THE SEVERITY SCALE OF RECURRENT APHTHOUS STOMATITIS AND ITS CORRELATION WITH HELICOBACTER PYLORI INFECTION AND AGES OF THE PATIENTS

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Abstract

A condition known as recurrent aphthous stomatitis is characterized by oral mucosal ulcers. This study aims to evaluate the severity scale of patients with recurrent aphthous stomatitis because the differences in the clinical features of recurrent aphthous stomatitis from patients to another, in addition to that we shall correlate the severity scale of recurrent aphthous stomatitis with age and Helicobacter pylori infection. It has been proposed that bacteria may have a role in the development of aphthae. One of the most prevalent and well-known pathogenic agents in the emergence of peptic ulcers is Helicobacter pylori. Recurrent aphthous stomatitis and Helicobacter pylori have been linked by certain researchers due to the histopathological similarity with peptic ulcers. The study's goals and objectives include

1- Evaluation of the severity scale of recurrent aphthous stomatitis patients.
1. Detection of the correlation between the severity scale of recurrent aphthous stomatitis and the ages of patients.
2. Determination of the correlation between the severity scale of recurrent aphthous stomatitis patients and infection with H.pylori using urea breath test.
3. Detection of the correlation between the ages of the recurrent aphthous stomatitis patients and infection with H.pylori.

Fifty patients with recurrent apthous stomatitis were participated in this study which at least occur four, or more times per year. It has been found that thirty one patients (62%) with recurrent aphthous stomatitis had mild symptoms, fifteen patients (30%) with moderate symptoms; whereas only four patients (8%) were with severe symptoms. The statistical analysis has shown that the number of patients who had mild symptoms of RAS was significantly higher than the number of patients who had moderate and severe symptoms, and the number of patients who had moderate symptoms of recurrent aphthous stomatitis was significantly higher than the number of patients who had severe symptoms. The ages of the patients with recurrent aphthous stomatitis showed statistically significant correlation with severity scale of recurrent aphthous stomatitis. Also, a strong positive linear correlation was found between the ages of recurrent aphthous stomatitis patients and urea breath test value, but Urea breath test values showed no correlation with severity scale of recurrent aphthous stomatitis. By these results we

concluded that there was a correlation between the severity scale of recurrent aphthous somatitis and the ages of the patients but there was no correlation between the severity scale of recurrent aphthous somatitis and helicobacter pylori infection.

Introduction

Recurrent aphthous stomatitis (RAS) is a recurrent painful ulcerative disorder that commonly affects the oral mucosa. Local and systemic factors such as trauma, food sensitivity, nutritional deficiencies, systemic conditions, immunological disorders and genetic polymorphisms are associated with the development of the disease [1]. Aphthous ulcers are classified into three different types, minor, major and herpetiform. Minor aphthae are generally located on labial or buccal mucosa, the soft palate and the floor of the mouth (non-keratinized mucosa).They can be singular or multiple, and tend to be small (less than 1 cm in diameter) and shallow. This type of RAS is the most common (80% of cases), and usually heals within 7-14 days [2]. Major aphthae also called as Sutton's disease; usually exceeds 1 cm cause deeper ulceration thus leave scar. It constitutes only 10-15% of RAS cases. These ulcers may remain about 10-20 days and may take months. The Herpetiform is least common variant of RAS that constitutes only 7-10% of RAS cases, ulcer size is very small measuring 2-3 mm in diameter; numerous in numbers (around 100 ulcers at once), can fuse together producing large irregular lesions that last for 7-10 days without leaving scars[3].

   The Helicobacter pylori (H. pylori) is a gram-negative, microaerophile bacteria, that colonizes the gastric mucosa and its infection is associated with the development of peptic ulcers, gastric mucosa associated lymphoid tissue lymphoma, and gastric cancer [4].Transmission of H.pylori is largely by the oral-oral or fecal-oral routes. Lack of proper sanitation, safe drinking water and basic hygiene, as well as poor diets and overcrowding, all play a role in the overall prevalence of infection[5].Considering the similarities of histological features between gastric ulcers and oral aphthous ulcers, and in view of the fact that the latter lesions often respond to treatment with broad-spectrum antibiotics such as tetracycline, it is reasonable to assume that H.pylori might also be involved in the development of recurrent oral aphthous ulcers. However, there is limited evidence regarding the colonization or the possible role of H.pylori in oral aphthous ulcers [6]. Invasive and non-invasive techniques are used to diagnose *H. pylori* infection. Invasive methods such as histology, rapid urease test (RUT), microbiological culture and polymerase chain reaction (PCR), require endoscopy and are also known as biopsy-based tests. Non-invasive tests include stool antigen test, serology and urea breath test (UBT) [7].The present study was designed as a case study to determine the correlation of severity of RAS and infection with H.pylori by using UBT.

The Aims and Objectives

1. Evaluation of the severity scale of recurrent aphthous stomatitis patients
2. Detection of the correlation between the severity scale of recurrent aphthous stomatitis and the ages of the patients.

3. Deteminination of the correlation between the severity scale of recurrent aphthous stomatitis and infection with H.pylori using urea breath test.

4. Detection of the correlation between the ages of the recurrent aphthous stomatitis patients and infection with H.pylori.

Subject, Materials and Methods

The study samples consisted of (50) patients with RAS referred from medical and dental centers in Baghdad City and other provinces in Iraq to department of Oral Medicine Clinic, College of Dentistry-University of Baghdad. The patients were estimated by dentist specialized in oral medicine to confirm the inclusion criteria.The collection of samples was from the period (January-2019) to (June-2019), Patients with RAS, which at least occur four, or more times in the year. Patients with systemic conditions and aphthous like lesion were excluded. Urea [C13] breath test kits (Heliforce)®, and Infrared (IR) Force spectrometer machine were used . Ethical approval committee of College of Dentistry-University of Baghdad approved this in vivo case study. After completing the extra oral examination, all the patients were examined intraorally to distinguish the RAS and to write the characteristic feature of the ulcer (size, number, sit, frequency and duration). The severity of the aphthous ulcer was recorded depending on Albanidou –Farmaki et al., 2005 scale [8]. which includes:-

0 = No symptoms

1 = Mild symptoms; recorded as the presence of one or two lesions, with duration of 4-7 days and frequency of recurrence of every 2-3 months.

2 = Moderate symptoms; recorded as the presence of two to five lesions with duration of 10-15 days and frequency of recurrence every one month.

3 = Severe symptoms; recorded as more than five lesions with duration of more than 15 days and continuation in most of the days.

After that all the patients were supervised and instructed not to eat or drink anything (only water) 3 hours at least before doing the test. The researcher filled out the required information on the sample bags, asked each patient and to hold his or her breath for 10 second, then exhale into first air bag marked "before" or (O minute), and make it full of gas as much as possible and immediately close it, then the participant asked to ingest 75 mg of non- radioactive isotopic urea (^{13}C), Labeled urea comes into contact with mucus, here, hydrolysis by H.pylori by urease enzyme Produced ammonia and labeled Carbone dioxide.

Urea rapidly, passed down its concentration gradient, into the epithelial blood and within minutes appears in the breath. After 30 minute, the participant asked to exhale into second bag labeled (after) or 30 minute, and immediately close it. After that, the two bags were attached to an Infrared (IR)-force spectrometer, which looked for labeled ^{13}C and displayed the value of UBT.

Result

It has been found that thirty one patients (62%) with RAS had mild symptoms, fifteen patients (30%) with moderate symptoms; whereas only four patients (8%) were with severe symptoms as
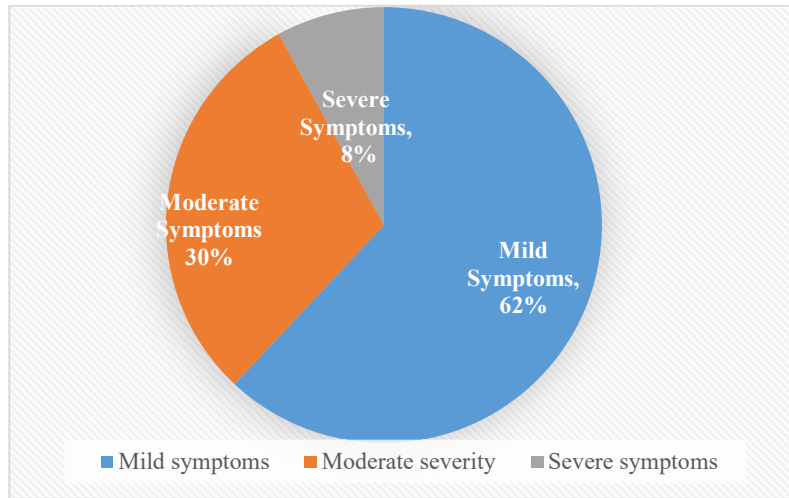
shown in Figure (1).

Figure (1):- Distribution of patient with RAS according to severity scale

The statistical analysis showed that the number of patients who had mild symptoms of RAS was significantly higher than the number of patients who had moderate and severe symptoms (p<0.001), and the number of patients who had moderate symptoms of RAS was significantly higher than the number of patients who had severe symptoms (p=0.005); Table (1)

Table (1):-Clinical presentation of patients with RAS (Severity scale RAS)

* Mild symptoms	* Moderate symptoms	* Severe symptoms	Z.test	P.value	
31	15	-----------	3.21	<0.001	Significant
31	----------	4	5.66	<0.0001	Significant
----------	15	4	2.80	0.005	Significant

 *N. of patients with

The age of the patients with RAS showed statistically significant correlation with severity scale of RAS (r=0.427, P=0.002). Also, a strong positive linear correlation was found between the age of RAS patients and UBT values (r=0.51, P<0.001), Table (2), but Urea breath test values showed no correlation with severity scale of RAS (r=0.189, p>0.05).

Table (2): Correlations coefficient test between study variables within RAS patients

Variables	Age	Urea Breath test
Age (years)	---	Pearson Correlation 0.512 P value <0.001

Severity Scale of RAS	Spearman Correlation 0.427 P value 0.002	Spearman Correlation 0.189 P value 0.109

Discussion

The results of current study showed that the number of patients with mild symptoms of RAS higher than those patients with moderate and severe symptoms. This result agrees with a study done by Maleki *et al.* (2009) who found that mild symptoms were recorded in 23 patients (53.5%). Nineteen cases (44.2%) were with moderate symptoms and only one patient (2.3%) with severe symptoms [9]. Also, the present study showed that the ages of the patients showed highly significant positive linear correlation with UBT values, this result agrees with the result of a study on RAS done by Maleki *et al*. (2009), suggested that the age of the patient associated with a positive UBT breath test. The elderly appear to be predisposed to a variety of diseases and, therefore, aging facilitates the onset and progression of many diseases, including gastrointestinal diseases. Albanidou-Farmaki *et al*. (2005) showed that the RAS patients with H.pylori infection suffered from more severe symptoms compared with H.pylori negative patients; while UBT values in present study showed no correlation with severity scale of RAS. Study done by Karaca *et al*. (2008) showed that, there were no significant correlations among the intensity of H.pylori with the recurrence rate, number, diameter of aphthous ulceration[10], the result of this study agrees with the result of present study that showed no correlation between the H.pylori infection and severity scale of RAS. Although there is a correlation between the severity scale of RAS and ages of the patients; and the ages of the patient have a correlation with UBT Value, but the results showed that the severity scale of RAS has no correlation with UBT Value, which means that the H pybri infection is not the only reason for increasing the severity of RAS with aging .Thus, more studies are needed to investigate in the causes of increasing the severity of RAS with aging.

Conclusions

There was a significant correlation between the age and the severity scale of RAS patients but there was no correlation between the H. pylori infection and severity scale of RAS.

Research Ethical Approval: Research Ethical Approval was obtained from the Faculty of Dentistry, University of Baghdad.

Conflict of Interest Statement: The authors declare that there is no conflict of interest.

References

1. Carolina-Cavaliéri G. , Ricardo-Santiago G. , Lívia-Guimarães Z., Fabrício-Rezende A., Recurrent aphthous stomatitis and Helicobacter pylori . Med Oral Patol Oral Cir Bucal. 2016 Mar 1;21 (2):e187-91.
2- Greenberg MS, Glick M, Ship J A: Burkett's oral medicine. Eleventh ed. "Recurrent Aphthous Stomatitis" 2008; Chapter 3, Pp: 57-60

3- Sharma D, Garg R (2018) A Comprehensive Review on Aphthous Stomatitis, its Types, Management and Treatment Available. J Develop Drugs 7: 189.

4. Gatta L, Vakil N, Vaira D, Scarpignato C. Global eradication rates for Helicobacter pylori infection: systematic review and meta-analysis of sequential therapy. BMJ. 2013;347:f4587.

5. Hunt RH, Xiao SD, Megraud F, Leon-Barua R, Bazzoli F, van der Merwe S, Vaz Coelho LG, Fock M, Fedail S, Cohen H, Malfertheiner P, Vakil N, Hamid S, Goh KL, Wong BCY, Krabshuis J, Le Mair A. Helicobacter pylori in developing countries. J Gastrointestin Liver Dis. 2011 Sep;20(3):299-304.

6. Birek C, Grandhi R, McNeill K, Singer D, Ficarra G, Bowden G: Detection of Helicobacter pylori in oral aphthous ulcers. J Oral Pathol Med 1999; 28: 197–203. 5. Peng NJ, Lai KH, Lo GH, Hsu PI. Comparison of noninvasive diagnostic tests for *Helicobacter pylori* infection. *Med Princ Pract.* 2009;18:57–61.

7. Peng NJ, Lai KH, Lo GH, Hsu PI. Comparison of noninvasive diagnostic tests for *Helicobacter pylori* infection. *Med Princ Pract.* 2009;18:57–61.

8. Albanidou-Farmaki E,Giannoulis L, Markopoulos A, Fotiades S, Aggouridaki X, Farmakis K, et al. Outcome following treatment for Helicobacter pylori in patients with recurrent aphthous stomatitis. Oral Dis. 2005;11:22-6.

9. Maleki Z, Sayyari AA, Alavi K, Sayyari L, Baharvand M. A study of the relationship between Helicobacter pylori and recurrent aphthous stomatitis using a urea breath test. J Contemp Dent Pract. 2009; 10:9-16.

10. Karaca S, Seyhan M, Senol M, Harputluoglu MM, Ozcan A. The effect of gastric Helicobacter pylori eradication on recurrent aphthous stomatitis. Int J Dermatol. 2008; 47:615-7