Clinical Evaluation of Recurrent Aphthous Stomatitis and Its Correlation with Helicobacter Pylori

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Abstract

Recurrent aphthous stomatitis is a disorder distinguished by ulcers restricted to the oral mucosa. Because of the histological similarities between peptic ulcers and recurrent aphthous stomatitis and the identified role of Helicobacter pylori in peptic ulcer, the possibility of bacterial involvement in the progression of aphthae has been suggested. Helicobacter pylori are one of the most common, well-known pathogenic agents in the development of peptic ulcers. Some investigators have shown a relationship between Helicobacter pylori and recurrent aphthous stomatitis. However, this relationship is controversial. The aims and objectives of this study were 1- Clinical evaluation of patients with recurrent aphthous stomatitis.2- Determination of the association between Helicobacter pylori and recurrent aphthous stomatitis using the urea breath test.

Eighty-five subjects were participated in this study; they are divided into two groups. Fifty patients with recurrent aphthous stomatitis, which at least occur four, or more times per year, thirty-five healthy subjects of the same age group as controls.

The results showed that ,the mean age of patients with recurrent aphthous stomatitis lie around 3rd decade and the percentage of female with recurrent aphthous stomatitis was higher than male,the clinical findings showed that the number of patients with minor recurrent aphthous stomatitis was higher than patients with major and Herptiform recurrent aphthous stomatitis , No difference between the number of patients who had single recurrent aphthous stomatitis and number of patients who had multiple recurrent aphthous stomatitis was found . According to the site of ulcers, the result founded that the number of patients who had RAS on the non-keratinized mucosa was higher than patients who had RAS on the keratinized mucosa and those who had recurrent aphthous stomatitis on keratinized and non-keratinized oral mucosa.

Regarding the laboratory findings, the percentage of patients with recurrent aphthous stomatitis who urea breath test positive was higher than percentage of control group,also the mean value (Delta Over Base) of urea breath test in recurrent aphthous stomatitis patients was statistically higher than that of healthy controls. By these results we concluded that there was a correlation between recurrent aphthous somatitis and H.pylori by using urea breath test in patients with recurrent aphthous stomatitis when compared with controls.

Keywords: *Recurrent aphthous stomatitis; H.pylori ; Clinical Evaluation; Health.*

Introduction

Recurrent aphthous stomatitis (RAS) is a very common condition characterized by solitary or multiple small, round, recurrent oral ulcers, with erythematous haloes and circumscribed margins[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

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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 etiopathogenesis of RAS so far remains not fully understood. The potential trigger factors include genetic predisposition, viral and bacterial infections, food allergies, vitamin and microelement deficiencies, systemic diseases (e.g., celiac disease, Crohn's disease, ulcerative colitis, AIDS), increased oxidative stress, hormonal defects, mechanical injuries and anxiety [4].

In genetically predisposed patients, the effect of certain trigger factors initiates the cascade of proinflammatory cytokines, directed against selected regions of the oral mucosa[5],The Helicobacter pylori (H. pylori), is a microaerophilic, Gram-negative spiral organism that has been shown to be the causative factor in a large proportion of patients with stomach ulcers and gastritis [6].

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[7].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 [8].

Diagnostic tests currently used for the detection of H.pylori fall into two categories: invasive and noninvasive, the former requiring endoscopy. The invasive methods, which are biopsy-based, include culture, rapid urease test (RUT) and histology. Non-invasive testing for H.pylori can be done by the urea breath test (UBT), serology and analyzing body materials such as faeces, urine and saliva. The UBT requires instruments such as mass spectrometer and infrared spectrometer, which are not always available in routine clinical laboratories [9, 10]. The present study was designed as a case-control study to determine probable H.pylori infection in patient with RAS by using UBT.

The Aims and Objectives

1- Clinical evaluation of patients with recurrent aphthous stomatitis.

2. Determination of the association between H. pylori and RAS using the urea breath test (UBT).

Subject, Materials and Methods

The study samples consisted of (85) subjects, (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, (35) healthy group, they were not suffering from aphthous ulcer during their life, and with no signs and symptoms of any systemic disease.

The participants 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 and the control group were included in the study. 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-control 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).

After that all the participants 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 participant (patient and healthy subject 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 result as positive or negative.

Results

The mean age of patients with RAS was (36.0±14.8) years with age range from (16-73) years, they were thirty females (60%) and twenty (40%) were males. The results showed that (40) patients (80%) had minor aphthous ulceration, whereas (6) patients (12%) had major aphthous ulceration and (4) patients (8%) had both minor and major ulcers .Herpetiform type of ulcers was not found in those patients (Fig.1), according to the number of ulcer, (24) patients(48%) had single ulcer, whereas(26)patients(52%)were with multiple ulcers at the time of examination(Fig.2). Thirty-eight patients (76%) with (RAS) had oral ulcer(s) located on non-keratinized mucosa. While two patients (4%) had oral ulcer on keratinized mucosa and ten patients (20%) had RAS on both keratinized and non-keratinized oral mucosa (Fig.3).The mean value of urea breathe test in RAS patients (11.146±9.446),which was statistically significant (P< 0.001) higher than that of healthy controls (3.606±5.025) (Table 1) .The UBT was positive in thirty-six (72%) patients and negative in fourteen(28%),while out of thirty five of control group the UBT was positive in eleven(31.4%) subjects and negative in twenty-four(68.6%)subjects (Table 2).These results were highly statistically significant (P<0.001).

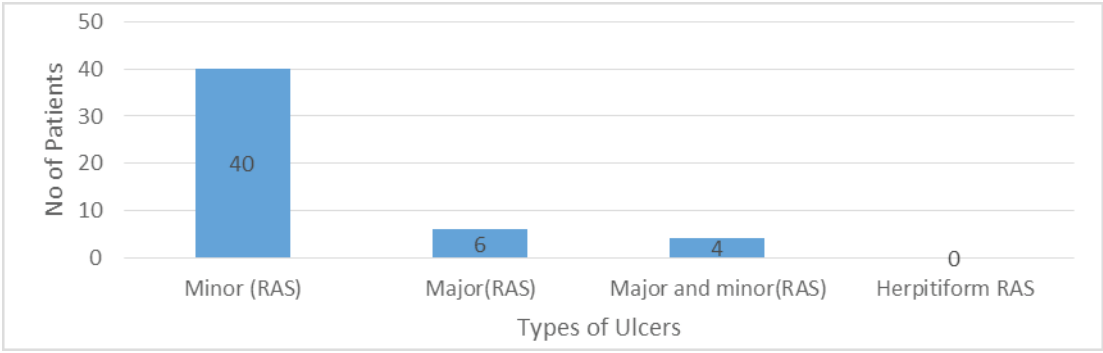

Figure (1):- Distribution of patients according to the clinical presentation (types of ulcers).

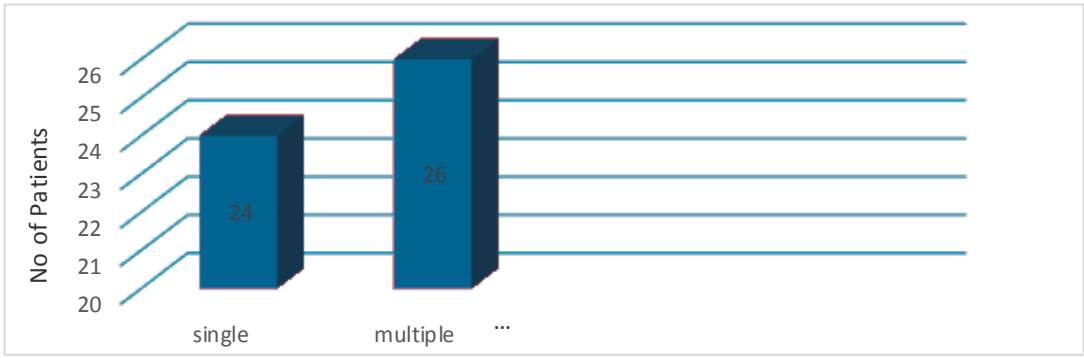

Figure (2):-Distribution of patients according to the clinical presentation (Number of ulcers)

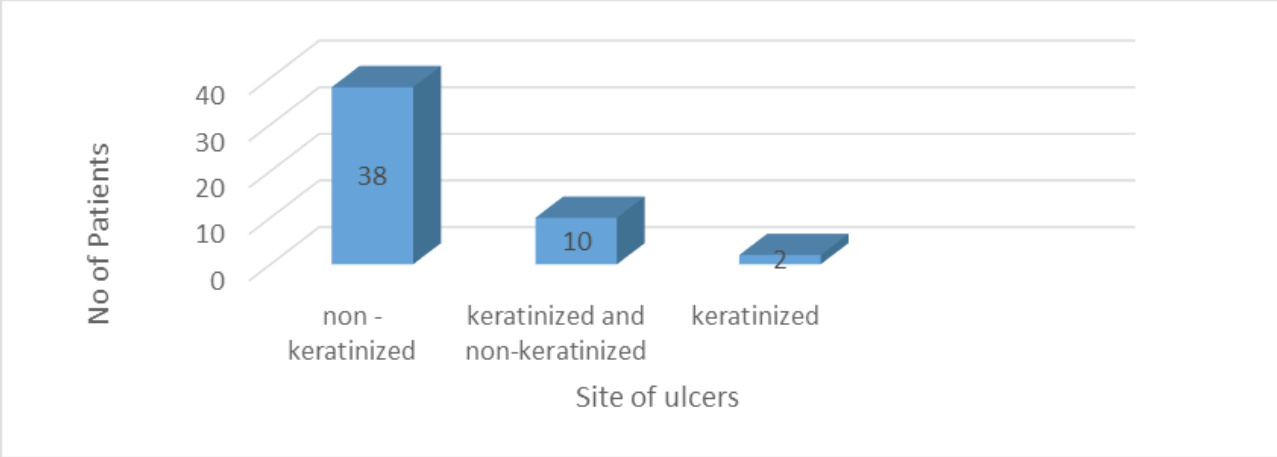

Figure (3):- Distribution of patients according to the site of ulcers

Table (1):- The Mean and Standered Deviation (SD) of UBT in all study groups

Test	Study Group	N	Test Value Mean	SD	Test result	P value	
Urea Breath Test (DOB)	Case	50	11.146	9.446	386.0 C	< 0.001	High-Significant
	Control	35	3.606	5.025			
T, C Mann-Whitney SD; Slandered Deviation DOB;Delta Over Base							

Table (2):- Distribution of Study groups according to the results of UBT

Urea Breath Test	Study Groups				Test Result	P value
	Case		Control			
	N=50	100%	N=35	100%		
· Positive	36	72.0%	11	31.4%	13.709 B	<0.001
· Negative	14	28.0%	24	68.6%		
B Chi-square test N: Number						

Discussion

The results showed that the mean age of patients with RAS lie around 3rd decade this result agreed with other studies [11, 12].While, other study have noted that the average age group was in the 4th decade [13]. Wheras Maleki *et al*. (2009) showed that the mean age ±SD was 25.0±ed .9.4 years in RAS patients [14].

The percentage of female with RAS was higher than male; this was reported in most other studies, which suggested female predilection [11, 15, 16].While other study by Taher(20018) suggested a male predilection [17], such results may be due to the limited number of patients.

The clinical findings showed that the number of patients with minor RAS was higher than patients with major and Herptiform RAS This result agreed with other studies[2,11,14,18].The result of this study showed that there was no difference between the number of patients who had single RAS and number of patients who had multiple RAS, this is in positive agreement

with the epidemiological study on RAS by Safadi (2009) demonstrated that approximately half of participants reported that ulcerations were single, while the other half reported them as multiple ulcerations[19].

The result showed that the number of patients who had RAS in the non-keratinized mucosa was higher than patients who had RAS in the keratinized mucosa and those who had RAS in keratinized and non-keratinized mucosa, this could be explained on the basis that the non-keratinized mucosa areas were movable structure and mostly affected by trauma and least resistant to infection. This result agreed with other studies [11, 17].

The mean value (DOB) of urea breath test in (RAS) patients was higher than that of healthy controls, which was statistically significant (P< 0.001),the percentage of RAS patients with positive UBT was significantly higher than percentage of control group (P<0.001)

It has been found by this result a potential association between RAS and H.pylori infection ,this result agreed with the results of two studies on patients with RAS were submitted to endoscopy biopsy to detect H. pylori. Both studies showed a positive relationship between the presence of the bacteria in the stomach and the occurrence of RAS in the mouth. In these studies by Karaca *et al*. (2008) and Tas *et al.* (2013) 87% and 65% of the patients with RAS, respectively, showed the bacteria in the gastric mucosa. There were significant decreases in the recurrence rate and healing time of RAS by eradication therapy [20, 21].

Maleki *et al*.(2009) had cases and control groups disregarding age and gender. The UBT was used to detect H. pylori infection. It was found that, 37.2% of individuals among the RAS patients and 31.8% individuals in the control group had a positive UBT. The difference was not found to be statistically significant (*P*=0.597). In other words, no correlation was detected [14].

Also the result of present study aggred with study by Birek *et al*. (1999) reported that 23 of 32 (71.9%) of recurrent aphthous ulcers detected by PCR assay were positive for H. pylori and suggested a relationship between H. pylori and recurrent aphthtous ulcers [8].

There are many studies in the last few years focused on the effect of H,pylori infection on the homeostasis of different micronutrients including iron, vitamin B12, folic acid, a-tocopherol, vitamin C and b-carotene[22], Öztürk *et al*.(2015)concluded that in Helicobacter pylori-positive children, many trace elements and mineral metabolism may change[23].

Conclusions

A potential association between RAS and H.pylori Infection in the stomach by using the mean value (DOB) and the results (positive and negative) of UBT in patients with (RAS) when compared with controls.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: The authors declare that they have no conflict of interest.

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