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Original Article

Evaluation of Mean Platelet Volume in Patients of Recurrent Aphthous Stomatitis

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ABSTRACT

One of the most prevalent conditions affecting the oral mucosa is recurrent aphthous stomatitis (RAS), which is characterized by uncomfortable ulcerations on the movable or non-keratinized oral mucosa. **Objective:** To compare mean platelet volume (MPV) in patients of recurrent aphthous stomatitis (RAS) versus healthy control. **Methods:** This non-probability sampling case-control research included 56 RAS patients and 56 healthy controls. Patients who presented for dental treatment and have RAS in oral cavity were included. Patients with systemic inflammatory illnesses, autoimmune diseases like pemphigus, or infectious diseases like herpes who attended for dental treatment and exhibited RAS in the oral cavity were excluded. The healthy control group had no mouth ulcers or blood problems. A Student t-test compared MPV between cases and controls based on age, gender, and MPV. **Results:** The mean age of the participants was 29.35 ± 8.28 years, with 57 (50.89%) females and 55 (49.11%) males. The mean MPV in the RAS group (8.86 ± 0.33) was significantly higher ($p < 0.001$) than in the control group (6.95 ± 0.2). The univariable model coefficient of 1.91 (95% CI = 1.81-2.01, $p < 0.001$) indicates that the RAS group had a significantly higher MPV than the Control group. For gender, males had a lower MPV compared to females ($\beta = -0.36$), but it was not statistically significant ($p = 0.056$). **Conclusions:** RAS patients have higher platelet activity indicated by higher mean platelet volume (MPV) than healthy controls.

INTRODUCTION

Recurrent aphthous stomatitis are ulcers of inflammatory origin which have a distinct clinical picture of a well demarcated ulcer with an erythematous halo [1-3]. It is caused by multiple factors which are still under research. Although a definitive etiology does not exist, several factors are suspected as possible causes for RAS [4]. 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 [5-7]. Among them stress and nutritional deficiency play a major role in initiating the inflammatory state of the body [8, 9]. Inflammation can be quantified by measuring marker of inflammation [10]. Platelets play a crucial role in coordinating inflammation by interacting with neutrophils a, monocytes, endothelium and lymphocytes [11]. Mean platelet Volume in Complete Blood Count gives information of the size of the platelets and their function. We can utilize this value as an indicator of inflammation [12]. The use of inflammatory markers can aid in the diagnosis of recurrent aphthous ulcer by establishing the inflammatory nature of the presented

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ulcer. Among the various markers available, complete blood count (CBC) has been found to be the most cost-effective option. In addition, CBC results are easily obtainable within hours, making it convenient for researchers to track and record reports. Therefore, CBC can be a useful tool in aiding clinicians to diagnose recurrent aphthous ulcer [13]. International research conducted by Sereflican *et al.*, showed significant difference in the value of MPV in patients of recurrent aphthous stomatitis as compared to control group [14]. In another study by Biyik et *al.*, they found no statistical difference in values of MPV in control group and patients of RAS [15]. This could be attributed to retrospective nature of study and improper screening of controls. In a study by Karaer *et al.*, showed a Mean platelet volume (fL) in patients with RAS of 9.8 ± 0.17 as compared to controls 10 ± 0.19 (p=.35) [16]. A positive correlation between recurrent aphthous ulcers and an increased MPV value can guide clinicians in diagnosing inflammatory ulcers. This information can help clinicians determine if the ulcer is of inflammatory origin, which can aid in patient counseling and provide reassurance that the disease. The objective of this study was to compare mean platelet volume in patients of recurrent aphthous stomatitis versus healthy control

METHODS

This case-control study was conducted at the Dental OPD of Sharif Medical and Dental College/Affiliated Hospital, Karachi from 1st July, 2022 to 28th February, 2023 on 58 participants using non-probability consecutive sampling. The sample size was calculated using WHO calculator to estimate a mean at a confidence level of 95% and an acceptable difference of 0.05, assuming a mean of MPV in RAS patients of 10 ± 0.19 (from the study by Karaer *et al.*,) [16]. The required sample size was 56 (55 RAS and 56 controls). Ethical approval was obtained from the hospital and verbal informed consent was obtained from all participants. The inclusion criteria were patients who presented to the Dental OPD for dental treatment and had RAS in the oral cavity. Patients with underlying systemic inflammatory conditions who presented with complaints other than RAS, autoimmune diseases such as pemphigus, or infectious diseases such as herpes were excluded from the study. The cases were patients who had recurrent aphthous stomatitis (RAS), while the controls were healthy subjects who did not have any oral ulcers or blood disorders. RAS was diagnosed by physical examination as the presence of one or multiple round-to-ovoid, shallow, punched-out-appearing, painful oral ulcers. The normal range for mean Platelet Volume is 8.9-11.8 fL. Demographic data like age, gender and contact details were recorded. Performa was filled of patients fulfilling the inclusion criteria. Blood samples were collected from each participant (both case and control groups) using a sterile needle and syringe or a vacutainer system. Appropriate safety precautions were used and standard phlebotomy protocols were followed. The blood sample was transferred to an EDTA tube and inverted several times to ensure proper mixing of the anticoagulant. The sample was processed within 2 hours of collection to prevent platelet activation and degranulation. The MPV was measured using an automated hematology analyzer, and the manufacturer's instructions for operating the analyzer were followed to ensure that it was calibrated properly. MPV was reported in femtoliters (fL). Our hypothesis was that value of Mean Platelet Volume will be increased in patients presenting with Recurrent Aphthous Ulcers. The data were entered and analyzed using R programming version-4.1.2. Descriptive statistics were computed for all variables. An independent samples t-test was performed to compare MPV values between cases and controls. Linear regression was run to control for confounding variables, using MPV as the dependent variable and comparators (case and control), age, and gender as independent variables. A significance level of $p < 0.05$ was used to determine statistical significance.

RESULTS

The mean age of the participants was 29.35 ± 8.28 years. There was a total of 112 participants in the study, with 57 (50.89%) being female and 55 (49.11%) being male. In terms of age group, the majority of participants were in the 26-40 age group, with 63 (56.25%) participants falling into this category. 42 (37.50%) participants were in the 13-25 age group, and only 7 (6.25%) were in the 41-65 age group (Table 1).

Table 1: Distribution of gender and age group

Variables	Characteristic	n (%)
Gender	Female	57 (50.89)
	Male	55 (49.11)
Age group (years)	13-25	42 (37.50)
	26-40	63 (56.25)
	41-65	7 (6.25)

The mean age of RAS (25.75 ± 4.36) was lower than controls (32.95 ± 9.64) statistically ($p<0.001$). The females were more in RAS (60.71%) than control group (41.07%) and the difference was statistically significant (Table 2).

Table 2: Comparison of age and gender between case and control

Characteristic	Aphthous, N = 56	Control, N = 56	p-value
Age (yrs), Mean ± SD	25.75 ± 4.36	32.95 ± 9.64	<0.001*
Gender, n (%)			
Female	34 (60.71)	23 (41.07)	0.038**
Male	22 (39.29)	33 (58.93)	

*Student t-test, **chi-square test

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The mean MPV for the Control group is 6.95 ± 0.20 (mean ± standard deviation), while for the RAS group, it is 8.86 ± 0.33. The p-value for the comparison of MPV between the two groups is <0.001, indicating that the difference between the means of the two groups is statistically significant (Table 3).

Table 3: Comparison of mean platelet volume between cases and control

Characteristic	Control, n = 56	RAS, n = 56	p-value
MPV, Mean ± SD	6.95 ± 0.20	8.86 ± 0.33	<0.001

*Welch Two Samples t-test

The univariable model coefficient of 1.91 (95% =1.81-2.01, p<0.001) indicates that the RAS group has a significantly higher MPV than the Control group. The multivariable model coefficient of 1.97 (95% =1.85-2.09, p<0.001) indicates that even after adjusting for other variables, the RAS group still has a significantly higher MPV than the Control group. For gender, the negative coefficient (-0.36) indicates that on average, males have a lower MPV compared to females, but difference is not statistically significant (p=0.056). The coefficient for the multivariable analysis indicates the change in the MPV for males compared to females after controlling for age group, but it is also not statistically significant. The coefficients for the univariable analyses show the difference in MPV between the reference group (13-25) and the other age groups. The negative coefficients for 26-40 and 41-65 indicate that on average, these age groups have lower MPV compared to the reference group. Both coefficients are statistically significant, with p-values less than 0.001. The coefficients for the multivariable analyses show the change in the MPV for each age group after controlling for other confounders. The coefficient for the 26-40 age group (p =0.089), and 41-65 age group are not statistically significant (p=0.145) (Table 4).

Table 4: Multivariate analysis of mean platelet volume (MPV) among cases and controls, stratified by gender and age group

Dependent: Mean platelet volume	Characteristics	Unit Value: Mean SD	Coefficient (univariable)	Coefficient (multivariable)
Group	Control	6.9 ± 0.2	-	-
	RAS	8.9 ± 0.3	1.91 (1.81 to 2.01, p<0.001)	1.97 (1.85 to 2.09, p<0.001)
Gender	Female	8.1 ± 1.0	-	-
	Male	7.7 ± 1.0	-0.36 (-0.73 to 0.01, p=0.056)	0.02 (-0.09 to 0.12, p=0.722)
Age group (year)	13-25	8.4 ± 0.9	-	-
	26-40	7.7 ± 1.0	-0.72 (-1.09 to -0.36, p<0.001)	0.10 (-0.02 to 0.22, p=0.089)
	41-65	7.0 ± 0.2	-1.37 (-2.11 to -0.63, p<0.001)	0.18(-0.06 to 0.42, p=0.145)

DISCUSSION

Our findings show that MPV is statistically higher in patients with RAS as compared to healthy control and the mean value of PV was higher in females and younger ages. Recurrent aphthous stomatitis (RAS), also called canker sores, is a condition where painful sores or ulcers appear in the mouth [17]. The cause is not fully known, but it's believed to be linked to genetics, the immune system, and environmental factors. Triggers may include stress, mouth injuries, certain foods, hormonal changes, and infections [8]. Platelets are tiny blood cells that play a crucial role in blood clotting, wound healing, and inflammation. The MPV test measures the size of platelets in the blood, with larger platelets indicating increased platelet activity [9]. Research has suggested that higher MPV levels may be associated with increased inflammation and more severe inflammatory conditions [6, 18]. Our findings showed that the mean MPV in the RAS group (8.86 ± 0.33) was significantly higher (p<0.001) than in the control group (6.95 ± 0.2). In a previous matched case-control study that included 80 cases of RAS and controls, the MPV values between cases (262.3±43.89 K/µL) and controls (253.6 ± 67.37 K/µL) were not significantly different (p >0.05) [19]. Many factors can play a role in the differences observed in these results, such as differences in the selection criteria of the study participants, inclusion of patients with more severe or active RAS, variations in the laboratory methods used to measure MPV values, and differences in the demographic or clinical characteristics of the study participants, such as age, gender, medical history, or medication use. Ekiz *et al.*, conducted a study that included 60 patients diagnosed with RAS, as well as 60 healthy individuals as a control group [18]. They reported that the RAS patients had significantly higher mean platelet volume (MPV) compared to the control group. This finding suggests that platelet activity may be higher in RAS patients and may contribute to the development or severity of the condition. The current study found that the mean MPV value was higher in females and younger age groups. This could be attributed to hormonal changes that occur during menstruation, which can affect platelet function and increase MPV levels [20]. Another matched case control prospective study by Turan *et al.*, on 260 participants reported the MPV was significantly less in RAS than healthy control. They also reported that erythrocyte sedimentation rare and neutrophil count was higher in RAS than healthy control [21]. Due to a more responsive and active immune system, young age participants may also have high platelet count resulting in increased platelet activity and inflammation. The differences in MPV values between aphthous patients and healthy controls may due to other factors, like lifestyle habits (smoking and drinking alcohol), underlying medical conditions (autoimmune disorders), or medication use [22]. However, to explore the underlying mechanism for association of MPV and RAS and their

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predicting factors, more rigorous research is warranted.

CONCLUSIONS

The study provides some evidence that patients with RAS have higher mean platelet volume (MPV) compared to healthy controls, indicating increased platelet activity and potential involvement in the pathogenesis of RAS. The study also suggests that the mean MPV value is higher in females and younger age groups.

Authors Contribution

Conceptualization: MN
Methodology: UM, MN
Formal analysis: SA, AA
Writing-review and editing: UT, SAAZ, AK

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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