Inflammatory biomarkers in rosacea patients

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Abstract

Aim: Rosacea is an inflammatory disease characterized by telangiectasia, papules and pustules associated with immune response. Several factors, especially inflammatory factors, have been investigated in its etiopathogenesis. The Systemic Immune Inflammation Index (SII) is a new inflammation marker. It has recently been used to evaluate the inflammatory and immune status of the patients. Also, several studies investigated other inflammation markers like neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR). The present study aims to investigate the correlation between rosacea, an inflammatory disease, and inflammatory markers such as platelet (PLT), lymphocyte (LYM), neutrophil (NEU), NLR, PLR, and especially SII.

Materials and Methods: The study was conducted with 100 papulopustular rosacea patients and 100 healthy controls. The patient and control groups were similar in age and gender. Participant data and laboratory results were obtained retrospectively from the patient files.

Results: Seventy-eight of the rosacea patients were female and 22 were male. The mean participant age was 47.97. There was no significant difference between rosacea patients and the control group based on age and gender. The PLT and LYM markers were significantly lower in the patient group when compared to the control group, and NLR, PLR and SII markers were significantly higher in the patient group (p<0.05).

Conclusion: The significant difference between the investigated inflammatory parameters suggested that rosacea could be a systemic inflammatory disease rather than a simple skin inflammation. More comprehensive studies are required to clarify this premise and the correlation between rosacea and systemic inflammation.

Introduction

Rosacea is a common chronic inflammatory dermatosis. Rosacea characterized by erythema, telangiectasia, papules/pustules, especially on the cheeks, nose, forehead, and chin [1]. It could be observed at any age; however, it usually onsets between 30 and 50. It is more common in females; however, the number of male patients has increased in recent years [1]. Rosacea is a skin disease that affects an average of 5.46% of the adult population globally [2]. Rosacea is generally categorized into four subtypes based on morphological properties: erythema telangiectatic, papulopustular, phymatous, and ocular rosacea [3].

Although the etiology of the disease is characterized by the induction of innate immune response and abnormal neurovascular signal by various environmental stimuli and endogenous factors, the diversity in clinical forms has prevented the clear understanding of the pathophysiology of rosacea [4,5].

The Systemic Immune Inflammation Index (SII) is a new inflammation marker that employs platelet, neutrophil and lymphocyte counts (platelet count × neutrophil/lymphocyte ratio). It has recently been used to evaluate the inflammatory and immune status of patients. Systemic inflammation has been considered an indicator of prognosis, disease severity and survival in several inflammatory and malignant diseases [6-8]. In dermatology, the correlation between SII and hidradenitis suppurativa, psoriasis, psoriatic arthritis, Behçet’s disease, recurrent aphthous stomatitis has been investigated [6,7,9,10]. Furthermore, several studies investigated inflammation markers like neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) [11].

The present study aimed to investigate the correlation between rosacea, an inflammatory disease, and inflammatory markers such as platelet (PLT), lymphocyte (LYM), neutrophil (NEU), NLR, PLR, and especially SII.
Materials and Methods
The research was approved by the Fırat University Non-invasive Research Ethics Committee (Number: 2023/12-11). One hundred patients who were presented to Health Sciences University, (XXX ???) Urban Dermatology Clinic between January 2022 and April 2023 and were diagnosed with papulopustular rosacea based on clinical examination were included in the study. Papulopustular rosacea patients without any concomitant dermatological, systemic, or local inflammatory diseases who were 18-65 years old, were not pregnant, did not abuse alcohol or substances, no history of anti-inflammatory medicine intake in the previous 3 months in the system were included in the study group. Patients who met the study criteria at the specified time were included. The control group included 100 healthy individuals who presented to the hospital for screening. The healthy control group included individuals without a dermatological, systemic, or local inflammatory disease who were between 18 and 65 years old, were not pregnant, and without a history of anti-inflammatory drug use in the previous 3 months in the system. The patient and control group members has similar age and gender distribution. The correlations between PLT, LYM, NEU, NLR, PLR, and SII parameters were investigated in the patient and control groups. Participant data and laboratory findings were obtained retrospectively from patient files.

Statistical analysis
The study data were analyzed with the Statistical Package for Social Science for Windows (SPSS) 24.0 software. Kolmogorov Smirnov test was applied to test whether the data were normally distributed and all parameters were found to be normally distributed (p>0.05). Therefore, parametric tests were used in data analysis. Independent samples t-test was used to investigate the differences between PLT, LYM, NEU, NLR, PLR and SII of the patient and control groups. Furthermore, the statistical difference between the gender distribution of the groups was determined with the chi-square test. Roc Analysis was conducted on the SII figures of the patient group and the cut off, sensitivity and specificity values are presented. The findings were considered significant at 95% (p<0.05) confidence levels.

Results
Seventy-eight percent of the rosacea patients were female and 22% were male. The mean participant age was 47.97. There was no significant difference between rosacea patients and the control group based on age and gender. The differences between the analyzed parameters in the groups are presented in Table 1.

There were significant differences between rosacea and control group PLT (t=-3.056; p<0.05), LYM (t=3.320; p<0.05), NLR (t=3.168; p<0.05), PLO (t=1.924; p<0.05) and SII (t=2.316; p<0.05) findings. Thus, the patient PLT and LYM findings were lower when compared to the controls, the patient NLR, PLR and SII findings were higher. The Roc curve analysis revealed that the SII cut-off was 586.95 with 84.6% sensitivity and 82.3% specificity (Area under the curve: 0.892; 95% (CI) confidence interval: 0.806 - 0.977; p=0.000<0.05).

Discussion
Rosacea is a chronic inflammatory skin disease characterized by erythema, papules and pustules associated with immune response [12]. Several studies reported that inflammatory pathways play a key role in the pathogenesis of rosacea [13-15]. In the present study, we investigated the role of systemic inflammation in rosacea pathogenesis based on various parameters. Belli et al. [16] compared the NLR, monocyte/high-density lipoprotein (HDL), cholesterol (MHR), and PLR ratios of rosacea patients and controls. NLR, mean low-density lipoprotein (LDL) and total cholesterol, triglyceride, C-reactive protein (CRP), systolic and diastolic blood pressures, and insulin resistance (IR) were significantly higher in rosacea patients when compared to controls. MHR was significantly higher in rosacea patients with IR and metabolic syndrome. Caf et al. [17] compared rosacea patients and the control group for endothelial dysfunction, systolic and diastolic blood pressures, hemogram, CRP, erythrocyte sedimentation rate (ESR), total cholesterol, triglyceride, LDL, HDL, NLR, PLR, mean platelet volume and fasting blood sugar. Metabolic syndrome, blood pressure, and NLR were higher in the patient group. These findings suggested that rosacea

Table 1. The differences between PLT, LYM, NEU, NLR, PLR and SII in rosacea patients and the control group.

<table>
<thead>
<tr>
<th>Parameter (mean ± sd)</th>
<th>Rosacea (n:100)</th>
<th>Control (n:100)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLT</td>
<td>273.53±60.28</td>
<td>296.47±76.47</td>
<td>.005*</td>
</tr>
<tr>
<td>LYM</td>
<td>2.10±0.61</td>
<td>2.36±0.82</td>
<td>.003*</td>
</tr>
<tr>
<td>NEU</td>
<td>4.26±1.42</td>
<td>4.17±1.41</td>
<td>.586</td>
</tr>
<tr>
<td>NLR</td>
<td>2.28±1.46</td>
<td>1.89±0.79</td>
<td>.002*</td>
</tr>
<tr>
<td>PLR</td>
<td>140.25±49.12</td>
<td>135.28±47.91</td>
<td>.042*</td>
</tr>
<tr>
<td>SII</td>
<td>602.34±60.82</td>
<td>562.66±77.19</td>
<td>.021*</td>
</tr>
</tbody>
</table>

Independent Samples t-Test, *p<0.05. (PLT: Platelet, LYM: Lymphocyte, NEU: Neutrophil, NLR: Neutrophil Lymphocyte Ratio, PLR: Platelet Lymphocyte Ratio, SII: Systemic Immune Inflammation Index).

Figure 1. ROC Analysis.
could lead to an atherogenic effect and exhibit systemic involvement.

Karaosmanoglu et al. [13] retrospectively analyzed CBC, CRP, ESR, triglyceride, HDL and LDL findings in rosacea patients. NLR, monocyte/lymphocyte ratio and PLR, MHR and SII were compared between patient and control groups. Monocyte and platelet counts, SII, ESR and CRP were significantly higher in rosacea patients, and no statistically significant difference was determined between other parameters. Ertekin et al. [18] compared various inflammatory parameters (high-sensitivity C-reactive protein, interleukin-1 beta, interleukin-6, tumor necrosis factor alpha) between rosacea and healthy controls. And they found the levels of these parameters to be significantly higher in the patient group.

**Limitations**

This is a retrospective study. Thus, although a meticulous screening was conducted, the details of medical patient data were limited by the data available in hospital system. In the study, only certain inflammatory parameters were analyzed, and inflammatory markers such as CRP, ESR, interleukins and tumor necrosis factors were not analyzed. Prospective studies that would be conducted with larger samples and more inflammatory markers would provide further knowledge that could clarify the issues associated with rosacea.

**Conclusion**

Blood inflammatory parameters are inexpensive and easily determined inflammation markers. Significant findings in rosacea patients could be employed as inflammatory biomarkers. Similar to the above-mentioned studies, we determined significant differences between inflammatory parameters in rosacea patients and healthy controls. PLT and LYM were significantly lower in rosacea patients when compared to the control group, NLR, PLR and SII were significantly higher in the patient group. The significant difference between the analyzed blood inflammatory parameters, especially the SII, suggested that rosacea could be a systemic inflammatory disease rather than just a skin inflammation. The association between rosacea and systemic inflammation and metabolic conditions has been reported in various studies [19-21]. However, it is not clear whether rosacea could lead to systemic and metabolic conditions or whether these conditions induce rosacea. Further comprehensive studies are required to clarify this ambiguity and the correlation between rosacea and systemic inflammation.

**Ethical approval**

This research was approved by the Fırat University Non-invasive Research Ethics Committee (Number: 2023/12-11).

**References**