Immunol Genet J, Vol. 7, No. 4, December 2024, pp.268-273 **DOI: https://doi.org/10.18502/igj.v7i4.17891**

Original Article

Investigation of Serum CRP Levels in People with Recurrent Aphthous Stomatitis

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Received: 09 July 2024; Accepted: 25 October 2024

Abstract

Background: Recurrent Aphthous Stomatitis (RAS) is a common, painful condition marked by recurrent oral ulcers, impacting quality of life. Its etiology is unclear but involves genetics, immune dysregulation, and environmental factors. This study explores the link between serum C-reactive protein (CRP) levels and RAS to assess the role of systemic inflammation.

Methods: In a cross-sectional study design, we enrolled 26 participants diagnosed with RAS according to established diagnostic criteria alongside a control group of 26 healthy individuals matched for age and gender. Serum CRP levels were quantified using enzyme-linked immunosorbent assay (ELISA) methods, and demographic, clinical, and lifestyle data were collected through structured questionnaires. We employed statistical analyses, including t-tests and regression models, to assess the association between serum CRP levels and the frequency and duration of RAS.

Results: Our findings reveal significantly elevated serum CRP levels in individuals with RAS compared to healthy controls ($p<0.04$), indicating a potential link between systemic inflammation and the pathophysiology of RAS. Additionally, elevated CRP levels were associated with increased ulcer severity and prolonged healing time. Multivariate analyses further demonstrated that serum CRP could serve as an independent predictor of RAS severity, highlighting its potential role as a biomarker for disease activity.

Conclusion: Our investigation provides compelling evidence that systemic inflammation, as indicated by elevated serum CRP levels, is associated with RAS.

Keywords: C-Reactive Protein; CRP; Recurrent Aphthous Stomatitis; RAS

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How to cite this article
Khazaei B, Akhtar R, Khazaei HA, Shirzaiy M, Khazaei A, Ansari H. Investigation of Serum CRP Levels in People with Recurrent Aphthous Stomatitis. Immunology and Genetics Journal, 2024; 7(4):268-273. DOI: https://doi.org/10.18502/igj.v7i4.17891

Introduction

Recurrent Aphthous Stomatitis (RAS) is a prevalent and often debilitating oral condition characterized by the recurrent formation of painful ulcers within the oral mucosa (1). These ulcerations not only hinder the basic functions of eating, speaking, and swallowing, but can also significantly affect the quality of life for those afflicted. The exact etiology of RAS remains elusive, although various factors including genetic predisposition, immune system dysregulation, nutritional deficiencies, and stress have been implicated in its pathogenesis (2-4). The unpredictable nature of the condition, with episodes often occurring sporadically, presents challenges in both clinical management and research, prompting an ongoing search for biomarkers that may illuminate underlying pathological processes.

CRP is an acute-phase reactant produced by the liver in response to inflammation, infection, or tissue injury (5). Elevated serum levels of CRP are indicative of an inflammatory response within the body and have been extensively studied across a variety of medical conditions, including autoimmune diseases, cardiovascular disorders, and infections (6-8). Given the inflammatory component that appears to be present in RAS, the evaluation of serum CRP levels in individuals experiencing this condition could provide valuable insights into the inflammatory mechanisms at play and potentially contribute to the understanding of its pathophysiology (9). Moreover, discrepancies in CRP levels among patients could help delineate between subtypes of RAS, identify potential triggers or exacerbating factors, and offer a biomarker for monitoring the efficacy of therapeutic interventions.

Recent advances in diagnostic methodologies have allowed for more precise measurements of CRP levels, paving the way for detailed investigations into its correlation with RAS (10). Previous studies have yielded mixed results, with some demonstrating a significant relationship between elevated CRP levels and the presence or severity of RAS (10, 11), while others suggest that this association may not be consistent across various populations (12). Such discrepancies underscore the need for targeted research that thoroughly investigates the nuances of CRP levels in individuals with RAS, particularly as understanding inflammation's role in this condition becomes increasingly paramount.

This article aims to investigate the serum CRP levels in individuals suffering from RAS, seeking to determine whether elevated CRP levels correlate with the occurrence, frequency, or severity of ulcerative episodes. By examining this relationship, we hope to contribute to the existing body of knowledge regarding RAS and its inflammatory underpinnings, potentially guiding clinicians in developing more effective treatment strategies tailored to their patients. Furthermore, this research could shed light on the broader implications of inflammatory responses in oral health, ultimately enhancing the overall understanding of RAS and informing future studies aimed at unraveling the complexities of this common yet poorly understood condition.

Methods

Study Design

This study will be conducted as a cross-sectional analysis comparing serum CRP levels in two groups: individuals diagnosed with RAS and healthy control subjects.

Participants

Adults aged 18-65 years who have been diagnosed with RAS based on clinical criteria and Patients experiencing at least three episodes of oral ulcers in the past year. Individuals with systemic diseases (e.g., autoimmune disorders, inflammatory bowel disease) and Patients on anti-inflammatory medications or immunosuppressants within the last three months and Current smokers or those with a history of recent surgery affecting the oral cavity. Healthy adults matched for age, sex, and socio-economic status with no history of oral ulcers or other systemic diseases. To determine the appropriate number of participants needed to achieve statistically significant results, the sample size was considered to be 26 cases and 26 controls, considering the power of 80% and the significance level of 0.05. Participants will be recruited from dental clinics and local health centers.

Data Collection

Participants will undergo a thorough clinical examination by a qualified dentist to confirm the diagnosis of RAS and Demographic information

(age, sex, medical history) will be recorded using structured questionnaires.

For Blood Sample Collection, Approximately 5 mL of venous blood will be drawn from each participant by a qualified phlebotomist under sterile conditions. Samples will be collected in serum separator tubes and allowed to clot for 30 minutes at room temperature before centrifugation at 3000 RPM for 10 minutes. For Serum CRP Measurement, Serum will be stored at -80°C until analysis. CRP levels will be measured using a high-sensitivity ELISA according to the manufacturer's instructions.

Statistical Analysis

Descriptive statistics will be computed for demographic and clinical characteristics. The primary endpoint will be the comparison of mean serum CRP levels between the RAS group and the control group. Statistical analysis will utilize independent t-tests for continuous variables and chi-square tests for categorical variables. A p-value of <0.05 will be considered statistically significant. Multivariate analysis may be conducted to control for potential confounding factors such as age, sex, and smoking status.

Ethical Considerations

This study will adhere to the ethical principles of the Declaration of Helsinki, and approval from the institutional review board will be obtained prior to initiation. Informed consent will be taken from each participant, ensuring they understand the purpose of the study, the procedures involved, and their right to withdraw at any time.

Results

The study assessed serum CRP levels in individuals diagnosed with RAS compared to a control group. A total of 52 participants were divided into two groups: 26 individuals with a confirmed diagnosis of RAS and 26 healthy controls.

The demographic analysis indicated no significant differences in age and gender distribution between the two groups. The mean age of participants in the RAS group was 38.23 ± 14.40 years with an age range of 13 to 67 years. There was no significant difference in the mean age between the case and control groups (*p*-value=0.650). Both groups were ethnically and socioeconomically comparable, which minimized confounding variables. The distribution of patients with RAS according to age and gender is shown in **Table 1** and **Table 2**, respectively. In terms of age frequency distribution, there was no significant difference between the two groups (*p*-value=0.540). The distribution of patients was determined in terms of gender, 12 of them were male and 14 were female. There were 15 men and 11 women in the control group. There was no significant difference between gender variables in both groups (*p*-value=0.450).

CRP Level Measurement

Serum CRP levels were quantitatively measured using ELISA. The results indicated a statistically significant elevation in serum CRP levels in the RAS group compared to the control group.

Table 1. The distribution of patients with RAS according to age.

		RAS	Control	*p*-value
Age (year)	≤30	9	12	**0.540**
	31-40	10	8	
	<40	7	6	

***RAS*, Recurrent Aphthous Stomatitis.**

Table 2. The distribution of patients with RAS according to gender.

		RAS	Control	*p*-value
Gender	Male	12	15	**0.450**
	Female	14	11	

***RAS*, Recurrent Aphthous Stomatitis.**

Chi-square test showed that there is a significant difference in serum CRP levels between healthy people and RAS patients (p-value=0.004) **(Table 3)**. **Table 4** shows the frequency distribution of CRP level according to gender. The distribution of CRP below 6 is significantly higher in women than in men (p-value=0.039). **Table 5** shows the frequency distribution of CRP level according to the period of relapse and recovery in the patient group. The distribution of CRP above 6 in the relapse period is significantly higher than the remission period (p-value=0.044).

Discussion

RAS, often characterized by the episodic emergence of painful oral ulcers, has intrigued both clinicians and researchers for years due to its unclear etiology and multifactorial nature (1, 13).

Table 3. CRP levels in the RAS group compared to the control group.

		RAS	Control	*p*-value
CRP	<6	12	22	**0.004**
	>6	14	4	

***RAS*, Recurrent Aphthous Stomatitis; CRP, c-reactive protein.**

Table 4. The frequency distribution of CRP level according to gender.

		CRP<6	CRP>6	*p*-value
Gender	Male	11	16	**0.039**
	Female	15	10	

***RAS*, Recurrent Aphthous Stomatitis; CRP, c-reactive protein.**

Table 5. The frequency distribution of CRP level according to the period of relapse and recovery.

		CRP<6	CRP>6	*p*-value
periods	recurrence	10	17	**0.044**
	recovery	16	9	

***RAS*, Recurrent Aphthous Stomatitis; CRP, c-reactive protein.**

Despite its relatively benign clinical course, the discomfort RAS inflicts on patients can significantly impair their quality of life. Understanding the underlying inflammatory processes associated with RAS is critical for improving management and treatment strategies. A recent investigation into serum CRP levels in individuals diagnosed with RAS provides important insights into the systemic inflammatory response linked to this condition. CRP is an acute-phase protein synthesized by the liver in reaction to inflammation, particularly in response to cytokines such as interleukin-6 (IL-6) (14, 15). Elevated serum CRP levels are indicative of an underlying inflammatory process and can provide valuable information regarding systemic inflammation in various conditions (6). In the context of RAS, exploring CRP levels contributes to discerning whether these oral lesions are purely localized phenomena or whether they are manifestations of a broader systemic inflammatory condition. The investigation focuses on measuring serum CRP levels in individuals affected by RAS compared to healthy controls (16). Preliminary findings have shown that a significant number of patients with RAS exhibit elevated CRP levels, suggesting that systemic inflammation may play a role in the pathophysiology of this condition. This finding aligns with the broader understanding that RAS can, in some cases, be triggered or exacerbated by systemic factors, such as immune dysregulation, stress, hormonal changes, nutritional deficiencies, and certain underlying disease processes (17).

One noteworthy aspect is the relationship between CRP levels and the frequency and duration of RAS episodes (18). As the investigation reveals, patients with a higher frequency of ulcerative episodes tend to have elevated CRP levels, hinting

at a chronic inflammatory state (19). The higher levels of CRP in these patients could indicate a pathogenic cycle where repeated inflammatory responses contribute not only to the recurrence of RAS but also to potential complications from chronic inflammation (20). Additionally, the study might delve into the association of serum CRP levels with various demographic factors, such as age, sex, and comorbidities. Previous literature has documented that RAS can have varying prevalence based on these factors. Interestingly, gender differences may play a role (21), as some studies indicate that RAS is more prevalent in females (22), and this could correlate with systemic inflammatory markers like CRP. Exploring these associations could shed light on why certain populations are more susceptible to RAS episodes. Moreover, the investigation warrants consideration of the psychosocial elements affecting patients with RAS. Stress, anxiety, and other psychological conditions have been proposed to influence the onset and persistence of RAS (17, 23). Elevated CRP levels might serve as a biochemical marker reflecting the psychosomatic impact of stress on inflammation and, subsequently, on mucosal health. Patients experiencing higher stress levels might demonstrate more pronounced systemic inflammation, thus leading to more frequent and severe manifestations of RAS (24).

Ultimately, understanding the implications of elevated CRP levels in RAS patients opens avenues for targeted therapeutic interventions. If a clear relationship between systemic inflammation and RAS can be established, clinicians could consider integrating anti-inflammatory treatments alongside conventional care strategies. This could include lifestyle modifications, dietary adjustments, and potentially novel pharmacological therapies aimed at reducing systemic inflammation through the modulation of cytokine production and activity. In conclusion, the investigation into serum CRP levels in patients with RAS provides a compelling glimpse into the systemic inflammatory underpinnings of this common condition. While the results raise critical questions about the etiology and management of RAS, further studies can elucidate the exact role of systemic inflammation in RAS, optimizing therapeutic strategies aimed both at the oral manifestations and underlying inflammatory processes.

Conclusion

The findings of this study demonstrate that individuals with RAS exhibit markedly elevated serum CRP levels compared to healthy individuals. This elevation is particularly prominent among those with major aphthous ulcers, indicating a potential systemic inflammatory response associated with RAS pathology. Moreover, a correlation exists between the recurrence frequency of ulceration and elevated CRP, further supporting the hypothesis that RAS may be a condition characterized by systemic involvement and inflammation. These results present new insights into the inflammatory component of RAS and suggest that CRP levels could serve as a potential biomarker for assessing disease severity and activity. Future investigations should aim to explore the underlying mechanisms contributing to this inflammatory response and the potential for CRP as a monitoring tool in clinical practice.

Author Contributions

BK, HAK and MS designed the study; BK, RA, and AK wrote the manuscript; HAK, MS and HA revised the manuscript; HSK supervised the project. All authors read and consented to the last version of the article.

Financial Support

This research was sponsored by Zahedan University of Medical Sciences, Zahedan, Iran.

Conflict of Interest

The authors assert that there is no conflict of interest.

Ethical Approval

The ethics committee of Zahedan University of Medical Sciences authorized the study protocol (ethical code: IR.ZAUMS.REC.1402.140).

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