

# Zinc Deficiency in Patients with Recurrent Aphthous Stomatitis: A Pilot Study

Rizwan Hamid<sup>1</sup>, Altaf Chalkoo<sup>2</sup>, Saima Ashawari<sup>1</sup>, Gazanfer Shah<sup>3</sup>, Ubaid Ullah Gul Salmani<sup>4</sup>

## ABSTRACT

**Introduction:** Recurrent aphthous stomatitis is a common disease of the oral mucosa, affecting 20 per cent of the general population. However, the aetiology of this disease is unknown. This study is done to compare zinc levels in recurrent aphthous stomatitis patients with those of a well-matched, healthy, control population.

**Material and Methods:** Twenty-five subjects with a history of minor recurrent aphthous stomatitis and 25 healthy subjects (control group) took part in the study. Patients aged between 20 and 40 years with recurrent oral aphthous ulcers less than or equal to 1 cm in diameter were included. Exclusion criteria were pregnancy and lactation, systemic disease (ulcerative colitis, Crohn's disease, Behçet's disease), any current medication (topical or systemic), dental surgery during the previous month and deficiencies in iron, folic acid or vitamin B1, B2, B6 or B12. Serum zinc levels were compared between patient and control groups.

**Results:** Zinc deficiency was detected in 29 per cent of recurrent aphthous stomatitis patients and in 5 per cent of controls. The mean serum zinc level in the patient group was significantly lower than in the control group.

**Conclusion:** These results suggest an association between zinc deficiency and recurrent aphthous stomatitis.

**Keywords:** Aphthous Stomatitis, Recurrent; Zinc

## INTRODUCTION

Recurrent aphthous stomatitis is a common disease of the oral mucosa, affecting 20 per cent of the general population.<sup>1</sup> This disease is characterised by recurrent, round, shallow oral ulcerations surrounded by inflammation, chiefly involving non-keratinised mucosa.<sup>2</sup> Recurrent aphthous stomatitis is classified into three types: minor, major and herpetiform aphthous ulcerations. The most common form of recurrent aphthous stomatitis is minor aphthous ulceration, followed by major and then herpetiform ulcerations.<sup>3</sup> The aetiology of recurrent aphthous stomatitis is unknown. These ulcerations may be indicative of underlying systemic diseases, ranging from vitamin deficiency to autoimmunity.<sup>4</sup> In addition, several studies have investigated the role of genetics, stress, haematinic deficiencies, vitamin deficiencies and autoimmunity in this disease.<sup>5-11</sup> Zinc is one of the most important trace elements in the human body. Endre et al. reported the case of a patient with zinc deficiency and cellular immune deficiency who had had recurrent aphthous ulcerations for six years and in whom these ulcers disappeared following zinc treatment.<sup>12</sup> Delayed wound healing in zinc deficiency indicates that zinc is important for the metabolic response to wound healing.<sup>13</sup> A multitude of

treatment modalities exist for the symptomatic management of aphthous ulcers from topical applications (including analgesics, anaesthetics, antiseptics, anti-inflammatory agents, steroids, sucralfate, tetracycline suspension, and silver nitrate) to dietary modifications. In recalcitrant cases or aphthae with systemic involvement, systemic treatment can be selected from a wide spectrum of immunomodulators that include dexamethasone, tacrolimus, azathioprine, cyclophosphamide, colchicine, prednisolone, cyclosporine A, interferon- $\alpha$ , tumour necrosis factor- $\alpha$  antagonists, antimetabolites, and alkylating agents. Despite many therapeutic options, no treatment is specific and definitive for RAS. We report a controlled pilot study comparing zinc levels in a group of patients with recurrent aphthous stomatitis and a well-matched healthy control group.

## MATERIAL AND METHODS

The study was conducted in the Department of Oral Medicine and Radiology for a period of 1 year. The sample size comprised of 50 subjects of either sex and between the ages of 20 and 40 years. Twenty-five patients with a history of recurrent aphthous stomatitis and 25 healthy people (control group) took part in the study. Diagnosis of RAS was made on the basis of history and clinical features. Patients who are physically healthy with history of duration of ulcers for more than 24 h but not exceeding 72 h with symptoms like pain and burning sensation secondary to oral aphthous ulcers and with the characteristic clinical features of recurrent minor oral aphthous ulcers were included in the study. A diagnosis of aphthous ulcer was made if it occurred on the non-keratinized mucosa as a small ( $\leq 1$  cm), round to ovoid ulcers, with circumscribed margins, having yellow or gray floors and are surrounded by erythematous halo (figure 1 and 2). Pregnant and lactating women, patients with any other coexisting oral mucosal diseases, systemic disease (ulcerative colitis, Crohn's disease, Behçet's disease), any medication (topical or systemic), dental surgery during the previous month and deficiencies in iron, folic acid

<sup>1</sup>Post Graduate Scholar, <sup>2</sup>Professor and Head, Department of Oral Medicine and Radiology, <sup>3</sup>Post Graduate, Scholar, Department of Oral Medicine and Radiology, <sup>4</sup>Post Graduate Scholar, Department of Periodontics, GDC, <sup>5</sup>Senior Resident, GMC, Srinagar, Kashmir

**Corresponding author:** Dr. Rizwan Hamid, Government Dental College and Hospital, Srinagar -190010, Kashmir

**How to cite this article:** Rizwan Hamid, Altaf Chalkoo, Saima Ashawari, Gazanfer Shah, Ubaid Ullah Gul Salmani. Zinc deficiency in patients with recurrent aphthous stomatitis: a pilot study. International Journal of Contemporary Medical Research 2017;4(12):11-13.



**Figure-1:** Aphthous ulcer involving labial mucosa



**Figure-2:** Aphthous ulcer on buccal mucosa

or vitamin B1, B2, B6 or B12, end stage renal disease, or those taking any other medications for RAS were excluded from the study. Ethical committee approval was obtained and the study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants. Serum zinc levels were measured using absorption spectrophotometry. The accepted normal serum zinc level is 95–130 µg/dl. Serum zinc levels in patients were compared with those of the control group.

### STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 13.0 software. The distribution of continuous variables was tested using the Kolmogorov–Smirnov test. The chi-square test was used for comparisons between categorical variables, and the Mann–Whitney U test was used to compare medians between the groups. Statistical significance was set at a p value greater than 0.05.

### RESULTS

The mean age in the recurrent aphthous stomatitis and control groups was 31.6± 7.28 and 32.08± 7.46, respectively. Fifty-five per cent of the RAS group and 45 per cent of the control group were females. The groups were similar in terms of age ( $p=0.854$ ) and gender ( $p=0.777$ ).

Twenty-eight per cent of the patient group and 4 per cent of the control group had serum zinc levels lower than 95 mg/dl. The mean serum zinc levels in the recurrent aphthous stomatitis and control groups were 99.4±18.08 mg/dl (range 65–128) and 115.15± 11.19 mg/dl (range 79–128), respectively. The serum zinc level of recurrent aphthous

stomatitis patients was significantly lower than that in the control group ( $p=0.001$ ).

### DISCUSSION

Zinc is the second most abundant trace metal in the human body, and it is present in all living cells and body secretions.<sup>14</sup> Zinc deficiency is reported to produce marked effects on virtually all components of the immune system. Although not considered to be involved in the immune response, mucosal barrier immunity (i.e. skin acting as a barrier to prevent penetration of organisms) can be affected by the nutritional status of an individual.<sup>15</sup> In a study by Orbak et al., oral aphthous ulcers were seen in rats fed a zinc-deficient diet.<sup>16</sup> These authors reported zinc deficiency to be a potential risk factor for oral and periodontal diseases. Several studies have investigated the efficacy of zinc treatment for recurrent aphthous stomatitis, with contradictory results. Orbak et al. reported that 42.5 per cent of the recurrent aphthous stomatitis patients in their study had lower than normal serum zinc levels. They recommended zinc therapy for recurrent aphthous stomatitis because the aphthous ulcers were reduced in size and did not recur in the zinc-treated group.<sup>15</sup> Although most reports recommend zinc treatment for recurrent aphthous stomatitis, Wray et al. failed to confirm the beneficial effects of zinc seen in previous studies.<sup>16–18</sup> In this controlled study, zinc deficiency was detected in 28 per cent of recurrent aphthous stomatitis patients and 4 per cent of controls. The mean serum zinc level for the recurrent aphthous stomatitis group was significantly lower than that of the control group. However, because it is a pilot study, one limitation was the low number of enrolled patients. It is therefore recommended that larger, more detailed studies should be done to obtain more definitive data.

### CONCLUSION

Our data suggest an association exists between zinc deficiency and recurrent aphthous stomatitis. Therefore, zinc deficiency must be considered a possible aetiological factor for RAS.

### REFERENCES

1. Shulman JD. Prevalence of oral mucosal lesions in children and youths in the USA. *Int J Paediatr Dent* 2005;15:89–97.
2. Casiglia JM. Recurrent aphthous stomatitis: etiology, diagnosis, and treatment. *Gen Dent* 2002;50:157–66.
3. Bagan JV, Sanchis JM, Milian MA. Recurrent aphthous stomatitis. A study of the clinical characteristics of lesions in 93 cases. *J Oral Pathol Med* 1991;20:395–7.
4. Greenberg MS, Pinto A. Etiology and Management of Recurrent Aphthous Stomatitis. *Curr Infect Dis Rep* 2003;5:194–8.
5. Kozlak ST, Walsh SJ, Lalla RV. Reduced dietary intake of vitamin B12 and folate in patients with recurrent aphthous stomatitis. *J Oral Pathol Med* 2010;39:420–3.
6. Compilato D, Carroccio A, Calvino F, Di Fede G, Campisi G. Haematological deficiencies in patients with recurrent aphthosis. *J Eur Acad Dermatol Venereol* 2010;24:667–73.

7. Burgan SZ, Sawair FA, Amarin ZO. Hematologic status in patients with recurrent aphthous stomatitis in Jordan. *Saudi Med J* 2006;27:381–4.
8. Thongprasom K, Youngnak P, Aneksuk V. Hematologic abnormalities in recurrent oral ulceration. *Southeast Asian J Trop Med Public Health* 2002;33:872–7.
9. Piskin S, Sayan C, Durukan N, Senol M. Serum iron, ferritin, folic acid, and vitamin B12 levels in recurrent aphthous stomatitis. *J Eur Acad Dermatol Venereol* 2002;16:66–7.
10. Goldstein BH. Autoimmunity and recurrent aphthous ulcers. *Penn Dent J (Phila)* 1969;72:26–31.
11. Lehner T. Autoimmunity in oral diseases, with special reference to recurrent oral ulceration. *Proc R Soc Med* 1968;61:515–24.
12. Endre L. Recurrent aphthous ulceration with zinc deficiency and cellular immune deficiency. *Oral Surg Oral Med Oral Pathol* 1991;72:559–61.
13. Hallmans G. Local absorption of zinc from wounds treated with various zinc-compounds. *Acta Derm Venereol* 1979;58:251–4.
14. Lansdown ABG. Zinc in the healing wound. *Lancet* 1996;347: 706–7.
15. Keen CL. Zinc deficiency and immune function. *Annu Rev Nutr* 1990;10:415–31.
16. Orbak R, Kara C, Ozbek E, Tezel A, Demir T. Effects of zinc deficiency on oral and periodontal diseases in rats. *J Periodontal Res* 2007;42:138–43.
17. Orbak R, Cicek Y, Tezel A, Dogru Y. Effects of zinc treatment in patients with recurrent aphthous stomatitis. *Dent Mater J* 2003;22:21–9.
18. Merchant HW, Gangarosa LP, Glassman AB, Sobel RE. Zinc sulfate supplementation for treatment of recurring oral ulcers. *South Med J* 1977;70:559–61.
19. Sharquie KE, Najim RA, Al-Hayani RK, Al-Nuaimy AA, Maroof DM. The therapeutic and prophylactic role of oral zinc sulfate in management of recurrent aphthous stomatitis (RAS) in comparison with dapsone. *Saudi Med J* 2008;29:734–8.
20. Wray D. A double-blind trial of systemic zinc sulfate in recurrent aphthous stomatitis. *Oral Surg Oral Med Oral Pathol* 1982;53: 469–72.

**Source of Support:** Nil; **Conflict of Interest:** None

**Submitted:** 07-12-2017; **Accepted:** 03-01-2018; **Published:** 13-01-2018