



Factors predispose to aphthous ulcer

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Abstract:

Background: Aphthous stomatitis also known as recurrent aphthous ulcers, is a common and non-contagious infection of the mouth in otherwise healthy individuals

Objective: To study the relationship between aphthous ulcer and vitamin D and iron level in adults .

Materials and methods: Forty patients with aphthous ulcer and 20 controls were subjected to history taking, clinical examination, and laboratory investigations mainly to correlate the level of vitamin D and iron in patients with the aphthous ulcer.

Results: This study showed that vitamin D deficiency or insufficiency is insignificant in cases suffering from aphthous ulcer than normal controls. Also, the results of the study of iron level showed no statistically significant difference between both groups.

Conclusions : No relation between aphthous ulcer and vitamin D or iron level.

Key words: Aphthous ulcer- Vitamin D - Iron

Introduction:

Aphthous stomatitis also known as recurrent aphthous ulcers, is a common and non-contagious infection of the mouth in otherwise healthy individuals. ¹⁻²

It is a shallow ulcer on the unattached oral mucous membranes which may cause pain, difficulty in swallowing and may be severe up to absolute dysphagia. ³⁻⁴

The only or the main cause is still unknown but involves a T cell-mediated immune response triggered by a variety of factors. Different individuals have different triggers, which may include nutritional deficiencies, local trauma, stress,

hormonal influences, allergies, genetic predisposition or other factors .These ulcers occur periodically and heal completely between attacks. ⁵⁻⁶

The presence of vitamin D receptors in several tissues suggests that vitamin D may play a role in the etiopathology of diseases. Vitamin D receptors have been described in all immune system cells, particularly cells producing antigens, such as active T-lymphocytes, active macrophages and dendritic cell. ⁷⁻⁹

Patients and Methods:

Patients:

The study was done on two groups of adults:

1 -Group A: 40 cases who were diagnosed as having aphthous ulcer by history, and examination .

2-Group B: 20 healthy controls adults who were free .

The study had been carried out in outpatient clinic and department of otolaryngology at Assiut university hospital.

Inclusion criteria: patients suffering from aphthous ulcer, adults, both sexes.

Exclusion criteria: patients suffering from cancer, patients receiving cytotoxic drugs, patients receiving radiotherapy.

This study was approved by the Institutional Ethics and Research Committee of the Faculty of Medicine, Assiut University, Assiut, Egypt. The whole study was explained to the patients and a written consent was taken. They were completely free to be included in the study or not.

Each patient was subjected to history taking, clinical examination and laboratory investigations.

***Clinical features of ulcer :**

It must be round or oval, raised edges, covered by yellow-gray fibrinous membrane that can be scraped away and is surrounded by cherry halo. It may be small, medium and large.

We divided ulcers into three sizes to categorize them easily. An ulcer less than 0.5 cm is considered small sized ulcer, 0.5-1.0 cm is medium sized ulcer and more than 1.0 cm is large sized ulcer).

It is found in tongue, inner surface of lips, inner surface of the cheeks, anterior pillar of tonsils or palate. It is either single ulcer or multiple ulcers.

We asked each patient about recurrence rate. If it is recurrent ulcer or not.

***Laboratory investigations:**

Blood sample (3cm) was taken immediately after the diagnosis of Aphthous ulcer in the laboratory for measuring.

1 -Serum 25 (OH) vitamin D.

2 -Iron level.

Specimen collection and handling for vitamin D and Iron :

1- Serum used for the assay: collect the whole blood by a venipuncture and allow clotting.

2- The blood sample intubated at 37°C for 20 minutes and stored at -20°C till performing analysis .

Principle of vitamin D test:

The kit is a solid phase enzyme-linked immunoassay (ELIZA), based on the principle of competitive binding. Anti-vitamin D antibody coated well are incubated with vitamin D standards, controls samples, and vitamin D- Biotin conjugate at room temperature for 90 minutes.

Serum 25 (OH) D was done on ELIZA reader.

- Levels between 30-100 ng/ml were regarded as normal.
- Levels between 10-30 ng/ml were considered as vitamin D insufficient.
- Levels below 10 ng/ml were categorized as vitamin D deficient.

Principle of Iron test :

Iron bound to transferrin is released in an acidic medium as ferric iron and is then reduced to ferrous iron in the presence of ascorbic acid. Ferrous iron forms a blue complex with ferene.

The absorbance at 595 nm is directly proportional to the iron concentration.

Serum iron level is measured by BT1500 machine.

- Levels between 65-175µg/dl were regarded as normal level in males.

- Levels between 50-170µg/dl were regarded as normal level in females.
- Levels below 65µg/dl in males, 50 µg/dl in females were categorized as abnormal iron level.

Statistical analysis:

The statistical package for social science version 16 was used for data analysis. Quantitative variables will be expressed as Mean \pm SD and qualitative variables will be expressed as number and percentage.

To compare the results between the two groups a paired sample independent t-test was used, and qualitative variables were compared by Chi-square and Fishers exact tests. P value < 0.05 was considered as significant.

Results:

Sixty adults included in this study 40 patients and 20 controls. The mean age of the cases was 40.60 \pm 13.82 years, and 33.20 \pm 18.32 years for the controls, the range of age is 18:62 years. 17(42.5%) of the case group were males and 23(57.5%) were females, compared to 10(50%) males and 10(50%) females in the control group seen in table 1.

Table 1: Shows the distribution of age and sex in the patients and control.

	Case		Control		P-value
	No.	%	No.	%	
Age	40.60 \pm 13.82		33.20 \pm 18.32		0.085
Sex:					0.582
Male	17	42.5	10	50.0	
Female	23	57.5	10	50.0	

Among the patients we noticed that 30 (75%) patients have rounded ulcers and 10 (25%) patients have oval ulcers.

We noticed that the tongue is the most common site for aphthous ulcer 22 (55%) of patients and the anterior pillar of the left tonsil and the palate (uvula) are the least common sites for aphthous ulcer (2.5%) of patients.

Table 2: Shows different affected sites.

Site	No.	%
Tongue	22	55.0
Inner surface of lips	13	32.5
Inner surface of the cheeks	3	7.5
Anterior Pillar of left tonsil	1	2.5
Palate (uvula)	1	2.5

Within the tongue there are different parts from which the ulcer arises as seen in Fig.2.

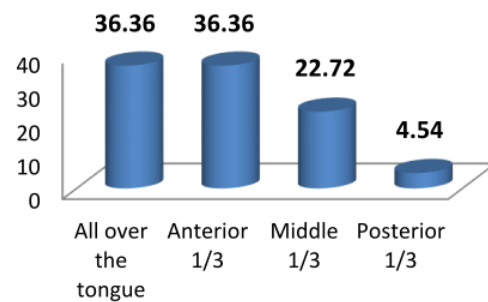


Fig.1: Shows the different affected sites of the tongue.

There were different sizes of aphthous ulcer as 19 (47.5%) of patients had small sized ulcers, 11 (27.5%) of patients had medium sized ulcers and 10 (25%) of patients had large sized ulcers. Small ulcer is less than 0.5 cm diameter, medium ulcer is 0.5 :1.0 cm diameter and large ulcer is more than 1.0 cm diameter.

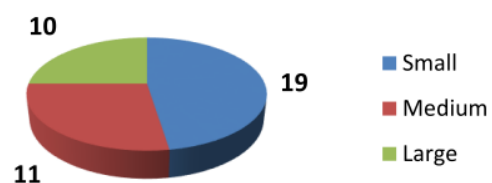


Fig. 2: Shows size of the ulcers.

Sixteen (40%) patients have negative past history of aphthous ulcers compared to 24(60%) patients have positive history of aphthous ulcers.

Twenty-five (62.5%) patients just have single ulcer only compared to 15(37.5%) patients have multiple ulcers in the same attack.

Nineteen (47.5%) patients had no other diseases with ulcers, but the rest had diseases. The most common one was diabetes 7(17.5%) and the least common one was renal disease 1(2.5%).

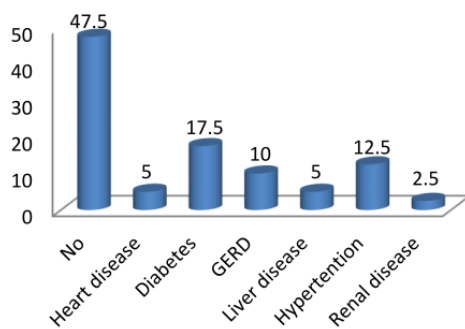


Fig.3: Shows cases with other diseases with the ulcer.

According to statistical analysis, comparing 25(OH) vitamin D levels in the study group versus the control group. All the values are expressed as mean \pm standard error of the mean. It was noted that vit D deficiency and insufficiency is statistically insignificant in cases with aphthous ulcer group and in control group. As seen in table 3.

It was noted that iron abnormal levels are statistically insignificant in cases with aphthous ulcer group and in control group. As seen in table 4.

Table 3: shows comparison between vit. D levels in the patients and control

No. Vit D. level	Groups				P. value
	Case		Control		
	No.	%	No.	%	
Normal	21	52.5	4	20	0.06
insufficient	19	47.5	16	80	
Deficient	0	0	0	0	

*Statistically significant difference ($p < 0.05$).

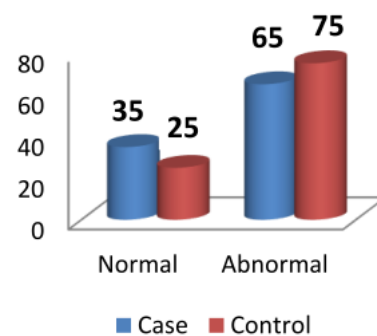


Fig 4: shows comparison between iron levels in the patients and control

Table 5: shows Values of vitamin D and iron and their mean \pm SD in the case and control groups.

	Groups		P. value
	Case	Control	
Vitamin D level	29.75 \pm 7.40	24.55 \pm 9.30	0.022*
iron level	49.02 \pm 20.54	45.18 \pm 19.90	0.494

* Statistically significant difference ($p < 0.05$).

Discussion :

Aphthous stomatitis (persistent aphthous ulcers) is the most common oral mucosal lesion which may cause significant morbidity. ¹

These ulcers are seen as shallow, agonizing ulcers on the unattached non

keratinizing epithelial surface of oral mucous membranes.²

It lasts about 7-10 days and heals without scarring and its recurrence rate is about 3-6 times per year. Larger ulcers may take weeks to months to heal and its healing may leave a scar. These ulcers may involve keratinizing epithelial surface. Symptoms may be mild or severe as interference with eating and drinking, up to causing weight loss due to malnutrition.¹⁰

In this study there were 17(42.5%) males and 23(57.5%) females in the case group, these results were close to the results of **Krawiecka et al 2017** that was done on 66 cases 24 (36.4%) males and 42(63.6%) females.¹¹

We found that 30(75%) of cases have rounded ulcer compared to 10(25%) of cases have oval ulcer. Other study made by **Akbar et al 2016** showed that round ulcer is more predominant than other shapes as 162(66%) of cases have rounded ulcers compared to 85(34%) of cases have other shapes of ulcer.¹²

The most common site of ulcers in this study is the tongue (55%) and the least common sites are anterior pillar of left tonsil and the palate 1(2.5%) for each. While the research of **Prithi and Dharman 2016** found that the most common site is the buccal mucosa 67(45%) and the least common site is the base of the tongue 13(9%).¹³

We found that 19(47.5%) of cases have small ulcers, 11(27.5%) of cases have medium sized ulcer and 10(25%) of cases have large ulcer. Also, the results of **Akbar et al 2016** showed 38% of cases have small ulcer, 13.9% of cases have medium sized ulcer, 8.3% have large ulcer and 39.8% of cases have not sure measures of ulcer. Most researchers found that small ulcer is the commonest ulcer.¹²

About the recurrence of ulcers, we found that 16 (40%) of cases have

negative history of recurrent ulcers compared to 24 (60%) of cases had past positive history of ulcers. As regard the number of ulcers during the same attack we found single ulcer in 25(62.5%) compared to multiple ulcers in 15(37.5%). On the other hand, **Prithi and Dharman 2016** did their research on 300 persons (150 cases and 150 controls). They mentioned that 46(30.6%) of cases have negative history of recurrent ulcer compared to 104(69.9%) of cases have positive history of ulcers, but our study is compatible with the same study in the number of ulcers as they found single ulcer in 99(66%) compared to multiple ulcers in 51 (34%) . may be the change in the results is due to the difference in number of cases between us in our studies. We studied on 40 patients and 20 controls, while Prithi and Dharman studied on 150 patients and 150 controls.¹³

In this study we found that 19(47.5%) of cases have no other associated diseases compared to 21(52.5%) of cases have other diseases. The most common one is diabetes mellitus 7(17.5%) and the least common one is renal diseases 1(2.5%). This is against the results of **Akbar et al 2016** which show 48(16.5%) of cases have no other diseases with ulcer compared to 202(83.5%) of cases have other diseases.¹²

Vitamin D level in our cases was normal in 21(52.5%), insufficient in 19(47.5%) and no cases have deficient level compared to control group which is normal in 4(20%), insufficient in 16(80%) and no controls have deficient level. These results differ from the results made by **Krawiecka et al 2017** on 66 cases who found that vitamin D level is normal in 5(7.6%), insufficient in 16(24.2%) and deficient in 45(68.2%) compared to control group

which is normal in 8(12.1%), insufficient in 18(27.3%) and deficient in 40(60.6%). There was no statistical significance in the difference of vitamin D deficits between the case and the control groups. And so, no correlation was detected between affection with aphthous ulcer and serum vitamin D level.¹¹

Iron level in our cases was normal in 14(35%) and low in 26(65%) compared to iron level in control group which is normal in 5(25%) and low in 15(75%). These results are against that made by **Sumathi et al 2014**, who made study on 50 cases and 25 controls and found iron level in the cases is normal in 17(34%) and low in 33(66%) compared to iron level in the control group which was normal in all of them.¹⁴

Conclusion:

Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosa diseases. It affects 5–25% of the population, with a predominance among women (particularly in the second and third decades of life). The condition is chronic and self-limiting in immunocompetent patients. It is characterized by recurrent onsets of shallow, clearly defined, round (or oval) and painful erosions (or ulcers) surrounded by an erythematous halo. Aphthous lesions are likely to occur on non-keratinized, non-attached oral mucosa. Some studies stated that vitamin D deficiency predispose to ulcerations in cases of ulcerative colitis.

This study was done on 40 cases diagnosed as aphthous ulcer and 20 healthy persons as a control group. We studied vitamin D and iron levels in the two groups to discover if there is relationship between vitamin D level (deficiency or insufficiency) and iron

deficiency and the occurrence of aphthous ulcer.

This study showed that vitamin D deficiency, insufficiency is insignificant in cases suffering from aphthous ulcer than normal controls. Also, the results of study of iron level showed no statistically significant difference between both groups.

Conflicts of interest:

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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