

Relationship of blood types (ABO/Rh) with recurrent aphthous ulcers: A case-control study

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Background: Recurrent aphthous stomatitis (RAS) is among the most common oral lesions and pain is often the chief complaint of patients. The main etiology of RAS is unknown but several predisposing factors have been suggested. This study aims to assess the correlation of blood types (ABO/Rh) with RAS.

Methods: We conducted this prospective screening study on 50 patients with RAS and 50 controls. Both groups received a questionnaire and underwent serum screening for detection of blood type (ABO/Rh). The collected data were analyzed by the independent t-, Fisher's exact, and chi square tests. $P < 0.05$ was considered statistically significant.

Results: There was no significant difference observed between cases and controls in terms of age ($P = 0.065$), sex ($P = 1.000$), blood type (ABO; $P = 0.531$), and Rh ($P = 1.000$).

Conclusion: Based on the results, blood type (ABO/Rh) is not a predisposing factor for RAS. However, future studies with larger sample sizes are recommended.

Keywords: recurrent aphthous stomatitis, blood groups, oral ulcer

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INTRODUCTION

Recurrent aphthous stomatitis (RAS) is among the most common oral ulcers with a prevalence rate of 5% to 20% in the general population ¹. Clinically, RAS lesions appear in the form of round or oval, well-defined recurrent painful ulcers with an erythematous inflammatory halo in the non-keratinized mucosa of the oral cavity, and are often covered with a gray pseudo-membrane ²⁻⁵. There are three forms of RAS - minor, major, and herpetiform in the oral cavity. The minor form

is most commonly seen in which the ulcer heals within 7 to 10 days ^{1,2,5}. RAS is more common in females, subjects under 40 years of age, Caucasians, non-smokers, and those with higher socioeconomic status ².

The main etiology of RAS remains unknown but it seems to be multifactorial ⁴. Predisposing factors include genetics, immunological factors, local trauma, cigarette smoking, hormonal factors, nutrition, stress, hypersensitivity, and allergy; microorganisms may also be involved in the pathogenesis of RAS ^{3,4,6,7}. Immunological changes

such as cytotoxicity of T cells against oral mucosal epithelium, antibody-dependent cell-mediated cytotoxicity, immune complex deposits in the oral mucosa, changes in the ratio of CD4 to CD8 cells, and increased levels of interleukin 2, interferon gamma, and tumor necrosis factor alpha (TNF α) have been reported in patients with RAS^{3,8}.

Although self-limiting aphthous ulcers manifest periodically, the pain and discomfort are due to ulcers that interfere with normal oral function such as eating, deglutition and speech, and negatively affect the quality of life of patients^{1,7}. Since the main reason behind the development of ulcers is not known, a wide range of treatments are available for this disease; however, none are completely successful⁶. The most commonly used treatment modality for aphthous ulcers is symptomatic treatment; whereas, the treatment of RAS must include wound healing and prevention of recurrence. Thus, prior to treatment, the underlying causes of disease must be identified and eliminated¹.

The blood groups were first described by Landsteiner in 1900⁹. The blood group ABH antigens are carbohydrates found abundantly on the surface of red blood cells and in epithelial tissue¹⁰. Since these antigens are made of polysaccharides which are similar to some polysaccharide bacterial structures, they may directly or indirectly affect the function of the immune system and reinforce or compromise it. Thus, assessment of the role of blood type as a predisposing factor for diseases based on cell-mediated and humoral immunity can provide new insight into this topic¹¹.

Several studies have assessed the prevalence malignancies, stomach ulcers, infections, and coagulation disorders in patients with different blood types¹². Possible relationships have been sought in several dermatologic disorders such as lichen planus, vitiligo, pemphigus, and psoriasis¹³.

Some studies also assessed the correlation of blood type antigens with oral diseases such as gingivitis, periodontitis, denture stomatitis, angular cheilitis, oral lichen planus, and oral cancer^{9,10,14-16}. We took into consideration the role of immunological factors such as cell-mediated immunity and hypersensitivity reactions in etiopathogenesis of RAS⁸ and immunological differences that exist among subjects with different blood types¹¹ and attempted to assess the correlation of blood type

with susceptibility to RAS. For the first time, we have sought to determine whether blood type is a predisposing factor for the development of recurrent aphthous ulcers.

PARTICIPANTS AND METHODS

The Ethics Committee of Shiraz University of Medical Sciences approved this study. The 100 enrolled patients provided written informed consent. Patients were selected from among those who presented to the Oral Medicine Department of Shiraz University, School of Dentistry from March to September, 2013. We evaluated 50 patients with RAS and 50 controls. Inclusion criteria consisted of: written informed consent and diagnosis of RAS confirmed by an oral medicine specialist. Exclusion criteria consisted of systemic conditions, oral drug intake, other oral diseases, cigarette smoking, and alcohol consumption. After enrollment, patients completed a demographic questionnaire. Blood samples obtained from the patients were analyzed for blood type and Rh by a technician blinded to the group allocation of specimens. At the end of the study, patients were informed about the results. Data were collected and analyzed using SPSS version 11.5, the independent "t", Fisher's exact, and chi square tests. $P < 0.05$ was considered statistically significant.

RESULTS

The mean age of patients was 29.3 ± 10.9 years in the case group and 25.6 ± 8.4 years in the control group, which was not significant based on the independent t-test ($P = 0.065$). There were 30 males and 20 females in the case and 29 males and 21 females in the control groups. Based on the Fisher's exact test, the two groups did not significantly differ in terms of gender ($P = 1.000$). Clinically, 46 had minor and 4 had major aphthous ulcers; 36 patients had less than 4 ulcers, 11 had between 5 to 10 ulcers, and 3 had more than 10 ulcers. Analysis of blood types revealed that 8 patients (16%) in the case group and 14 (28%) controls had blood type A; 7 (14%) in the case group and 6 (12%) in the control group had blood type B; 7 (14%) of the cases and 7 (14%) controls had blood type AB; and 28 (56%) of the cases and 23 (46%) controls had blood type O (Table 1). The chi square test showed

Table 1. ABO/Rh blood types in the case and control groups.

Blood Groups	Patients		Controls		OR (95% CI)	P
	n	(%)	n	(%)		
ABO blood group						
A	8	(16)	14	(28)	0.442 (0.138, 1.291)	0.531
B	7	(14)	6	(12)	1.214 (0.335, 4.397)	
AB	7	(14)	7	(14)	0.853 (0.25, 2.909)	
O	28	(56)	23	(46)	---	
Rh blood group						
Rh positive	45	(90)	45	(90)	1.000	1.000
Rh negative	5	(10)	5	(10)	1.000	

that no significant difference existed between the two groups in terms of ABH blood group antigens ($P=0.531$). Evaluation of Rh antigen demonstrated that in both the case and control groups, there were 45 (90%) Rh positive subjects and 5 (10%) Rh negative. Based on the chi square test, there was no significant difference between the two groups for Rh antigen ($P=1$).

DISCUSSION

The current study, as with previous studies on RAS, found a higher prevalence of aphthous lesions in young adults. In terms of gender, male patients significantly outnumbered female patients, which contrasted previous studies^{2,17}. The frequency of different blood types in the current study differed slightly from the results of an epidemiological study on a population in Fars Province¹⁸. A study conducted in Fars Province in 2001 reported that from patients who presented to the blood donation agency, 40.5% had blood type O, 27.9% had blood type A, 24.9% had blood type B, 5.7% had blood type AB, 86.9% were Rh positive, and 13.1% were Rh negative; these results differed from the current study findings. This difference might be attributed to ethnic and racial differences, the time difference of the studies, immigrations, and different study sample sizes¹⁸.

Our results could not find a correlation between blood types and RAS, which might be due to the small sample size. Future studies that enroll more patients from other populations (due to genetic differences) might yield different results⁹. Nikawa *et al.*, in their study on 442 patients, showed that denture stomatitis had a direct correlation with blood type. Patients with blood type O had more susceptibility to this condition¹⁶. Mosharaf and Jamshidi reported similar results. In their study, blood type O was reported to be a risk factor for

denture stomatitis¹⁹. Khozeimeh *et al.*, in a study on 300 patients, demonstrated that patients with blood type O had a higher mean number of *Candida albicans* colonies compared to the other groups; however, this was not a statistically significant difference²⁰.

In a study by Pai *et al.* on 750 patients, a significant association existed between periodontitis and blood type. Subjects with blood types A and B had increased susceptibility to periodontitis. There were more subjects that had blood types O and AB in the control group¹⁵. Koregol *et al.* showed that periodontitis was more common in patients with blood type O while patients with blood type A had a higher prevalence of gingivitis¹⁴. In a study by Ghalyani Esfahani *et al.* on 1521 patients, it was found that gingivitis and periodontitis had a direct correlation with blood type. They believed that blood type antigens could serve as receptors for microbial pathogens responsible for gingivitis and periodontitis²¹.

These carbohydrates are related to differentiation of epithelial cells in non-keratinized oral mucosa because the H antigen, the precursor of the ABO blood group antigens, is expressed on the surface of basal cells while A and B antigens are expressed on the surface of squamous cells^{10,22}. In contrast to the current study, Kumar *et al.* have studied the association of oral lichen planus with blood type. They screened 32877 patients and reported that this condition was more common in subjects with blood type A. However, subjects with blood type O had less susceptibility to this condition. Therefore, oral cancer was less frequently seen in this group. These researchers concluded that determination of blood type as an adjunct diagnostic tool could be suggested for oral lichen planus⁹. However, in another study in Shiraz, the researchers observed no association between blood types and oral lichen planus²³.

Jaleel and Nagarajappa reported that oral cancer was more common (1.46 times) in subjects with blood type A²⁴. Gao *et al.*, in their study on oral cancer, have concluded that 67% of subjects with oral cancer did not express A and B antigens¹⁰. Antibodies play a role in cytotoxicity and immunity against tumor cells via activation of the complement system and antibody-dependent cell-mediated cytotoxicity, as well as enhancement of the role of natural killer cells and macrophages in pathogenesis. The O and A blood types confer greater immunity against tumor disorders and provide higher levels of IgA immunoglobulin compared to other blood groups¹¹.

Mucosal IgA on the body surface acts as the first barrier against microbial pathogens. On the other hand, high levels of immunoglobulins can result in destructive immune reactions such as types II and III hypersensitivity via the function of IgM and IgG antibodies or formation of antigen-antibody complexes. These complexes can occur with a high probability in subjects that have blood types A and O compared to other types¹¹. The role of cell-mediated immunity and types I, III and IV hypersensitivity reactions in the etiopathogenesis of RAS, increased concentration of immunoglobulins in serum of patients with this condition⁸, and the effect of blood type antigens on cell-mediated and humoral immunity^{11,12,22} indicate that the proposed correlation of blood type with RAS should be elucidated in future, larger studies.

Considering the limitations of this study, further studies with larger sample sizes are required on other populations.

We have found no association between blood types and RAS in the current study.

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