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Original Article

The role of hematological markers in prediction of severity of psoriasis and associated arthritis

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Abstract

Background Nowadays, role of hematologic markers including neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), as cost-effective and reliable tests, in recognition of chronic inflammatory and autoimmune diseases, as well as prediction of their prognosis has been elucidated. In this study we investigate role of these factors in prediction of severity of psoriasis and associated arthritis.

Methods This is a retrospective cross-sectional study on thirty moderate-to-severe psoriasis patients, hospitalized in dermatology ward, and thirty aged- and sexed-matched healthy adults. NLR/PLR in psoriasis patients was compared to healthy controls. Furthermore, NLR/PLR of classic type of psoriasis was compared to other types of psoriasis (including psoriatic arthritis and erythrodermic psoriasis) by variance analysis. Correlation of demographic features with NLR/PLR was assessed via chi-square test and independent t test.

Results Mean age of patients in psoriasis and control groups was 35.66±16.62 and 39.8±11.18, respectively. Psoriasis patients had significantly higher NLR/PLR compared to control groups (3.47±3.83 vs. 1.37±0.55 and 133.26±83.99 vs. 96.25±40.72, respectively). The highest and lowest NRL/PLR belonged to erythrodermic and vulgaris types, respectively. Moreover, there was no significant correlation between NLR/PLR and psoriasis patients, with or without underlying disease.

Conclusion NLR/PLR can be a useful indicator for psoriasis severity and associated arthritis. It might be helpful in selection of type of treatment in psoriasis patients and employed as a prognostic factor in prediction of disease course and possible accompanied morbidities.

Key words
Psoriasis; Hematological markers; Psoriatic arthritis.

Introduction

Psoriasis is an autoimmune dermatologic disease affecting 0.6-4.8% of population worldwide. Infiltration of inflammatory cells especially neutrophils and lymphocytes have a crucial role in the pathogenesis of the disease. Production of tumor necrosis factor (TNF)-α by lymphocytes and plasmacytoid dendritic cells is a key factor in proliferation of keratinocytes and promotion of systemic inflammation. Furthermore, interleukin (IL)-17, produced by Thelper-17 (TH-17) lymphocytes as well as neutrophils, mast cells and macrophage, can provoke production of other inflammatory mediators associated to TH-1. Chronic inflammatory status can also lead to extracutaneous co-morbidities in psoriasis patients including metabolic syndrome,

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cerebrovascular and cardiovascular events as well as psoriatic arthritis.[1-3]

Psoriasis and severity index (PASI) score can be used for assessing psoriasis severity; however it is a time-consuming measurement method and has limited applicability in clinical practice. Other acute phase reactants such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are useful tools in risk assessment for possible co-morbidities in psoriasis.[4,5] Nowadays, role of hematologic markers including NLR and PLR, as cost-effective and reliable tests, in recognition of other chronic inflammatory and autoimmune diseases as well as prediction of prognosis has been elucidated.[6-8] In this study we investigate possible role of these factors in prediction of severity of psoriasis and associated arthritis.

Methods

This is a retrospective cross-sectional study on thirty moderate-to-severe psoriasis patients, hospitalized in dermatology ward of Afzalipour hospital, and thirty aged- and sexed-matched healthy adults. Inclusion criterion was psoriasis patients with more than 20% body surface area (BSA) involvement. Exclusion criteria were pregnancy, lactation, smoking, and patients who have been under systemic therapies such as immunosuppressive drugs, biologic therapies and retinoid since six months ago and affected by any other serious dermatologic or systemic diseases (such as chronic renal failure, hepatic insufficiency, metabolic syndrome, malignancy and overt infection). Firstly, demographic features (sex and age) and clinical features of patients were recorded. Then, hematologic indexes of the patients including neutrophil count, lymphocyte count and platelet count at the time of admission were recorded. After that, NLR and PLR were calculated by dividing neutrophil or platelet counts to lymphocyte count, respectively. Finally, NLR and PLR were compared to healthy controls, with no other dermatologic or systemic diseases, that were referred to dermatology clinic for cosmetic reasons. Furthermore, NLR/PLR of classic type of psoriasis was compared to those in psoriatic arthritis and erythrodermic psoriasis. This proposal was approved with ethical code IR.KMU.AH.REC.1398.158.

Statistical analysis Data were analyzed by SPSS 16 (software IBM, Armonk, NY, USA). Descriptive data demonstrated by mean, standard deviation, frequency and percentage. Correlation of demographic features with NLR/PLR was assessed via chi-square test and independent t test. Correlation between psoriasis patients and control group was evaluated by independent t test. Furthermore, correlation between different types of psoriasis and NLR/PLR was assessed by variance analysis.

Results

Thirty psoriasis patients (66.7% male) and thirty healthy controls (56.7% male) were enrolled the study. Mean age of the patients in psoriasis and control groups was 35.66±16.62 (range 5-66) years and 39.8±11.18 (range 20-68) years, respectively. There was no significant difference regarding age and gender between two groups (P=0.263 and P=0.426, respectively). Average NLR in psoriasis and control groups were 3.47±3.83 (range 0.75-20.8) and 1.37±0.55 (range 0.5-2.8), respectively, and the difference was statistically significant (P=0.004). Average of PLR was 133.26±83.99 (range 12.70-400.8) and 96.25±40.72 (range 46.2-191.6), respectively, and the difference was statistically significant (P=0.034).Furthermore, there was no significant difference between demographic features and NLR/PLR in both case and control groups (P>0.05).

Table 1 The hematologic markers depends upon types of psoriasis and underlying diseases.

	NLR ratio	*P. value*	*PLR ratio*	*P. value*
Psoriasis vulgaris	1.66 ± 0.23		94.77 ± 11.24	
Erythrodermic psoriasis	5.14 ± 1.62	0.083	160.37 ± 26.20	0.12
Psoriatic arthritis	3.96 ± 1.13		156.64 ± 44.36	
Psoriasis with underlying disease	1.66 ± 0.23	0.156	75.03 ± 117.67	0.383
Psoriasis without underlying disease	4.35 ± 2.8		145.18 ± 90.64	

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio;

Most of the patients had psoriasis vulgaris (40%; 66.7% male), and the remaining were erythrodermic psoriasis (36.7%; 54.5% male) or psoriatic arthritis (23.3%; 85.7% male). The highest mean NRL/PLR was in erythrodermic type, and the lowest ratio belonged to vulgaris type; however the difference was only significant for NLR **(Table 1)**. Moreover, there was no significant correlation between psoriasis and NLR/PLR in psoriasis patients with or without underlying disease **(Table 1)**.

Discussion

Psoriasis is a chronic inflammatory condition with dysregulation of both innate and adaptive immune system due to genetic and environmental factors. Increased inflammatory cytokines and chemokines [such as IL-6, IL-8, IL-12, IL-18, IL-Iβ, tumor necrosis factor (TNF)-α, E-selectin, intra-cellular adhesion molecule-1 (ICAM-1] have been demonstrated in the pathogenesis of psoriasis.[1-3]

Neutrophils release enzymes such as elastase, matrix metalloproteinase (MMP) and inflammatory cytokines that promote inflammatory status. Moreover, platelets have pro-thrombotic and inflammatory effects via release of p-selectin, platelet glycoprotein Ib-α and CD40-ligand.[7-20] Nowadays, there is growing evidence emphasizing the importance of NLR/PLR in determination of prognosis, disease activity in chronic inflammatory conditions such as autoimmune and inflammatory diseases (vitiligo, urticaria, atopic dermatitis, bullous pemphigoid, pemphigus vulgaris, systemic lupus erythematous, Behcet's syndrome and rheumatoid arthritis), neoplasms, cardiovascular and cerebrovascular events as well as metabolic syndrome.[6-15] Thereby, NLR/PLR may be a suitable simple rapid test to predict severe cases of psoriasis and patients who might more likely have co-morbidities such as metabolic syndrome and cerebrovascular/ cardiovascular attacks.[6-15]

To date, there are several studies evaluating NLR/PLR in psoriasis patients with conflicting results **(Table 2)**.[7-25] The results demonstrated that both NLR and PLR had significantly higher ratio in psoriasis patients compared to healthy adults. Furthermore, there was a significant positive correlation between NLR and severity of psoriasis based on PASI score. Most of the studies enrolled both mild and severe psoriasis cases.[7-25] Regarding increased risk of extracutaneous co-morbidities only in moderate-to-severe psoriasis; in the current study, only moderate-to-severe psoriasis patients were enrolled. In this study, significantly higher NLR/PLR was demonstrated in psoriasis compared to healthy controls. Moreover, erythrodermic and vulgaris types of psoriasis demonstrated the highest and lowest NRL/PLR, respectively; nevertheless, the result was only statistically significant for NLR.

Gruchata *et al*. demonstrated significantly higher level of CRP in psoriatic arthritis compared to psoriasis vulgaris. They also reported higher NLR and PLR in psoriatic arthritis than classic type of psoriasis (2.28 vs. 2 and 111.61 vs. 121.85, respectively).[8]

Table 2 The overall literature review of NLR and PLR ratio in psoriatic patients.

First author (Y)	*Study type*	*Number/sex*	*Mean age (Y)*	*Mean NLR ratio (%)*	*Mean PLR ratio (%)*	*Results*
Ustuner (2018)[7]	P	27 F 18 M	42.2 ± 13.3	2.08 ± 0.57	193.66 ± 29.18	No significant correlation between PASI and NLR/PLR ratio Significant reduction in NLR/PLR after TX
Gruchata (2019)[8]	R	PSV: 35 F; 45 M PSA: 46 M; 34 F	PSV: 48.48 ±16.08 PSA: 49.45 ±13.74	PSV: 2 PSA: 2.28	PSV: 111.61 PSA: 121.85	Significantly higher NLR/PLR ratio in PSA compared to PSV
Aktas Karaby (2020)[9]	R	94 (NA)	38.28 ± 12.48	1.96	106.94	Significantly higher NLR ratio in psoriatic patients compared to control No significant difference in PLR ratio in psoriatic patients compared to control Significantly higher NLR/PLR ratio in moderate-to-severe psoriasis compared to mild psoriasis.
Yurtdas (2014)[10]	P	19 F 32 M	39 ± 9 (20-52)	4 ± 3	124 ± 98	Significantly higher NLR ratio in psoriatic patients compared to control No significant difference in PLR ratio in psoriatic patients compared to control
Toprak (2016)[11]	P	22 F 17 M	34 ± 16	2.39	NS	Significantly higher NLR ratio in psoriatic patients compared to control No significant difference in NLR ratio after TX compared to baseline.
Ataseven (2014)[12]	R	67 F 37 M	38.50 (14-83)	2.19 ± 1.11	-	Significantly higher NLR ratio in psoriatic patients compared to control No significant correlation between NLR and PASI
An (2019)[13]	P	37 F; 38 M	38.7 ± 14.8	1.78 ± 1.02	123.14±62.83	Significant reduction in NLR/PLR after TX compared to baseline
Wang (2021)[14]	NA	PSV: 241 M; 106 F GPP: 20 M; 17F PSE: 39 M; 6 F PSA: 15 M; 10 F	PSV: 43.11±14.23 GPP: 41.24±14.16 PSE: 49.47±13.88 PSA: 43.04±14.31	PSV: 2.41±1.21 GPP: 5.90±5.15 PSE: 3.02±1.34 PSA: 3.49±1.56	PSV: 134.03±56.82 GPP: 221.82 ±126.01 PSE: 182.99 ±82.45 PSA: 199.06 ±74.24	Significantly higher NLR ratio in psoriatic patients compared to control No significant correlation between NLR and PASI Significantly lower NLR ratio in PSV compared to other types of psoriasis
Kim (2016)[15]	R	PSV: 62 M; 49 F PSA: 13 M; 12 F	PSV: 38±16.6 PSA: 42.4±8.3	PSV: 2.15±1.65 PSA: 2.95±.16	PSV: 140.7±114.9 PSA: 170.4±90.3	Significantly higher NLR ratio in PSV/PSA compared to control No significant difference in PLR ratio between PSA/PSV and control Significantly higher NLR/PLR ratio in PSA compared to PSV Significant correlation between PASI and NLR/PLR ratio
Arisoy (2017)[16]	P	34 F; 40 M	41±14	2.4±1.2	-	Significantly higher NLR ratio in psoriatic patients compared to control
Cerman (2016)[17]	NA	30 M; 19 F	42.33±15.47	2.62±1.46	-	Significantly higher NLR ratio in psoriatic patients compared to control No significant correlation between PASI and NLR ratio
Pektas (2016)[18]	NA	84 M; 88 F	42.17±11.98	2.19±0.83	137.53±61.3	Significantly higher NLR/PLR ratio in psoriatic patients compared to control Significant correlation between PASI and NLR/PLR ratio
Yildiz (2014)[19]	P	18 M; 16 F	37.4±12.8	2.66±1.22	-	Significantly higher NLR ratio in psoriatic patients compared to control
Dey (2021)[20]	P	63 M; 35 F	50±12.7	2.32±1.13	-	Significant correlation between PASI and NLR ratio No significant reduction in NLR ratio after TX with non-biologic drugs compared to base-line Significant reduction in NLR ratio after TX with biologic drugs
Sen (2014)[21]	P	78 M; 60 F	40.4±12.3	2.71±1.25	-	Significantly higher NLR ratio in psoriatic patients compared to control Significant correlation between PASI and NLR ratio
NajarNobari (2020)[22]	P	37 F; 43 M	40.38±13.19	4.76±2.12	8.34±3.40	Significant correlation between PASI and NLR ratio Significant reduction in NLR ratio after TX compared to base-line No significant correlation between nail/joint involvement and NLR ratio
Asahina (2017)[23]	P	PSV: 46 F; 140 M PSA: 12 F; 38 M	PSV: 54.6±15 PSA: 48.8±13.1	PSV: 2.71±1.66 PSA: 3.53±1.84	PSV: 153.5±67.7 PSA: 178.7±89.4	Significantly higher NLR/PLR ratio in PSA compared to PSV Significant reduction in NLR ratio after TX with biologic drugs
Polat (2017)[24]	R	21 F; 25 M	36.58±9.82 (2-53)	2.78±1.74	159.18±64.22	Significant correlation between PASI and NLR/PLR ratio Significantly higher NLR/PLR ratio in psoriatic patients compared to control
Solak (2016)[25]	R	88 M; 111 F	44.1±14.4	2.19±0.81	-	Significant correlation between PASI and NLR ratio

Likewise, Kim *et al.* in a retrospective study evaluated NLR and PLR in psoriasis patients compared to healthy control. They showed higher levels of white blood cells (WBC), neutrophils, monocytes and platelets, and also higher NLR/PLR in psoriasis patients compared to healthy ones. Furthermore, these hematological markers have significant positive correlation with PASI score. Moreover, hematological markers were significantly higher in psoriasis arthritis compared to psoriasis vulgaris. It was concluded that theses markers can be strong indicators for severity of psoriasis and presence of arthritis in these patients; with the NLR being the strongest predictor[15]. Similarly, Wang *et al.* demonstrated significantly lower NRL/PLR in classic type of psoriasis compared to other types, especially generalized pustular psoriasis (GPP).[14] These results were compatible with another retrospective study by Asahina *et al.* that demonstrated reduction in NRL/PLR in psoriasis patients after one year treatment with biologic drugs including adalimumab, ustekinomab and infliximab as well.[23]

Limitations of this study were low sample size and lack of evaluation of correlation between PASI score and NLR/PLR. However, all of the patients had moderate-to-severe psoriasis with more than 20% BSA involvement. Moreover, although we exclude psoriasis patients with other dermatologic and serious systemic diseases from the study; noticeable percentage of psoriasis patients had underlying diseases such as controlled hypertension or hyperglycemia. However, there was no significant difference between NLR/PLR in psoriatic patients with or without underlying disease.

Conclusion

Psoriasis patients had significantly higher percentage of NLR/PLR compared to healthy adults. The highest and lowest NLR/PLR was reported in erythrodermic and vulgaris types of psoriasis, respectively. Thereby, NLR/PLR can be a useful predicting indicator in psoriasis severity and associated arthritis.

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