

The Connection Between Recurrent Aphthous Stomatitis (RAS) and Psychological Stress in Patients at RSGM Nala Husada

Nur Tsurayya Priambodo*, Kharinna Widowati*, Aulia Dwi Maharani**, Kurnia Hayati*

*Departement of Oral Medicine, Faculty of Dentistry, Universitas Hang Tuah Surabaya, Indonesia

**Department of Dental Public health, Faculty of Dentistry, Universitas Hang Tuah Surabaya, Indonesia

Online submission : 14 November 2023

Accept Submission : 10 Desember 2023

ABSTRACT

Background: The most common oral soft tissue disease at RSGM Nala Husada is recurrent aphthous stomatitis. RAS is a condition marked by inflammation of the orakl mucosa, which manifests as one or more ulcers that recur over time. RAS can be influenced by various predisposing factors, with stress being a common trigger. Stress refers to the body's reaction to challenges or pressures that lead to uncomfortable feelings, which are perceived differently by each person. **Objective:** To determine the relationship between stress in patients with recurrent aphthous stomatitis at RSGM Nala Husada. **Materials and Methods:** The population and samples of all RAS patients who visited RSGM Nala Husada were taken by purposive sampling with a total of 100 people. The level of stress experienced by a person measured from the Depression Anxiety Stress Scale (DASS) questionnaire which consists of 42 questions. Data on RAS were taken from subjective examination and intra-oral examination. Processing of data using correlation test with Spearman test in SPSS program. **Results:** The results of the Spearman test are a weak correlation, which can be seen from $R= 0.115$ ($Sig = 0.175.> 0.05$). A positive R value means that the relationship is in the same direction. **Conclusion:** In this study there was no significant relationship between psychological stress in RAS patients at RSGM Nala Husada. Therefore, it is necessary to review further the severity, duration and intensity of stress that can trigger the emergence of RAS and reconsider other predisposing factors related to RAS besides stress.

Keywords: Depression Anxiety Stress Scale (DASS), Psychological Stress, Recurrent Aphthous Stomatitis (RAS)

Correspondence: Nur Tsurayya Priambodo, Department of Oral Medicine, Faculty of Dentistry, Universitas Hang Tuah Surabaya, Arif Rahman Hakim No. 150, Surabaya, East Java, Indonesia. Phone +6281331121988. E-mail: nur.tsurayya@hangtuah.ac.id

INTRODUCTION

One of the most common oral tissue disorders is Recurrent Aphthous Stomatitis (RAS). RAS is a recurring inflammation of the oral mucosa characterized by the presence of white ulcers. Recurrent aphthous stomatitis (RAS) is classified into three types based on factors such as the number, size, duration, and scarring of the lesions: Minor RAS, Major RAS, and Herpetiform RAS. Minor RAS is the most common type, affecting about 85% of individuals. It usually appears on non-keratinized oral mucosa, including the lips, cheeks, floor of the mouth, and the lower or side surfaces of the tongue. The ulcers in Minor RAS are typically small, with a diameter under 1 cm, often around 4-5 mm, and may number between 1 and 5. Their shape varies with location. Although the ulcers can recur over time, Minor RAS generally heals within 1-2 weeks without causing any scarring.

Major RAS, which occurs less often, accounts for about 10-15% of RAS cases. Although it shares some similarities with Minor RAS, Major RAS ulcers are larger (more than 1 cm in diameter), deeper, and frequently cause scarring. These ulcers can last for several weeks to months and are usually found on the lips, tongue, soft palate, and hard palate, often accompanied by significant pain.¹⁻³

RAS herpetiformis only occurs in 5-10% of all RAS cases. Ulcers in RAS Herpetiformis are small (1-2 mm) and appear in multiples (10-100) simultaneously. They are typically found on the lateral edges and underside of the tongue, as well as the floor of the mouth. These ulcers are small but cause pain and difficulty in eating and speaking. A single attack of ulcers in RAS Herpetiformis usually lasts about 1-2 weeks, with remission periods between attacks varying. Sometimes these ulcers may coalesce to form larger ulcerated areas, often with erythema^{3,4}.

RAS is a relatively mild disease, not life-threatening and non-infectious, but RAS can cause pain and discomfort that interferes with

masticatory, swallowing, and speech functions. RAS can attack non-keratinizing oral mucosa, namely buccal, labial, lateral and ventral mucosa of the tongue, floor of the mouth, soft palate and oropharyngeal mucosa with a characteristic clinical picture in the form of necrotic ulcers with clear boundaries and surrounded by an erythematous halo⁵⁻⁸.

The precise cause of recurrent aphthous stomatitis (RAS) remains unclear, but stress is recognized as a contributing factor. A study conducted by Wowor et al. in 2019 identified a significant link between stress and RAS among students in the Dentist Education Study Program at Sam Ratulangi University. This result is consistent with the findings of Kusumastuti in 2023, who observed that stress affects the incidence of RAS in dental professional students at IIK Bhakta. These studies suggest that psychological conditions, such as stress, can contribute to the onset of RAS^{9,10}.

Diagnosing RAS relies on evaluating the patient's history and the clinical features of the ulcer. Special attention should be given to the patient's history, especially concerning potential predisposing factors. Stress is a key factor closely associated with the condition¹¹. When an individual experiences stress, it activates the central nervous system (CNS) through the HPA axis (Hypothalamic Pituitary Adrenal). This activation prompts the hypothalamus to release CRH (Corticotropin Releasing Hormone), which in turn triggers the pituitary gland to produce ACTH (Adrenocorticotropic Hormone). ACTH prompts the production of cortisol and catecholamines. As cortisol levels increase in the bloodstream, the immune system's response becomes less effective. During stress, the rise in cortisol, which binds to receptors on all leukocytes, including lymphocytes, regulates the immune system. High cortisol levels suppress immune function by inhibiting both the phagocytic system and overall immune response. Stress-induced damage to the oral mucosa often results in both acute and chronic inflammation¹².

MATERIALS AND METHODS

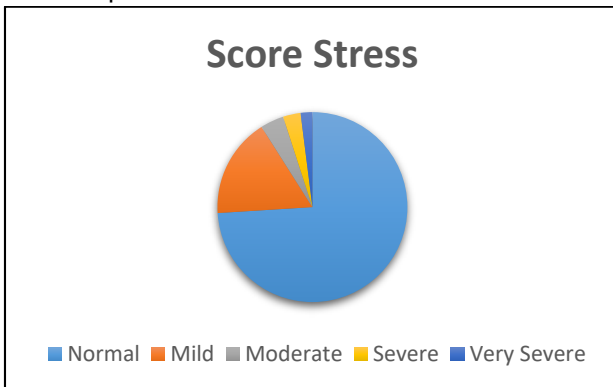
This research is an analytical observational study employing a cross-sectional design and was carried out at the Department of Oral Medicine, RSGM Nala Husada. The research population was all patients in the Oral Medicine Departement of RSGM Nala Husada in 2020. The study included a sample size of 100 participants selected through purposive sampling. Stress levels were assessed using the Depression, Anxiety, Stress Scale-42 (DASS-42), a validated and reliable questionnaire with 42 items aimed at measuring negative emotional states related to depression, anxiety, and stress.¹³. RAS data is taken from the results of subjective and objective examinations by Oral Medicine Specialist. The collected data were analyzed using the SPSS software and processed with the Spearman correlation test, due to the presence of nominal data scales. Analysis is used to obtain a description of each variable and is presented in table form. Data is said to be significant if $p < 0,05$.

RESULT

Table 1. Frequency distribution based on gender

Sex	Frequency	(%)
Male	26	26.0
Female	74	74.0
Total	100	100.0

Table 2. Score stress in the relationship between recurrent aphthous stomatitis and psychological stress in patients at RSGM Nala Husada research



The measurement of stress level is done by giving a Depression Questionnaire, Anxiety Stress Scale-42 (DASS-42). DASS-42 is a psychological measurement tool that is widely used as an initial screening of stress. The DASS questionnaire contains 42 questions. The results of the DASS-42 questionnaire were grouped into 5 groups according to the scores, namely normal 0-14, mild 15-18, moderate 19-25, severe 26-33, very severe >34. Respondents found that the normal condition was 0 and there was severe stress with a score of 34. The results of the stress score can be seen in table 2.

Table 3. The relationship between stress and the incidence of RAS in the study of the relationship between recurrent aphthous stomatitis and psychological stress in patients at RSGM Nala Husada

		RAS	Score Stress
RAS	Correlation Coefficient	1.000	.115
	Sig. (2-tailed)	.	.175
	N	100	100
Score Stress	Correlation Coefficient	.115	1.000
	Sig. (2-tailed)	.175	.
	N	100	100

Based on the results of the analysis test, the Spearman test there is no significant relationship, it can be seen from $R = 0.115$ ($Sig = 0.175 > 0.05$). A positive R value means the relationship is in the same direction. can be seen from table 3, it was found that the correlation $0.115 =$ very weak correlation almost non-existent ($Sig = 0.175 > 0.05$). This indicates that there is no significant association between thrush and stress in this study.

DISCUSSION

Recurrent aphthous stomatitis (RAS) or recurrent aphthous stomatitis (RAS) is an inflammation of the oral mucosa with a clinical picture in the form of single or multiple ulcers that appear repeatedly. Ulcers can appear in various sizes and numbers, so that they can be



classified into 3 types, specifically minor, major and herpetiform. RAS Minor with shallow, oval, diameter < 1 cm, visible white center, surrounded by an erythematous margin. Mayor RAS is characterized by the presence of round or oval-shaped ulcers with clear boundaries, 1 cm in diameter and accompanied by pain. Herpetiformis RAS is a rare type of focal ulceration of the oral mucosa. The striking feature of this type of RAS is the presence of multiple ulcers, 20 to 200 ulcers, 1-3mm in diameter, round shape, the mucosa around the erythematous ulcer and is expected to be painful¹. RAS can occur at any age and based on the 2018 report on result of national basic health research, the highest prevalence of RAS is at the age of 19-24 years, which is 9.6% and the lowest is at the age of 3-4 years. The data obtained was that the age range of respondents who experienced RAS was 18-59 years old^{6,14,15}.

Several studies have shown that RAS is more common in women than men, one of which is Abdullah's study which showed a higher prevalence of RAS in women than men, with a percentage of 55.4% in women and 44.6% in men. According to the literature, RAS was more common in women, 74 respondents, while 26 respondents were male¹⁵.

The diagnosis of RAS can be made with accurate subjective examination and accurate objective examination. Subjective examination is closely related to the history of RAS. RAS appears recurrently and can change locations in the oral cavity. Subjective examination begins with taking a history, where in the early stages, patients usually report a burning sensation on the oral mucosa about 2 to 48 hours before the ulcer appears. At this stage, the area may already look reddish (erythema). Once the ulcer appears, patients complain of pain at the ulcer site, which can be more intense in large ulcers. In addition to significant pain, patients may also experience discomfort when speaking and eating^{1,2,4,14}. The data analysis of this study obtained non-significant results. The non-significant results in this study were influenced

by many factors, one of which was due to the background of patients who were not willing to explain in detail about the appearance of their ulcers. In fact, to get the right diagnosis of RAS, it needs to be confirmed by an accurate subjective examination.

To this day, the etiology of RAS is idiopathic or the cause is still unknown. However, there are several predisposing factors that play a significant role in the development of this condition, including genetic predispositions, immune system responses, hormonal imbalances, stress, systemic diseases, local mechanical trauma, viral and bacterial infections, nutritional intake, smoking habits, and allergic reactions. This research specifically examines psychological stress as a triggering factor. During stressful situations, cortisol levels in the blood rise, which can lead to an increase in the number of leukocytes and inflammation, ultimately triggering RAS. Physiologically, stress triggers stimulation of two main systems, namely the sympathetic nervous system and the hypothalamic pituitary adrenal (HPA) axis. Activation of the HPA axis causes the secretion of cortisol, a stress hormone that regulates metabolism and vascular reactivity. Elevated cortisol levels can lead to increased inflammatory activity, which in turn can trigger RASs with higher relapse rates¹⁷. Stress can cause the body to react via the Hypothalamus-pituitary-adrenal cortex (HPA) axis which is activated by a series of stress reactions that lead to the release of Corticotropin-releasing hormone (CRH) from the hypothalamus and glucocorticoids, including cortisol from the adrenal cortex. Increased cortisol levels are able to regulate components of the body's defense and inflammatory response. Increased salivary cortisol flow, decreased salivary levels, and changes in salivary pH can lead to an imbalance between the host and increased reactive microbial species making them more susceptible to infection in the dental and oral areas¹⁸.

Under stressful conditions, the adrenal cortex secretes cortisol, leading to a reduction in

the synthesis of IFN- γ and an increase in the formation of IL-10 and IL-4 (type 2 cytokines). This shift results in a greater type 2 cytokine response. Recent studies suggest that this imbalance in type 1/type 2 cytokine levels plays a crucial role in connecting the effects of stress to the immune system. Various immune responses occur in this context, including a decrease in the number of CD4 lymphocytes, an alteration in the CD4 ratio, reduced regulatory activity of CD4 CD25 Tregs, an increase in B lymphocytes, a rise in T cells, a decrease in HSP expression, an enhanced immune complement system, a higher number of NK cells, reactivation and hyperreactivity of neutrophils, decreased expression of anti-inflammatory cytokines produced by Th2 and TGF, and increased expression of pro-inflammatory cytokines such as those produced by Th1, including IL-2, IL-12, IFN- γ , and TNF α .

In the humoral response, salivary IgA levels in patients with RAS rise during the acute phase and then decrease during the regression and recovery phases. Alongside IgA, levels of IgG and IgM also increase. IgG and complement function together as opsonins to assist each other. IgG possesses effective opsonin properties because phagocytic cells, such as monocytes and macrophages, have receptors for the Fc region of IgG. This interaction enhances the binding between phagocytes and target cells. Consequently, these changes can result in pathological conditions in the oral mucosal epithelial cells, making them more responsive to stimuli⁸.

The level of stress can be assessed using the Depression Anxiety and Stress Scale (DASS). This scale includes 42 questions that are intended to evaluate the negative emotional states associated with depression, anxiety, and stress. The stress scale in depression anxiety stress scale consists of 42 questions and is very sensitive to the level of non-specific chronic causes. The stress scale was used to measure the level of relaxation, the appearance of nervous breakdowns, the level of anger,

overreaction, and the level of patience. The results of respondents answers based on experience for a week will be evaluated with a stress severity index, and calculated based on a score system. DASS-42 questionnaire were grouped into 5 groups according to the scores, namely normal 0-14, mild 15-18, moderate 19-25, severe 26-33, very severe >34. Respondents found that the normal condition was 0 and there was severe stress with a score of 34^{2,14,19}. In this study, there was no relationship between RAS and psychological stress, this was due to the severity of stress and the duration of stress experienced by patients was low or mild.

The non-significant results in this study were also influenced by the many overlapping predisposing factors of RAS, especially in this study genetic, hormonal, allergic and trauma. Genetic factors have an influence on the emergence of RAS almost more than 40%. Patients with genetic RAS from parents can be inherited up to 90%. Genetic factors are related to human leukocyte antigen (HLA). HLA detection can reflect genetic conditions because each individual has different HLA. Several HLA antigens such as HLA-A33, HLA-B35, and HLA-B81 have been associated with an increased incidence of RAS^{10,16,20,21}. The hormonal conditions experienced in patients in this study also indirectly affect the predisposing factors of stress. This is another possible cause of insignificant research results. Hormonal factors often occur in women are menstruation, pregnancy, contraceptive use, breastfeeding and menopause. During menstruation, a decrease in progesterone hormone levels will inhibit the maturation of epithelial cells which will facilitate bacterial invasion so that RAS can occur¹⁶.

Allergic factors are often associated with a higher prevalence of RAS in patients. Immune molecules like immunoglobulins and eosinophil cationic protein (ECP) are key indicators of the body's allergic response. Potential allergens such as certain food ingredients (including milk,

food additives, carbonated drinks, and nuts), toothpaste components, and dental care products may also trigger allergic reactions^{8,20}. Trauma is another significant predisposing factor for RAS. It can lead to edema, cause inflammation of cells, and increase the viscosity of the submucosal extracellular matrix, thereby making RAS more likely to occur. Trauma can be caused by mechanical, chemical, thermal, iatrogenic trauma, such as biting, brushing teeth too hard, consuming hot food, e-cigarettes, sharp dentures, rough dental fillings, sharp tooth root residues, and others²⁰. Therefore, the existence of several predisposing factors is also the reason for this study, why the relationship between stress and RAS patients is not significant.

CONCLUSION

The study's results indicate that there is no significant connection between stress and recurrent aphthous stomatitis in patients at RSGM Nala Husada. Further research is necessary with various other triggering factors, a sharper and more accurate subjective examination, a more diverse population, a longer research time so that the results can be used in general to improve the degree of oral health, especially those related to the field of oral disease.

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