European Review for Medical and Pharmacological Sciences 2023; 27: 9267-9272

Evaluation of systemic immune and inflammatory biomarkers in hidradenitis suppurativa

Z. UTLU

Department of Dermatology and Venereology, Health Sciences University Erzurum Regional Training and Research Hospital, Erzurum, Turkey

Abstract. – OBJECTIVE: We aimed to investigate the interrelation of HS with CBC parameters and new inflammatory indicator parameters, systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI).

PATIENTS AND METHODS: 102 patients diagnosed with HS and 99 healthy controls were included. The medical records and laboratory findings of the participants were reviewed retrospectively. Patients and control group neutrophil, lymphocyte, monocyte, and platelet counts, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), monocyte-lymphocyte ratio (MLR), mean platelet volume (MPV), platelet distribution width (PDW) and red cell distribution width coefficient of variation (RDW), SII and SIRI were compared.

RESULTS: The patient and control groups differed significantly concerning CRP, neutrophil count, lymphocyte count, monocytes count, platelet count, PLR, and MHR ($p<0.05$), whereas the mean of MPV and NLR did not show a significant difference in control individuals. SII and SIRI were significantly higher in patients with HS than in controls ($p=0.005$, $p<0.001$).

Correlation analyses of SII and SIRI with each other and CRP were performed. It was determined that SIRI had a moderate correlation with CRP (r=0. 346, $p<0.001$). The correlation between SII and CRP was low (r=0.256, $p<0.001$). In addition, we analyzed the correlation between SII and SIRI and we determined a high level of correlation (r=0.675, $p<0.001$).

CONCLUSIONS: Our study has objectively demonstrated that SII and SIRI are more reliable biomarkers than other inflammation parameters in HS patients. Thus, SII and SIRI would be used to evaluate treatment response and follow-up in HS as new indicators.

Key Words:
Hidradenitis suppurativa, Systemic immune-inflammation index, Systemic inflammation response index.

Introduction

Hidradenitis Suppurativa (HS) is a chronic, recurrent inflammatory disease of apocrine sweat glands. It is characterized by recurrent abscesses, nodules, sinus tracts, fistules, and scarring at intertriginous areas[1].

Follicular occlusion is considered the main factor in its pathogenesis, while inflammatory pathophysiology could not be determined precisely[2]. Effective usage of anti-inflammatory drugs in the treatment and the absence of pathogenic bacteria suggest the idea that the inflammatory system has a critical role in pathogenesis[1].

Besides dysregulated immune-mediated inflammatory response, genetic predisposition, smoking, and obesity are often discussed risk factors[3,4].

CBC is a cost-effective and easily accessible diagnostic test. Current research displays the potential role of complete blood count (CBC) parameters, such as the ratio of leukocyte subtypes (neutrophil-lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), mean platelet volume (MVP), and red blood cell distribution width (RDW) as inflammatory indicators[3-7].

Also, the utilization of the systemic immune-inflammation index (SII) and systemic inflammation response index (SIRI) is an escalator approach to evaluate the activity of various inflammatory diseases and predict prognosis in cancer patients[8-11].

In this research, we aimed to investigate the interrelation of HS with CBC parameters and new inflammatory indicator parameters SII and SIRI.

Patients and Methods

A retrospective study was conducted on patients with HS admitted to the Dermatology

Corresponding Author: Zeynep Utlu, MD; e-mail: dr.zeynep.utlu@gmail.com

Department of Erzurum Regional Training and Research Hospital, Turkey, between January 2019 and April 2020. All patients who presented to our clinic were diagnosed with HS and were retrospectively reviewed. In total, 102 patients satisfying the following inclusion criteria were included: diagnosed with HS by a dermatologist, had complete blood count analysis results during follow-up, did not have any systemic and/or chronic inflammatory diseases (e.g., cardiac diseases, diabetes mellitus, hypertension, hyperlipidemia, and rheumatoid arthritis). Patients with missing data were excluded from the study. The control group comprised 99 healthy volunteers from outside the hospital. It consists of volunteers who did not have known systemic and/or inflammatory disease, did not smoke, did not have acne vulgaris or chronic dermatological disease, and did not use regular medication. The hematological parameters including hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), RDW, white blood cells (WBCs), neutrophils, lymphocytes, platelets, and MPV, platelet distribution width (PDW) and red cell distribution width coefficient of variation (RDW-CV) were recorded, and NLRs, SII, SIRI were calculated. SIRI and SII were defined as follows: SIRI neutrophil count x monocyte count/lymphocyte count and SII platelet count x neutrophil count/lymphocyte count, respectively. Neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), and platelet-lymphocyte ratio (PLR) were determined. The demographic characteristics of the patient group are shown in Table I.

Statistical Analysis

All procedures were performed using Statistical Package for Social Sciences (SPSS Inc., Armonk, NY, USA, v21.0) software. After checking the normality distribution of scale variables by the Kolmogorov-Smirnov test, continuous parameters were compared using Kruskal-Wallis H and/or Mann-Whitney U tests according to the number of samples. The exact significance test for the Mann-Whitney U test was performed when the sample size was not sufficient. Pearson's Chi-square or Fisher tests were used to compare independent categorical variables according to the sample sizes. Continuous variables were stated as mean ± standard deviation or median (interquartile range), and categorical variables as numbers (percentages). Bonferroni correction was applied as post-hoc if significant results were obtained in more than two-sample comparisons. CRP, SII, and SIRI values were compared with Spearman's correlation test and presented with a simple scatterplot. The p-values achieved after post-hoc analysis were tabulated in an adjusted manner. A two-sided p-value <0.05 was considered statistically significant.

Results

A total of 102 patients [42 (41.2%) women and 60 (58.8%) men] with a mean age of 30.56 years participated in the study. The age and sex distribution of healthy volunteers were similar to that of the patients (Table I).

The comparison results of the two groups in terms of hemogram measurements and measurements calculated with formulas are given in Table II. The patient and control groups differed significantly concerning CRP, neutrophil count, lymphocyte count, monocyte count, platelet count, and PLR ($p<0.05$), whereas the mean of MPV and NLR did not show a significant difference in control individuals. SII was 729.41 (IQR: 150.1-7298.8) and SIRI was 1.86 (IQR:0.39-19.4) in patients with HS, while it was 536.35 (IQR: 180.2-1637.8) and 1.07 (IQR:0.34-3.44) in the control group. SII and SIRI were significantly high-

Table I. Comparison of age and gender of HS patients and controls.

		Patient Group	Control Group
Gender	Female	42 (41.2%)	51 (51.5%)
	Male	60 (58.8%)	48 (48.5%)
Age	Between 18-30	53 (52.0%)	52.0
	Between 31-40	22 (21.6 %)	21.6
	41 and above	27 (26.4%)	26.4
N		102	99

Table II. Comparison of laboratory parameters HS patients separately with the healthy control group.

Parameters	Patients (n=102)	Healthy control (n=99)	*p*-value
Hemoglobin (g/dl)	15.04±1.6	14.7±1.4	0.136
Neutrophil (10^9/l)	5,875±2,280	4,289±1,816	**< 0.001**
Lymphocyte (10^9/l)	2,792±904	2,313±637	**< 0.001**
Monocytes (10^9/l)	742±392	545±162	**< 0.001**
Platelet (10^9/l)	296±66	274±59	**0.007**
MPV (fl)	10.12±0.83	10.14±1.14	0.581
NLR (10-2)	242±204	193±80	0.072
PLR	118±61	125±39	**0.028**
CRP (mg/l)	13.2±17	2.6±1.4	**< 0.001**
SII	729±756	536±269	**0.005**
SIRI	1.86 ±2.11	1.07±0.63	**< 0.001**

Data were expressed as mean±standard deviation. Mann-Whitney U test was used. Significant values were shown in bold. MPV: Mean platelet volume; NLR: Neutrophil/lymphocyte ratio; PLR: Platelet/lymphocyte ratio; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; SII: Systemic immune-inflammation index; SIRI: systemic inflammation response index.

er in patients with HS than in controls (p=0.005, p<0.001). No significant difference was found between the patient and control individuals in terms of characteristics other than these.

The SII and SIRI calculation parameters, neutrophil, lymphocyte, and platelet counts, might already be expected to correlate with SII and SIRI. Therefore, correlation analyses of SII and SIRI with each other and CRP were performed. It was determined that SIRI had moderate correlations with CRP (r=0.346, p<0.001) Table III. The correlation between SII and CRP was low (r=0.256, p<0.001; Table III). In addition, we analyzed the correlation between SII and SIRI and we determined a high level of correlation (r=0.675, p<0.001; Table III).

Discussion

The inflammatory pathophysiology of hidradenitis suppurativa (HS) has not been precisely defined yet. However, inflammatory indicators like the number of leukocytes, erythrocyte sedimentation rate (ESR), and CRP are used for diagnosis and follow-up of the disease[12]. Leukocyte sub-types, including neutrophils, lymphocytes, and monocytes, are the non-specific cellular indicators of systemic inflammation. It is known that cellular components of blood and their ratio could provide insights into the severity of the continuing inflammation[13].

Recently, a tendency to benefit from inflammatory indexes like NLR, MLR, and PLR to evaluate the activity of various inflammatory diseases and as prognostic indicators to predict survival has developed[14-17].

In the literature, most of the research on NLR and PLR values at HS show that NLR and PLR values are higher in HS patients compared to control groups, while Çelikarslan et al[18] have not spotted any significant difference among HS patients and control groups in terms of NLR and PLR. Furthermore, Gambichler et al[3] have found that PLR is significantly lower in HS patients and stated that PLR might not be a suitable biomarker of disease activity and severity.In our research, neutrophil, lymphocyte, and monocyte numbers were

Table III. The correlation between SII, SIRI, and CRP.

	CRP		SIRI		SII	
	rs	*p*	*rs*	*p*	*rs*	*p*
CRP			0.346**	<0.001	0.256**	<0.001
SIRI	0.346**	<0.001			0.675**	<0.001
SII	0.256**	<0.001	0.675**	<0.001		

Spearman's correlation test was used. CRP: C-reactive protein; SII: Systemic immune-inflammation index; SIRI: systemic inflammation response index. *p<0.05 **p<0.01.

higher in HS patients than in the control group, whereas NLR elevation was not statistically significant. PLR is detected higher with a statistically moderate significance in the patient group. Conflicting results in the literature and our data caused us to deduce that NLR and PLR might be inadequate biomarkers in HS patients.

Thrombocytes play a significant role in normal homeostasis. MPV is a thrombocyte function indicator. Since chronic inflammatory diseases might be related to coagulopathies, changes in MVP have been investigated in many different diseases. In some of these cases, MVP was not found concerning disease activity, while in others, it was increased or decreased[19,20].

Authorities suggested that high MVP could be a risk factor for thrombosis. It is proclaimed that increased MVP could be a risk factor in numerous inflammatory diseases like ankylosing spondylitis and rheumatoid arthritis[21].

Also, in many up-to-date types of research, it is obtained that MVP is significantly high in Bechet's disease[19,22]. In contrast, Altunışık et al[23] could not determine a significant difference between acne rosacea patients and control groups in terms of MPV and RDW values. Similarly, retrospective research on patients with alopecia areata by İslamoğlu and Demirbaş[24] has not shown any significant difference in MPV, RDW, and NLR values.

MPV has also been investigated on HS, and no consensus has been settled on the outcomes. Even though Ünal et al[25] detected significantly higher MPV values in HS patients compared to control groups, Miller et al[26] stated they had not found any difference in MPV values. Although there is chronic recurrent inflammation in HS, it might not be connected to a hyper-coagulative or pro-thrombotic event.

In our results, platelet numbers were higher in our patients compared to the control groups, while no statistically significant difference was present among MPV values. These conflicting findings show the requirement for other prospective studies with more patients to decide whether MPV could be used on HS patients as an inflammatory and prognostic indicator or not.

Both systemic immune inflammation index (SII) and systemic inflammation result index (SIRI) are recently defined inflammatory biomarkers related to prognosis and treatment response[27]. Also, SII is identified as an inflammatory indicator of various dermatologicaldiseases[8,13]. Dincer Rota et al[28] showed that SII could be a predictor for psoriasis in patients with psoriasis. Tanacan et al[29] revealed that high SII values are associated with disease severity in patients with RAS.

It has also been reported that SII may have a high prognostic value in cancer patients and that a high pre-treatment SII value may be associated with poor outcomes[11].

Recent studies[27-30] show that since thrombocyte number could be accepted as an inflammation marker, SII is a more complicated and solid index to evaluate the relation between inflammatory disease and their comorbidities than NLR. SII could be used to identify HS patients at risk for high blood pressure, insulin resistance, metabolic syndrome, and cardiovascular comorbidities[3,30].

SIRI is another new prognostic factor based on peripheral neutrophil, monocyte, and lymphocyte numbers to forecast prognosis and treatment response in some malignancies[9,31].

In their meta-analysis, Wei et al[32] declared that SIRI is related to the poor prognosis of malignancies and could be used as an efficient predictor of cancer treatment.

There is not much research on SIRI in dermatologic patients in the literature. A recent study with acne patients who use isotretinoin displays that after ISO treatment, SIRI declined significantly, yet there was no difference in initial SIRI values between patients and healthy controls[27].

According to the result of our study, SII and SIRI values were significantly higher in patients with HS. One of the most striking findings of our study was SIRI's positive correlation with CRP. In addition, a high correlation between SII and SIRI in HS patients is detected. Our results support the hypothesis of SII and SIRI being suitable biomarkers for patients with HS.

Limitations

The present study has several limitations. Firstly, it has a relatively small sample size and is a single-center study. Also, because of its retrospective design, the authors could not obtain much information about the disease staging and the extent of the involved areas.

Conclusions

Even though the relation of NLR and PLR with HS has been investigated previously, this is the first research on the interrelation of HS with SII and SIRI, as far as we know. Since there are conflicting results in the literature on NLR,

MPV, and PLR, a significant elevation of SII and SIRI may highlight SII and SIRI over other markers. Thus, SII and SIRI would be used to evaluate treatment response and follow-up in HS as new indicators. More advanced prospective controlled research is needed to clarify the connection between SII, SIRI, and HS.

Conflict of Interest
The authors declare that they have no conflict of interests.

Informed Consent
Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Ethics Approval
This study was approved by the Ethics Committee of Erzurum Regional Training and Research Hospital (#ID2022/07-87) and conducted according to the Helsinki Declaration of Human Rights.

Authors' Contributions
U.Z.; methodology, validation, investigation and data collection, writing-original draft preparation, and writing-review and editing.

Funding
We declare no financial support or relationships that may pose a conflict of interest.

ORCID ID
Zeynep Utlu: 0000-0002-0178-2871

References

1) Yaşar NF, Uylas MU, Baspinar M, Sarsilmaz H, Ates E, Erkasap S, Sahin A. Evaluating the Use of Hematological Parameters in Staging Hidradenitis Suppurativa. Wounds 2016; 28: 87-91.
2) Gibson RS, Porter ML, Kimball AB. Erythrocyte sedimentation rate, rather than C-reactive protein, maybe the preferred biomarker for hidradenitis suppurativa. JAAD Int 2022; 19: 47-48.
3) Gambichler T, Hessam S, Cramer P, Abu Rached N, Bechara FG. Complete blood collection-based systemic inflammation biomarkers for patients with hidradenitis suppurativa. J Eur Acad Dermatol Venereol 2022; 36: 1593-1596.
4) Jiménez-Gallo D, de la Varga-Martínez R, Ossorio-García L, Albarrán-Planelles C, Rodríguez C, Linares- Barrios M. The Clinical Significance of Increased Serum Proinflammatory Cytokines, C-Reactive Protein, and Erythrocyte Sedimentation Rate in Patients with Hidradenitis Suppurativa. Mediators Inflamm 2017; 2017: 2450401.
5) Aktaş Karabay E, Aksu Çerman A, Demir D, Kıvanç Altunay I. The Effects of Systemic Psoriasis Therapies on the C-Reactive Protein and the Neutrophil-Lymphocyte Ratio. Ann Dermatol 2019; 31: 60-610.
6) Eraldemir FC, Musul M, Duman AE, Oztas B, Baydemir C, Hulagu S. The relationship between neutrophil/lymphocyte and platelet/lymphocyte ratios with oxidative stress in active Crohn's disease patients. Hippokratia 2016; 20: 368-373.
7) Zareifar S, Farahmand Far MR, Golfeshan F, Cohan N. Changes in platelet count and mean platelet volume during infectious and inflammatory disease and their correlation with ESR and CRP. J Clin Lab Anal 2014; 28: 245-248.
8) Tezcan D, Turan Ç, Yılmaz S. The effect of colchicine treatment on complete blood cell count-based parameters in patients with Behçet's disease. J Health Sci Med 2022; 5: 517-522.
9) Chao B, Ju X, Zhang L, Xu X, Zhao Y. A Novel Prognostic Marker Systemic Inflammation Response Index (SIRI) for Operable Cervical Cancer Patients. Front Oncol 2020; 13: 766.
10) Wu J, Yan L, Chai K. Systemic immune-inflammation index is associated with disease activity in patients with ankylosing spondylitis. J Clin Lab Anal 2021; 35: 23964.
11) Fest J, Ruiter R, Mulder M, Groot Koerkamp B, Ikram MA, Stricker BH, van Eijck CHJ. The systemic immune-inflammation index is associated with an increased risk of incident cancer-A population-based cohort study. Int J Cancer 2020; 146: 692-698.
12) Lapić I, Padoan A, Bozzato D, Plebani M. Erythrocyte Sedimentation Rate and C-Reactive Protein in Acute Inflammation. Am J Clin Pathol 2020; 153: 14-29.
13) Yorulmaz A, Hayran Y, Akpinar U, Yalcin B. Systemic Immune-Inflammation Index (SII) Predicts Increased Severity in Psoriasis and Psoriatic Arthritis. Curr Health Sci J 2020; 46: 352-357.
14) Stefaniuk P, Szymczyk A, Podhorecka M. The Neutrophil to Lymphocyte and Lymphocyte to Monocyte Ratios as New Prognostic Factors in Hematological Malignancies - A Narrative Review. Cancer Manag Res 2020; 12: 2961-2977.
15) Gao K, Zhu W, Liu W, Ma D, Li H, Yu W, Wang L, Cao Y, Jiang Y. Diagnostic value of the blood monocyte-lymphocyte ratio in knee osteoarthritis. J Int Med Res 2019; 47: 4413-4421.
16) Pilaczyńska-Cemel M, Gołda R, Dąbrowska A, Przybylski G. Analysis of the level of selected

parameters of inflammation, circulating immune complexes, and related indicators (neutrophil/lymphocyte, platelet/lymphocyte, CRP/CIC) in patients with obstructive diseases. Cent Eur J Immunol 2019; 44: 292-298.

17) Ji Y, Wang H. Prognostic prediction of the systemic immune-inflammation index for patients with gynecological and breast cancers: a meta-analysis. World J Surg Oncol 2020; 18: 197.
18) Çetinarslan T, Türel Ermertcan A, Özyurt B, Gündüz K. Evaluation of the laboratory parameters in hidradenitis suppurativa: Can we use new inflammatory biomarkers? Dermatol Ther 2021; 34: 14835.
19) Ataş H, Canpolat F, Eskioglu F. Evaluation of Mean Platelet Volume in Patients With Behcet's Disease as an Indicator of Vascular Thrombosis. Arch Iran Med 2018; 21: 234-239.
20) Lippi G, Buonocore R, Cervellin G. The Mean Platelet Volume Is Decreased in Patients Diagnosed with Venous Thromboembolism in the Emergency Department. Semin Thromb Hemost 2016; 42: 632-635.
21) Kisacik B, Tufan A, Kalyoncu U, Karadag O, Akdogan A, Ozturk MA, Kiraz S, Ertenli I, Calguneri M. Mean platelet volume (MPV) as an inflammatory marker in ankylosing spondylitis and rheumatoid arthritis. Joint Bone Spine 2008; 75: 291-294.
22) Masoumi M, Shadmanfar S, Davatchi F, Shahram F, Akhlagi M, Faezi T, Kavosi H, Moradi S, Balasi J. Correlation of clinical signs and symptoms of Behçet's disease with mean platelet volume (MPV) and red cell distribution width (RDW). Orphanet J Rare Dis 2020; 15: 297.
23) Altunisik N, Turkmen D, Sener S. Investigation of the relationship between inflammatory blood parameters and rosacea and Demodex infestation. J Cosmet Dermatol 2020; 19: 2105-2108.
24) İslamoğlu ZGK, Demirbaş A. Evaluation of complete blood cell and inflammatory parameters in patients with alopecia areata: Their association with disease severity. J Cosmet Dermatol 2020; 19: 1239-1245.
25) Ünal A. Evaluation of mean platelet volume and platelet count in patients with hidradenitis suppurativa. Turkderm-Turk Arch Dermatol Venereol 2021; 55: 189-192.
26) Miller IM, Johansen ME, Mogensen UB, Zarchi K, Ellervik C, Jemec GB. Coagulation Status in Hidradenitis Suppurativa: A Danish Population- and Hospital-Based Cross-Sectional Study. Dermatology 2015; 231: 119-126.
27) Cosansu NC, Yuksekal G, Turan U, Umitfer F, Yaldiz M, Sevimli Dikicier B. Investigation of systemic immune-inflammation index and systemic inflammation response index as an indicator of the anti-inflammatuary effect of isotretinoin in patients with acne vulgaris. Cutan Ocul Toxicol 2022; 41: 174-178.
28) Dincer Rota D, Tanacan E. The utility of systemic-immune inflammation index for predicting the disease activation in patients with psoriasis. Int J Clin Pract 2021; 75: e14101.
29) Tanacan E, Dinçer Rota D, Oktem R, Erdogan FG. The correlation of systemic immune-inflammation index, neutrophil-to-lymphocyte ratio, derived neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio with disease severity in recurrent aphthous stomatitis. J Cosmet Dermatol 2022; 21: 4858-4863.
30) Sánchez-Díaz M, Salvador-Rodríguez L, Cuenca-Barrales C, Arias-Santiago S, Molina-Leyva A. Exploring the role of systemic immune-inflammation index and neutrophil-lymphocyte ratio in cardiovascular risk stratification for patients with hidradenitis suppurativa: A cross-sectional study. J Dermatol 2022; 49: 1238-1244.
31) Chen L, Chen Y, Zhang L, Xue Y, Zhang S, Li X, Song H. In Gastric Cancer Patients Receiving Neoadjuvant Chemotherapy Systemic Inflammation Response Index is a Useful Prognostic Indicator. Pathol Oncol Res 2021; 27: 1609811.
32) Wei L, Xie H, Yan P. Prognostic value of the systemic inflammation response index in human malignancy A meta-analysis. Medicine (Baltimore) 2020; 99: 23486.