



## A Comparative Study on Hematological Inflammation Markers in Acne Vulgaris

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### Authors' contributions

This work was carried out in collaboration among all authors. Author ND designed the study, collected data, did the literature search and also wrote the first draft of the manuscript. Authors EU and VM collected data and wrote part of the manuscript. All authors read and approved the final manuscript.

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### ABSTRACT

**Aim:** The literature does not include sufficient data on the hematological inflammation markers in acne vulgaris. The present study aimed to investigate potential of neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and mean platelet volume as inflammatory markers in acne vulgaris.

**Study Design:** This is a a case-control, comparative clinical study conducted with the approval of ethical review board.

**Place and Duration of Study:** Department of Dermatology between March 2015 and July 2015.

**Methodology:** The study included 45 moderate/severe acne patients and 30 age- and sex-matched controls. Demographic data, medical history were recorded. Laboratory parameters, including total leucocyte, neutrophil, lymphocyte, platelet counts, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and mean platelet volume were retrospectively evaluated before treatment, and after 3-months of oral isotretinoin treatment. Parameters of the patient group (pre-treatment) and the control group, additionally pre-treatment and post-treatment parameters of the patient group were compared.

**Results:** The mean total leucocyte count (P < 0.001), neutrophil count (P < 0.001), and

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neutrophil/lymphocyte ratio ( $P = 0.047$ ) were significantly higher, and mean platelet volume ( $P < 0.001$ ) was significantly lower in the patient group (pre-treatment) compared to the control group. Additionally, the mean post-treatment leucocyte count ( $P = 0.001$ ), neutrophil count ( $P < 0.001$ ), and neutrophil/lymphocyte ratio ( $P < 0.001$ ) were significantly lower compared to pre-treatment parameters.

**Conclusion:** Acne vulgaris is associated with systemic inflammation, and isotretinoin treatment has systemic anti-inflammatory effects. Especially, neutrophil/lymphocyte ratio is indicative of systemic inflammation in acne, and may be used as a follow-up marker during treatment.

*Keywords: Acne; inflammation; isotretinoin; neutrophil/lymphocyte ratio; platelet/lymphocyte ratio.*

## 1. INTRODUCTION

Acne vulgaris is a common chronic inflammatory skin disease characterized with hyperkeratinization, elevated sebum production associated with androgenic stimulation of sebaceous gland, *Propionibacterium acnes* colonization, innate immune system activation and inflammation [1].

In recent years, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and mean platelet volume (MPV) are used as inflammation markers, and have been associated with chronic inflammation in various disorders including malignancies, cardiovascular disorders, inflammatory bowel disease, and systemic lupus erythematosus [2-12].

White blood cell count subtypes reflect different aspects of inflammatory processes. The immune response to various conditions is characterized by neutrophilia and relative lymphopenia. NLR can easily be calculated using the neutrophil and lymphocyte counts in peripheral blood count. Calculating NLR is a simpler and cheaper method compared to measuring inflammatory cytokines [2-8].

In addition, there is a link between inflammation and platelet activation. During the inflammatory processes, platelet count and function are increased. Platelet volume is an indicator of platelet activation. In several studies, it has been reported that platelet indices such as platelet count, PLR and MPV may indicate inflammation process [9-12].

Studies with hematological inflammation markers in patients with acne are limited. Therefore the present study aimed to investigate these markers among a group of acne patients.

## 2. MATERIALS AND METHODS

The study included 45 patients with moderate/severe acne diagnosed according to

European Acne Guideline criteria [13] that were followed-up at our dermatology department, and treated with at least 3 months of oral isotretinoin and 30 age- and sex-matched controls without a history of chronic inflammatory disease. Patients and controls under the age of 16 were excluded from the study, and apart from acne, neither patients nor control participants had any other disorder, including hematological disorders. Demographic data, medical history were recorded. Laboratory parameters in complete blood count (CBC), including total leucocyte, neutrophil, lymphocyte, platelet counts, MPV, NLR, and PLR were retrospectively evaluated. CBC parameters were measured on the analyzer (Beckman Coulter LH780, USA) using electrical impedance method.

Both patients and controls with any abnormality in any CBC parameter were excluded from the study. CBCs of control patients were compared with pre-treatment CBCs of patients. Additionally, pre-treatment CBCs were compared with post-treatment CBCs (CBCs after 3 months of oral isotretinoin therapy) in the patient group.

Statistical analyses were performed using SPSS v.18.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as mean  $\pm$  standard deviation, and categorical variables as frequencies and percentages. The chi-square test was used to determine associations between categorical variables. Differences between patient and control groups were determined using the independent samples t-test. Differences before and after treatment in patient group were determined using the paired-samples t-test. The study protocol was approved by the Afyon Kocatepe University, Ethics Review Boards (Ethics Committee approval number is 2015/03-97).

## 3. RESULTS

The study included 45 acne patients and 30 controls. In all, 73% of the acne patients were

female (mean age: 19.51±2.36 years) and 83% of the controls were female (mean age: 19.90±2.91 years). Acne and control groups were both age- and sex-matched (P = 0.464/0.177).

The mean total leucocyte count was 6326±1241/mm<sup>3</sup> in the control group vs. 7666±1581/mm<sup>3</sup> in the patient group (P < 0.001). The mean total neutrophil count was significantly higher in the patient group (4771±1239 in the patient group vs. 3768±951 in the control group, P < 0.001). Additionally, the mean MPV was significantly lower in the patient group (8.83±1.27 fL in the patient group vs. 9.91±1.05 fL in the control group, P < 0.001). The mean NLR in the patient and control groups were 2.21±0.64 and 1.93±0.54, respectively (P = 0.047). With regard to other parameters, there weren't any significant differences between the 2 groups. Detailed comparison of the patient and control groups was given in Table 1.

The mean post-treatment leucocyte count was significantly lower than pre-treatment count (7011±1350/mm<sup>3</sup> vs. 7666±1581/mm<sup>3</sup>, P = 0.001). Additionally, the mean neutrophil count (4037±1111/mm<sup>3</sup> vs. 4771±1239/mm<sup>3</sup>, P < 0.001), and NLR (1.81±0.57 vs. 2.21±0.64, P < 0.001) were significantly lower in post-treatment CBCs. Although the difference was not significant, in the post-treatment CBCs, the mean MPV was higher (8.88±1.15 vs. 8.83±1.27, P = 0.595). Detailed comparison of pre-treatment and post-treatment CBCs in the patient group was given in Table 2.

#### 4. DISCUSSION

Previous studies investigating hematological inflammation markers in acne vulgaris are very limited. Ataseven et. al retrospectively evaluated neutrophil, lymphocyte counts, and NLR in

patients receiving 3-months of systemic isotretinoin for acne vulgaris, and found no difference between pre-treatment and post-treatment levels [4]. Recently Seçkin et. al [5] reported no meaningful difference of the systemic isotretinoin treatment on the NLR. In contrast, in the present study we found significant differences between pre-treatment and post-treatment neutrophil counts, and NLRs. Unlike the present study, previous 2 studies did not include a control group which makes it impossible to compare the findings. As one of the main results of the present study, we found that NLR was significantly higher in the untreated acne patients compared to control, and NLR significantly decreased after treatment. In recent years, increasing studies have shown the association of NLR with systemic inflammation and poor prognosis in various systemic disorders including cardiovascular disorders, malignancies, type 2 diabetes mellitus, chronic renal failure, and familial mediterranean fever [2,3,6-8]. In recent years, there is ongoing evidence that many inflammatory pathways are involved in acne etiopathogenesis [1]. Especially innate immune system-mediated inflammation and Toll-like receptor-mediated cytokines play role in acne formation [14]. Furthermore, there is also evidence that acne vulgaris is associated with inflammatory state even without appearance of clinical lesions [1]. This may suggest that only cure of clinical lesions may not be enough for complete recovery of inflammation. Therefore, new follow-up markers other than clinical signs are needed to evaluate complete recovery. The present study findings provide more evidence that acne vulgaris is associated with systemic inflammation and isotretinoin treatment has an anti-inflammatory effect. Additionally the present study findings support that NLR is indicative of systemic inflammation, and may be used as a follow-up marker to assess systemic recovery during treatment.

**Table 1. Comparison of the control and patient groups, according to CBC parameters**

Parameter	Patient (n = 45)	Control (n = 30)	P value
Mean leucocyte count (/mm <sup>3</sup> ) ± SD	7666±1581	6326±1241	< 0.001
Mean neutrophil count (/mm <sup>3</sup> ) ± SD	4771±1239	3768±951	< 0.001
Mean platelet count (/mm <sup>3</sup> ) ± SD	284444±60258	269000±45110	0.235
Mean lymphocyte count (/mm <sup>3</sup> ) ± SD	2235±545	2034±527	0.117
Neutrophil/lymphocyte ratio ± SD	2.21±0.64	1.93±0.54	0.047
Platelet/lymphocyte ratio ± SD	142.62±48.03	138.15±33.1	0.712
Mean platelet volume MPV(fL) ± SD	8.83±1.27	9.91±1.05	< 0.001

**Table 2. Comparison of the pre-treatment and post-treatment CBC parameters in the patient group**

Parameter	Pre-treatment (n = 45)	Post-treatment (n = 45)	P value
Mean leucocyte count (/mm <sup>3</sup> ) ± SD	7666±1581	7011±1350	0.001
Mean neutrophil count (/mm <sup>3</sup> ) ± SD	4771±1239	4037±1111	< 0.001
Mean platelet count (/mm <sup>3</sup> ) ± SD	284444±60258	290756±71004	0.263
Mean lymphocyte count (/mm <sup>3</sup> ) ± SD	2235±545	2312±545	0.282
Neutrophil/lymphocyte ratio ± SD	1.81±0.57	2.21±0.64	< 0.001
Platelet/lymphocyte ratio ± SD	142.62±48.03	129.31±34.40	0.059
Mean platelet volume MPV(fL) ± SD	8.83±1.27	8.88±1.15	0.595

In addition, many studies have found that a decrease in MPV is indicative of systemic inflammation and disease activity in various infectious and inflammatory disorders including cardiovascular diseases, rheumatoid arthritis, acute rheumatic fever, inflammatory bowel disease, and acute pancreatitis [2,9-12]. Similarly, in the present study, we found that MPV was lower in patients compared to controls, however although post-treatment MPV was higher than pre-treatment MPV, this did not reach significance level. Similarly, Seçkin et. Al [5] also observed no meaningful difference of 3-months isotretinoin treatment on MPV value.

The limitations of the present study are its retrospective design and the small number patients included. And it would have been useful to investigate the correlation between markers in the present study with erythrocyte sedimentation rate, and C-reactive protein, which could not be performed because of retrospective nature.

In conclusion, we found that moderate/severe acne is associated with systemic inflammation, and isotretinoin treatment has systemic anti-inflammatory effects. Especially, NLR is a promising marker of systemic inflammation in moderate/severe acne and may be used at follow-up.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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