

Ferritin and vitamin b12 levels in patients with recurrent aphthous ulcers

Moin Sabeer Tidgundi¹, Khaja Moinuddin^{2*}, Mirza Sharif Ahmed Baig³

¹Associate Professor, ²Assistant Professor, ³Professor, Dept. of Biochemistry, Khaja Banda Nawaz Institute of Medical Sciences, Kalaburagi, Karnataka

* Corresponding Author:

Email: drkhajamoinuddin@gmail.com

Abstract

Background: Recurrent aphthous ulcers (RAU) are one of the most common ulcerative lesions of the oral cavity with a prevalence rate of approximately 50-66%. The prevalence of hematinic deficiencies including ferritin and vitamin B12 deficiencies and their role in the prophylaxis and development of RAU is not well known. Some studies have reported no association between RAU and deficiencies of iron, folate or vitamin B12. While other studies have demonstrated a high prevalence of hematinic deficiencies in patients with RAU. Hence the present study was conducted to determine the association between levels of vitamin B12 and serum ferritin in patients with RAU.

Materials and Method: This was a case control study conducted in a tertiary care hospital in South India from May 2015 to May 2016. The study was approved by the institutional ethics committee. Informed consent was taken from all the patients. After recording patients demographics like age, gender, occupation, address 3ml blood was drawn from cases and controls centrifuged at 3000 rpm for 10 minutes for the analysis of serum Ferritin by Enzyme Linked Immunosorbent Assay (ELISA) method and serum B12 by radio immunoassay. The data was expressed as Mean \pm SD. Students Unpaired 't' test is used for comparing biochemical parameters between cases and controls and P value of <0.05 was considered as statistically significant.

Results and Discussion: Most cases were in males aged between 35 - 45 years. Most cases of RAU were minor, only four cases were herpetiform. The patients were classified as having minor aphthous ulcers, major aphthous ulcers, or herpetiform aphthous ulcers according to the criteria of Lehner. In the present study, 64% of the patients had low serum ferritin levels and 54% of the patients had low serum vitamin B12 levels. In the present study, statistically significant differences were observed in the serum levels of ferritin and vitamin B12 between the two groups

Conclusion: In the present study, 64% of the patients had low serum ferritin levels and 54% of the patients had low serum vitamin B12 levels. Screening aphthous ulcer patients by measuring serum ferritin and vitamin B12 levels is necessary, as to prevent recurrent aphthous ulcer. It is also essential for recurrent aphthous ulcer patients to have nutritional diet containing iron and vitamin B12

Keywords: Iron Deficiency Anaemia, Serum Ferritin, Aphthous Ulcer, Vitamin B12.

Introduction

Recurrent aphthous ulcers (RAU) are one of the most common ulcerative lesions of the oral cavity with a prevalence rate of approximately 50-66%.⁽¹⁾ RAU are prone for recurrences and is estimated that three-month recurrence rates are as high as 50 %.⁽²⁾ They usually present as small round/oval ulcers with a yellow-grey colour and erythromatous "halos" and usually heal, with no permanent scarring.⁽³⁾ The exact etiology of aphthous ulcers remains unknown although many factors have been implicated in the pathogenesis of RAU, such as smoking, immunological factors, stress, hematological disorders, hormonal imbalance, infections, vitamin deficiencies, and genetic factors.⁽³⁻⁵⁾

The prevalence of hematinic deficiencies including ferritin and vitamin B12 deficiencies and their role in the prophylaxis and development of RAU is not well known. Some studies have reported no association between RAU and deficiencies of iron, folate or vitamin B12.^(6,7) While other studies have demonstrated a high prevalence of hematinic deficiencies in patients with RAU.⁽⁸⁻¹⁰⁾ Vitamin B12 deficiency is rare and usually occurs in late adulthood.⁽¹¹⁾ Deficiency anemia, particularly iron deficiency, vitamin B12 deficiency and folic acid

deficiency, cause occurrence of recurrent aphthous stomatitis.⁽¹¹⁾

Ferritin is a globular protein which is present intracellularly, in which iron is stored in a soluble, non-toxic form. Serum ferritin is most sensitive test for iron deficiency anaemia. Since the etiology of RAU is unknown, diagnosis is entirely based on history and clinical criteria as there are no laboratory investigations to confirm the diagnosis.^(12,13) There are few studies conducted on association between RAU and levels of vitamin B12 and serum ferritin in this region, hence the present study was conducted to determine the association between levels of vitamin B12 and serum ferritin in patients with RAU.

Materials and Method

This was a case control study conducted in a tertiary care hospital attached to KBNIMS from May 2015 to May 2016. The study was approved by the institutional ethics committee. Informed consent was taken from all the patients. The following criteria was used for selection of subjects.

Inclusion criteria: Patients attending otorhinolaryngology clinic with recurrent oral ulceration aged between 30-60 years.

Diagnosis was made by oral medicine specialist based on the presence of round symmetrical yellowish white ulcers less than 1 cm in diameter with an erythematous halo covered with a detachable membrane, which recovered without any scars.

Exclusion criteria:

1. Chronic Smokers and alcoholics.
2. Patients with history of medical disorders such as hypertension, hepatic, renal, cardiac disorders, Behcet's disease, hematological disorders, Crohn's disease and ulcerative colitis.
3. Subjects on medications such as sulphonamides, rifampicin, vancomycin, cytotoxic agents like methotrexate and non-steroidal anti-inflammatory drugs.

After recording patients demographics like age, gender, occupation, address 3ml blood was drawn from cases and controls centrifuged at 3000 rpm for 10 minutes for the analysis of serum Ferritin by Enzyme Linked Immunosorbent Assay (ELISA) method and serum B12 by radio immunoassay. The data was expressed as Mean \pm SD. Students Unpaired 't' test is used for comparing biochemical parameters between cases and controls and P value of <0.05 was considered as statistically significant.

Results

A total of 64 cases and 60 controls were included in the final analysis. The demographic characteristics of the subjects is shown in Table 1.

Table 1: Demographic data of the cases and controls

Variable	Cases	Controls
Number of subjects	64	60
Age	39.4 \pm 7.56	37.7 \pm 4.78
Male: Female	35:29	34:26
Type of RAU		
Minor	45	-
Major	15	-
Herpetiform	4	-

RAU = Recurrent aphthous ulcer

Most cases were in males aged between 35 - 45 years.

Most cases were of RAU were minor, only four cases were herpetiform. The patients were classified as having minor aphthous ulcers, major aphthous ulcers, or herpetiform aphthous ulcers according to the criteria of Lehner.⁽¹⁴⁾

Table 2: Comparison of vitamin B12 and serum ferritin levels in cases and controls

Variable	Cases (64)	Controls (60)
Vitamin B12 (pg/ml)		
Low	35	11*
Normal	29	59
Mean \pm SD	294.72 \pm 112.56	365.34 \pm 94.32*
Serum ferritin (ng/ml)		
Low	41	9*
Normal	23	51
Mean \pm SD	87.78 \pm 71.56	114.23 \pm 63.68*

Normal serum vitamin B12 level = 180-910 pg/ml

Normal serum ferritin level = For males 17-230 ng/ml and 14-150 ng/ml for females

* $p \leq 0.05$ = Significant

Discussion

The present study was conducted to evaluate the serum levels of ferritin and vitamin B12 in patients with recurrent aphthous ulcers. Discomfort in patients with recurrent aphthous ulcers is relatively high. RAU increase the flow of saliva and interfere with day to day activities like eating, drinking, speaking and can have significant effect on patients quality of life. Since the etiology of RAU is unknown, the treatment is aimed mainly to relieve pain.⁽¹²⁾

The demographic characteristics of the cases and controls is shown in Table 1. There was no statistically significant difference between the demographic between cases and controls. The most common RAU affected were males and in the age group of 35-45 years. The age incidence is similar with other studies but other studies have reported females were more affected with RAU.⁽¹⁵⁻¹⁷⁾ The high incidence of RAU in females as reported by other studies may be explained by the fact that women have high predisposition to become anaemic.⁽¹⁸⁾ But some studies have reported haematitic deficiencies regardless of gender.^(19,20)

According to published studies, 80% of all RAU lesions are minor RAU in nature.⁽²¹⁾ In the present study minor RAU were the most common type of RAU. Various studies have reported no association between RAU and deficiencies of iron, folate or vitamin B12.^(6,7) While other studies have demonstrated a high prevalence of hematinic deficiencies in patients with RAU.⁽⁸⁻¹⁰⁾ In the present study, statistically significant differences were observed in the serum levels of ferritin and vitamin B12 between the two groups (Table 2).

In the present study, 64% of the patients had low serum ferritin levels. Other studies have reported similar but with varying percentage of serum ferritin levels. Some have reported 60% of patients having low serum ferritin levels while some others have reported as low as 20%.^(4,9,19,20) A recent study it was found that 37.8% of the subjects had reduced serum ferritin, which was statistically significant compared to controls.⁽²²⁾

Vitamin B12 deficiency suppresses the cell mediated immunity and is the most frequently found haematinic deficiency, producing changes in the epithelium of the oral cavity.⁽²³⁾ In the present study, 54% of the patients had low serum vitamin B12 levels. Other studies have also reported similar findings but with varying percentage of vitamin B12 deficiency.^(9,12,22,23) In addition, some studies conducted on replacement therapy with vitamin B12 in RAU with a proven vitamin B12 or folate deficiency improved rapidly on replacement therapy, while those with iron deficiency had shown a less response.^(24,25)

Vitamin B12 deficiency suppresses the cell mediated immunity, changes in the epithelium of tongue and the buccal mucosa.^(23,26) Serum B12 is essential for the synthesis of DNA, and its deficiency results in the development of megaloblastic anaemia, especially in developing countries including India.⁽²⁷⁾ Vitamin B12 deficiency impairs the metabolism of folate which can lead to folic acid deficiency. Therefore, in addition to Vitamin B12 measurement, folic acid should also be measured in cases of RAU. One study has reported that there is possible role of folic acid in the etiology of RAU,⁽⁴⁾ but another study has rejected the role of folic acid in RAU.⁽²⁸⁾

Folic acid helps in regeneration and healing process of oral epithelium and is also essential for the synthesis of DNA. A study conducted in Pakistan reported folate deficiency of 16%.^(29,30) In the present study we did not measure folic acid levels, which is a limitation of the study. Future studies, preferably should be controlled therapeutic trials having large sample size and also include supplementary methods to measure folic acid in order to examine the relationship between this folic acid and RAU.

Conclusion

In the present study, 64% of the patients had low serum ferritin levels and 54% of the patients had low serum vitamin B12 levels. Screening aphthous ulcer patients by measuring serum ferritin and vitamin B12 levels is necessary, as to prevent recurrent aphthous ulcer. It is also essential for recurrent aphthous ulcer patients to have nutritional diet containing iron and vitamin B12.

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