



# Effect of Systemic Isotretinoin use on Neutrophil/Lymphocyte Ratio in Acne Patients: A Retrospective Study

## Akne Hastalarında Sistemik İzotretinoin Kullanımının Nötrofil/Lenfosit Oranı Üzerine Etkisi: Retrospektif Bir Çalışma

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### Abstract

**Objective:** Acne vulgaris (AV) describes a chronic inflammatory condition that occurs in the pilosebaceous unit, which is common in the community. Increase in sebum production, abnormal follicular keratinization, Propionibacterium acnes (P.acnes) colonization and inflammation play a role in acne development. ISO, comedolytic, is the only agent that has an effect on all four conditions that determine the pathogenesis of acne, such as a large reduction in sebaceous gland size, suppression of sebum production and reduction in inflammation. In this study, it was aimed to compare the N/L ratio values at the beginning of the treatment and at the 4<sup>th</sup> month of the treatment in acne vulgaris patients receiving systemic ISO treatment.

**Material and Method:** 50 patients with acne vulgaris who applied to the dermatology outpatient clinics of Karaman Training and Research Hospital between October 2020 and February 2021, had moderate and severe acne vulgaris and were started on oral isotretinoin were included in the study. The medical records of the patients were reviewed retrospectively. The neutrophil/lymphocyte (N/L) ratio values of the patients at the beginning of isotretinoin treatment and after four months were recorded.

**Results:** The mean age of the patients was 23.1±6.23, 52.0% (26 persons) were male. There was a significant decrease in the N/L ratio in total and in both genders with isotretinoin use ( $p<0.01$ ). A positive correlation was found between the initial and post-treatment N/L rates.

**Conclusion:** Prospective studies with larger series and control groups may show that N/L ratio may be an important parameter in the follow-up of acne vulgaris patients receiving systemic therapy.

**Keywords:** Acne vulgaris, severe acne, systemic therapy, isotretinoin, neutrophil-lymphocyte ratio, inflammation

### Öz

**Amaç:** Akne vulgaris (AV), toplumda sık rastlanan, pilosebase üniteye ortaya çıkan kronik inflamatuvar bir durumu tanımlar. Akne gelişiminde sebum üretiminde artış, anormal foliküler keratinizasyon, Propionibacterium acnes (P.acnes) kolonizasyonu ve inflamasyon rol alır. ISO, komedolitik, sebase bez boyutlarında büyük oranda küçülme, sebum üretimini baskılama ve enflamasyonda azalma gibi akne patogenezi belirleyen dört durumun hepsine etkisi bulunan tek ajandır. Bu çalışmada, sistemik ISO tedavisi alan akne vulgaris hastalarında tedavi başlangıcında ve tedavinin 4. ayında N/L oranı değerlerinin karşılaştırılması amaçlanmıştır.

**Gereç ve Yöntem:** Ekim 2020-Şubat 2021 tarihleri arasında Karaman Eğitim ve Araştırma Hastanesi Dermatoloji polikliniklerine başvuran, orta ve şiddetli akne vulgaris olan ve oral izotretinoin başlanan 50 akne vulgaris tanılı hasta çalışmaya alındı. Hastaların tıbbi kayıtları retrospektif olarak incelendi. Hastaların izotretinoin tedavisi başlangıcında ve dört ay sonrasındaki nötrofil /lenfosit(N/L) oranı değerleri kaydedildi.

**Bulgular:** Hastaların yaş ortalaması 23,1±6,23, %52,0 (26 kişi) erkekti. İzotretinoin kullanımı ile N/L oranında toplamda ve her iki cinsiyette anlamlı düşüş vardı ( $p<0,01$ ). Başlangıç ve tedavi sonrası N/L oranları arasında pozitif korelasyon tespit edildi.

**Sonuç:** Daha geniş serilerde ve kontrol grupları ile yapılacak prospektif çalışmalar, sistemik tedavi alan akne vulgaris hastalarının takibinde N/L oranının önemli bir parametre olabileceğini gösterebilir.

**Anahtar Kelimeler:** Akne vulgaris, şiddetli akne, sistemik tedavi, izotretinoin, nötrofil/lenfosit oranı, inflamasyon



## INTRODUCTION

Acne vulgaris (AV) describes a chronic inflammatory condition that occurs in the pilosebaceous unit, which is common in the community. Acne lesions consist of open or closed comedones, inflammatory papules or pustules, nodules and cysts that can cause scar development and pigmentation disorders. Increase in sebum production, abnormal follicular keratinization, Propionibacterium acnes (P.acnes) colonization and inflammation play a role in the development of acne.<sup>[1]</sup> Isotretinoin (13-cis retinoic acid) (ISO), a retinoid derivative, is the first-choice treatment for nodulocystic acne, severe papulopustular acne, that is resistant to other treatments, or acne that heals with scarring. It is widely used in dermatology practice.<sup>[2]</sup> ISO is the only agent that has an effect on all four conditions that determine the pathogenesis of acne, with its effects such as comedolytic, greatly reducing the size of the sebaceous glands, suppressing sebum production and reducing inflammation.<sup>[3]</sup> Recently, the neutrophil-lymphocyte (N/L) ratio has been used to determine the systemic inflammatory response.<sup>[4]</sup> (N/L) ratio, found by dividing the neutrophil count by the lymphocyte count, is an easily accessible inflammatory marker to determine the risk of myocardial infarction and high coronary artery disease (CAD).<sup>[5,6]</sup> In many studies, (N/L) ratio associated chronic low-grade inflammation was found to be associated with risk factors such as diabetes mellitus (DM), hypertension, metabolic syndrome (MetS), obesity, hyperlipidemia, smoking and endothelial dysfunction.<sup>[7,8]</sup> In this study, we aimed to compare the N/L ratio values at the beginning of the treatment and at the 4<sup>th</sup> month of the treatment in acne vulgaris patients receiving systemic ISO treatment.

## MATERIAL AND METHOD

The study was carried out with the permission of Karamanoğlu Mehmet Bey University, Faculty of Medicine Ethics Committee (Date: 27.04.2022, Decision No: 04-2022/09). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. We included 50 acne vulgaris patients who applied to Karaman Training and Research Hospital Dermatology outpatient clinics between October 2020 and February 2021, had moderate and severe acne vulgaris according to the Global Acne Rating System,<sup>[9]</sup> and were started on oral ISO. We reviewed the medical records of the patients retrospectively. We recorded the age, gender, duration of illness, neutrophil/lymphocyte (N/L) ratio at the start of isotretinoin treatment and after four months of the acne patients included in the study. We did not include patients who have a disease that affects hematological parameters or who use drugs that affect these parameters (nonsteroidal anti-inflammatory drugs, anticoagulants, immunosuppressants, etc.), malignancy, those who use cigarettes and alcohol, and those under the age of 18 and over 60 years of age.

## Statistical Analysis

IBM SPSS (Statistics for Windows, Version 22.0, Armonk NY) program was used in the statistical analysis of the data. The normal distribution of data was evaluated with the Kolmogorov Smirnov test. It was found that the data were normally distributed. Mean±Standard Deviation values were given in the descriptive findings according to the characteristics of the variables. The paired t test was used to compare the N/L values, and the Pearson correlation test was used to evaluate the correlation of numerical data. A p-value of <0.05 was considered statistically significant.

## RESULTS

Of the 50 acne patients, 24 were women and 26 were men; mean age was  $23.1 \pm 6.23$  yrs. (Table 1).

**Table 1.** Demographic and descriptive characteristics

	Mean	SD
Age	23.1	6.23
Duration of Acne (year)	5.6	2.97
N/L beginning	2.0	0.90
N/L after treatment	1.5	0.45
Male	52.0% (n:26)	26
Female	48.0% (n:24)	24

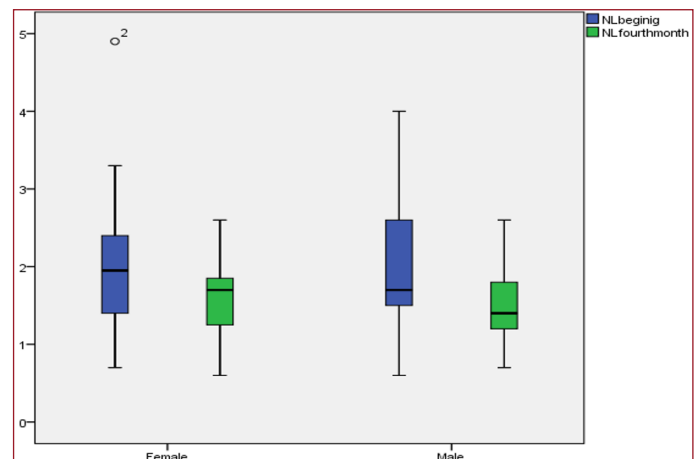
With the use of isotretinoin, there was a significant decrease in the N/L ratio in total and in both genders (Table 2).

**Table 2.** Change of N/L ratios with treatment

	Mean of difference	SD	t	p
Total participants*	0.4668 (n:50)	0.5897	5.598	<0.001
Female	0.4167 (n:24)	0.5872	3.476	0.002
Male	0.5131 (n:26)	0.5997	4.362	<0.001

\* Row percentage used

The variation of N/L ratios by gender with the use of isotretinoin is given in Figure 1.



**Figure 1.** The variation of N/L ratios by gender with the use of isotretinoin

We found a positive correlation between the initial and post-treatment N/L rates (Table 3).

	N/L 1	N/L 2	Age	Duration of Acne (year)
	r, p	r-p	r-p	r-p
N/L 1		0.829**-<0.001	0.191-0.184	0.211-0.141
N/L 2			0.242-0.090	0.191-0.184

r=Correlation Coefficient \*\*Correlation is significant at the 0.01 level (2-tailed).

## DISCUSSION

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous unit.<sup>[10,11]</sup> The presence of inflammatory markers in microcomedones, which is the initial appearance of acne, has been demonstrated by immunohistochemical methods. In inflammatory lesions, an increase in IL-1 was detected in the comedonal content in the early stages. An increase in perifollicular CD 4+ T cells, macrophages and cytokines was also detected in closed comedones where the inflammation is not advanced.<sup>[12]</sup> Neutrophils are activated by enzymes such as myeloperoxidase, elastase and acid phosphatase. The proportion of circulating leukocytes varies in the case of an inflammatory reaction. Relative to the increase in neutrophils, lymphopenia occurs. In the literature, it has been suggested that N/L ratio is a prognostic marker in many important diseases such as cardiovascular diseases and diabetes mellitus, hypertension and malignancies.<sup>[13]</sup> These values return to normal levels upon termination of treatment.<sup>[14]</sup> Özüğüz et al. evaluated the effect of ISO treatment on N/L ratio level in 67 acne vulgaris patients and did not detect a statistically significant decrease in N/L ratio values before and after treatment at the 3<sup>rd</sup> month.<sup>[15]</sup> Karadağ et al.<sup>[16]</sup> included 70 acne vulgaris patients in their study. They stated that only a moderate increase in the number of platelets was observed among the hematological parameters of the patients. In the same study, no change was found in other hematological values after the use of ISO. Unlike in our study, a significant decrease was found in N/L ratios. The age and sex ratios of the acne vulgaris patients included in the study may have been effective in this result.

## CONCLUSION

The N/L ratio is an easy to measure, inexpensive, and hemogram-determined value. Prospective studies with larger series and control groups may show that N/L ratio may be an important parameter in the follow-up of acne vulgaris patients receiving systemic ISO treatment.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of of Karamanoğlu Mehmet Bey University, Faculty of Medicine Ethics Committee (Date: 27.04.2022, Decision No: 04-2022/09).

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

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The author has no conflicts of interest to declare.

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**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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