).

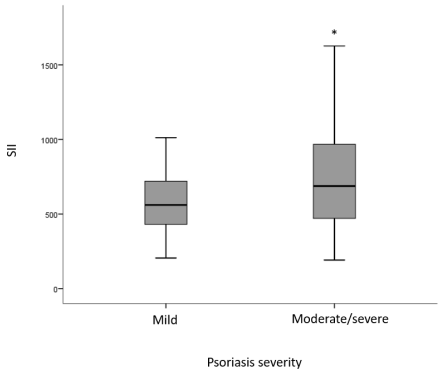

Figure 2. The effect of psoriasis severity on SII. Increased SII values observed in patients with moderate/severe psoriasis (*: p<0.05).

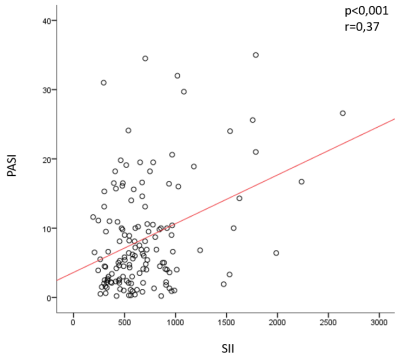

Figure 3. The positive correlation between SII and PASI.

The correlation between SII and PASI was significant in patients with moderate/severe psoriasis (p=0.046, r=0.28), while it was not in patients with mild psoriasis (p=0.13, r=0.16).

The median SII in patients with and without arthritis were, respectively, as follows: 672.1 (IQR: 491.1-726.1) and 548.2 (IQR: 395.3-802.2).

SII was higher in patients with arthritis than patients without arthritis (p=0.018) (Figure 4).

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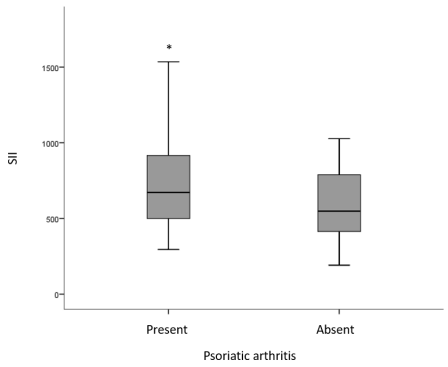

Figure 4. The influence of arthritis on SII. Increased SII values observed in patients with arthritis (*: p<0.05).

The median SII was significantly lower in patients with family history when compared with patients without [539 (IQR: 414-681.9), 632.4 (IQR: 46.,2-903.2), respectively; p=0.025)].

SII values did not differ between patients with or without nail involvement (p=0.12).

There were not any significant correlations between SII and age (p=0.39, r=-0.05), SII and disease duration (p=0.15, r=-0.12), SII and age of disease onset (p=0.37, r=0.08).

ROC analysis showed that the cut-off value of SII that demonstrated the maximum sensitivity and specificity for differentiating moderate/severe psoriasis from mild psoriasis was 490.

Employing this cut-off value, the sensitivity and specificity of SII for identifying moderate/severe psoriasis was 64.5% and 64.8%, respectively (Figure 5).

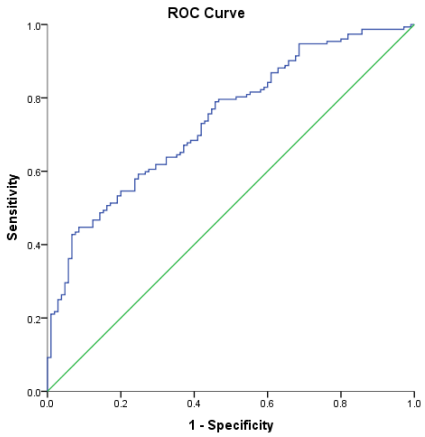

Figure 5. Receiver operating curve analysis of SII.

Discussion

Psoriasis is a common immune-mediated inflammatory dermatosis.

Recent studies shed light on the intricate web of involved factors and pathways in the pathogenesis of psorasis. Immune dysfunction is the hallmark feature of psoriasis leading to chronic inflammation, which manifests itself as uncontrolled keratinocyte proliferation.

It is well-known that psoriatic plaques are not only characterized by hyperproliferation and abnormal differentiation of keratinocytes, but also dermal infiltration of immune cells and increased dermal vascularity.

There is still an ongoing debate on whether the actual trigger to initiate the pathophysiological cascade of inflammatory events in psoriasis is keratinocytes or immune cells.

Despite the perplexity in understanding the underlying mechanisms, one of the most supported assumption is that psoriasis is a multisystem inflammatory disease, that involves a constant interplay between keratinocytes, immune cells and many other cells [1-3,5-10].

Subtypes of WBCs, which include neutrophils, lymphocytes and monocytes are widely known as systemic non-specific cellular markers of overall inflammation.

CBC is an inexpensive and easily available diagnostic test.

Cellular components of blood and their ratios may give insight into the extent of ongoing inflammation.

In recent years, there has been a trend in clinical practice to utilize inflammation-based indexes, such as the NLR, MLR and PLR as assessment tools for disease activity of various kinds of inflammatory diseases and prognostic indicators in survival of the patients with malignant tumors [4,11-18].

The SII, which is a novel inflammation-based biomarker, integrates neutrophils, platelets and lymphocytes.

SII covers NLR and platelets and is calculated by the formula platelet x NLR. SII, combined with other hematological inflammatory indexes, appears to be a simple and inexpensive tool in prediction of progression of a diverse number of diseases [4,15-19].

According to result of our study, SII was significantly higher in patients with psoriasis than in controls.

Moroever, WBC, neutrophil counts, RDW-CV, NLR, MLR and PLR were all higher in patients than in controls.

To the best of our knowledge, our study is the first to evaluate these inflammation indicators in psoriasis.

Results of our study strongly correlate with the evidence that psoriasis is a systemic inflammatory disease [3,6,7,9,10].

One of the most outstanding findings of our study was the demonstration of the positive correlation of SII with PASI.

SII was significantly higher in patients with moderate/severe psoriasis than in patients with mild psoriasis.

This positive correlation reveals the significance of SII as an indicator for the poor prognosis in patients with psoriasis.

In this study, ROC analysis was performed to determine the optimal prognostic cutoff value of SII.

According to ROC analysis, a SII level of 490 had the maximum sensitivity and specificity for differentiating moderate/severe psoriasis from mild psoriasis.

We suggest that a SII value of 490 should be employed as the cut-off value for determining severity in patients with psoriasis and psoriatic arthritis.

Psoriasis is a systemic inflammatory disease. But, why we did not detect a positive correlation between SII and PASI in patients with mild psoriasis?

Our findings were in line with the aim of the study, which was the demonstration of the role of SII as a powerful prognostic indicator in patients with psoriasis.

In our opinion, the fact that the correlation between SII and PASI was not significant in patients with mild psoriasis was due to lack of quantification of systemic inflammation in mild psoriasis.

All the hematological indexes of the study group proved the inflammatory nature of psoriasis, but the overall inflammation in mild psoriasis might not be prominent enough to be detected with these systemic inflammation markers.

A recent study by Sokolova et al. has questioned the assessment of systemic inflammation in psoriasis [20].

They investigated systemic inflammation markers, including C-reactive protein (CRP), calprotectin, lipocalin 2, beta-defensin 2, interleukin-8 (IL-8), IL-22, IL-17 and IL-23 in patients with psoriatic arthritis and found out that the majority of the patients exhibited remarkable marker elevations.

However, despite active skin disease, CRP was not increased or hardly increased in most of the patients with psoriatic arthritis.

It has been concluded that the determination of systemic inflammation in psoriasis is difficult and lack of elevation of inflammation markers does not mean absent systemic inflammation. Instead it means different kinds of markers are required to validate systemic inflammation in psoriasis [20].

One of the noteworthy findings of this study was the description of lower SII values in patients with family history when compared with patients without family history.

It is well-known that both genetic and environmental factors are involved in the pathogenesis of psoriasis.

In patients without family history, extrinsic environmental factors are the primary drivers of psoriasis pathogenesis.

Infections, including Streptococcus pyogenes, Staphylococcus aureus, Candida albicans and human immunodeficiency virus can provoke or exacerbate psoriasis [21].

In our opinion, the higher SII values in patients without family history may be related with extrinsic risk factors, particularly infections, which are closely linked with systemic inflammation.

Conclusion

In this study, complete blood count results of the patients and the controls were evaluated retrospectively in order to evaluate the utility of inflammation-based indexes, particularly SII for disease progression and severity in patients with psoriasis and psoriatic arthritis.

As far as we know, this is the first report to demonstrate the prognostic role of SII in patients with psoriasis and psoriatic arthritis.

We suggest that SII has a high diagnostic value for moderate/severe psoriasis and might serve as an indicator for the poor prognosis in patients with psoriasis.

Combined with subtypes of WBCs, RDW-CV, NLR, MLR and PLR, SII might serve as a non-invasive and cost-effective marker of systemic inflammation.

These independent and inexpensive predictors should be used as objective markers that reflect the balance between host inflammatory and immune response status in patients with psoriasis.

Moreover, this study investigated ROC curves to determine the SII value that predicted moderate/severe psoriasis.

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Accordingly, the cut-off value determined by ROC analysis for SII was 490.

We suggest a SII of 490 as the cut-off value to define moderate/severe psoriasis.

Conflict of interests

None to declare.

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Corresponding Author: Ahu Yorulmaz, Ankara Bilkent City Hospital, e-mail: ahuyor@gmail.com