

Research Article

Salivary irisin in relation to recurrent aphthous ulcerand weight status in Diyala city/Iraq

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Received date: 03-05-2022

Accepted date: 20-06-2022

Published date: 15-03-2024



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<https://doi.org/10.26477/jbcd.v36i1.3587>

Abstract: Background: Recurrent aphthous stomatitis remains the most common ulcerative disease of the oral mucosa that exists as painful round shallow ulcers with a well-defined erythematous margin and a yellowish grey pseudomembranous centre. Salivary irisin is an identified adipomyokine and research has revealed that it has an anti-inflammatory effect and is a novel myokine; it is synthesized in skeletal muscle and adipose tissue. The aim of the present study was to evaluate the relation of salivary irisin to recurrent aphthous ulcers and weight status in Diyala City / Iraq. Materials and methods: A cross-sectional comparative study was carried out during the period from the end of December (2021) until the end of March (2022). The total sample size composed of all patients attending a specialised dental center in Ba'aquba / Diyala governorate with recurrent aphthous ulcers of both gender and ages ranged from 20-30 years (100 patients consider the study group) assessed according to the directions suggested by the WHO (1997) and compared to the control group free from this lesion (100 patients consider the control group) matching in age and sex. The weight status was assessed using the digital weight scale. The sub samples of 45 from each study and the control group were selected to analyse salivary irisin. The description of data, presentation, and analysis process is carried out through the use of the SPSS package (SPSS version 22, Chicago, Illinois, USA). For the quantitative variable mean, the standard deviation (SD) was used. Frequency and percentage are used for the qualitative variable. The independent sample T test was used for the difference between the two groups. Pearson's correlation was used for the linear correlation between two quantitative variables. Results: The highest percentage of recurrent aphthous ulcer was found in the lower lip. The mean value of irisin was higher among the study group than in the control group. The mean value of the body mass index among the control group was higher than that of the study group. When correlating the body mass index with salivary irisin, it is a positive weak not significant correlation. Conclusions: This study concluded that there is an elevated level of irisin among recurrent aphthous ulcers, in addition to that, the recurrent aphthous ulcer decreases the body mass index.

Keywords: Irisin, recurrent aphthous ulcer, weight status.

Introduction

Recurrent aphthous ulcer is also known as canker sores or recurrent aphthous stomatitis (RAS) which is deemed the most widespread oral mucosal disease evenly both in children and adults ⁽¹⁾. RAS is diagnosed from a history of recurrent ulcers together with an oral examination. These are considered recurrent, round or ovoid, small, multiple, ulcers with bounding margins having yellow or gray floors. They seem to be encircled by erythematous haloes that exist first during childhood or adolescence ⁽²⁾. There are three types Minor aphthous ulcers occur mainly in the 10-40 years age group and are frequently 2-4 mm in diameter, major aphthous ulcers occur mainly in childhood and adolescence, and are larger, even more than 1 cm in diameter. Furthermore, Herpetiform ulceration came to exist in a slightly older age group, starting with vesiculation which seems to pass almost rapidly into multiple, minutes (2 mm). The differential diagnosis for RAS may gradually vary from idiopathic or unknown causes to connective

tissue disease, or even sometimes can be caused by inflammatory bowel diseases. A detailed review of the system may play a respectable role in characterizing or pointing out if it belongs to a systemic inflammatory process or if it is completely idiopathic⁽³⁾.

Saliva is an aqueous fluid secreted by specialized glands in the oral cavity and composed of a mixture of secretary products (inorganic and organic products) which are derived from these salivary glands plus substances from the oropharynx, upper airway, gastrointestinal reflux, gingival sulcular fluid, food deposits, and blood-derived compounds^(4,5). Irisin is an adipomyokine and research has revealed that it has anti-inflammatory effects and a novel myokine, has been one of the most investigated peptides⁽⁶⁾, and exhibits autocrine and paracrine effects, it is made up of 112 amino acids primarily produced in skeletal muscle and adipose tissue⁽⁷⁾ as well. Moreover, irisin is present in peripheral or marginal nerve cells, sebaceous glands of the skin, in addition to many organs and tissues. It covers the alteration of white adipose into brown adipose tissue. Besides, it controls and adjusts thermogenesis, energy outflow, weight loss, and fundamentally glucose homeostasis through augmenting uncoupling protein 1 in brown adipose tissue⁽⁸⁾. Irisin, is also termed an exercise hormone, that is created by splitting or cleavage of fibronectin type III domain-containing protein 5 (FNDC5), the extracellular portion of type I membrane protein, which follows the process of activation by peroxisome reproduction- activated receptor- γ coactivator α , that is substantially was considered as a myokine secreted in reaction to physical load on the part of skeletal muscle. Eventually, it has also been discovered to be emitted or secreted out of adipose tissue⁽⁹⁾. Many previous studies demonstrate that irisin plays a role in the inflammation process such as Bilski which reported an increase in plasma irisin levels in colitis⁽¹⁰⁾. The study of Bakal showed increased irisin levels in cases of acute appendicitis⁽¹¹⁾. The anti-inflammatory, anti-oxidative and anti-apoptotic properties of irisin have received a great role of attention from the scientific society⁽¹²⁾. Mazur and his team illustrate that irisin elevates the inflammatory activation of macrophages stimulated by lipopolysaccharide (LPS). And another study found that increasing the levels of serum irisin in gastric cancer (GC) patients can play a great role in the early diagnosis of GC patients^(13, 14). While Altay *et al.*, 2021 demonstrated elevated irisin levels in RAS patients⁽⁶⁾.

Nutritional status, generally, is defined as a process of measuring the level of the individual's physiologic need for food. On the other hand, World Health Organization considers the nutritional status as a consequence of the diversified amount of socio-economic conditions. It can be a highly-susceptible indicator of the total level of development, in addition to the idea of estimating food supplied⁽¹⁵⁾. A study found that the concentrations of irisin have been correlated positively with Body Mass Index (BMI) in healthy women⁽¹⁶⁾, another study revealed that the level of irisin has a positive correlation to BMI in non-diabetic individuals⁽¹⁷⁾, while a study suggested plasma irisin levels are higher in obese compared to anorexia nervosa⁽¹⁸⁾. Contrastingly, they reported a negative relationship between irisin level with BMI, fat mass in men and ratio of waist-hip⁽¹⁹⁾. Choi *et al.* Stated that BMI has a negative correlation to serum irisin⁽²⁰⁾, and such a result of similarity may be due to adipogenesis mechanisms associated with irisin in fatty tissue during ulceration. Moreover, it was also reported that BMI may demonstrate sort of different associations with circulated irisin because numerous studies have revealed that BMI has shown different associations with diverse health conditions^(21, 22).

To the best of our knowledge, no Iraqi study was found to evaluate the relation of salivary irisin to recurrent aphthous ulcer and weight status in Diyala City / Iraq for reason this study was conducted with the null hypothesis that there is no relation of recurrent aphthous ulcer to the oral health condition, nutritional status and salivary constituents among patients.

Materials and Methods

A cross sectional comparative study has been conducted. The sample includes all patients with RAS attending specialized dental centers in Ba'aquba / Diyala governorate of both gender age range 20-31 years, during the period from the end of December 2021 till the end of March 2022 with the following inclusion criteria for the study group: the patient had oral ulceration clinically diagnosed as RAS, and agree to participate in this study, as well as free from any systemic disease associated with oral ulcer, not a smoker and not receiving any multivitamins, calcium and vitamin D3 supplements from the total study group included 100 patients of them complaining from recurrent aphthous ulcer without any systemic diseases were selected, the control group include 100 patients free from the recurrent aphthous ulcer. Ethical approval was achieved from the University of Baghdad, all participants revealed their consent, and the procedures and protocol of the study had been approved and certified by ethical committee.

In the absence of a stimulant, salivary samples were collected by mixing into the test tube according to the Munro method prior to clinical evaluation between 9 am and 11 pm, using a timer for 10 minutes⁽²³⁾. The instructions were given to all patients that they should be free from acute or chronic diseases, have no medications, eat or drink only water one hour before collection, not smoke or exercise heavily. After saliva collection, saliva samples were centrifuged for about 20 minutes at about 2000-3000 rpm, and all samples were stored at about -20 C until biochemical and immunological analysis. All patients were examined by a single examiner under standard conditions, and the oral cavity was examined with chairs and mirrors.

Recurrent aphthous ulcer was assessed according to directions suggested by the WHO⁽²⁵⁾. The examination begins with the upper and lower lips, sulcus, retro-molar pad area, buccal mucosa, hard and soft palate, dorsum and margins and ventral surfaces of the tongue then the floor of the mouth, for all participants case sheets were filled, which include demographic information regarding age and gender. Medical history, the site, frequency, and type of RAS were classified according to the criteria of Burkit (1998) into minor ulcer: less than 1 cm in diameter and heal without a scar, major ulcer: over 1 cm in diameter; takes longer time to heal and often heal with a scar and herpetiform: considered as a distinct clinical entity that manifests as recurrent crops of dozens of small ulcers throughout the oral mucosa. Weight status was assessed by using the digital weight scale, BMI index is a number calculated from the patient's weight and height, according to the formula (WHO, 2000)⁽²⁶⁾: $BMI = \text{Weight (Kg)} / \text{Height (m}^2\text{)}$.

The value of nutritional indicators is compared to the international reference value, and the use of the reference population defined by the National Centre for the Prevention and Promotion of Chronic Diseases and the Use of the CDC Growth Chart (Center for Disease Control and Prevention, 2000)⁽²⁷⁾.

Statistical analysis

The description of data, presentation and analysis process is carried out through the use of the SPSS package (SPSS version 22, Chicago, Illinois, USA). The standard deviation (SD) is used for the quantitative variable average. Frequency and percentage are used as qualitative variables. An independent sample T test was used to determine the differences between the two groups. Pearson correlation was used to compare linear correlation between two quantitative variables. For the significance level as Unsignificant $P > 0.05$, Significant $P \leq 0.05$.

Results

The distribution of samples by ulcer's site is shown in Table 1, this table shows that a higher percentage of the patients had RAS in the lower lip (47%) followed by buccal mucosa and border of the tongue (11% for each), while the least frequencies of RAS was seen in the upper lip (8%), gingiva (7%), the tip of the tongue (7%), hard palate (4%), the floor of mouth (3%) and the soft palate (2%).

The mean value of irisin among the study and control group is shown in table 2 as it illustrates that the mean value of irisin was higher among the aphthous ulcer group than in the control group with a non-statistically significant difference between them.

Table 3 demonstrates irisin level according to type and frequency of ulcer, the mean value of irisin was higher among the group of one-time ulcer episode than ≥ 3 group episodes, with a non-statistically significant difference between them. While the mean value of irisin was higher in minor ulcers than in major ulcers with a non-statistically significant difference between them.

In the Table 4 the mean value of BMI among the control group was higher than that study group with a statistically significant difference between them. However, the relation between the BMI and salivary Irisin was not significant in a positive direction Table 5.

Table 1: Distribution of samples by ulcer's site.

Site	No.	%
Lower lip	47	47.00
Buccal mucosa	11	11.00
Gingiva	7	7.00
Border of tongue	11	11.00
Tip of tongue	7	7.00
Upper lip	8	8.00
Hard palate	4	4.00
Soft palate	2	2.00
Floor of mouth	3	3.00

Table 2: Descriptive and statistical test of Irisin (ng/mL) among study and control groups.

Vars.	Groups				Statistic	
	Study		Control		T test	P value
Salivary Irisin	Mean	\pm SD	Mean	\pm SD		
Irisin	1.719	0.354	1.530	0.536	1.980	0.051 NS

Table 3: Descriptive and statistical test of salivary Irisin by frequency and type of recurrent aphthous stomatitis

Recurrent aphthous stomatitis	Cats	Salivary irisin		T test	P value ^
		Mean	\pm SD		
Frequency	One time	1.595	0.340	1.388	0.172
	≥ 3	1.449	0.362		
Type	Minor	1.552	0.355	0.721	0.475
	Major	1.463	0.357		

Table 4: Descriptive and statistical test of Body Mass Index among study and control groups.

Groups	Mean	±SD	T test	P value
Study	22.506	3.392	2.823*	0.005 Sig.
Control	24.105	4.534		

*Significant P≤0.05

Table 5: Correlation between Body Mass Index and salivary Irisin by study and control groups.

Groups		Salivary Irisin	
		r	P^
Study	BMI	0.164	0.283
Control	BMI	0.253	0.093

Discussion:

The majority of recurrent aphthous ulceration in the oral cavity have been found an extreme variation regarding sites in which Queiroz and his colleagues found that the majority of RAS lesions were located in the tongue ⁽²⁸⁾, Chatterjee’s study showed lower vestibule was the main site and Oyetola’s finding was lower lip ^(29,30), while this study found that the lower lip where the most site affected by RAS (47%), Therefore, the relation between RAS and site was mostly variable from study to another which could be related to the differences in samples of the population selected on each one.

The present study showed that non significantly elevated level of irisin in recurrent aphthous ulcer patients, this result is in agreement with Altay and his team⁽⁶⁾ which demonstrated the elevated level of irisin in RAS patients. Recurrent aphthous ulcer is the most common inflammatory condition in oral mucosa characteristic by the recurrent onset of painful ulcer, it was hypothesized that elevated level of irisin in RAS can by explained its anti-inflammatory effect to overcome the inflammation of RAS. There are many previous studies demonstrate that irisin plays a role in the inflammation process ⁽¹¹⁻¹⁴⁾.

In the present study, the circulating irisin was correlated with BMI and found positive non-statistical significant relation, this result comes to agree with previous studies ⁽²⁸⁻³⁰⁾ while it does not agree with others ^(19,20), thus, other studies with a larger number of sample consisting of different subjects are guaranteed in future to investigate the definite association of irisin with BMI.

In this study, the mean value of BMI was lower among the study group than in the control group with statistically significant differences between them. Besides, BMI value was lower in patients with three or more time ulcer episodes per month than one-time episode and such a result has disagree with previous studies, some research demonstrated that recurrent aphthous ulceration is quite a common condition affecting the oral cavity, as it is painful and may be the cause of distress. Additionally, this can demonstrate interference with normal and everyday life activities by affecting eating and swallowing processes ⁽³¹⁾, and even the RAS episode three or more times per month effect the eating pattern and furthermore affect the BMI more than one-time episode.

Conclusion

This study concluded that a higher percentage of the patients had RAS in the lower lip and there is an elevated level of irisin among recurrent aphthous ulcers, in addition to that, the recurrent aphthous ulcer decreases the body mass index.

Conflict of interest

The authors have no conflicts of interest to declare.

Author contributions

AKT and NJSR contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript

Acknowledgement and funding

None

Ethical approval

All of the individuals were given thorough information about the study and the procedures involved, and their informed consent was acquired on a form approved by the ethics committee of the University of Baghdad \ College of Dentistry.

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الاريسين اللعابي وعلاقته بقرحة الفم المتكررة وحالة الوزن في محافظة ديالى ايه كنعان طاهر, ندى جعفر محمد حسن الشيخ راضي

المستخلص:

الخلفية: التهاب الفم القلاعي المتكرر يعتبر من أكثر الأمراض التقرحية شيوعاً في الغشاء المخاطي للفم. تتواجد كتقرحات دائرية مؤلمة مع حافة حمراء وواضحة مع مركز الغشاء المصفر. الاريسين اللعابي هو اديبيومايوكاين وأظهرت الأبحاث أن له تأثيراً مضاداً للالتهابات ومايوكاين جديد. ويتكون في العضلات والهيكل العظمي والأنسجة الدهنية. التغذية تشير إلى العمليات التي تدخل في تناول الأطعمة واستخدامها من أجل نمو الجسم وصيانته وإصلاحه. تتكون العينة الاجمالية من 200 عينه تم اختيارها من المركز التخصصي لطب الاسنان في ديالى من نهاية ديسمبر (2021) حتى نهاية مارس (2022) وبفئات العمرية (20-31). تم تقييم القرحة القلاعية المتكررة وفقاً للإرشادات التي اقترحتها منظمة الصحة العالمية في (1997). و تقييم حالة الوزن باستخدام مقياس الوزن الرقمي، ورقم محسوب من وزن المريض وطوله. كانت الأغلبية من تقرحات الفم في الشفة السفلى، وكانت متوسط القيمة للاريسين اللعابي اعلى في المرضى الذين يعانون من القرحة مقارنة بالطبيين، ان متوسط قيمة الوزن كانت اقل في المرضى الذين يعانون من التقرحات مما عليه في الطبيعي وكانت العلاقة ايجابية ضعيفة بين المتوسط الوزني والاريسين اللعابي. استنتجت الدراسة الى ارتفاع في مستوى الاريسين اللعابي في الحالات التي تعاني من تقرحات الفم ووجدت علاقة ايجابية ضعيفة بين المتوسط الوزني والاريسين اللعابي إضافة الى ان قرحة الفم المتكرره تقلل من مؤشر كتله الجسم