

Mean Platelet Volume, Neutrophil-To-Lymphocyte Ratio, and Platelet-To-Lymphocyte Ratio as Inflammatory Markers in patients with Recurrent Aphthous Stomatitis

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ABSTRACT

Objective: The aim of this study is to examine the associations between white blood cell (WBC), hemoglobin (Hb), neutrophil, lymphocyte, platelet, mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels in patients with recurrent aphthous stomatitis (RAS).

Materials and Methods: For this study, 137 patients with RAS and 137 healthy controls were recruited. The study participants had no systemic diseases except RAS. Serum WBC, Hb, neutrophil, lymphocyte, platelet, MPV, PLR, NLR, ESR, and CRP levels were recorded in the active period for all patients with RAS and controls.

Results: There was no statistically significant difference in the WBC, Hb, neutrophil, lymphocyte, platelet, MPV, NLR, PLR, ESR, and CRP levels between patients with RAS and controls.

Conclusion: No differences were observed for WBC, Hb, neutrophil, lymphocyte, platelet, MPV, NLR, PLR, ESR, and CRP levels between patients with RAS and controls. These parameters therefore cannot be used as markers for inflammation or inflammation severity in patients with RAS.

Keywords: C-reactive protein, erythrocyte sedimentation rate, inflammation, recurrent aphthous stomatitis, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio

Introduction

Recurrent aphthous stomatitis (RAS) is an oral mucosa disease characterized by chronic inflammation. It is one of the most common painful lesions and can have negative effects on quality of life, oral health, and nutritional status [1]. Diagnosis of RAS depends on exclusion of other causes of ulcerative stomatitis [2, 3]. Recurrent aphthous stomatitis accounts for 25 percent of recurrent ulcers in adults and 40 percent in children [4]. The severity of stomatitis is represented by one of three subtypes: minor, major, and herpetiform RAS. Minor RAS is the most common form and is generally confined to the lips, tongue, and buccal mucosa. These are superficial, round ulcerations with a diameter < 10 mm. Major RAS has extensive spread (commonly extending to the gingiva and pharyngeal mucosa), is larger in size (> 10 mm), and has a longer duration of eruption. Herpetiform RAS are large and deep ulcers that are often joined, and exhibit irregular contours [5]. According to another classification by Bagan et al. [6], the disease can be categorized into three types. In type one, intervals of aphthous lesions occur over three months, while in type two, the eruption of lesions occur in one-to-three month intervals. In type three, aphthous lesions are constantly present.

Although a definitive etiology does not exist, several factors are suspected as possible causes for RAS. These include trauma, genetic background, hematological disorders, immunological factors, smoking cessation (cigarettes), stress, microbial factors, nutritional factors (such as folate and B-complex vitamin deficiencies), and allergies [7]. In general, during the inflammatory response, levels of neutrophils and monocytes increase and levels of lymphocytes decrease in the peripheral blood stream. The effect of various trigger factors initiates the cascade of proinflammatory cytokines directed against selected regions of the oral mucosa in RAS. Microscopic evaluation of RAS found the disease released significant infiltration by leukocytes, which varies depending on disease extent and severity [8].

Platelets, mean platelet volume (MPV), hemoglobin (Hb), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) were shown to be associated with inflammation and the severity of inflammation in several diseases [9, 10]. Serum C-reactive protein (CRP) is a positive acute phase reactant protein that is synthesized by the liver, and its blood level increases within hours in response to inflammation and infection [11]. Erythrocyte sedimentation rate (ESR) is a type of blood test that measures how quickly erythrocytes (red blood cells) settle at the bottom of a test tube containing a blood sample. Typically, red blood cells settle relatively slowly. A faster-than-normal rate may indicate inflammation in the body [12].

The aim of this study was that determine whether the serum levels of white blood cells (WBC), Hb, neutrophils, lymphocytes, platelets, MPV, NLR, PLR, ESR, and CRP were altered in patients with minor RAS.

Materials and Methods

A prospective case-control study was carried out in the Department of Otolaryngology of Malatya Training and Research Hospital, Turkey. This study was approved by the Ethics Committee of the Malatya Training and Research Hospital (number: 23536505-604.02), and was conducted in accordance with the ethical standards of the Helsinki Declaration of 2000. Written informed consent was obtained from patients.

A total of 274 participants were enrolled in the study. The study involved two groups:

- Patients with minor RAS, which comprised 137 patients (60 male and 77 female) with a mean age of 34.7 ± 2 (min. 15 y, max. 63 y).
- A healthy control group comprising 137 patients (55 male and 82 female) with a mean age of 33.6 ± 2.5 (min. 15 y, max. 62 y).

All patients in the study group had minor clinical RAS features and were all characterized by type two disease; intervals between eruptions were three or more than three times in one month. We used the ulcer severity score (USS) to assess and monitor oral ulcers. The six clinical USS features, i.e., number of ulcers, ulcer size, ulcer duration, ulcer-free period, pain, and site of ulcers were recorded [13]. Patients with chronic disease (such as anemia, diabetes mellitus, chronic hypertension) were excluded from the study. In addition, patients who used drugs, alcohol, and tobacco were excluded from the study. All laboratory parameters were obtained from patients with RAS in an active period. Laboratory param-

eters were obtained prior to the start of any medical treatment.

The controls exhibited either no evidence of active RAS or history of RAS. Patients with any systemic disorders that were related to stomatitis (such as Behcet's disease, celiac disease, and other gastrointestinal or dermatological diseases), or who evidenced drug intake, or had a history of immunosuppressive or immunomodulatory treatment were excluded from the study.

Statistical Analysis

All analyses were conducted using The Statistical Package for the Social Sciences (SPSS) v.15.0 (SPSS Inc., Chicago, IL, USA). Data distribution was analyzed using the Kolmogorov-Smirnov test. The variables that were normally distributed are shown as mean \pm SD, whereas non-normally distributed data are indicated as median \pm interquartile range (IQR). Comparisons of parameters were conducted using the Student t-test or Mann-Whitney U test. A two-tailed $p < 0.05$ was considered statistically significant.

Results

There was no statistically significant difference between cases and controls regarding age. The mean USS score was 28.6 ± 4.1 in patients with RAS. The mean WBC value was 6.9 ± 0.34 K/ μ L in patients with RAS and 6.96 ± 0.35 K/ μ L in controls. The median hemoglobin value was 14.2 (12.5-15.3) in patients with RAS and 13.7 (13.1-14.9) in controls. The median neutrophil value was 3.5 (2.9-4.9) K/ μ L in patients with RAS and 3.7 (3.0-4.5) K/ μ L in controls. The median lymphocyte value was 2.1 (1.1-2.5) K/ μ L in patients

with RAS and 2.3 (1.8-2.7) K/ μ L in controls. The median platelet value was 278 (237-343) K/ μ L in patients with RAS and 263 (237-302) K/ μ L in controls. The mean MPV values were 9.8 ± 0.17 fL in patients with RAS and 10 ± 0.19 in controls. The median NLR value was 1.8 (1.4-2.5) in patients with RAS and 1.6 (1.2-2.1) in controls. The median PLR values was 127.4 (101-154.7) in patients with RAS and 129 (90.4-170.2) in controls. The mean value of ESR was 12.5 ± 1.15 (mm/h) in patients with RAS and 10.7 ± 1.19 (mm/h) in controls. The median and IQR values of CRP was 0.2 (0.09-0.44) mg/L in patients with RAS and 0.23 (0.09-0.43) mg/L in controls. The mean vitamin B12 value was 356 ± 55 in patients with RAS and 346.4 ± 24 μ g/dL in controls.

There was no statistically significant difference between patients with RAS and the controls regarding WBC, Hb, neutrophil, lymphocyte, platelet, MPV, NLR, PLR, ESR, and CRP levels. In addition, there was no statistically significant difference in vitamin B12 levels between patients with RAS and the controls. Laboratory findings for both groups are presented in Table 1.

Discussion

In the present study, we found that WBC, Hb, neutrophil, lymphocyte, platelet, MPV, PLR, NLR, ESR, and CRP values displayed no significant differences between patients with RAS and healthy controls. These parameters therefore cannot be used as markers of inflammation and/or severity of inflammation in patients with RAS.

We found that blood WBC, Hb, neutrophil, lymphocyte, and platelet levels were not significantly

Table 1. Clinical characteristics and laboratory parameters of study participants

	Patients with RAS n=137	Controls n=137	p
Age (y)	34.7 \pm 2.0	33.6 \pm 2.5	0.64
USS score	28.6 \pm 4.1	-	
Vitamin B ₁₂	356 \pm 55	346.4 \pm 24	0.94
Hemoglobin	14.2 (12.5-15.3)	13.7 (13.1-14.9)	0.74
White blood cells	6.9 \pm 0.34	6.96 \pm 0.35	0.55
Neutrophils (K/ μ L)	3.5 (2.9-4.9)	3.7 (3-4.5)	0.92
Lymphocytes (K/ μ L)	2.1 (1.1-2.5)	2.3 (1.8-2.7)	0.49
Platelets (K/ μ L)	278 (237-343)	263 (237-302)	0.26
Mean platelet volume (fL)	9.8 \pm 0.17	10 \pm 0.19	0.35
Neutrophils/lymphocytes ratio	1.8 (1.4-2.5)	1.6 (1.2-2.1)	0.11
Platelets/lymphocytes ratio	127.4 (101-154)	129 (90.4-170.2)	0.48
CRP (mg/L)	0.2 (0.09-0.44)	0.23 (0.09-0.43)	0.93
ESR (mm/h)	12.5 \pm 1.15	10.7 \pm 1.19	0.20

Normally distributed variables are shown as mean \pm SD, whereas non-normally distributed data are shown as median \pm IQR. CRP; C-reactive protein; ESR; erythrocyte sedimentation rate; USS; ulcer severity score; RAS; recurrent aphthous stomatitis.

different between case and control participants. In a previous study, higher WBC and neutrophil levels and a lower lymphocyte level were associated with inflammation response [14]. Likewise, high levels of platelets can cause vascular occlusion and perfusion problems, and may be related to several diseases such as sudden sensorineural hearing loss [14]. In agreement with this study, Sereflican et al. [15] found that WBC, Hb, neutrophil, and lymphocyte levels were not higher in patients with RAS, compared with controls. Although Terzi et al. [16] found lymphocyte and platelet level to not indicate statistically significant differences between patients with RAS and controls, they observed that WCB and neutrophil levels were higher in patients with RAS than in controls.

In the present study, we found MPV level showed no statistically significant difference between the two groups. In contrast, Ekiz et al. [17] showed that patients with RAS had significantly higher MPV compared to controls. In agreement with the current study, other research found no statistically significant difference regarding MPV level between patients with RAS and controls [15, 16].

In the present study, we found both PLR and NLR did not indicate statistically significant differences between patients with RAS and healthy controls. Both a higher level of PLR and NLR was found to be linked to higher levels of inflammation in the body [18]. Additionally, NLR and PLR have been defined as potential new markers in several inflammatory diseases (e.g., Behçet's diseases and sudden sensorineural hearing loss) [18, 19]. Selected studies have reported NLR level as significantly higher in patients with RAS than controls [16, 20]. In addition, NLR level was linked to oral ulcer activity and pain severity [16, 20]. A study by Sereflican et al. [15], however, demonstrated a lack of any statistically significant difference between patients with RAS and controls as it relates to NLR and PLR levels.

In this study we found that CRP and ESR were not valuable parameters of inflammation in patients with minor RAS. Some infections, autoimmune diseases, and malignancies are associated with high ESR and CRP levels [21]. In contrast to our research, other studies found higher ESR or CRP levels in patients with RAS [15, 17].

This study observed no systemic inflammation in RAS in terms of WBC, Hb, neutrophil, lymphocyte, platelet, MPV, NLR, PLR, ESR, and CRP val-

ues. Different studies published previously in the literature and all results were different each one. The present study was performed with a larger patient group than previous studies. Patients' laboratory values were taken during the active period, when aphthous stomatitis was most intensely experienced. All patients were assessed by the same otolaryngology expert. These factors represent the strengths of our research.

In conclusion, WBC, Hb, neutrophil, lymphocyte, platelet, MPV, NLR, PLR, ESR, and CRP levels did not differ significantly among patients with RAS. These parameters can therefore not be used as markers of inflammation or inflammation severity in patients with RAS. Further studies involving larger populations are needed to confirm these findings.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Malatya Training and Research Hospital (number: 23536505-604.02).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author has no conflict of interest to declare.

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