

A Narrative Review of the Oral Manifestations Encountered in COVID-19 Patients

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Abstract

This article aims to review the literature regarding oral manifestations found in patients with COVID-19 to aid dental professionals in diagnosing the condition if it presents in their dental offices.

A search was made in the international literature and all the articles, found in the English language, on the stated objectives, were included. Articles published between January 2020 to December 2022 were included. A review was done of the available literature.

The review was conducted on a total of 30 articles. The oral manifestations reported were dysgeusia, anosmia, dry mouth, herpetiform-like ulcers, erythematous lesion, ulceration of the palate, and oral blisters and aphthous-like ulcers.

Keywords: Oral, manifestations, COVID-19, aid dental professionals, diagnosing, review, ulceration.

INTRODUCTION

In December 2019, the coronavirus disease (COVID-19) emerged in Wuhan, China, and manifested itself as a severe acute respiratory syndrome. It was declared a public health emergency on 30th January 2020 by WHO and a pandemic on 11th March 2020 [1]. Globally, 760,360,956 confirmed cases and 6,873,477 deaths due to COVID-19 have been reported to WHO as of 11:31 am CET, 16 March 2023 [2]. Regions of the American subcontinent accounted for nearly half of the cases (48%) and more than half the mortalities (55%) with Argentina, Brazil, and the United States of America accounting for the greatest numbers of new cases and deaths in the region [3].

Based on the phylogenetic study of the viral genome, COVID-19 is also a part of the beta coronavirus family. It attaches to the angiotensin-converting enzyme 2 (ACE-2) receptor, which is the same entry receptor to which SARS-CoV attaches. The virus cannot attach to any cell which does not have an ACE2 receptor. The strong association between ACE2 and SARS-CoV protein suggests that humans with a greater expression of ACE-2 might be more prone to COVID-19 [4].

Transmission of the virus from human to human is by direct contact with secretions or eye, nasal and oral mucous membranes, and droplet transmission via aerosols formed by secretions. Aerosols may also be generated during clinical procedures leading to the spread of the virus [5].

The mean incubation period of the virus is 5.8 days but it may range from 2 to 14 days [6]. Cough and fever are

the most common presenting symptoms with 33-60% of patients presenting with chest X-ray abnormalities [7]. However, extrapulmonary manifestations of the disease have also been reported including myocardial injury, acute kidney injury [7], cutaneous manifestations [8], gastrointestinal symptoms, hepatocellular injury [9], and involvement of the oral cavity [10].

As an upsurge is being reported in COVID-19 cases in our community, it is pivotal to our role as dental and medical practitioners to be aware of the oral manifestations of this pandemic so that we can provide a timely diagnosis of the disease in our clinics. The objective review of this narrative review is to summarize the findings in various case reports and articles and aid the clinicians the better recognizing the condition if it presents itself.

METHODS

A literature search was performed on Google Scholar, PUBMED, and LIVIVO. The MESH terms used to perform the search were: (oral manifestations) and (COVID-19).

All relevant articles that could be found up till December 2022 were included in the study. All kinds of studies that reported oral manifestations of the disease were included in the study. We went through the abstracts of studies for which free full text was not available and studies in a language other than English were excluded.

During the first read in which we only read the title and abstracts of the studies, all duplicate articles were removed. All studies that were considered eligible for the review were shortlisted and were then gone through comprehensively.

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A manual search of the references of the articles selected from the initial search was also conducted to detect any other articles which were relevant to our study and could be included.

RESULTS

A total of 30 articles were reviewed. These included case series, case reports, letters to the editor, reviews, and systemic reviews. A summary of the different cases reported in these studies is prepared in **Table 1**.

Table 1 : A summary of the different cases reported.

Patient	Age	Gender	Clinical presentation and location	Symptoms	Presumptive clinical diagnosis
1.	41	F	Bulla Hard palate	Asymptomatic	Angina bullosa hemorrhagic-like lesion [11]
2.	51	F	Macule, papule Hard palate	Asymptomatic	Vascular Disorder [11]
3.	55	F	Bulla Tongue	Asymptomatic	Angina bullosa hemorrhagic-like lesion [11]
4.	41	M	Small macules Hard Palate	Burning sensation	Nonspecific mucositis [11]
5.	81	M	Aphthous like +necrosis Upper and lower lip, Tongue	Painful	Not registered [12]
6.	71	F	Aphthous like Upper and lower lip, Tongue	Painful	HSV-1 positive [12]
7.	83	F	Ulcer Tongue, hard palate	Painful	Not registered [12]
8.	72	M	Hemorrhagic ulcerations Upper & lower lip	Painful	HSV-1 positive [12]
9.	32	F	Multiple ulcers Tongue	Painful	Not registered [12]
10.	35	M	Ulcer Tonsillar pillar	Painful	Not registered [12]
11.	29	M	Ulcer Ventral tongue	Painful	Not registered [12]
12.	28	M	Aphthous like ulcers Labial mucosa	Painful	Not registered [12]
13.	45	F	Ulcer Dorsal side of the tongue	Painful then asymptomatic	Not registered [12]
14.	56	M	Herpetic like ulcers Palate	Painful	Not registered [13]
15.	58	M	Ulcers Palate	Painful	Not registered [13]
16.	65	F	Vesicles Lips	Painful	Not registered [13]
17.	43	F	Aphthous like lesions Tongue depapillation	Burning sensation	Not registered [14]
18.	53	M	Commissural fissures	Burning	Commissural cheilitis [14]
19.	78	F	Lesions Tongue, palate, commissure	Painful	Pseudomembranous candidiasis Angular cheilitis [14]
20.	56	M	Ulcers Palate	Painful	Herpetic recurrent stomatitis [15]

21.	58	M	Ulcers Palate	Painful	Not registered [15]
22.	65	F	Desquamative gingivitis and blisters on labial mucosa	Painful	Not registered [15]
23.	42	M	Ulcer Buccal mucosa	Painful	Not registered [16]
24.	63	M	Extensive ecchymosis	Not registered	Not registered [17]
25.	71	M	Ischemic mucosa and petechiae,	Not registered	Not registered [17]
26.	M	88	Chronic ulcer	Not registered	Not registered [17]
27.	F	39	Ischemic mucosa and chronic ulcer	Not registered	Not registered [17]
28.	M	64	Ischemic extensive ulcer	Not registered	Not registered [17]
29.	F	23	Vesiculobullous lesions and petechiae	Not registered	Not registered [17]
30.	M	31	Vesiculobullous lesions and petechiae	Not registered	Not registered [17]
31.	M	56	Multiple minor ulcers and petechiae	Not registered	Not registered [17]
32.	F	53	Reddish macule and chronic ulcer	Not registered	Not registered [17]
33.	M	45	Extensive areas of ischemic mucosa	Not registered	Not registered [17]
34.	M	69	Chronic ulcer and ecchymosis	Not registered	Not registered [17]
35.	M	72	Painful chronic ulcers and reddish macules	Not registered	Not registered [17]
36.	M	66	Petechiae	Not registered	Not registered [17]
37.	F	70	Reddish macules and chronic ulcer	Not registered	Not registered [17]

Taste Alterations

Disorders encompassing changes in and malfunction of the sense of taste and/or smell are known as chemosensory disorders. Taste disorders are one of the earliest and easily detectable symptoms that give the patient an insight into his contracting the disease and orient him towards self-isolation. This contributes to containing the quick spread of the disease, which is especially beneficial in areas that have reduced testing facilities [10]. In a meta-analysis performed on patients affected by COVID-19 to evaluate the incidence of gustatory, out of a total of 1390 COVID-19 patients recorded in 9 studies, 626 reported some degree of dysfunction of the gustatory system. Individual studies performed on gustatory dysfunction reported a prevalence ranging from 5.61% to 92.65% [18]. In an analysis by Biadsee *et al.* an impaired sense of taste was reported by 25.8% of the patients with an impaired sense of smell also reported in the absence of any other symptom [5]. Angiotensin-converting enzyme 2 (ACE2) has been reported to be the main host cell receptor of human coronaviruses, and it plays a critical role in the entry of the virus into the cell

to cause the infection [19]. A study by Xu *et al.* indicated that tongue epithelial cells and epithelial cells of the oral mucosa express ACE-2 and are highly enriched with this receptor [20]. This abundance of ACE2 receptors on the tongue mucosa is suspected to be a cause of taste alteration [21]. In 2022, a study was carried out to study the expression of Angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) in different oral tissues. The authors found strong expression of both ACE2 and TMPRSS2 in the squamous epithelia of buccal mucosa and tongue epithelia and concluded that SARS-CoV-2 can propagate in the supra-basal zone of the squamous epithelium of oral mucosa and disseminate into taste buds, parotid gland, trigeminal nerve and microvessel contributing to the reported oral manifestations [22].

Xerostomia

A systematic review was conducted to study the prevalence of xerostomia in patients infected with COVID-19 and the overall prevalence was found to be 43% [23]. Xerostomia in COVID-19 patients is pathogenically related to cellular viral protein expression, ACE2 system disturbance, inflammation of the salivary glands, cranial neuropathy, zinc deficiency, medications, and other comorbidities [24]. It has also been hypothesized that dysgeusia, which is a well-reported symptom of COVID-19, might be occurring secondary to xerostomia as an alteration in the composition and quantity of saliva may cause gustatory dysfunction [25].

Oral Mucosal Lesions

Aspecific erosions and ulcers, aphthous-like ulcers, erythema multiforme-like erosions, macules, petechiae, urticarial, chicken pox-like lesions, vesicles, and bullae have been reported in several studies [26-30]. The lesions are most commonly found in the tongue, palate, and lips [31]. In one study it was hypothesized that other factors such as stress during COVID due to social life restrictions, financial problems during the lockdown and lack of oral hygiene might also be contributing factors in oral mucosal lesions [30]. However, an immunohistochemical analysis for SARS-CoV-2 spike protein was performed on the lip biopsy of a woman with vesiculobullous lesions on her lower lip. The spike protein was found to be present in keratinocytes and inflammatory endothelial cells, and acinar and ductal cells of the minor salivary glands [29].

Periodontal Disease

It has been hypothesized that persistent inflammation in the severe form of COVID-19 may lead to periodontal

disease due to activation of the coagulation cascade and an increase in fibrinogen degradation [32]. A case report was published in which a 35-year-old female patient with all systemic symptoms of COVID-19 presented to the dental emergency with the complaint of intense gingival pain, bleeding, and halitosis. On examination, she was found to have necrotic interdental papillae, edematous and erythematous gingivae, and severe halitosis. Although COVID-19 was strongly suspected, testing could not be provided to her [33].

DISCUSSION

In summary, clinical and biological data reinforces that oral mucosa is a pioneer entry site for SARS-CoV-2 and that oral symptoms, including dry mouth and loss of taste/smell, might be one of the earliest symptoms of COVID-19 [34]. Given the meager number of reported studies, there is only limited data available on which taste disturbances are the most frequently reported oral manifestation. The prevalence of gustatory disorders globally in patients affected by COVID-19 is 45%. Oral manifestations reported in the different studies included desquamative gingivitis, necrotizing ulcerative periodontitis, concomitant herpes infection, white and erythematous plaques, small blisters, aphthous like ulcers, irregular ulcers, and petechiae. Buccal mucosa, tongue, gingiva, lips, and palate were most affected [10].

A review of the literature published in 2021, stated that impairment of taste, ulcers, petechiae, reactivation of plaque-like lesions, plaque-like lesions, desquamative gingivitis, and geographic tongue was among the most commonly reported symptoms. However, the review stated that a causal link has not been established between the reported symptoms and COVID-19 [35]. In a brief review conducted by Paradowska AM once again the most reported oral manifestation was dysgeusia while other findings in the oral cavity included oral pain, aphthous stomatitis, ulceration, increased incidence of other viral infections such as herpes simplex virus and varicella zoster virus and exacerbation of all autoimmune diseases which can be explained by a reduction in immunity [36].

A six-month update of a previously published living systematic review on the oral manifestations of COVID-19 published in 2021, reported that the incidence of xerostomia was 43% which is almost half the patients. The most prevalent clinical pattern of the oral mucosal lesions reported in the update was aphthous-like lesions followed by herpetic lesions. Geographic tongue, candidiasis, angular cheilitis, and parotitis were also reported with the tongue, lips and

palate is the most commonly affected sites [37]. In an observational study conducted in India in 2021, xerostomia was found to be the most prevalent symptom while ulceration, difficulty swallowing, bleeding gums, difficulty chewing, and burning sensation were the other symptoms reported by the participants [38]. A systematic review conducted by Fakhruddin *et al.* reported the mucocutaneous manifestations of COVID 19 which were found to be most prevalent on the palate, tongue, buccal mucosa, lips, and gingivae. The reported mucocutaneous lesions included blisters, papillary hyperplasia, ulcers, glossitis, mucositis, erosions, and macules. Those who fell severely ill and had poor oral hygiene were more likely to have ulcerations and necrotic gingiva while angina bullosa and petechiae were mostly observed as a result of side effects of COVID-19 therapy [39]. ACE 2 enzyme which is the main target of SARS-CoV, is present in periodontal sites and might be the reason for periodontal involvement [40]. Extensive ecchymosis, ischemic mucosa, chronic ulceration, petechiae, vesiculobullous lesions, and reddish macules were reported in a clinicopathologic study conducted by Ciro DS. The authors also recognized that the lesions were either caused by hemorrhage and/or ischemia or secondary to inflammation due to viral load [17]. A systematic review conducted in 2022 reported that prolonged intake of corticosteroids for the treatment of COVID-19 led to immunosuppression which increased the incidence of opportunistic infections in the oral cavity like aspergillosis and mucormycosis. Secondary manifestations such as enanthematous lesions were also reported due to poor oral hygiene and immunosuppression. Like previous studies, this review also reported that the most common oral manifestations were, loss of taste sensation, anosmia, and xerostomia [41]. An analytical study conducted in 2022 reported that non-specific solitary ulcers, candida-like lesions, and depapillation of the tongue were also found in addition to the most commonly reported symptoms of dysgeusia and xerostomia. The authors further noted that many of the COVID-19 infected patients had co-morbidities such as diabetes Mellitus which might be the reason for xerostomia seen in the patients, hence further work needs to be done to eliminate such confounding factors [42].

It is yet to be determined whether these findings are a result of SARS-COV2 or a result of the immunosuppression resulting from the infection making the patient infection-prone. It should be noted that the majority of patients reported in case studies were old-age patients

with other comorbidities resulting in immunosuppression. Clinical studies and biopsies of the lesions are needed to demonstrate a relationship between oral lesions and COVID-19.

CONCLUSION

There are several oral manifestations of COVID-19, however, they are underreported due to a lack of evaluation of the oral cavity in this subset of patients. Considering the high incidence of some oral manifestations such as xerostomia, all COVID patients must be screened for oral manifestations and proper care provided.

CONFLICT OF INTEREST

The author declare no conflict of interest.

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AUTHOR'S CONTRIBUTION

All the authors contributed equally to the publication of this article.

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