

Recurrent Aphthous Stomatitis and Allergy: is it Related?

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Abstract

Recurrent aphthous stomatitis is one of the most common ulcerative disorders associated with oral mucosa. The etiology of recurrent aphthous stomatitis remains unclear and is considered idiopathic. Several plausible triggers have been studied as predisposing to recurrent aphthous stomatitis, where one of the predisposing factors is allergy.

This study aimed to determine the relationship between recurrent aphthous stomatitis and allergy through a history of allergy and IgE levels. The study involved 50 recurrent aphthous stomatitis patients. The inclusion criteria included patients with minor type recurrent aphthous stomatitis, who do not have a systemic disease or take any drug, do not use orthodontic appliances, and are voluntarily willing to be the study subject. Recurrent aphthous stomatitis is diagnosed with anamnesis to determine the recurrence of recurrent aphthous stomatitis and history of allergy and clinical examination to examine the ulcer of recurrent aphthous stomatitis. After that, patients had blood samples taken for IgE levels. The data obtained were then analyzed for the relationship between allergy history and IgE with chi-square. Patients with a history of allergy mainly had a high value of IgE with 12 (85,7%). There was a significant relationship between the history of allergy and IgE levels of recurrent aphthous stomatitis patients with a p-value of 0.013 ($p < 0.05$).

It can be concluded that it is crucial to examine the history of allergy and perform laboratory examinations to search for predisposing factors in recurrent aphthous stomatitis patients.

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Introduction

Recurrent aphthous stomatitis (RAS) is one of the most common ulcerative disorders associated with oral mucosa.¹ RAS affects 10-20% of the population and can be observed at any age.² RAS affects up to 25% of adults and 40% of children.³ It is characterized by extremely painful, recurring, solitary, or multiple ulcers in the upper throat and oral cavity ulcers.¹

The etiology of recurrent aphthous stomatitis remains unclear and is considered idiopathic. Several plausible triggers have been

studied that influence its precipitation. There are several local factors and underlying systemic diseases and conditions that predispose to recurrent aphthous stomatitis, including genetic factors, food allergens, local trauma, endocrine alterations (menstrual cycle), stress and anxiety, smoking cessation, certain chemical products, and microbial agents.⁴⁻⁶

Allergy is an altered or changed immune system response to foreign proteins.⁷ Allergy diagnosis was based on a history of allergy, clinical examination, and laboratory examination. Several biomarkers have been reported for allergy, including immunoglobulin E (IgE), blood or sputum eosinophilia, fractional exhaled nitric oxide [FeNO], serum interleukin (IL)- 5 and IL- 13 or are under current investigation (e.g., pro-inflammatory mediators, genes, microRNAs (miRNAs), markers of epithelial barrier integrity, microbiomes). Individuals with a clinical history of this disease have a positive mark on immunoglobulin E.^{8,9}

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This study aimed to determine the relationship between recurrent aphthous stomatitis and allergy. The allergy was examined through a history of allergy and IgE levels.

Materials and methods

Research Design and Sample

This is an analytical study with a cross-sectional approach conducted at the Oral Medicine Installation at the Universitas Sumatera Utara Dental Hospital and Prodia Clinical Laboratory Medan. Diagnosis of recurrent aphthous stomatitis was carried out at the Oral Medicine Installation at the Universitas Sumatera Utara Dental Hospital. IgE examination was carried out at the Prodia Clinical Laboratory.

The study involved 50 recurrent aphthous stomatitis patients. The sampling method in this study was non-probability sampling with the purposive sampling method. All subjects who met the inclusion and exclusion criteria were included. Inclusion criteria include patients with minor type recurrent aphthous stomatitis, who do not have a systemic disease or take any drug, do not use orthodontic appliances, and are voluntarily willing to be the study subject.

Recurrent aphthous stomatitis is diagnosed with anamnesis and clinical examination. Anamnesis was done to determine the recurrence of recurrent aphthous stomatitis and a history of allergy. Clinical examination was done to examine the ulcer of recurrent aphthous stomatitis. After that, all patients had blood samples taken for IgE levels. Professional analysts in the laboratory then analyze the blood.

Data Analysis

The data obtained were then analyzed using SPSS 20.0 version. The relationship between the history of allergy and IgE was analyzed with chi-square. $p < 0.05$ was considered as the significance level.

Ethical Clearance

This study followed national and international ethics guidance and was approved by the Research Ethics Committee of Universitas Sumatera Utara No. 730/KEP/US/2021. All patients were also given informed consent.

Results

Fifty recurrent aphthous stomatitis patients were included in this research. The

results of this study showed that patients were mainly in late adolescence (17-25 years), with 37 (74%) patients, and subjects in the early adolescence (12-16 years) category were 5 (10%) patients. Meanwhile, 4 (8%) patients were in early adulthood (26-35 years) and late adulthood (36-45 years) categories (Figure 1).

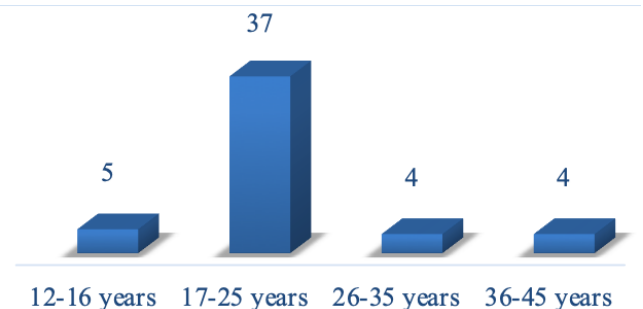


Figure 1. Distribution of patients' age.

The patients in this study were primarily female, with 35 (70%) patients. Meanwhile, only 15 (30%) patients were male. The distribution of patients based on gender can be seen in Figure 2.

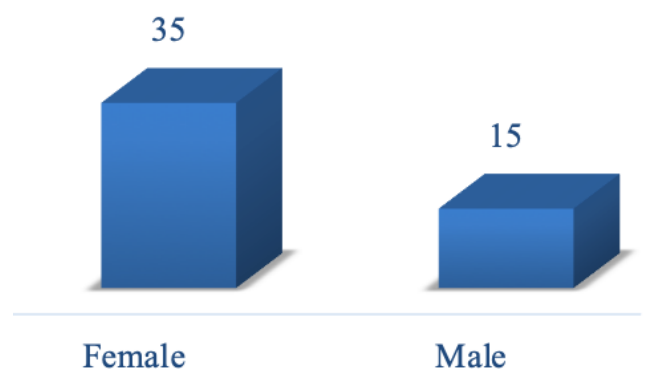


Figure 2. Distribution of patients' gender.

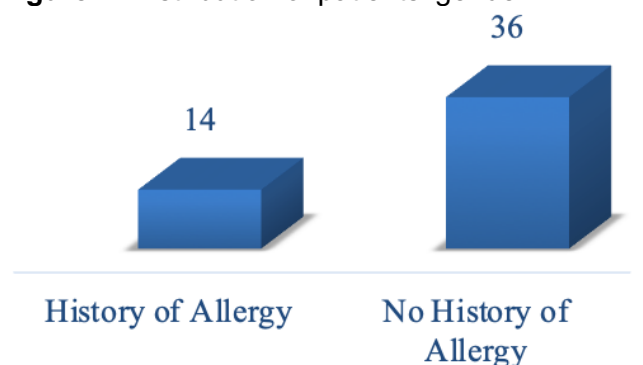


Figure 3. Distribution of the history of allergy in recurrent aphthous stomatitis patients.

Figure 3 shows the distribution of the history of allergy in recurrent aphthous stomatitis

patients. The results showed that 14 (28%) patients have a history of allergy. Meanwhile, 36 (72%) patients have no history of allergy.

Table 1 shows the relationship between the history of allergy and IgE in recurrent aphthous stomatitis patients. Patients with a history of allergy mainly had a high value of IgE with 12 (85,7%). There was a significant relationship between the history of allergy and IgE levels of recurrent aphthous stomatitis patients with a p-value of 0.013 ($p < 0.05$).

History of Allergy	IgE		Total	p-value
	Normal	High		
Allergy	2	12	14	p=0.013
No Allergy	19	17	36	

Table 1. The relationship between the history of allergy and IgE in recurrent aphthous stomatitis patients.

Discussion

The first episodes of recurrent aphthous stomatitis most frequently begin during the The second decade of life.¹⁰ This study showed that 37 (74%) patients with RAS are mainly in late adolescence (17-25 years). This result was in accordance with the study by Jabbar et al. in 2018, which showed that 71.3% of recurrent aphthous stomatitis patients were in the second decade of life.¹¹ The onset of ulcers usually occurs during childhood. The disorder is most prevalent among individuals in their 20s, with a tendency to diminish in frequency and severity with age.¹²

Several studies have reported a higher incidence of recurrent aphthous stomatitis among females, non-smokers, white races, and people with high socioeconomic status.¹² The present study showed that the most commonly affected recurrent aphthous stomatitis patients were female, with 70% of patients. This study's results align with the study conducted by Queiroz in 2018 showed that, out of 68 recurrent aphthous stomatitis cases, 40 (59.2%) were female and 28 (40.8%) were male.¹³ This study is also similar to the study by Bandagi, which showed that in 50 patients reporting to the Department of Oral Medicine with RAS, 70% were female, and 30% were male.¹⁴ The change in hormonal balance could cause a high incidence of recurrent aphthous stomatitis among females. During

menstruation and pregnancy, the hormonal changes in females can play an important role in recurrent aphthous stomatitis development. The decrease in estrogen levels results in decreased blood supply to the peripheral organs and disruption of the cell types in the oral cavity, slowing the keratinization process so that oral tissues become more susceptible to local irritation and can easily develop recurrent aphthous stomatitis. Women also are more sensitive to emotional situations and stress, which can involve the immune system. This high prevalence in women also can be explained by the fact that women seek more medical attention.¹⁵⁻¹⁷

The etiology of recurrent aphthous stomatitis is poorly understood, but several risk factors may cause it. Physical examination should be used to screen for trauma secondary to dental appliances, widespread vesiculobullous eruptions, and signs of hormone imbalance. The presence of fever should prompt a workup for infection, and if the fever is recurrent, fever syndromes. Blood work should be used to rule out hematologic or nutritional deficiencies and antibodies related to autoimmunity.¹⁸ Allergy has always been considered a possible cause of recurrent aphthous stomatitis.^{3,19} The mouth is subjected to various antigenic agents in food components such as beef, cow's milk, chocolate, coffee, beans, cereals, almonds, strawberries, cheese, tomatoes, wheat flour (containing gluten), and food additives. Allergic and irritant reactions to such agents can manifest in various ways and lead to recurrent aphthous stomatitis.²⁰⁻²²

The role of allergy in causing recurrent aphthous stomatitis is unknown, and the pathogenesis is unclear. However, it is known that allergy plays a vital role in recurrent aphthous stomatitis.²³ The presence of allergens could initiate the cytokine cascade leading to the formation of aphthae.¹² Hypersensitivity to certain food substances, oral microbes, and microbial heat-shock proteins has been suggested as a causative factor in recurrent aphthous stomatitis. Recent literature suggests that 15-50% of patients with recurrent aphthous stomatitis have a positive patch test, but only 20% are clinically relevant.^{24,25}

This study evaluated the role of allergy as the cause of recurrent aphthous stomatitis with a detailed anamnesis followed by relevant IgE laboratory tests. Diagnosis of oral allergy

requires a history of previous exposure to the allergen, clinical features and symptoms, and a record of disease progression after removal of the allergen. Several examinations can also help diagnose allergies, such as measuring serum IgE.^{9,20,22} This study showed that only 14 (28%) recurrent aphthous stomatitis patients have a history of allergy. This finding was in accordance with studies of Shirzaiy that showed that out of the 326 recurrent aphthous stomatitis subjects, only 32 subjects (9.8%) had an allergy history.¹⁵ Similarly, in a study by Kamat, the authors reported that only 44,6% (78 Populations) with recurrent aphthous stomatitis have a history of allergy out of 442 populations with recurrent aphthous stomatitis. This might happen because patients usually do not recognize what causes their recurrent aphthous stomatitis.²⁶

It is known that IgE will increase when an allergy occurs so IgE can be used as a potential allergy biomarker.^{2,5} Given the possible relationship between allergy and recurrent aphthous stomatitis, evaluation of allergy-related biomarkers, including IgE, can be helpful in patients with aphthous stomatitis.²³ IgE was classically considered important in allergy. When allergy occurred, IgE was produced.^{24,27} In this study, 14 patients with a history of allergy have high levels of IgE serum. There was a significant relationship between the history of allergy and IgE levels of recurrent aphthous stomatitis in this study, with a p-value of 0.013 ($p < 0.05$). These results were similar to the study by Almoznino in 2014, which also showed the positive association of increased IgE levels with recurrent aphthous stomatitis.²⁴ The study by Farhad-Mollashahi in 2020 showed that salivary levels of IgE in patients with recurrent aphthous stomatitis showed that patients with oral aphthous had higher salivary levels of IgE and there was a significant difference in the salivary IgE between recurrent aphthous stomatitis group and control group. IgE is one of five isotypes of human immunoglobulins, IgG, IgA, IgM, IgD, and IgE. Alterations in IgD and IgE serum levels have been reported in recurrent aphthous stomatitis patients.^{23,24,28} IgG and complement work together to help each other as an opsonin in antigen destruction. IgG has effective opsonin properties because phagocyte, monocyte, and macrophage cells have receptors for the Fc fraction of IgG to strengthen the relationship between phagocytes and target cells. IgG

molecules bind to their cognate antigens via their two fragment antigen-binding (Fab) sites and are, in turn, recognized by specific receptors on the membrane of leukocytes. These receptors bind the Fc (fragment crystallizable) domain of IgG; thus, they are named Fcγ receptors (FcγR). IgG antibodies are the bridge between the two arms of the immune system, bringing together the specificity of recognition of the adaptive immune system and the destructive potential of the innate immune system cells. Crosslinking these receptors on the surface of leukocytes leads to the activation of several effector cell functions. Depending on the cell type and the Fcγ receptor type, these functions include phagocytosis, cell degranulation, production of various cytokines and chemokines, antibody-dependent cell-mediated cytotoxicity (ADCC), and activation of genes. These effector functions are geared toward destroying pathogens and the induction of an inflammatory state that can cause tissue damage. These changes can lead to pathological conditions in the oral mucosal epithelial cells so that epithelial cells are more sensitive to stimulation.^{29,30}

Conclusions

In conclusion, allergy was well known as a predisposing factor for recurrent aphthous stomatitis. This study showed a significant relationship between the history of allergy and IgE levels as the biomarker of allergy in recurrent aphthous patients. Therefore, dentists should always examine the possibility of allergy in recurrent aphthous stomatitis patients. Future research recommends comparing the history of allergy and IgE levels in patients with and without recurrent aphthous stomatitis.

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Declaration of Interest

The authors report no conflict of interest.

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