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Review Article **Oral Surgery**

The Reported Oral Manifestations of COVID 19 Viral infection: A Review Article

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Abstract

The new SARS-CoV-2 virus has become a worldwide emergency. It is recognized as a multiorgan disease and post-acute sequalae are seen in many systems. Many oral symptoms have been reported in relation to COVID-19. Cause- effect relationship between coronavirus and the appearance of such oral lesions still cannot be established. Immunosuppression state of positive cases could explain appearance of oral lesions. Oral hygiene is an aspect that should not be left aside, and it is of great importance to encourage the patient to reinforce hygiene techniques.

Keywords: Outbreak, Covid-19, SARS-CoV-2, Dysgeusia, Chemesthesis, immunosuppression, Oral lesions.

INTRODUCTION

A global crisis had emerged with the outbreak of novel coronavirus SARS-CoV-2 challenging the healthcare systems worldwide [1]. Coronaviruses are a family of viruses that were first described in 1960, characterized by having a corona-like structure formed by the spike proteins. In 2019, SARS-CoV-2 was discovered as a new type of coronavirus, generating the coronavirus disease 2019 (COVID-19) that is responsible of the current pandemic [2, 3].

Coronavirus comprises a single plus strand of RNA (+ssRNA). SARS-CoC-2 is a β-CoV that mainly affects respiratory, gastrointestinal, and central nervus system of humans and mammals; that is transmitted through respiratory droplets, aerosols, contact and fomites [4].

The most common clinical symptoms are fever, headache, sore throat, dyspnea, dry cough, abdominal pain vomiting and diarrhea [5]. Severe cases might develop pneumonia; sever acute respiratory syndrome, and kidney failure. That is all life-threatening conditions [6, 7]. Patients affected with SARS-CoV-2 are mostly develops moderate symptoms (80%), while those who display severe disease symptoms are 20 %; of which 5% may become critically ill [8].

It has been proposed that the oral cavity might be a viral reservoir as the gingival sulcus is a well-established niche where inflammatory enzymes and molecules accumulate and promote the colonization of microorganisms. The oral cavity is one of the entry routs of the virus, as transmission could be directed through fomites or droplets of saliva (generated while talking, coughing or sneezing) [9].

Within the clinical manifestations that are generated after infection by SARS-CoV-2, oral cavity lesions have been also described; and the aim of this review is to go through those reported oral manifestations and lesions related to the SARS-CoV-2 infection.

Oral Manifestations of COVID-19 Infection

Various manifestations have been reported in the literature related to COVID-19 infection.

Gustatory Impairment

The perception of flavors is complex and involves the senses of taste and smell as well as chemesthesis. Chemesthesis contributes to perception of certain food characteristics, such as spiciness or cold, through sensitive afferents of trigeminal nerve [10]. Dos Santos *et al.*, (2020) systematic review reported that gustatory impairment was the most comment oral manifestation, with a prevalence of 45% [11]. It was

further described as 38% for dysgeusia, 35% for hypogeusia, and a 24% of ageusia. Orilisi G. *et al.*, (2021) systematic review included these alterations as functional disorders. Their systematic review suggested that these alterations could be related directly to SARS-CoV-2 and could be considered as early manifestation of COVID-19 infection [12]. The exact pathogenesis is still not known but had been related to angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in abundance on the respiratory epithelium and oral mucosa specially the tongue [13]. Farid H. *et al.*, (2021) discussed different proposed mechanisms of taste alteration in COVID-19 infection. It was classified as: Inflammatory response, Neurological response and Zinc Imbalance [11]. Figure 1 shows the proposed mechanisms for taste alteration in COVID-19 [11].

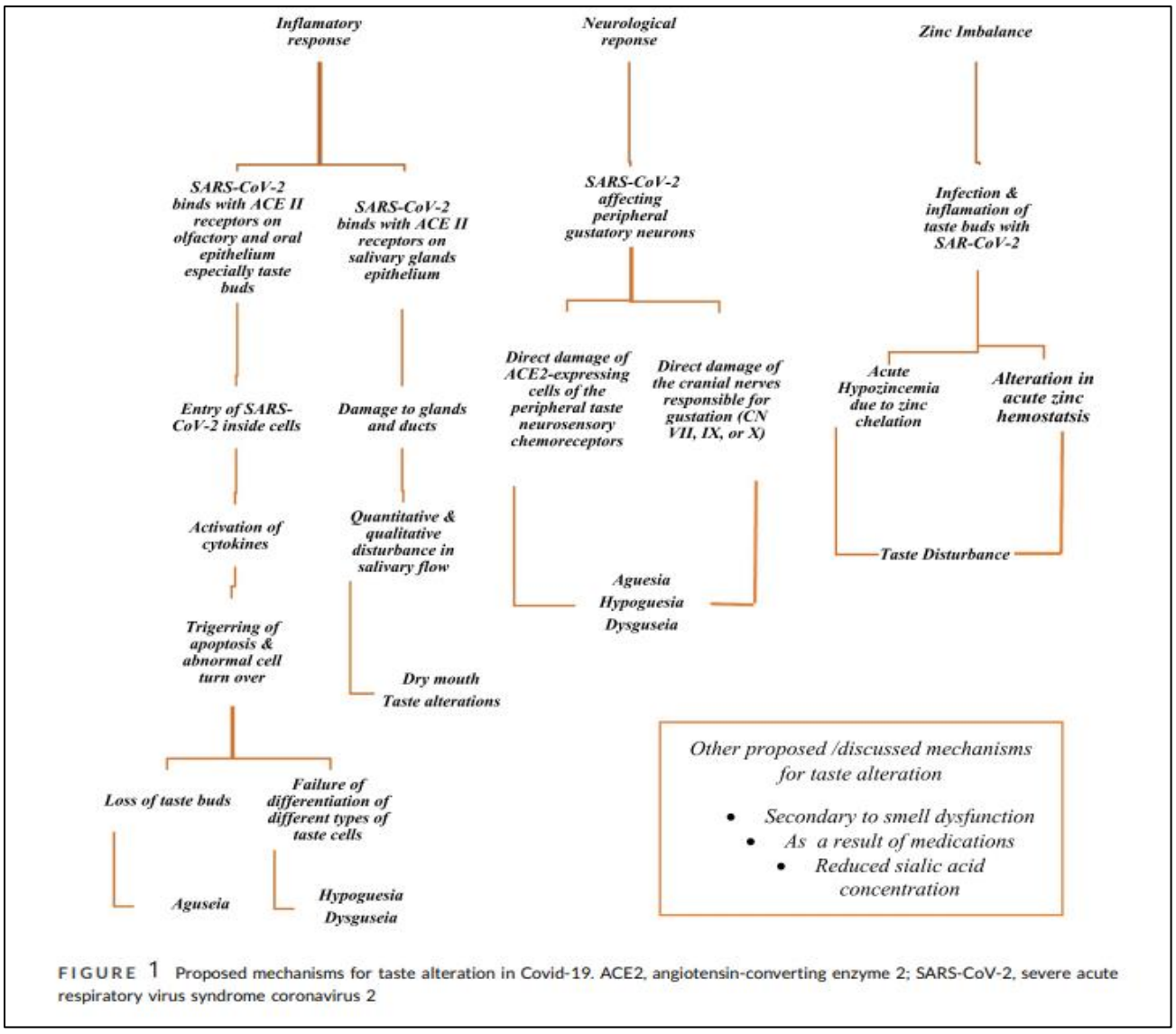

FIGURE 1 Proposed mechanisms for taste alteration in Covid-19. ACE2, angiotensin-converting enzyme 2; SARS-CoV-2, severe acute respiratory virus syndrome coronavirus 2

Lozada-Nur *et al.*, (2020) proposed that dysgeusia (with or without olfactory symptoms) had been reported as an early or lone symptoms of COVID-19 before involvement of the lungs or other organs. They hypothesized that dysgeusia results from alterations in localized cellular zinc homeostasis in the oral gustatory cells due to the immune responses to SARS-CoV-2 viral replication, with or without hypozincemia [14].

Other Functional Disorders

Masticatory muscle weakness, salivary gland ectasia, TMJ abnormalities, and facial tingling were reported [15]. It was suggested that salivary gland ectasia reflected the hyperinflammatory response to SARS-CoV-2, as shown by the significant relationship with C-reactive protein and lactate dehydrogenase levels at hospital admissions and antibiotic use during acute disease [12]. Early reports in the pandemics showed a good number of PCR Positive of COVID-19 patients presenting with dry mouth symptoms [15, 16]. Halitosis, tongue and masticatory muscle pain and swelling, geographical tongue, hyperplasia of papilla associated with taste changes and macroglossia were reported with fatigue and other major symptoms of COVID-19 [16-18]. Muthyam A, *et al.*, (2022)

observational study showed that xerostomia was the commonest symptom (44%) in their COVID-19 positive patients during and after the disease illness. Swallowing difficulty (16%), chewing problems (7%), and burning sensation (4%) were reported also [19].

Oral Mucosal lesions

Mucosal lesions that are reported in COVID-19 include ulcers, erosions, plaque-like lesions, reactivation of herpes simplex virus 1 (HSV1) and geographic tongue [11].

Ulcers and erosions are of the most common oral lesions associated with COVID-19 confirmed or suspected patients [20-22]. Reports showed that ulcerative and erosive lesions appear as painful lesions with irregular borders. Tongue (dorsum and lateral borders) is the most reported site of these ulcers, followed by hard palate and buccal mucosa [11]. Muthyam *et al.*, reported oral ulcerations in 10% of their study pool [19] De Medeiros *et al.*, (2021) concluded that ulcerative and erosive lesions were the most common orofacial manifestation of COVID-19 before and during hospitalization [23]. Gabusi A, *et al.*, (2021) suggested that those ulcerative and erosive lesions, appeared a few days after the onset of the respiratory symptoms and worsened during hospitalization, due to persistent immunological impairment, and lesions did not heal after SARS-CoV-2 eradication [24].

Aphthous-like lesions were also reported. These lesions are probably appearing due to the distribution of ACE2 receptor on the oral mucosa, however, one case report had reported a patient with minor aphthous ulcer which was diagnosed with Sweet syndrome related to COVID-19 [25, 26] Taskin B *et al.*, (2020) reported a 61-year-old-female with a positive PCR of COVID 19, presented with several erythematous nodules on scalp, trunk, and extremities and minor aphthous ulcers on her hard palate and buccal mucosa. Skin biopsy showed diffuse neutrophilic infiltration in the upper dermis with granulomatous infiltration in the lower dermis and subcutaneous area that was compatible with erythema nodosum-like Sweet syndrome [32]. Stress and immunosuppression secondary to COVID-19 could be other possible cause of such lesions [27] Aphthous like lesions without necrosis were observed in younger patients with mild symptoms, whilst those with necrosis and hemorrhagic crusts were observed more frequently in older patients with immunosuppression and severe infection. Healing of these lesions takes 5 to 15 days [28].

Different factors including drug eruption (to NSAID), vasculitis or thrombotic vasculopathy secondary to COVID-19 were suggested as causes for development of ulcerative and erosive lesions [29-31].

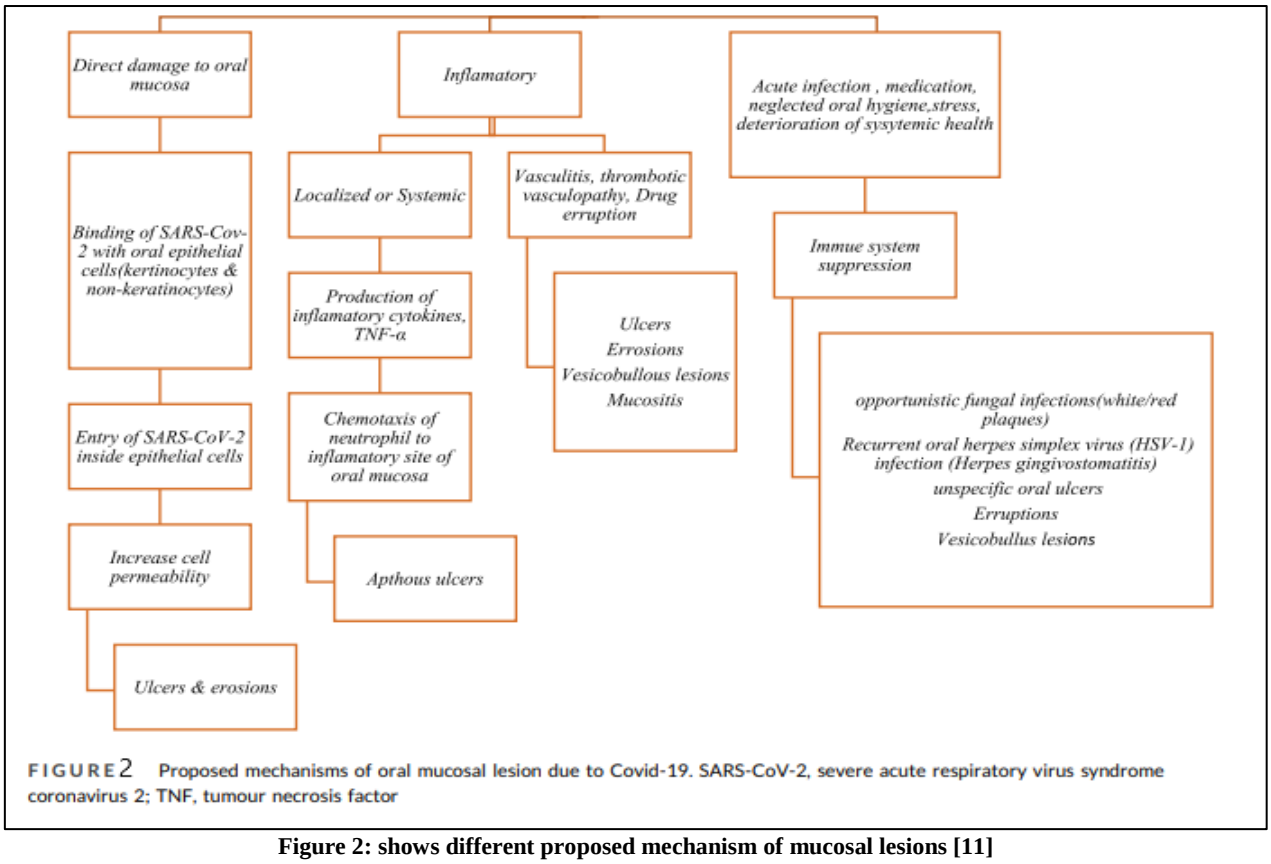

FIGURE 2 Proposed mechanisms of oral mucosal lesion due to Covid-19. SARS-CoV-2, severe acute respiratory virus syndrome coronavirus 2; TNF, tumour necrosis factor

Figure 2: shows different proposed mechanism of mucosal lesions [11]

Reactivation of Herpes Simplex 1 (HSV1) was also reported. Hadou *et al.,* (2020) reported this reactivation in one intubated patient in intensive care. Although cutaneous manifestations disappeared with median time of 48 hours, no information regarding resolution of Herpes Simplex provided [32]. One more study reported multiple yellow tiny ulcers resembling the late stages of herpetic recurrent infection, on the dorsum of the tongue along with geographic tongue in one positive case.

Iranmanesh B, *et al.,* (2020) review presented many reported other oral lesions, as: [5]

1. White/red plaques.
2. Erythema Multiforme like lesions.
3. Angina Bullosa like lesions.
4. Melkerson-Rosenthal Syndrome.
5. Kawasaki-like disease.
6. Necrotizing periodontal disease.
7. Vesicles and pustules.
8. Petechiae.
9. Nonspecific lesions (mucositis).
10. Post -inflammatory pigmentation.

John Wiley and Sons in 2020 presented 3 cases with positive RCR test of SARS-CoV-2 with oral manifestations. First case was for a 43-year-old female who developed fever, malaise, dysgeusia and anosmia, diarrhea, pneumonia and blood laboratories suggested a high risk of thrombosis. During her stay in the isolation, she reported aphthous like-lesions, burning sensations, and tongue de-papillation. Second case was for a 53-year-old male, tested RCR positive of SARS-CoV-2 and needed hospital admission. After discharge in his dental visit, he reported having burning mouth sensation, dysgeusia and anosmia, and cheilitis at the commissural fissures. These lesions were healed after using the prescribed triamcinolone acetonide, but the dysgeusia and anosmia persist. The third case was for a 78-year-old female tested positive for SARS-CoV-2 with hospital admission. Lesions were noticed on the tongue, palate and commissure compatible with pseudomembranous candidiasis. Patient was complaining of intense sensation of dryness in the mouth that she never had before [33].

DISCUSSION AND CONCLUSION

COVID-19 is recognized as a multiorgan disease and post-acute sequalae are seen in pulmonary, hematologic, cardiovascular and many other systemic involvements. Few incidences were reported of multisystem inflammatory syndrome in children. The pathophysiological mechanisms behind this could be related to any of these: direct viral toxicity, endothelial damage and microvascular injury, immune system, dysregulation and stimulation of a hyperinflammatory state, hypercoagulability with resultant in situ thrombosis, and macrothrombosis, and maladaptation of the angiotensin-converting enzyme 2 (ACE2) pathway [34].

With respect to oral symptoms, observational studies concluded that subjects who were aged and with comorbidities had high pre- and post- oral symptoms like xerostomia, chewing and swallowing difficulties, altered taste, and mouth ulcerations, and this could be linked it to compromised/ suppressed immune system and long-term pharmacotherapy in COVID-19 disease. Another cause for xerostomia may be dehydration and atrophy of acinar cells in salivary glands, which is common in viral infections leading to burning mouth and swallowing difficulty as secondary manifestation and intermittent ulcers may be the sign of vitamins deficiency. Production of antibodies against viral infections requires vitamins like vitamin A, B-complex, and E, whereas vitamin C and D act as immune boosters, so their requirement exceeds daily required dietary allowance (9RDA) values. Hence, COVID-19 patients need to continue these supplements during and after the disease along with a good diet [19, 35].

Oral hygiene is an aspect that should not be left aside, and it is of great importance to encourage the patient to reinforce hygiene techniques. Recent studies have shown that patients with poor oral hygiene increase the severity of COVID-19 symptoms. In contrast, in patients who maintained good oral hygiene, the symptoms of COVID-19 decreased significantly [36].

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