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Original Article

Importance of Iron Deficiency in Patients with Recurrent Aphthous Stomatitis

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ABSTRACT

Aphtha is a Greek word for ulceration which is a common problem in dentistry for diagnosis and treatment. **Objective:** To assess serum levels of iron among patients with RAS and its comparison with the control group. **Methods:** The analysis involved 150 subjects alienated into 2 groups as a group with recurrence of aphthous ulcer and a control group. The 75 patients were encompassed in the control group and 70 in the aphthous ulcer matched for age and sex. Based on the history and clinical examination, the diagnosis of RAS was made. By ELISA test and ELX 800 Absorbance Microplate Reader tool, Serum ferritin was measured, while micro-lab 300 was used to evaluate serum hemoglobin and iron levels. **Results**: Grounded on standard values of laboratory investigations, serum levels of iron were suggestively lower in patients of RAS in comparison to the control group. Minor RAS type was observed in 71 patients (94.7%), while major RAS was reported in 4 patients (5.3%). Out of 75, 20% had multiple ulcers and 80% had a single ulcer. While RAS was localized in non-keratinized mucous membrane in 64 patients (85.3%), in 6 patients (8%); RAS was located in keratinized mucous membrane and both non-keratinized and keratinized mucosa were seen in 5 subjects (6. 7%). **Conclusion:** The presence of iron deficiency has been linked to recurrent aphthous stomatitis.

INTRODUCTION

Aphtha is a Greek word for ulceration which is a common problem in dentistry for diagnosis and treatment [1-2]. A feature of RAS is erythematous ulcers of the oral mucosa, which might be multiple or single, with a history of shallow necrotic center surrounded by raised margins and recurrence, with erythematous halo and gray-yellow pseudo-membrane. A patient with RAS will experience pain in the mouth, ranging from simple discomfort to soreness with normal oral functions such as chewing and swallowing [3-4]. Children are apparently up to 39% more affected, and patients who have positive family history are most likely to progress towards RAS than without family history [5]. These recurrent ulcers are classified by size, type, healing time as large or minor RAS, and herpetic ulcers and numbers of RAS. The maximum communal type is minor one, accounting for 82% of all types [6-7]. This disease is of unknown etiology and multifactorial. The utmost probable triggers are localized injury, stress and genetic predisposition. The nutritional deficiencies, systemic diseases, endocrine disorders, food allergies and cessation of smoking might also be taken as related factors [8]. It is assumed that the contributory agents cause oxidative stress, but the particular reason of RAS is still not clear. The exact pathogenesis and etiology of RAS has not been recognized. Hematological deficits also suggested to be a possible etiological factor, but the data presented are still contradictory, possibly due to ethnic, geographical and dietary differences [9-10]. Since oral epithelium may thin

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out and atrophy in the absenteeism of blood cells, RAS may be due to anemia in the absence of any complications. Oral epithelial atrophy makes it more susceptible to injury and creates a favorable environment for the penetration of the bacterial antigen, one of the reasons tangled in the RAS pathogenesis. In Pakistan, hematological abnormalities are common in 19% to 29% of the over-all population, and about 1.4% of individuals suffer from anemia [11]. This morbidity is instigated by iron deficiency and can be detected by non-invasive approaches such as serum ferritin (SFer), serum iron (SI) and hemoglobin (Hgb) [12]. This study was designed to assess serum levels of iron among patients with RAS and its comparison with the control group.

METHODS

This case-control study was held in the dental outpatient department (OPD) of Hamdard University, Karachi for six-months duration from July 2021 to December 2021. Formal approval of the Ethics Review Committee was obtained prior to the start of the research. Total 150 subjects were included using a non-probability technique of sampling, and after meeting the inclusion and exclusion criteria, they were alienated into 2 groups: patients with RAS from group I (75) and controls from group II (75). The criteria of selection for group I were subjects of all ages and sexes with an active aphthous lesion with a history of recurrent attacks of mouth ulcers at least three times a year. Healthy subjects with no history of any systemic disease and aphthous stomatitis were encompassed in control group. Recurrent aphthous ulcer was identified on the base of clinical examination and history. The criteria of exclusion was aphthous ulcers in the last 2 months, lactation, pregnancy, alcohol use, smoking and any oral lesions other than iron supplementation, use of immunomodulatory agents, taken any therapeutic regimen, multivitamins and steroids. Demographic information, namely gender, age, history of systemic diseases and occupation was recorded. The oral mucosa was carefully examined for the size, type, location and number of the ulcers. Venous blood was collected from study participants and submitted to a laboratory for evaluation. By ELISA test and ELX 800 Absorbance Microplate Reader tool, Serum ferritin was measured, while micro-lab 300 was used to evaluate serum hemoglobin and iron levels. The collected data was entered into the SPSS 21.0 for analysis. Gender is articulated as frequency and percentage and arithmetic variables such as ferritin, age, iron and Hb levels are stated as standard and mean deviation. The significant difference was determined with an independent t-test in means amid patients and controls. P values less than or equal to 0.05 were measured significant with the confidence interval of 5%.

RESULTS

In RAS group I; there were 50 women (66.7%) and 25 men (33.3%), while in control group II; there were 43 women (57.3%) and 32 men (42.7%). The RAS group mean age was (29.02± 8.95) years, and that of the control group was (31.11± 7.2) years. The mean ages comparison among the RAS and the control group was not significant ($p > 0.05$).

Demographic Features	Group I (RAS) n= (75)	Group II (Control) n = (75)
Age(years)10-20 years	13(17.3%)	10 (14.2%)
21-30 years	39 (52%)	32 (45.7%)
31-40 years	23 (30.7%)	28 (40%)
Gender		
Male	25 (33.3%)	32 (42.7%)
Female	50 (66.7%)	43 (57.3%)

Table 1: Demographic Features of Patients and Control Group

The features of patients in group I and II by age and sex is presented in Table 1. It was found that the change in the level of ferritin among the control and RAS group was significant in the 21-30 years and 30-40 years age group ($p < 0.005$). When comparing the gender, a significant difference was found at $p < 0.05$ for women, Table 2.

Demographic Features	Group I (RAS) n= (75)	Group II (Control) n = (75)	p-value
Age (years)	Ferritin (ng/ml) Mean±SD	Ferritin (ng/ml) Mean±SD	
10-20 years	28.01±11.2	35.64± 20.1	0.39
21-30 years	24.10±13	36.0± 14	0.003
31-40 years	24.2±11	36.20± 16	0.003
Gender			
Male	37.9±15.9	42.31± 10.1	0.43
Female	28.2±14.8	41.02± 18.2	0.00

Table 2: Demographic Features Conferring to The Patient's and Control's Serum Ferritin Levels

Mean hemoglobin levels in the 21-30 and 31-40 age-group in the RAS group were significantly lower than the control group ($p\ 0.05$) (Table 3).

Demographic Features	Group I (RAS) n= (75)	Group II (Control) n = (75)	p-value
Age (years)	Hemoglobin (g/dl) Mean±SD	Hemoglobin (g/dl) Mean±SD	
10-20 years	12.1±1.3	12.9±2.4	0.11
21-30 years	11.8±1.9	15.1±1.8	0.01
31-40 years	13.1±1.5	14.8±1.2	0.01
Gender			
Male	15.1±1.2	14.9±0.9	0.10
Female	12.9±2.3	15.1±1.1	0.01

Table 3: Demographic Features Conferring to The Patient's and Control's Serum Hemoglobin Levels

Minor RAS type was observed in 71 patients (94.7%), while major RAS was reported in 4 patients (5.3%). Out of 75, 20% had multiple ulcers and 80% had a single ulcer. While RAS was localized in non-keratinized mucous membrane in 64 patients (85.3%), in 6 patients (8%); RAS was located in

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keratinized mucous membrane and both non-keratinized and keratinized mucosa were seen in 5 subjects (6.7%).

Age (years)	(n=75) Group I (RAS)	(n = 75) Group II (Control)	p-value
	(g/dl) iron Mean±SD	(g/dl) iron Mean±SD	
10-20 years	12.1±1.3	12.9±2.4	0.11
21-30 years	11.8±1.9	15.1±1.8	0.01
31-40 years	13.1±1.5	14.8±1.2	0.01
Gender			
Male	15.1±1.2	14.9±0.9	0.10
Female	12.9±2.3	15.1±1.1	0.01

Table 4: Demographic Features Conferring to The Patient's and Control's

DISCUSSION

Many aspects institute to play a part in the pathogenesis of aphthous stomatitis. It is suggested that the hematological parameters are the most important influences in recurrent aphthous stomatitis. So, in this analysis, hematological parameters were determined among these patients [13]. The present research discovered that 28.76 years is the mean age of patients with RAS, which means they are in their third decade of life. The same situation is reported in the literature. In this study, women are more affected by RAS than men unlike other studies [14]. This may be because women are more prone to endocrine fluctuations and gestation, and are extra predisposed to mental stress. In this analysis, according to other studies, most RAS appear to be of a minor type. We also found that most ulcers are found in non-keratinized mucosa as it is mobile and therefore more susceptible to injuries that predispose to ulcer development. These results are in line with the Islamabad Dental Hospital study. Hematological failure was observed more frequently in patients with RAS in comparison to the group of control [15]. In one study, it is reported that 59% of RAS patients with hematological deficiencies improved after using replacement treatment, while 29% exhibited significant development [16-17]. This study found lower levels of ferritin and hemoglobin in the RAS group in comparison to the control group. These conclusions are reinforced by additional analyses. Due to the decrease level of Hb, the oxygen carrying capacity is reduced in anemic patients, ultimately causing the oral mucosa to atrophy and thus ulcerate [18]. Similarly, iron is necessary for the correct growth and function of oral epithelial cells. It is also a necessary component of the cytochrome oxidase enzyme, which is required for normal epithelial maturation. When there is iron deficiency, levels of cytochrome oxidase fall and ultimately cause atrophy of epithelium, putting the oral mucosa at danger of ulceration. In addition, iron deficiency causes abnormal formation of vascular channels, ensuing in atrophy and reduced blood flow [19-20]. The shortcomings of the study, in the inadequate sample size and study design, i.e., a cross-sectional study, but believe that this may be useful in signifying a causal association between hematological parameters and RAS. In order to create new treatment options and prophylaxis in patients with RAS, a larger trial of prospective stomatitis studies should be carried out.

CONCLUSION

patients with RAS have higher levels of iron deficiency than the control group, it was concluded that iron deficit was linked to recurrent aphthous stomatitis.

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