Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as inflammatory markers in psoriasis: a case-control study

Hao Trong Nguyen, Long Dinh Hoang Vo, Nguyen Nhat Pham

Ho Chi Minh City Hospital of Dermato-Venereology, Ho Chi Minh City, Vietnam

Abstract

Our case-control study of 60 patients with psoriasis vulgaris (PsV), 20 patients with psoriatic arthritis (PsA), and 34 healthy control participants in Ho Chi Minh City Hospital of Dermato-Venereology from October 2019 to September 2020 aimed to evaluate the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and associated factors in patients with PsV and PsA. Results showed that in the PsV group, significant correlations of NLR with Psoriasis Area and Severity Index and the high-sensitivity C-reactive protein (hs-CRP) level was noted (r=0.374 and r=0.352, respectively; P=0.003 and P=0.006, respectively). NLR was also related to PsA (P=0.007, OR=1.57). The area under the curve (AUC) for NLR in predicting PsA was 0.7554 (cut-off, 2.239; sensitivity, 85%; specificity, 61.67%). PLR was also related to PsA (P=0.008, OR=1.01). The AUC for PLR was 0.6513 (cut-off, 159.6; sensitivity, 55%; specificity, 88.33%). Thus, complete blood count parameters can reflect the inflammatory status of patients with PsV and PsA. NLR and PLR may be potential diagnostic markers for PsA in patients with psoriasis. Future studies should aim to assess the value and usage of these parameters.

Introduction

Although the pathophysiology of psoriasis is complex, chronic inflammation plays an important role in psoriasis and its comorbidities, such as cardiovascular diseases.[1] While the Psoriasis Area and Severity Index (PASI) and body surface area are used to assess the severity of the disease, these parameters cannot fully evaluate chronic inflammation. Thus, there is a need for simple, convenient, and reliable parameters to assess chronic inflammation.

Psoriatic arthritis (PsA) can precede, coexist with, or develop after psoriasis vulgaris (PsV), with a typical latency of approximately 10 years.[2] Early identification of PsA is important since this condition causes irreparable joint damage and negatively affects patients' quality of life. Thus, there is a need to identify markers to predict the presence of PsA in patients with psoriasis, and inflammatory markers such as interleukin (IL)-6, tumor necrosis factor (TNF)-α, E-selectin, high-sensitivity C-reactive protein (hs-CRP), and intercellular adhesion molecule 1 are usually evaluated for this purpose. However, assays for these markers are expensive and may be difficult to obtain, limiting their applicability and popularity.

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) can reflect systemic inflammation and are easily obtainable from a routine blood test. There has been accruing evidence of these simple-to-obtain inflammatory biomarkers about their broad utility in clinical practice such as predictors of disease course and outcome in a variety of medical conditions. Some reports have shown that the NLR and PLR increase in several diseases including diabetes mellitus, acute coronary syndrome, ulcerative colitis, Behcet's disease, tuberculosis, rheumatic arthritis, and cirrhosis.[3,4] More novel evidence includes the correlation of PLR with liver fibrosis in chronic hepatitis B patients, hyperfunction and malignancy of the thyroid, and irritable bowel disease.[5,6] Besides, NLR is another marker of inflammation derived from a hemogram and it's often evaluated in combination with PLR. Thus, NLR also showed some association with the conditions that PLR did in the same studies and others such as the active state of ulcerative colitis, the control level in diabetes mellitus type 2, the atrial fibrillation, and the outcome of cerebral hemorrhage.[7-10] In addition to the literature on many chronic and classical conditions, the potential use of PLR and NLR for more acute and novel diseases such as the identification of potentially severe COVID-19 cases is intriguing.[11]

Besides the wide range of studies in many specialties, to our best knowledge, no previous study has evaluated the NLR and PLR in patients with psoriasis and determined the correlation of these parameters with the PASI, hs-CRP level, erythrocyte sedimentation rate (ESR), and other factors. Therefore, we aimed to evaluate the association of NLR and PLR with disease-related factors in patients with PsV and PsA. We expect that the findings will yield a simple, convenient, and cost-effective tool to assess inflammation in psoriasis patients.

Correspondence: Hao Trong Nguyen, Ho Chi Minh City Hospital of Dermato-Venereology, 2 Nguyen Thong, Ward Vo Thi Sau, District 3, Ho Chi Minh City, 700000, Vietnam.
Tel.: +84.903639234.
E-mail: bshao312@yahoo.com

Key words: NLR, PLR, Psoriasis, Inflammation.

Acknowledgments: The authors acknowledge and thank the staff at the Psoriasis Clinic, Ho Chi Minh City Hospital of Dermato-Venereology, for their help with data collection.

Contributions: HTN, analysis of data, manuscript drafting, and publishing edition finalization; LDHV, data acquisition, analysis of data, and publishing edition finalization; NNP, data acquisition, analysis of data, and publishing edition finalization. All the authors approved the final version to be published.

Conflicts of interest: The authors declare no potential conflict of interest.

Funding: None

Ethical approval and consent to participate: The participants were clearly explained the study's objectives and protocols and written informed consent was obtained prior to study enrollment. The study did not cause any harm to the participants or change the management or course of their diseases. All costs were covered by the investigators, and the patients' identities were concealed to maintain their privacy. The study protocol was approved by the Research Ethics Committee of Ho Chi Minh City Hospital of Dermato-Venereology.

Availability of data and material: All data used to support the findings of this study are included within the article. Moreover, the Excel data used to support the findings of this study are available from the corresponding author upon request.

Informed consent: The participants were clearly explained the study's objectives and protocols and written informed consent was obtained prior to study enrollment.

Received for publication: 21 April 2022.
Accepted for publication: 13 July 2022.

Licensee PAGEPress, Italy
Dermatology Reports 2023; 15:9516
doi:10.4081/dr.2022.9516

Materials and Methods

Study design

We conducted a case-control study in adult patients with PsV and PsA who were diagnosed and treated at Ho Chi Minh City Hospital of Dermato-Venereology from October 2019 to September 2020.

Participants

We obtained a convenience sample of 60 patients with PsV, 20 patients with PsA, and 34 healthy control participants. Psoriasis vulgaris was clinically diagnosed, and PsA was diagnosed on the basis of a Classification Criteria for Psoriatic Arthritis score ≥3. Patients with chronic diseases or active infections and those receiving treatment with methotrexate, cyclosporin, systemic corticosteroid, or biologics within the previous month were excluded. The control participants were selected from healthy populations (medical students, medical staff, patients' caregivers) who did not currently have chronic diseases or active infections. The control participants were age- and sex-matched to the patients with PsA and PsV.

Procedure

The following clinical information was evaluated in patients with PsV and PsA: age, weight, height, cigarette and alcohol consumption, age of onset, duration of disease, and psoriasis and PsA characteristics. Finally, blood samples were collected to perform a routine complete blood count (CBC) and measurements of ESR and hs-CRP level. The control participants also underwent the aforementioned procedures. CBC and ESR evaluations were analyzed in Ho Chi Minh City Hospital of Dermato-Venereology by using the Cell-Dyn 3200 and Ves Matic Easy systems, respectively. The hs-CRP analysis was done at MEDIC Medical Center by using the Alinity system (Abbott).

Statistical analysis

Data analysis was performed using STATA version 14. Qualitative data were described by using frequency and percentage. Quantitative data were described by mean and standard deviation if they were normally distributed, and by median and lower and upper ranges if the data did not

Table 1. Characteristics of the study population.

Characteristics	PsV (n=60)	PsA (n=20)	Control (n=34)	P
Age (year), mean±SD	47.72±14.01	51.5±13.83	46.52±14.23	0.340**
Sex, n (%)				
Male	38 (63.33)	13 (65)	17 (50)	0.388***
Female	22 (26.67)	7 (35)	17 (50)	
BMI (kg/m^2), mean±SD	22.73±3.57	22.07±3.93	22.78±3.86	0.397**
Alcohol consumption, n (%)				
Yes	29 (36.25)	5 (25)		0.342***
No	31 (63.75)	15 (65)		
Cigarette smoking, n (%)				
Yes	18 (30)	7 (35)		0.676***
No	42 (70)	13 (65)		
Age of onset (years), mean±SD	36.17±15.75	40.60±16.65		0.411*
Duration (years), mean±SD	11.12±11.14	10.99±11.54		0.689*
PASI, mean±SD	7.85±6.33	11.71±5.60		0.003*

PsV, psoriasis vulgaris; PsA, psoriatic arthritis; BMI, body mass index; PASI, Psoriasis Area and Severity Index. *P-value extracted from Mann–Whitney U test; ** P-value extracted from Kruskal–Wallis test; *** P-value extracted from Chi-squared test.

Table 2. Comparison of blood cell counts and other inflammatory parameters among the psoriasis vulgaris, psoriasis arthritis, and control groups.

Parameters	PsV (n=60)	PsA (n=20)	Control (n=34)	P*	P**	P***
WBC (k/μL)	8.57±2.54	10.2±2.67	7.54±1.55	0.074	<0.001	0.009
Neutrophils (k/μL)	5.21±2.38	7.02±2.21	4.07±1.04	0.013	<0.001	0.001
Lymphocytes (k/μL)	2.32±0.60	2.13±0.75	2.57±0.72	0.135	0.117	0.722
Monocytes (k/μL)	0.70±0.23	0.81±0.26	0.59±0.13	0.008	<0.001	0.067
Eosinophils (k/μL)	0.28±0.22	0.18±0.07	0.23±0.17	0.268	0.950	0.515
Basophils (k/μL)	0.07±0.04	0.07±0.04	0.08±0.07	0.859	0.609	0.446
Platelets (k/μL)	254.2±51.8	330.2±180.9	246.9±49.4	0.694	0.259	0.421
Hemoglobin (g/μL)	14.08±1.38	12.06±2.53	13.78±1.35	0.427	0.014	0.001
ESR (mm)	26.48±20.38	60.12±24.75	25.96±18.11	0.774	<0.001	<0.001
hs-CRP (mg/L)	3.06±4.91	27,04±26,82	1.75±2.33	0.047	<0.001	<0.001
NLR	2.48±1.49	3.68±1.59	1.69±0.64	0.001	<0.001	<0.001
PLR	119.5±44.4	171.5±103.1	103.3±37.3	0.062	0.007	0.044

WBC, white blood cell; PsV, psoriasis vulgaris; PsA, psoriatic arthritis; hs-CRP, high-sensitivity C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio. *P-value extracted from Mann–Whitney–Wilcoxon test between control vs. PsV group; **P-value extracted from Mann–Whitney–Wilcoxon test between control *vs.* PsA group; ***P-value extracted from Mann–Whitney–Wilcoxon test between PsV group vs. PsA group.

Table 3. Correlation of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with psoriasis area and severity index, high-sensitivity C-reactive protein level, and erythrocyte sedimentation rate in the PsV and PsA groups.

Group	Parameters	NLR	PLR
PsV	PASI	p=0.003	p=0.114
		r=0.374	r=0.206
	hs-CRP	p=0.006	p=0.236
		r=0.352	r=0.155
	ESR	p=0.873	p=0.901
		r=-0.021	r=-0.017
PsA	PASI	p=0.784	p=0.360
		r=0.066	r=0.216
	hs-CRP	p=0.518	p=0.063
		r=0.153	r=0.423
	ESR	p=0.367	p=0.252
		r=-0.213	r=0.269

PsV, psoriasis vulgaris; PsA, psoriatic arthritis; hs-CRP, high-sensitivity C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PASI, Psoriasis Area and Severity Index. P-values and coefficients of correlation (r) extracted from Spearman test of correlation.

show a normal distribution. The Shapiro-Wilk test was used to test the normality of the quantitative data. The differences between two or more qualitative parameters were assessed by the Chi-squared (χ^2) test. If the quantitative data were normally distributed, the differences between two and more quantitative parameters were assessed using Student's test and ANOVA, respectively. Opposingly, when the quantitative data were not normally distributed, the Mann-Whitney U test and The Kruskal-Wallis test was performed to compare two or more groups. We also described the correlation between quantitative variables using Spearman's rank correlation test. Statistical significance was set at a P-value of 0.05.

Ethics

The participants were clearly explained the study's objectives and protocols and written informed consent was obtained prior to study enrollment. The study did not cause any harm to the participants or change the management or course of their diseases. All costs were covered by the investigators, and the patients' identities were concealed to maintain their privacy. The study protocol was approved by the Research Ethics Committee of Ho Chi Minh City Hospital of Dermato-Venereology.

Results

Characteristics of the participants

The study population included 60 patients in the PsV group, 20 in the PsA group, and 34 control participants. The characteristics of the study population are shown in Table 1. Overall, the three groups showed no significant differences in age, sex, body mass index (BMI), alcohol consumption, cigarette smoking, age at psoriasis onset, and duration of the disease (P>0.05). However, the PASI score was higher in the PsA group than in the PsV group (11.71±5.60 *vs*. 7.85±6.33, P=0.003, Mann-Whitney U test).

Table 4. Logistic regression models for predicting psoriasis arthritis in psoriasis patients.

Parameters	OR	95% CI	P
NLR	1.57	1.132-2.164	0.007
PLR	1.01	1.003-1.020	0.008
ESR	1.06	1.031-1.089	<0.001
hs-CRP	1.14	1.044-1.244	0.003

hs-CRP, high-sensitivity C-reactive protein; ESR, erythrocyte sedimentation rate; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; OR, odds ratio; CI, confidence interval.

Comparisons of inflammatory parameters between groups

The intergroup differences in inflammatory parameters were evaluated in three pairwise comparisons, namely, PsV *vs*. PsA, PsV *vs*. control, and PsA *vs*. control. All three pairwise comparisons showed significant differences in the neutrophil count and hs-CRP level, while none of the three pairs showed differences in lymphocyte, eosinophil, and basophil counts. Notably, NLR showed significant differences in all three pairwise comparisons, but PLR did not show a significant difference in the comparison between the PsV and control groups. The intergroup comparison data for the other parameters are demonstrated in Table 2.

Inflammatory parameters and severity

The PsV group showed positive correlations between NLR with PASI and hs-CRP level (r=0.374 and r=0.352, respectively), and the correlations were statistically significant (P=0.003 and P=0.006, respectively). However, PLR showed no correlation with PASI, hs-CRP level, and ESR. The corresponding data are presented in Table 3.

Prediction of psoriatic arthritis

Table 4 presents the results of logistic regression models for determining the ability of NLR, PLR, ESR, and hs-CRP levels to predict PsA in patients with psoriasis. NLR was related to PsA in patients with psoriasis (P=0.007, OR=1.57). The area under the receiver operating characteristic curve (AUC) of NLR value to predict PsA in patients with psoriasis was 0.7554. At the cut-off NLR of 2.239, sensitivity was 85% and specificity was 61.67% (data not shown). PLR was also related to PsA in patients with psoriasis (P=0.008, OR=1.01) with an AUC of 0.6513. At the cut-off PLR of 159.6, sensitivity was 55% and specificity was 88.33% (data not shown).

Discussion

Several studies have evaluated predictive biomarkers for PsV and PsA; however, no markers have been identified to date. To

this end, we conducted a study on hematological and inflammatory parameters and calculated the NLR and PLR to assess their value in detecting PsA in patients with psoriasis.

The true meaning of inflammatory biomarkers NLR and PLR has been widely exploited through studies. The predictive value of NLR and PLR values has been described for various inflammatory skin diseases such as erythema nodosum,[12] Behçet's disease,[3] and sarcoidosis,[13] and their value in patients with psoriasis is gaining increasing attention. These parameters were found to be elevated in patients with psoriasis complicated by comorbidities such as cardiovascular diseases.[4,14] Thus, there may be some potential in using NLR and PLR in psoriasis monitoring and prognosis, as well as to detect the presence of comorbidities.

Consistent with previous studies, we found higher NLR values in patients with PsA and PsV compared to healthy controls. NLR has been consistently shown to be higher in patients with psoriasis than in normal populations in many previous studies.[15-20] In addition, one of these studies showed a reduction in NLR in response to biological agents.[16] Our study found a positive correlation of NLR with PASI. This is consistent with the literature. We suggest that the higher NLR values may indirectly reflect increased levels of inflammation in psoriatic lesions and systemically. This inflammatory state may also increase the risk of cardiovascular disease and other comorbidities.[21,22] The NLR is a rapidly accessible and convenient marker that could be utilized in clinical practice to monitor both the progress of PsV and PsA, and of their comorbidities. However, to the best of our knowledge, there is no consensus on the threshold NLR value for evaluating psoriasis. In fact, the NLR can fluctuate significantly in healthy populations depending on demographic factors.[23] Additionally, the correlation in our study was weak (r=0.374), which may be due to the small number of participants. Therefore, further studies are warranted to confirm the value of the NLR and establish a clinically relevant threshold.

Although other studies showed a higher PLR in the PsA and PsV groups compared to controls, our results only showed differences between the PsA and control groups and between the PsV and PsA groups.[15,24] This may be attributed to differences in the ethnicities and disease severities among study populations and the small size of the individual groups. We also analyzed the correlations between PLR and PASI in both psoriasis groups and found no correlation. Contrastingly, Kim, *et al*. found a positive correlation between PLR and PASI.[15] This may be because, unlike the NLR, the PLR is not a strong biomarker of inflammation in psoriasis. Therefore, better-designed studies should aim to assess the significance of PLR in patients with psoriasis.

Kim, *et al*. previously demonstrated significantly higher CBC, white blood cell (WBC), neutrophil, monocyte, eosinophil, platelet, eosinophil, and hemoglobin levels in psoriasis patients compared to controls.[15] However, in our study, only WBC, neutrophil, monocyte, and hemoglobin levels were significantly higher in the PsA group compared to controls. The results of WBC and neutrophil count were comparable to those of Polat, *et al.* and Ataseven, *et al*., but these authors did not evaluate monocyte and eosinophil counts.[18,19] Gruchala, *et al*. also compared CBC differentials between PsV and PsA groups and noted significant differences in WBC, neutrophil, monocyte, hemoglobin, and platelets counts.[24] In our study, we also found that WBC, neutrophil, and hemoglobin levels were significantly higher in the PsA group compared to the PsV group. However, we found no differences in lymphocyte and platelet counts between the groups. These differences compared to previous studies may be because of the differences in the characteristics of the study populations.

Although ESR is usually used to assess and monitor acute and chronic inflammatory conditions, it is influenced by many factors, including age, sex, BMI, metabolic syndrome, smoking, alcohol consumption, and physical activity levels.[25,26] A few previous studies have evaluated the ESR in patients with psoriasis. Consistent to our findings for the PLR, we found significant differences in ESR between PsA and PsV groups, and between PsA and control groups. In other studies, the ESR was higher in PsA patients compared to PsV patients and in PsV patients compared to controls.[15,27]

hs-CRP is a well-established marker of inflammation and infection and can also predict the risk of cardiovascular disease.[28,29] In our study, the highest hs-CRP level was recorded in the PsA group, followed by the PsV group, and all the differences were statistically significant, consistent with the findings of other studies.[15,20] Our findings also reflected the systemic inflammation and, notably, the high risk of cardiovascular events in psoriasis and PsA in accordance with the CDC and ACC classification of hs-CRP.[30] Consistent with previous studies, we also found a positive correlation between NLR and hs-CRP.[16,20]

This study suggests that NLR, PLR, ESR, and hs-CRP levels are promising markers to detect PsA in patients with psoriasis. Logistic regression analysis showed that the NLR was the strongest predictor and the PLR was also considered an acceptable predictor of PsA in psoriasis patients. These results are consistent with those of a previous study that demonstrated the utility of NLR, PLR, and ESR values in predicting the presence of PsA in psoriasis patients and found that NLR was the strongest predictor.[15]

This study was limited by its single-center design and small number of participants; therefore, additional multicenter studies with a larger patient population are warranted to validate our results.

Conclusions

NLR and PLR may reflect the inflammatory status in patients with psoriasis and may serve as predictors of PsA. These ratios are clinically valuable as they are convenient and easy to measure using routine CBCs. Nevertheless, additional studies with larger patient populations are warranted to validate our results.

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