How to Cite:
Marsoul, R. D., Al- Qaysi, S. A., & Alsaady, M. (2022). Investigation of the serotonin role in the development of Recurrent Aphthous Stomatitis. *International Journal of Health Sciences*, *6*(S5), 6944–6948. https://doi.org/10.53730/ijhs.v6nS5.10209

Investigation of the serotonin role in the development of Recurrent Aphthous Stomatitis

Rajaa Dh. Marsoul
Collage of Medicine, Babylon University, Iraq
Corresponding author email: mahdi.muntadher535@gmail.com

Suhayr Aesa Al- Qaysi
Collage of Medicine, Babylon University, Iraq

Mohammed Alsaady
Collage of Medicine, Babylon University, Iraq

***Abstract*---**Background: Recurrent aphthous stomatitis (RAS) is a common disease characterized by repeated formation of non-contagious and benign oral ulcers. It is triggered by different factors and its cause is not completely understood. This study aimed to evaluate the role of serotonin in the patients with RAS, compared to that in the control subjects. Subjects and Methods: Present study involved 100 participants of which 50 subjects diagnosed with RAS and the others without (healthy controls). Blood samples obtained from participants for serum serotonin investigation by enzyme linked immunosorbent assay. Results: Serum serotonin concentrations were significantly ($P < 0.05$) lower in patients with RAS (mean ± standard deviation [SD]; 5.737±5.007) compared to control group (mean ± SD; 8.709±5.670). Conclusion: Serum serotonin decreased in Iraqi patients with RAS compared to controls. RAS is one of the significant variables that may relate to the low serum serotonin concentrations.

***Keywords*---**Recurrent ulcer, aphthous stomatitis, serotonin.

Introduction

Aphthous stomatitis is a common disease characterized by the repeated formation of non-contagious and benign oral ulcers called (aphthae) in otherwise healthy persons. The term (canker sores) used mainly in North America, although this may also refer to any ulcers inside the mouth. The cause for this condition is not completely understood but it involves a T cell-mediated immune response initiated and triggered by different factors. These factors may include local trauma,

nutritional deficiencies, stress, hormonal influences, certain foods, allergies, dehydration, genetic predisposition or certain food additives.

These sores occur periodically and completely heal between the attacks. In the majority of cases, the individual ulcers persist about (7–10) days, and the ulceration episodes occur (3–6) times per one year. Most of these ulcers appear on the non-keratinizing epithelial surfaces in the oral cavity – i.e. anywhere except in the attached gingiva, the dorsum of the tongue and the hard palate – although the more severe forms that are less common might also involve keratinized epithelial surfaces. Symptoms range from a minor nuisance to the interfering with the drinking and eating. The severe forms might be debilitating and even causing weight loss due to malnutrition.

This disease is very common; it is affecting about (20%) of the general population to some degree [1, 2]. The onset is often during adolescence or during childhood; and the condition usually remains for several years before gradually disappearing. There is no curing and the treatments like corticosteroids aim for managing pain, reducing of the healing time and reducing of the frequency of ulceration episodes. The precise aetiology and pathogenesis of RAS remains unclear, although several factors are generally considered as crucial in the development of RAS, such as nutrition, drugs, food hypersensitivity, hormones, infections, trauma, tobacco and psychological stress [3, 4].

Materials and Methods

Study design:
The present study includes 100 participants. These participants were divided into two groups, the first group includes 50 RAS patients and the second group includes 50 apparently healthy individuals (control group). The current study was carried out from the outpatient clinic (dental health centres and dental department in Al-Husain Medical City/ Holy Karbala province, Iraq), and the samples were under the supervision of oral diagnosis specialist dentists.

This study was performed in the laboratories of the Biochemistry Department in Faculty of the Medicine/ University of Babylon. In total, 50 patients (48 % of females and 52 % of males) were enrolled in the study with RAS based on the history and clinical features for RAS. Body Mass Index (BMI) was calculated by weight (kg) divided by the square of height (m), BMI = Weight (kg)/ Square Height (m^2) [5].

Exclusion criteria were the presence of chronic systemic diseases such as cardiovascular diseases, hypertension and hormonal disturbances, identified by a physician, and the presence of other seriously interfering diseases, subjects < 6 years old and non-agreement.

Sample collection:
Two milliliters of venous blood was taken from patients and drained into gel plain tube for serum preparation, which would be used in serotonin test. Blood in gel tube allowed to clot for 40 min at 37°C and then centrifuged at 3000xg for approximately 10 min. The serum has been stored at −20°C until the time of

assay. The concentrations of serum serotonin were determined at laboratories of Biochemistry Department, Faculty of Medicine, University of Babylon by enzyme-linked immunosorbent assay (ELISA) using human serotonin ELISA kit (PARS BIOCHEM) [6].

Data analysis

The data analyzed using the Software Package for Social Sciences version 21 (SPSS, IBM Company, Chicago, USA). The data were presented as a mean ± standard deviation (SD), the differences between studied groups were evaluated using unpaired Student's t-test. The association between serotonin levels was tested using Pearson's correlation coefficient.

Results

There was no significant difference in age and body mass index (BMI) (as mean) between control and RAS group (P = 0.97 and 0.61), as shown in Table 1. This age and BMI matching helps to eliminate differences in parameter results that may originate due to the significant variation in age and BMI. Serum serotonin concentrations were significantly (P < 0.05) lower in RAS patients (mean ± SD; 5.31 ± 2.38) than that of control group (mean ± SD; 8.86 ± 4.63) as illustrated in Table 2.

Table 1: Anthropometric parameters in the studied groups

			Groups		Total	P value
			Patients	Controls		
Age	≤20	N	7	6	13	0.97
		%	14.0%	12.0%	13.0%	
	21-30	N	14	16	30	
		%	28.0%	32.0%	30.0%	
	31-40	N	18	17	35	
		%	36.0%	34.0%	35.0%	
	41-50	N	11	11	22	
		%	22.0%	22.0%	22.0%	
BMI	Normal	N	4	7	11	0.61
		%	8.0%	14.0%	11.0%	
	Overweight	N	14	12	26	
		%	28.0%	24.0%	26.0%	
	Obesity	N	32	31	63	
		%	64.0%	62.0%	63.0%	

Table 2: Mean difference serum serotonin between RAS patients and controls

	Group	No.	Mean ± SD	P value
Serum serotonin	P	50	5.31 ± 2.38	< 0.05
	C	50	8.86 ± 4.63	

Discussion

RAS is the most common inflammatory disease of the oral mucosa with a global prevalence of 0.5% to 75% and female predilection [7]. The first episode of RAS most frequently commences in the second decade of life. The lesions usually begin with prodromal burning sensation 2 to 48 hours before an ulcer appears [8]. Oral aphthous ulcers typically occur as painful, symmetrically round fibrin-covered mucosal defects with an erythematous border and most commonly on non keratinized mucosa in healthy patients. However, it can be seen on the keratinized mucosa especially in patients with immune deficiency [9]. It was demonstrated that there was a significant ($P<0.05$) decrease in the level of serum serotonin in patients in comparison with the control (5.31 ± 2.38 vs. 8.86 ± 4.63) [10].

In previous studies, the levels of depression, anger, and stress in the patients suffering from RAS were determined using Hamilton Anxiety Depression (HAD) scale, and the psychological factors were demonstrated to be highly associated with RAS pathogenesis [11]. Approximately, 46% of the patients with RAS have a positive family history. Local trauma, iron deficiency anaemia, folic acid deficiency, vitamin B12 resorption defect [12], neutropenia, and psychological factors such as stress and anger [11] can play a role in RAS aetiology.

The *5-HTT* gene modulates the intensity and duration of serotonergic neurotransmission, thus, this gene polymorphism can influence the anxiety related behaviors [13, 14]. It has been recently reported that the L and S variants of the promoter polymorphism modulate SLC6A4 differently. The S allele is associated with reduced transcription of SLC6A4 and consequently a reduction in serotonin reuptake [13]. Several studies have evaluated the correlation between a variety of polymorphisms and aphthous lesions; however, none of them has assessed *5-HTT* gene polymorphism related to this disease.

References

1. Bruch JM, Treister N (2009). Clinical Oral Medicine and Pathology. Springer Science & Business Media. p. 53.
2. Recurrent aphthous stomatitis M Namrata, R Abilasha Department of Oral Pathology, Saveetha Dental College, Saveetha Dental College, Chennai, Tamil Nadu, India, 2017 , Volume : 1, Issue : 2, P : 43-47.
3. Porter SR, Scully C, Pedersen A (1998). Recurrent aphthous stomatitis. Crit Rev Oral Biol Med 9: 306-321.
4. Natah SS, Konttinen YT, Enattah NS, Ashammakhi N, Sharkey KA, et al. (2004) Recurrent aphthous ulcers today: a review of the growing knowledge. Int J Oral Maxillofac Surg 33: 221-224.
5. ALKatawe HM, Suhayr A. AlQaysi DH-H. Interleukin 1 beta Gene Polymorphism Synergetic with H.pylori Infection Contribute to Development Of Gastric Disease and Oxidative stress. Indian J Public Heal Res Dev 2019;10.
6. Takeshita S, Kikuno R, Tezuka K, Amann E. Osteoblast-specific factor 2: Cloning of a putative bone adhesion protein with homology with the insect protein fasciclin I. Biochem J 1993; 294: 271-8.

7. M. W. Liang and C. Y. Neoh, “Oral aphthosis: management gaps and recent advances,” Annals of the Academy of Medicine Singapore, vol. 41, no. 10, pp. 463–470, 2012.
8. M. S. Greenberg, M. Glick, and J. A. Ship, Burket’s Oral Medicine, BC Decker, Hamilton, Canada, 2008.
9. Mortazavi H, Safi Y, Baharvand M, et al. Diagnostic features of common oral ulcerative lesions: an updated decision tree. Int J Dent 2016; 2016:1–14. 10.
10. Avicenna J Med Biotechnol. 2018 Jan-Mar; 10(1): 56–60. Association of Serotonin Transporter Gene Polymorphism with Recurrent Aphthous Stomatitis
11. Shamsolmolouk Najafi, Mahsa Mohammadzadeh, Amirabbas Zahedi, Mansour Heidari, and Nima Rezaei.
12. Dwijaya, A., & Atmaja, M. H. S. (2022). Clinical and imaging findings of klippel-trenaunay syndrome: A case report. International Journal of Health & Medical Sciences, 5(1), 145-149. https://doi.org/10.21744/ijhms.v5n1.1860
13. Chiappelli F, Cajulis OS. Psychobiologic views on stress-related oral ulcers. Quintessence Int 2004;35(3): 223–227
14. Altenburg A, Abdel-Naser MB, Seeber H, Abdallah M, Zouboulis CC. Practical aspects of management of recurrent aphthous stomatitis. J Eur Acad Dermatol Venereol 2007; 21(8):1019–1026.
15. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. International Journal of Health Sciences, 6(1), i-v. https://doi.org/10.53730/ijhs.v6n1.5949
16. Amanlou M, Babaee N, Saheb-Jamee M, Salehnia A, Farsam H, Tohidast Akrad Z. Efficacy of Satureja khuzistanica extract and its essential oil preparations in the management of recurrent aphthous stomatitis. DARU J Pharm Sci 2007; 15(4):231–235.
17. Lesch KP, Balling U, Gross J, Strauss K, Wolozin BL, Murphy DL, et al. Organization of the human serotonin transporter gene. J Neural Transm Gen Sect 1994;95(2): 157–162