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The utility of systemic-immune inflammation index for predicting the disease activation in patients with psoriasis

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Abstract

Objective: To evaluate the utility of systemic-immune inflammation index (SII) in the management of patients with psoriasis.

Method: This retrospective case-control study was conducted on patients who were admitted to the dermatology outpatient clinic. Patients with psoriasis (n = 71) were compared with a age and gender-matched control group (n = 70) with other non-inflammatory dermatologic diseases. Study and control groups were compared in terms of clinical characteristics and SII values (neutrophil X platelet/lymphocyte). Afterwards, 50th percentile value (4.5) for psoriasis area severity index (PASI) was calculated for the study group. Two subgroups were formed according to PASI values: (1) PASI < 4.5 group (n = 36) and (2) PASI ≥ 4.5 (n = 35). Clinical characteristics and SII values were also compared between these two subgroups. Furthermore, SII values were compared according to the presence of scalp, joint, nail, and genital area involvement in the study group. Finally, a receiver operating characteristic (ROC) curve analysis was performed in order to assess the performance of SII in determining the activation of psoriasis in the study group.

Results: Significantly higher SII values were found in patients with psoriasis. PASI ≥ 4.5 subgroup and patients with nail and genital involvement had also significantly higher SII values ($P < .05$). A cut-off value of 575.8 was calculated with 66.7% sensitivity and 66% specificity for psoriasis activation.

Conclusion: SII may be used for the prediction of psoriasis activation.

What's known

Complete blood cell indices have been used as prognostic markers in various fields of medicine for years. Systemic-immune inflammation index (SII) (neutrophil X platelet/lymphocyte) is a new complete blood cell index that has been used in the prediction of disease progression especially in the field of oncology. As SII includes three main parameters of complete blood cell count, it may give a more precise opinion about chronic inflammation and other medical branches have also started to use SII.

What's new

To the best of our knowledge, there is no study in the literature evaluating the efficacy of SII in patients with psoriasis. The results of the present study indicated that SII was associated with psoriasis activation and severity. Moreover, this novel index might be used for the prediction disease activation in patients with psoriasis.

1 | INTRODUCTION

Psoriasis is a chronic inflammatory skin disease with an approximate worldwide prevalence of 0.5%-11.4% in the adult population.[1] Its pathophysiology is complex and altered immune-mediated response in individuals with genetic predisposition together with the presence of environmental triggering events are thought to be the main underlying factor behind psoriasis at present.[2-4] However, our knowledge is still limited and we have a long way to go in the enlightment of etiology and treatment of psoriasis. Apart from its pathognomonic skin manifestations such as scaling, induration, and erythema because of the hyperproliferation and abnormal differentiation of the epidermis, psoriasis may also involve specific parts of the body such as nails and joints.[5]

The main goal of the physician in the management of psoriasis is to improve quality of life and to suppress symptoms for the patients. Various topical and systemic treatment modalities may be used for this purpose.[6] The decision for optimal treatment option is made according to the clinical characteristics and extent of the disease. On the other hand, prediction of prognosis is challenging and there are not sufficient laboratory tests to foresee the disease progression for the time being.[7,8] For this reason, researchers are working on practical and effective methods to help clinicians in the management of psoriasis.[7,8]

Complete blood cell indices such as red cell distribution width (RDW), mean platelet volume (MPV), neutrophil to lymphocyte ratio (NLR), and platelet to lymphocyte ratio (PLR) have been used as prognostic markers in various fields of medicine for years.[9-12] They were also performed as supportive tests in the estimation of disease progression for psoriasis.[13-15] Systemic-immune inflammation index (SII) (neutrophil X platelet/lymphocyte) is a new complete blood cell index that has been used in the prediction of disease progression especially in the field of oncology.[16-18] As SII includes three main parameters of complete blood cell count, it may give a more precise opinion about chronic inflammation and other medical branches have also started to use SII.[19,20] To the best of our knowledge, there is no study in the literature evaluating the efficacy of SII in patients with psoriasis.

This study aims to evaluate the utility of SII in the management of patients with psoriasis.

2 | MATERIALS AND METHODS

This retrospective case-control study was conducted on patients who were admitted to the outpatient clinic of Department of Dermatology and Venereology, Ufuk University Hospital from January, 1, 2017 to December, 31, 2019. Patients with psoriasis were compared with a age and gender-matched control group with other non-inflammatory dermatologic diseases. Inclusion criteria for the study group were: (1) Patients with diagnosis of psoriasis (2) ≥18 years of age. Exclusion criteria were: (1) Presence of pregnancy or lactation. Written informed consent was obtained from all the participants, and the study was approved by the institutional ethics committee of Turkish Ministry of Health, Ankara City Hospital (E1-20-517). First, study and Control groups were compared in terms of their demographic features, clinical characteristics, and laboratory parameters. Age, gender, body mass index, comorbidities (presence of diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, Hashimoto's thyroiditis, inflammatory bowel disease) rate of smoking and alcohol consumption, laboratory test results (hemoglobin, hematocrit, white blood cell count, platelet count, neutrophil count, lymphocyte count, red blood cell distribution, erythrocyte sedimentation rate, C-reactive protein, and SII) were compared between study and control groups.

Afterwards, psoriasis area severity index (PASI) score were used for the assessment of disease severity. Four body parts (head, arms, trunk, and legs) are evaluated for the calculation of PASI score. Each part is scored individually based on the percentage of skin area involved and then combined for a total score ranging from grade 0 to 6. Additionally, the severity is estimated by three main clinical signs: erythema, induration, and desquamation. Severity parameters are measured on a scale of 0-4. Final score is calculated by using the sum of all three severity parameters, specific area scores, and weight of the respective sections.[21] Fifty percentile of PASI score for all psoriasis cases was calculated and the study group was divided into two subgroups according to their PASI score values: (1) Patients with PASI score < 50th percentile and (2) Patients with PASI ≥ 50th percentile. Previously mentioned demographic and clinical parameters were also compared between these two subgroups. Furthermore, SII values were compared according to the presence of scalp, joint, nail, and genital area involvement in the study group. Finally, a receiver operating characteristic (ROC) curve analysis was performed in order to assess the performance of SII in determining the activation of psoriasis in the study group.

Statistical Package for the Social Sciences 21 (SPSS 21, IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) software was used for the statistical analysis. The data were evaluated in terms of normal distribution criteria. Median and interquartile-range values were used for continuous variables while percentage values were used for categorical variables as the data were not normally distributed. Mann-Whitney U and chi-square tests were conducted for the comparison of variables between the groups. ROC curve analysis with Youden index was used for determining the cut-off value of SII in the prediction of psoriasis activation in the study group. A type-1 error of 0.05 was claimed statistically significant.

3 | RESULTS

There were 71 and 70 patients in the study and control groups, respectively. Comparison of demographic features and clinical characteristic between the study and control groups was shown in Table 1. Statistically significant differences were found between the groups for smoking rate, median hematocrit, platelet, neutrophil, lymphocyte,

TABLE 1 Comparison of demographic features and clinical characteristic between the study and control groups

Variables	Study group (n = 71)	Control group (n = 70)	*P* values
Age (years) (median, IQR)[a]	42 (25)	40 (21)	.32
Gender (n, %)[b]			
Male	27 (38%)	36 (51.4%)	.12
Female	44 (61.9%)	34 (48.5%)	
Body mass index (kg/m^2) (mean ± SD)	26.26 ± 4.85	25.12 ± 3.92	.13
Smoking (n, %)	38 (53%)	23 (32.8%)	**.005**
Alcohol consumption (n, %)	17 (23.9%)	13 (18.5%)	.13
Frequency of comorbidities(n, %)[b]			
Diabetes mellitus	7 (9.9%)	2 (2.9%)	.16
Hypertension	13 (18.3%)	9 (12.8%)	.48
Hyperlipidemia	39 (54.9%)	32 (45.7%)	.81
Coronary artery disease	1 (1.4%)	5 (7.1%)	.11
Hashimoto's thyroiditis	3 (4.2%)	5 (7.1%)	.49
Inflammatory bowel disease	1 (1.4%)	0 (0%)	.52
Others	4 (5.6%)	0 (0%)	.24
Laboratory parameters (median, IQR)[a]			
Hb(g/dL)	14.5 (1.87)	14 (1.73)	.31
Hct(%)	42.31 (5.3)	39.5 (5.05)	**<.001**
MCV (fL)	87.5 (4.56)	87 (5.68)	.61
WBC($10^3/mm^3$)	7.7 (2.40)	7.6 (1.7)	.061
Plt ($10^3/mm^3$)	261 (70.6)	223 (76)	**<.001**
Neutrophil ($10^3/mm^3$)	4.86 (1.99)	4.6 (1.30)	**.023**
Lymphocyte ($10^3/mm^3$)	2.18 (0.80)	2.51 (0.87)	**.001**
RDW (%)	12.7 (1.34)	12.4 (1.0)	**.052**
ESR (mm/h)	18 (18)	8.5 (8)	**<.001**
CRP (mg/dL)	4.5 (8.1)	0.23 (0.2)	**<.001**
SII ($10^3/mm^3$)	581.05 (436.86)	403.14 (179.41)	**<.001**

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; IQR, interquartile range; Plt, platelet; RDW, red blood cell distribution width; SII, systemic immune-inflammation index; WBC, white blood cell.

Statistically significant *P* values are highlighted in bold.

[a]Statistical analysis was performed by Mann Whitney U test.

[b]Statistical analysis was performed by Chi square test.

red blood cell distribution width, erythrocyte sedimentation rate, C-reactive protein, and SII values ($P < .05$). All of the mentioned parameters were higher in the study group except median lymphocyte count.

Fifty percentile PASI score value in the study group was calculated as 4.5. There were 36 patients whose PASI score was below 4.5 and there were 35 patients with PASI score ≥ 4.5. Clinical characteristics and laboratory changes of the patient with PASI score < 4.5 and PASI ≥ 4.5 were compared in Table 2. Significantly higher median white blood cell, neutrophil, erythrocyte sedimentation rate, C-reactive protein, and SII values were found in the PASI ≥ 4.5 group ($P < .05$). Other parameters were comparable between the groups.

There were 48, 18, 21, and 27 patients with scalp, joint, nail, and genital area involvement, respectively, in the study group. Comparison of SII values according to the presence of scalp, joint, nail and genital area involvement in the study group were shown in Table 3. Significantly higher SII values were present in patients with nail and genital involvement ($P < .05$).

Receiver operating characteristic curve analysis for assessing the performance of SII in the prediction of psoriasis activation was shown in Table 4 and Figure 1. A cut-off value of 575.8 was calculated with 66.7% sensitivity and 66% specificity (area under the curve was 0.65 and $P = .04$).

4 | DISCUSSION

The results of the present study indicated that SII was associated with psoriasis activation and severity. Moreover, this novel index might be used for the prediction disease activation in patients with psoriasis. The pathophysiological pathways behind psoriasis is complicated and mainly related to immune-mediated events including T lymphocytes, dendritic cells, and various cytokines leading to an excessive inflammatory process.[2-4,22] Thus, assessment of inflammation is important for clinicians to establish more effective management protocols. However, there is no optimal prognostic marker available at present and researchers are working on new methods to evaluate the degree of inflammation in this group of cases.[7,8]

Complete blood cell indices are practical and cost-effective markers that have been used in various fields of medicine for years.[9-12] As psoriasis is also an inflammatory skin disease, the utility of complete blood indices were investigated in several studies with promising results.[13-15] Red cell distribution width, mean platelet volume, neutrophil to lymphocyte ratio and platelet to lymphocyte ratio were the most common indices used in the literature. However, mentioned markers may be affected by various factors such as anemia, infection and other inflammatory conditions. Furthermore, the utility of these indices has not been validated by high-quality studies. For this reason, they cannot be used widely in routine clinical practice.[13-15] On the other hand, combination of various parameters may be useful and more data is necessary to reach more precise results.

SII is a novel index including three main parameters of complete blood cell count and it is regarded as an efficient ancillary test for the estimation of inflammation. The main strength of SII compared with NLR is the inclusion of platelet count. Platelets take part in crucial immune-mediated processes such as releasing anti-microbial proteins and producing inflammatory cytokines. Furthermore, they play a role in coagulation, fibrinolysis, tissue regeneration and angiogenesis.[23] Although, it was most commonly used in the field of oncology

TABLE 2 Clinical characteristic and laboratory changes of the patient with PASI score < 4.5 and PASI ≥ 4.5

Variables	PASI score < 4.5 (n = 36)	PASI score ≥ 4.5 (n = 35)	*P* values
Age (years) (median; IQR)[a]	38 (27)	42 (27)	.24
Body mass index (kg/m^2) (median, IQR)	25.59 (4.69)	26.31 (7.64)	.88
Smoking (n, %)	17 (47.2%)	21 (60%)	.26
Psoriatic arthritis (n, %)	5 (13.8%)	11 (31.4%)	.15
Alcohol consumption (n, %)	4 (11.1%)	9 (25.7%)	.83
Frequency of comorbidities (n, %)[b]			
Diabetes mellitus	3 (8.3%)	4 (11.4%)	.68
Hypertension	4 (11.1%)	9 (25.7%)	.21
Hyperlipidemia	15 (41.6%)	15 (42.8%)	.59
Coronary artery disease	0 (0%)	1 (2.8%)	.5
Hashimoto's thyroiditis	1 (2.7%)	2 (5.7%)	.5
Inflammatory bowel disease	0 (0%)	1 (2.8%)	.5
Laboratory parameters (median, IQR)[a]			
Hb (g/dL)	14.17 (2.13)	14.72 (1.73)	.95
Hct (%)	41.30 (5.37)	44.15 (4.84)	.54
MCV (fL)	87.03 (4.01)	88.8 (5.73)	.41
WBC (10^3/mm^3)	7.34 (2.31)	9.1 (2.69)	**.006**
Plt (10^3/mm^3)	262.4 (53.95)	252.5 (85.75)	.35
Neutrophil (10^3/mm^3)	4.55 (1.56)	5.47 (2.31)	**.003**
Lymphocyte (10^3/mm^3)	2.05 (0.71)	2.30 (0.95)	.55
RDW (%)	12.51 (1.67)	13.07 (1.38)	.15
ESR (mm/h)	8 (6)	18.5 (8)	**.001**
CRP (mg/dL)	2.65 (4.68)	6.1 (8.25)	**.033**
SII (10^3/mm^3)	532.656 (193.49)	681.98 (684.49)	**.007**

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; IQR, interquartile range; Plt, platelet; RDW, red blood cell distribution width; SII, systemic immune-inflammation index; WBC, white blood cell.

Statistically significant *P* values are highlighted in bold.

[a]Statistical analysis was performed by Mann Whitney U test.

[b]Statistical analysis was performed by Chi square test.

TABLE 3 Comparison of SII values according to the presence of scalp, joint, nail, and genital area involvement in the study group

(n, %)	involvement +	involvement –	*P* value
Scalp (48, 67.6%)	598.82 (431.9)	525.93 (442.16)	.22
Arthritis (18, 25.4%)	677.11 (657.26)	551.17 (315.97)	.098
Nail (21, 29.6%)	629.2 (687.1)	547.2 (370.7)	**.04**
Genital (27, 38%)	665.8 (551.1)	545.1 (324.1)	**.03**

Abbreviation: SII, systemic immune-inflammation index.

Statistically significant *P* values are highlighted in bold.

TABLE 4 ROC curve analysis for assessing the performance of SII in the prediction of psoriasis activation

(AUC: 0.65, 95% CI: 0.51-0.78)	Cut-off value for SII	Sensitivity	Specify	*P* value
	575.8	66.7%	66.0%	.04

Abbreviations: AUC, area under the curve; CI, confidence interval; ROC, receiver operating characteristic; SII, systemic immune-inflammation index.

in the past, other medical disciplines has started to utilize SII in recent years.[16-18] However, SII has not been used for the evaluation of psoriasis activation before and in our opinion it may be beneficial for physicians who work in this field. Of course, prediction of psoriasis prognosis is challenging and it is not possible to decide on the best management protocol just by one parameter. Thus, SII may be used as a supportive method along with physical examination and conservative laboratory tests. Furthermore, SII was also reported to be a promising marker for

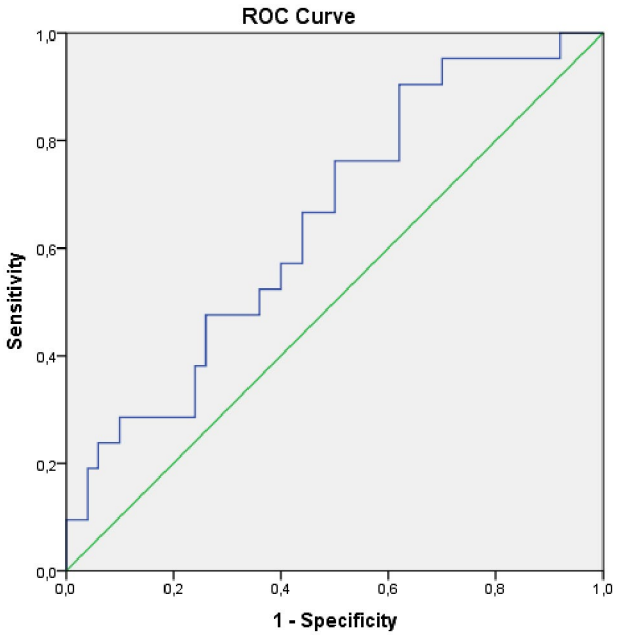

FIGURE 1 Receiver operating characteristic curve analysis for assessing the performance of SII in the prediction of psoriasis activation

the assessment of disease activation in other dermatologic pathologies such as Behçet's disease.[24] Thus, it may be used for the evaluation of other inflammatory skin diseases in the near future.

The main strengths of the present study were its novelty and inclusion of various study parameters. However, retrospective design and single center experience were the main limitations.

In conclusion, SII may be used for the prediction of psoriasis activation and physicians should be cautious in patients with SII values above 575.8.

DISCLOSURES

The authors state that they have no conflict of interest in this study.

AUTHOR'S CONTRIBUTIONS

DD: Study design, manuscript writing, supervision, ET: Data collection, literature review, manuscript writing.

DATA AVAILABILITY STATEMENT

The data of the manuscript is available.

CONSENT TO PARTICIPATE

Informed consent was obtained from all participants.

CONSENT FOR PUBLICATION

Necessary consent was taken from the patients for publication.

ETHICS APPROVAL

The study protocol was approved by Ministry of Health Ankara City Hospital Ethics Committee with reference number E1-20-517 and informed consent was obtained from all participants.

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