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ORIGINAL ARTICLE

Hematological parameters in patients with acnes

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Abstract

Objective: To compare complete blood count (CBC) parameters and inflammatory factors in the patients with different grade of acne vulgaris and healthy controls.

Methods: A total of 20 patients were enrolled in this study. Patients were divided into mild group and moderate-to-severe group based on the acne severity, and compared to controls. Inflammatory factors (TNF-α, IL-6, IL-8, and IL1-α) detected by ELISA and complete blood count parameters (MPV, NLR, dNLR, PLR, LMR, and SII) obtained by routine blood tests were compared among the three group.

Results: All CBC parameters were not significantly elevated in patients with acne compared to healthy controls. However, the present studies have found that the inflammatory factors in acne patients were significantly elevated relative to healthy controls, and increase with the acne grade.

Conclusions: Inflammatory factors are convenient parameters to show inflammatory response to acne vulgaris, and may be a new clinical method for judging the acne grades of objectively. Considering the use of antibiotic, we believe that this metric worth further study.

KEYWORDS
acne vulgaris, derived neutrophil-to-lymphocyte ratio, inflammatory factors, lymphocyte to monocyte ratio, systemic immune-inflammation index

1 | INTRODUCTION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous units which mainly localized on the face, chest, and back.[1] It is the eight most common skin disease and the most common skin condition in adolescents, affecting approximately 85% of teenagers.[2] Numerous people all around the world were also plagued by acne scar and other complications. The pathogenesis of acne vulgaris closely relates to the inflammatory response. Inflammatory factors (IFs) that include TNF-α, IL-6, IL-8, and IL1-α play important roles in a range of inflammatory processes of acne vulgaris,[3–5] and severe disease with a robust inflammatory response can leave permanent scarring and severely impact the psychological well-being and quality of life of patients.[6]

Mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), derived neutrophil-to-lymphocyte ratio (dNLR), platelet to lymphocyte ratio (PLR), lymphocyte to monocyte ratio (LMR), and systemic immune-inflammation index (SII) as diagnosis and prognostic biomarkers were used for the inflammatory disease and tumor,[7–10] illustrating hidradenitis suppurativa,[11] seborrheic dermatitis,[12] and gastric cancer.[13] Complete blood count (CBC) is one of the most common laboratory tests performed for patient, influenced by

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many conditions.[14] Novel biomarkers of CBC parameters for inflammation have been the subject of extensive studies, but few studies have evaluated the relationship between acne vulgaris and CBC parameters. Therefore, the aim of the current study was primarily to conduct a further extensive study to compare CBC parameters and IFs in the patient with different grades of acne vulgaris and healthy controls (HCs).

2 | METHODS

2.1 | Study subjects

Twenty outpatients diagnosed with acne were included from June 2022 to August 2022, 10 patients with mild acne and 10 patients with moderate-to-severe acne. In addition, 10 healthy controls were recruited. All enrolled patients were diagnosed by two specialist dermatologists according to acne severity (Table 1). In cases of discrepancy, state of patients was assessed by a third independent dermatologist and consensus derived.

Individuals aged 18–60 years with acne, who did not present other dermatology disorders and had not taken antibiotics, were included in this study. Exclusion criteria were are as follows.

1. Patients with other causes of inflammatory response, including seborrheic dermatitis, psoriasis, and inflammatory arthritis.
2. Patients with a history of drug use in the 2 months before inclusion, including the use of antibiotic and other anti-acne drugs.
3. Patients were considered to be in the immunocompromised state.
4. Pregnant or lactating patients were excluded.

2.2 | Study methods

Questionnaires were used to collect demographic and clinical details. Two peripheral blood samples (4 mL total) were collected via the cubital vein in the patients and HCs by EDTA tubes. One tube of samples was used for complete blood count analysis which were completed by the Clinical Laboratory Department, and the another one was used for inflammatory factors detection. Serological levels of IFs were detected by enzyme label analyzer RaytoRT-6100, Rayto Co. Ltd, China, using enzyme-linked immunosorbent assay kits (96 T, JiuBang Biology, China) according to manufacturer's protocols.

2.3 | Statistical analyses

Numerical variables were presented as Mean ± SD (standard deviation) Kolmogorov–Smirnov test and Shapiro–Wilk test were used to statistical. One-way ANOVA was utilized for data analysis, followed by Bonferroni's test. Correlation analysis was performed using the Pearson's correlation assay. Statistical analyses were performed with SPSS 24 software (IBM SPSS statistics 23) and the R statistical package. A p value <0.05 was considered statistically significant.

The CBC parameters (Leukocyte (×109 / L), neutrophils (×109 / L), monocytes (×109 / L), platelets (×109 / L), lymphocytes (×109 / L), NLR, dNLR, MPV, LMR, PLR and SII) and IFs (TNF-α, IL-6, IL-8, IL1-α) were compared among the three groups. PLR was computed as the ratio platelet count /lymphocyte count, NLR was calculated as neutrophil count /lymphocyte count, lymphocyte count /monocyte count was calculated by LMR, dNLR was used to calculate neutrophils/ (leukocytes minus neutrophils), and platelet count × neutrophil count/lymphocyte count was calculated by SII.

3 | RESULTS

3.1 | Patients' characteristics

Thirty Participants total were finally included in this study, with a median age of 22 years. Detailed characteristics of the study population were presented in Table 2. There were no significant differences in basic characteristics including age ($p = 0.580$), gender ($p = 1.000$), BMI ($p = 0.331$), family history ($p = 0.530$), time for sleep ($p = 0.630$), and constipation ($p = 0.660$) among the three groups.

3.2 | Comparison of CBC parameters

The results of CBC parameters were shown in the following Table 3. The median values of MPV, NLR, dNLR, PLR, LMR and SII were 10.30, 1.93, 1.43, 122.03, 5.43 and 462.51. The difference in the

TABLE 1 Classification criteria of the acne grade.

Grade of acne	Classification Criteria
Mild	Level I, Comedones were predominant, a small number of papules and pustules, the total number of lesions less than 30.
Moderate	Including level II and level III. Level II: pimples, papules and pustules of equal amount, and the total number of lesions ranged from 31 to 50; level III: a large number of papules and pustules, and occasionally large inflammatory lesions, which were widely distributed. The total number of lesions ranged from 51 to 100, with less than 3 nodules.
Severe	level IV, the main lesion was nodular/cyst acne or clustered acne; the total number of lesions was more than 100, and the number of nodules/cysts was more than 3.

TABLE 2 The demographic characteristics of the participants.

	All	Normal (%)	Mild (%)	Moderate-to-severe (%)	*p* value
Age					
Mean ± SD	22.37 ± 2.06	22.60 ± 0.70	22.70 ± 1.34	21.80 ± 3.29	0.580
BMI					
Mean ± SD	21.66 ± 3.14	20.44 ± 2.55	22.20 ± 2.89	22.35 ± 3.79	0.331
Gender					
Female	19 (63.33)	7 (70)	6 (60)	6 (60)	1.000
Male	11 (36.67)	3 (30)	4 (40)	4 (40)	
Family history					
Yes	8 (26.67)	0 (0)	3 (30)	5 (50)	0.530
No	22 (73.33)	10 (100)	7 (70)	5 (50)	
Time for sleep					
5–6 h	5 (16.67)	2 (20)	1 (10)	2 (20)	0.630
6–8 h	22 (73.33)	7 (70)	9 (90)	6 (60)	
>8 h	3 (10)	1 (10)	0 (0)	2 (20)	
Constipation					
Yes	8 (26.67)	2 (20)	2 (20)	4 (40)	0.660
No	22 (73.33)	8 (80)	8 (80)	6 (60)	

TABLE 3 Comparison of patient and control groups in terms of hematological parameters.

	All	Normal	Mild	moderate-to-severe	*p* value
Leukocyte count, ×109/L, median (IQR)	5.98 (4.72–8.10)	5.63 (4.58–7.35)	5.97 (4.78–8.55)	6.53 (5.19–8.38)	0.690
Neutrophil count, ×109/L, median (IQR)	3.42 (2.76–4.74)	3.37 (2.66–4.68)	3.21 (2.77–4.99)	3.60 (3.01–5.08)	0.770
Lymphocyte count, ×109/L, median (IQR)	2.01 (1.34–2.50)	1.86 (1,26–2.27)	2.15 (1.55–2.76)	2.00 (1.24–2.77)	0.571
Platelet count, ×109/L, median (IQR)	248.50 (221.75–279.75)	258.50 (225.25–279.75)	233.50 (213.00–260.50)	254.00 (204.00–294.00)	0.793
Monocyte count, ×109/L, median (IQR)	0.33 (0.27–0.44)	0.28 (0.22–0.43)	0.33 (0.27–0.49)	0.37 (0.28–0.48)	0.417
MPV, median (IQR)	10.30 (9.78–10.50)	9.80 (9.38–9.18)	10.50 (10.23–10.58)	10.45 (9.88–10.83)	0.266
NLR, median (IQR)	1.93 (1.43–2.83)	2.05 (1.62–2.39)	1.77 (1.24–2.38)	1.90 (1.42–2.70)	0.418
dNLR, median (IQR)	1.43 (1.17–1.93)	1.56 (1.24–1.87)	1.26 (1.05–1.93)	1.42 (1.17–2.07)	0.448
LMR, median (IQR)	5.43 (4.71–6.67)	5.17 (4.56–7.43)	5.65 (4.98–6.67)	5.24 (3.66–6.09)	0.431
PLR, median (IQR)	122.03 (104.95–166.09)	122.71 (110.34–213.14)	113.32 (96.10–136.68)	122.59 (110.11–169.55)	0.203
SII, median (IQR)	462.51 (379.66–595.70)	546.44 (444.32–617.77)	405.36 (318.07–477.99)	482.60 (384.10–625.67)	0.266

TABLE 4 Comparison of patient and control groups in terms of inflammatory factors.

	All	Normal	Mild	Moderate-to-severe	*p* value
TNF-α, median (IQR)	46.64 (37.84–67.89)	30.11 (23.30–40.67)	50.88 (41.82–65.18)	72.67 (57.40–77.43)	0.000
IL-6, median (IQR)	32.72 (27.32–36.78)	23.60 (22.23–30.73)	33.35 (29.31–37.65)	36.83 (34.12–45.83)	0.000
IL-8, median (IQR)	128.27 (95.71–164.81)	69.79 (58.66–104.14)	132.83 (109.59–147.52)	178.76 (149.51–201.41)	0.000
IL-1α, median (IQR)	39.50 (124.22–167.79)	94.79 (79.55–140.39)	158.32 (144.34–152.78)	166.27 (152.78–183.02)	0.000

value of these CBC parameters was not statistically significant (all $p > 0.05$).

3.3 | Comparison of the Serum levels of IFs

Serum levels of inflammatory factors among the three groups were summarized in Table 4. The expression of TNF-α, IL-6, IL-8, and IL-1α was different in each group (all $p < 0.05$). The inflammatory factors of the moderate-to-severe group were significantly higher than the other two groups ($p < 0.05$). Compared to the health controls, TNF-α, IL-6, IL-8, and IL-1α of the patients with mild acne were significantly higher ($p < 0.05$).

3.4 | CBC parameters and the Serum levels of IFs

Pearson correlation analyses were carried out to detect any correlations between CBC parameters and the serum levels of IFs. The data reveal a clear lack of correlation between the CBC parameters and the serum levels of IFs (all $p > 0.05$), but there are two notable exceptions. The results showed a certain correlation between mono counts and IL-6 ($r = 0.442$, $p = 0.014$). The analysis for the correlation of mono counts and IL-8 also suggests positive correlation ($r = 0.446$, $p = 0.014$).

4 | DISCUSSION

In this study, we compared the CBC parameters and inflammatory factors between patients with the different acne grades and HCs, and we found that CBC parameters were not significantly elevated in patients with acne compared to healthy controls. However, studies have found that the levels of inflammatory factors in acne patients were significantly elevated relative to HCs and increased with the severity of acne. The results of our study showed that CBC parameters did not have the potential to distinguish the severity of acne, and the detection of inflammatory factor levels is more hopeful to become an effective clinical means for the objectively judgment of the severity of acne.

Acne is a chronic inflammatory disease of follicular sebaceous unit. The pathogenesis is complex,[15] and it is still generally regarded as fact within the medical and lay community that Cutibacterium acnes (C. acnes, Propionibacterium acnes) stimulates inflammatory and immune responses through a variety of mechanisms.[16] C. acnes results in the release of inflammatory mediators including lipase that degrades triglyceride, protease that destroys the hair follicle wall, and chemokines, recruiting CD4+ lymphocytes, neutrophils, and monocytes to the affected site. C. acnes can also activate the immune system and result in the increasing of the pro-inflammatory factors release,[16,17] such as activating Toll-like receptor 2 on monocytes to induce the production of IL-8. Aside from that, it induces the release of inflammatory factors produced by hair follicle keratinocytes including IL-1α, IL-6, TNF-α, facilitating the formation of acne. Platelets also have positive effects on the inflammation processes, predominantly relating to the cytokines and chemokines release.[18,19]

Routine blood test is a common clinical examination to obtain CBC parameters including the mean platelet volume, white blood cell count, neutrophil count, monocyte count, lymphocyte count and platelet count and so on, and then, the values of MPV, NLR, dNLR, PLR, LMR, and SII can be obtained. Among them the NLR is a new cheap marker and an immensely sensitive indicator of infection, inflammation, and sepsis[20] verified by numerous studies. MPV is associated with thrombocyte function and activation, and it is related to a variety of pro-inflammatory diseases, including irritable bowel syndrome, thyroiditis[18] and so on. PLR has also been proposed as a marker of inflammation, although it is used less frequently in published studies. SII has been considered a good index that reflects the local immune response and systemic inflammation.[21] Its high clinical value has been proven over and over in several types of cancers such as pancreatic cancer, renal cell carcinoma and gastric cancer and inflammatory diseases.

Previous studies have proved that NLR and PLR are predictive biomarkers. Wentao Wang et al[13] demonstrated that pretreatment NLR and PLR together serve to independently predict tumor regression grade after neoadjuvant chemotherapy and surgery in patients with advanced gastric cancer (GC). In addition, it has been reported that NLR and PLR were found to be predictive markers of lymph node metastasis of GC patients, and NLR is better to predict overall survival than PLR.[22] The study by T Gambichler et al[11] is the first to analyzed the systemic inflammation biomarkers in hidradenitis suppurativa(HS) patients and controls, and reported that SII was considerably higher in HS patients, PLR was noticeably lower in HS patients compared with the control group. All systemic inflammation-based biomarkers investigated are associated with HS severity, to some extent. Mustafa Tosun et al[12] compared the SII, MPV, PLR, and NLR in the Seborrheic dermatitis (SD) patients and control group. They found that the levels of PLR and MPV in the patient group were statistically significantly higher than those in controls, which may be developed as novel inflammatory markers in SD.

Recent studies have investigated inflammatory markers with isotretinoin in the treatment of acne. The study carried out by Cağri Turan et al[23] investigated the differences in some inflammatory markers in patients with acne vulgaris after oral isotretinoin treatment compared with healthy controls and themselves, and found that NLR did not substantively differ from controls before and after treatment, while SII can be used as the indicator of anti-inflammatory effect of isotretinoin. Nur Cihan Cosansu et al[24] assessed the effectiveness of SII, systemic inflammatory response index (SIRI), and other inflammatory markers in patients with acne vulgaris treated with isotretinoin, and indicated that SII and SIRI were superior in being anti-inflammatory indicators for the effects of isotretinoin. Similar experiments have been done by Omer Kutlu et al[25] on the effect of ISO treatment on MHR and other inflammatory markers in patients with acne vulgaris. This was

the first study, to our knowledge, to describe the relationship between CBC parameters, inflammatory factors, and the severity of acne vulgaris. There are similarities between the study by Dursun Turkmen et al[26] and ours, along with differences. We would like to point out the following differences. Firstly, the grouping is not alike. They divided their participant into two groups, patient group and control group. As pointed out in the preceding paper, there were three groups in our study. Secondly, this study represented the first systematic analysis of the value of SII and dNLR in patients with the different acne grades. IFs (IL-1α, IL-6, IL-8, TNF-α) were also parts of our study. Summing up, more inflammatory markers were tested in this study, and more attention was paid to the relationship between hematological parameters and disease severity.

5 | LIMITATION

The limitations of this study include that this is a single-center study with a small sample size, which may lead to a certain deviation of the study results. A multicenter study with a large sample size should be conducted in the future to determine whether the CBC parameters and related IFs can be used as inflammatory markers of acne.

AUTHOR CONTRIBUTIONS

The study was designed by JC and TC. Samples were collected by TC, YC, and LL. Processing of the specimens was performed by JC and YL. The data were analyzed by TC and YP. The manuscript was written by TC, YC, and XS. All the authors reviewed and approved the final manuscript before submission.

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CONFLICT OF INTEREST STATEMENT

All authors declare no potential conflicts of interest, including any relevant financial interests, activities, relationships, or affiliations.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

This study was approved by the Ethics Committee of the First Affiliated Hospital, Chongqing Medical University (ID: 2022–83).

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