

REVIEW ARTICLE

COVID-19 from the perspective of dentists: A case report and brief review of more than 170 cases

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Abstract

A novel coronavirus which has appeared from China, has been circulating hastily around the world. We summarized the publications including oral manifestation of coronavirus disease 2019 (COVID-19) cases based on PubMed and Google Scholar data bases, and also present a case that highlights oral lesions 2 days prior to the first COVID-19 general symptoms. Two authors independently reviewed the papers, 17 studies of more than 170 confirmed cases between ages of 9 and 90 were included. The most common oral manifestation was dry mouth followed by dysgeusia and pseudomembranous fungal structure. Change in tongue sensation and ulceration, muscle pain during mastication, swelling in oral cavity, and herpetic lesions were other common symptoms. Associated symptoms, latency time, treatment, and prognosis have also been meticulously reviewed. We hope that careful clinical intraoral examination on all COVID-19 positive patients and equally on any patients who need dental care will pave the way for further studies.

KEYWORDS

coronavirus, COVID-19, oral examination, oral manifestations, review

1 | INTRODUCTION

A novel coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that triggers a new infectious respiratory disease, coronavirus disease 2019 (COVID-19) that has appeared from Wuhan, China, has been circulating hastily around the world. It has been declared as pandemic emergency by World Health Organization (WHO), on March 2020. Common clinical features of this virus infection include fever, cough, headache, diarrhea, fatigue, headache, and myalgia.¹ Two new symptoms, anosmia and ageusia, were also found to be widespread, according to the most recent reports.²

COVID-19 has an incubation time that ranges between 1 and 14 days. Early detection of symptoms is life-saving. Some of mucocutaneous manifestations of this viral infection can be helpful for the early diagnosis. Furthermore, recent reports discovered that loss of taste and smell may represent as the first and only manifestations of infection.³

An increasing number of literatures have been recently published sporadically on oral manifestations of COVID-19 patients,

suggesting that oral lesions could be a possible clinical characteristic of COVID-19. The epidemiologic significance of the oral manifestations remains uncertain and thus, in this brief review, we have tried to summarize the publications including oral manifestation of COVID-19 cases.

2 | METHODS

An electronic literature search was conducted on Medline (PubMed) and Google Scholar databases on October 2020 with the terms “((novel coronavirus) OR (Coronavirus disease 2019) OR (COVID-19) OR (SARS-CoV-2)) AND ((oral) OR (mucocutaneous) OR (manifestation) OR (mucositis)).” The time for publication was set to 2019 onwards. Two reviewers independently reviewed the articles. Case reports dealing with oral manifestations of COVID-19 were included. In addition, the patient of the case we report, provided written consent to publish the characteristics and picture of her case and the identity of the patient has been protected.

3 | CASE

A 56-years-old female with underlying health condition of hypertension and chronic sinusitis, reporting history of inverted papilloma lesion in the left maxillary sinus that was partially resected, presented with vesicles on lower lip mucosa. She was examined and followed up via video consultation and asked to send a picture of the lower lip mucosa. History of the oral manifestation revealed 2 days of dry mouth, acute dysgeusia, mild pain, and burning sensation in lower lip mucosa. She reported appearance of two vesicles in the same region and simultaneous systemic symptoms of COVID-19 after 2 days (Figure 1). Our subject systemic symptoms included: high fever, fatigue, and lack of appetite. She did not develop any cutaneous lesion. Polymerase chain reacted (PCR) assay resulted positive for COVID-19, and azithromycin, levofloxacin, montelukast, naproxen, and acetaminophen were immediately prescribed.

The patient reported previous history of herpetic infections. Although, recurrent HSV infections are less common within the mouth and typically involve the keratinized mucosa, such as gingiva and palate, they can occur on any mucosal site in immunocompromised patients.⁴ We proposed herpes PCR testing, however, but due to mild symptoms and financial issues, the patient refused to perform. After 7 days, oral lesions were healed and systemic symptoms regressed on day 14.

4 | RESULTS

Overall, 17 studies were included in the final analysis. More than 170 COVID-19 positive Patients developed oral manifestations, ranging from 9 to 90 years of age (Table 1). All the patients, with the exception of 24,⁵⁻⁷ presented with systemic symptoms such as fever, cough, weakness, shortness of breath, diarrhea, and dysgeusia.



FIGURE 1 The view of lower lip labial mucosa showing vesicles in the area

The most common oral manifestation was dry mouth, which was reported in 75 of the cases. 71 patients reported changes in taste sensation and a strong association with burning mouth and taste change was found.^{3,5,6,8-10} 67 patients developed pseudomembranous structure, white plaque or hairy tongue on the intraoral mucosa, with or without other symptoms like dry mouth and glossalgia, 11 of which on the tongue were identified by questionnaire, the etiology remained unknown, while in 55 other cases specimens were taken from the oral mucosa and fungal infection was confirmed, with *Candida albicans* as the most prevalent strain.^{3,5,8,11-13} 48 patients reported a change in their tongue sensation, 28 of whom suffered from painful ulcers in the area, 15 patients suffered from muscle pain during mastication with a mean VAS score of 3.8, and 10 patients indicated swelling in the oral cavity: four in the palate, four in the tongue, and two in the gums. Change in tongue sensation strongly correlated with swollen palate and plaque-like changes in the tongue.^{3,7,14,15}

Sporadic reports showed recurrent herpes simplex virus lesions in six cases: four on the hard palate, and two on the tongue.^{6,12,13,16} Four patients developed erythema multiforme-like eruptions, three of whom had palatal macules and petechiae and one of whom showed three blisters in the inner lip mucosa.^{6,17} Erosions, erythema, ulcers, necrotizing ulcerative periodontitis, and aphthous like lesions were also observed in single cases.^{5,8-10,14,15,18-21}

The details on the onset of the oral manifestation was recorded for the 95 of the cases, with a mean of 7.21 days after systemic symptoms, varying from -10 to 42 days. In 42 cases, oral lesions resolved spontaneously or with some basic treatment within 3 weeks, except gingival hyperpigmentation in one patient, detailed information was not documented in other cases.

5 | DISCUSSION

Several reports and systematic reviews investigated cutaneous lesions due to COVID-19. Sousa et al²² recently, highlighted the need for further epidemiological research on oral manifestation of COVID-19. As the virus has become a pandemic, there has been continuous production of additional data. We therefore conducted a study to briefly review papers on oral and mucosal symptoms of patients suspected or diagnosed with COVID-19.

The main impact of COVID-19 on oral mucosa seems to be multifactorial, the important role of the immune system is inevitable. Medicine, the nature of the virus and even stress could put the control of the Immune system at risk. A certain state of immune dysregulation may lead to opportunistic infections, drug eruptions, or the risk of exacerbating existing autoimmune conditions via cytokine storm. Moreover, some researchers assume that oral lesions contributed to COVID-19 are based on the assumption of an Inflammatory response that induces vascular inflammation.¹⁴ Nevertheless, we also noticed that oral manifestations may potentially be other overlapping diseases.

Smell and taste changes are early indicators of the COVID-19 pandemic and are effective in political decision making. While dry

TABLE 1 Articles on oral manifestations of Coronavirus disease 2019 (COVID-19)

Author and year	Nr of Cases	COVID-19 PCR test	Age and gender	COVID-19 manifestations	Cutaneous lesions	Treatment for COVID-19	Oral manifestation	Location of oral manifestation	Days after COVID-19 diagnosis	Treatment of oral symptoms	Healing of oral symptoms
Patel et al, 2020	1	Not provided	35, Female	CGS	None	None	Necrotizing gingivitis	Labial interdental papillae	3 days	Metronidazole, Chlorhexidine	5 days
Badsee et al, 2020	128	Positive	Ages NR 55%Female	CGS (especially cough and impaired sense of smell and taste)	NR	NR	Dry mouth (n = 72) Dysgeusia (n = 67) Change in sensation in the tongue (n = 20) Masticatory muscle pain (n = 15) Swelling of oral cavity (n = 10) Plaque-like changes in the tongue (n = 9) Oral bleeding (n = 6)	Tongue, Palate, Gums	NR	NR	NR
Ansari et al, 2020	2	Positive	56, Female75, Male	CGS	None	Antibiotics (Azithromycin) Supportive treatment Anti-viral(Remdesivir [n = 1])	Painful ulcers with irregular margins (Recurrent herpes simplex)	Tongue, Hard palate	5 days 7 days	Diphenhydramine, Dexamethasone, Tetracycline and Lidocaine.	7 days
Soares et al, 2020	1	Positive	42, Male	CGS	Present	Anti-inflammatory drugs (Dexamethasone, Dipyron)	Painful ulcer Multiple reddish macules	Tongue, Hard palate, Buccal mucosa, Lips	NR	None	3 weeks
Chaux-Bodard et al, 2020	1	Positive	45, Female	CGS (mild stage)	Present	None	Irregular ulcer (it was painful during 24 h, followed by 24 h of erythematous macula, which evolved into asymptomatic ulcer)	Tongue	-8 days	NR	10 days
Rodriguez et al, 2020	3	Positive	43, 78, Females 53, Male	CGS	None	NR	Dry mouth Apthous-like lesions Tongue depapillation Pseudomembranous candidiasis Commissural cheilitis (n = 2) Burning sensation (n = 2)	Tongue, Palate, Lips	since hospitalization, 7 days 42 days	Triamcinolone acetone, Neomycin, Nystatin	10 days, not reported, 15 days
dos Santos et al, 2020	1	Positive	67, Male	CGS	None	Hydroxychloroquine Antibiotics (Ceftriaxone, Azithromycin)	Ulcers (Recurrent herpes simplex) white plaque (Saccharomyces cerevisiae)	Tongue	24 days	Fluconazole, Nystatin, Chlorhexidine, and Hydrogen peroxide 1%	14 days

(Continues)

TABLE 1 (Continued)

Author and year	Nr of Cases	COVID-19 PCR test	Age and gender	COVID-19 manifestations	Cutaneous lesions	Treatment for COVID-19	Oral manifestation	Location of oral manifestation	Days after COVID-19 diagnosis	Treatment of oral symptoms	Healing of oral symptoms
Tomo et al, 2020	1	Positive	37, Female	CGS	None	Anti-inflammatory drugs (Dexamethasone, Dipyrrone)	Erythema and depapillation Dry mouth Dysgeusia	Tongue	9 days	Chlorhexidine	1,4 days
Martín Carreras-Presas et al, 2020	3	Suspicious (n = 2) Positive (n = 1)	65, Female 58, Males	CGS (One patient has no symptoms except the mucosal manifestation)	Present (n = 1)	Hydroxychloroquine Antibiotics Anti-inflammatory drugs (Dexamethasone) Antifungal Anti-viral (Lopinavir, Ritonavir)	Painful ulcers (Recurrent herpes simplex (n = 2)) Blisters (n = 1) Desquamative gingivitis (n = 1) Pain on tongue (n = 1)	Hard palate, Labial mucosa	Single manifestation (n = 1) Since the beginning (n = 1) 2 days (n = 1)	Hyaluronic acid, Chlorhexidine, Prednisolone and Valaciclovir	10 days, 7 days, 3 days
Aghazadeh et al, 2020	1	Positive	9, Female	CGS	Present	Supportive treatment	Vesicles and erosions	Lips, Tongue, Buccal mucosa	NR	None	7 days
Corchuelo et al, 2020	1	Positive	40, Female	Lymphadenopathy	Present	Antibiotics (Azithromycin) Anti-inflammatory drugs (Ibuprofen) Vitamin D2	Canker sores (<i>Candida albicans</i>) Apthous-like lesion Gingival hyperpigmentation	Tongue, Lips, Gingiva	3 weeks	Nystatin, Chlorhexidine	20 days, pigmentation not faded
Ciccarese et al, 2020	1	Positive	19, Female	CGS	Present	NR	Erosions and Ulcerations Petechiae	Lips, Palate, Gingiva	5 days	Palliative	10 days
Cebeci Kahraman et al, 2020	1	Positive	51, Male	CGS	None	Antibiotics (Clarithromycin)	Erythema, Petechiae, and Pustules	Oropharynx, Palate	10 days	None	A few days!
Sakaidaa et al, 2020	1	Positive	52, Female	CGS	Present	Antibiotics (Ampicillin/Sulbactam, Clarithromycin)	Erosions	Lips, Buccal mucosa	-10 days	Oral prednisolone	NR
Salehi et al, 2020	53	Positive	Mean age = 63 (age ≥ 50:80%) Female 57%	CGS (especially respiratory distress and fever)	NR	Anti-viral Antibiotics Anti-inflammatory drugs (Corticosteroids)	Pseudomembranous structures, white plaques	NR	Mean = 8 days	Fluconazole, Nystatin	NR
Galvina et al, 2020	1	Positive	40, Female	CGS (mild stage)	NR	NR	Recurrent herpes simplex Hairy tongue white lesions	Hard palate, Tongue	7 days	Acyclovir, Antiseptic, Nystatin, Panthenol, Local anesthetic	3 weeks

TABLE 1 (Continued)

Author and year	Nr of Cases	COVID-19 PCR test	Age and gender	COVID-19 manifestations	Cutaneous lesions	Treatment for COVID-19	Oral manifestation	Location of oral manifestation	Days after COVID-19 diagnosis	Treatment of oral symptoms	Healing of oral symptoms
Riad et al, 2020	26	Positive	Mean age = 37 Female 56%	CGS (n = 4) 22 patients had no symptom except the mucosal manifestation	NR	NR	Ageusia (n = 3) Painful tongue ulcers (all cases)	Tongue (dorsum and side)	Mean = 4 days after PCR test (ranging from 0–5 days)	Oral paracetamol, Chlorhexidine	7 days (n = 21) 14 days (n = 5)
Our case	1	Positive	56, Female	CGS	None	Antibiotics (Azithromycin, Levofloxacin) Anti-inflammatory and antiasmatic drugs (Montelukast, Naproxen and Acetaminophen)	Vesicles Dry mouth Dysgesia	Lower lip mucosa	–2 days	None	7 days

Abbreviations: CGS, common general symptoms (including: fever, cough, headache, diarrhea, or myalgia); NR, not reported.

mouth was the most prevalent oral symptom,^{3,8,9} invasion of the salivary ducts has been confirmed by animal model experiments as the first attack of the virus,²³ Provided that it may be the potential reason of acute sialadenitis and related symptoms including discomfort, swelling, pain, or secretory salivary glands dysfunction. Nonetheless, it is possible to cause chronic sialadenitis after recovery. Several studies have shown the possibility of an outbreak of opportunistic infections,^{3,5,8,12} especially, fungal co-infections. Accordingly, some risk factors may play a role, including lymphocytopenia, intensive care unit admission, invasive or non-invasive ventilation, corticosteroid, and broad-spectrum antibiotic usage, growing age, or having immunocompromised condition. Exanthematic lesions may be linked to viral etiology, for instance, hand-foot-and-mouth disease, herpetic recurrent stomatitis (affecting keratinized tissue), and erythema multiforme (affecting both keratinized and non-keratinized tissue) that may be triggered by direct virus invasion.

Various care and treatment protocols and guidelines existed among countries, which caused challenge of data analysis. The most prominent treatment approach for COVID-19 was the combination of anti-viral therapy with antibiotics. In addition, analgesics, antipyretics, and antitussives could be applied as Supportive treatment. Corticosteroids and antihistamines were used for anti-inflammation effects. Some case reports implied medication containing antiseptics mouthwash, corticosteroids, and palliative drugs for mucosal symptoms. Antifungal or antibacterial therapy was also prescribed, where the etiology was relevant. However, as in our case, some researchers refused to consider any therapy for mild or asymptomatic patients due to the nature of spontaneous recovery. Drug eruption can occur within the latency period.²⁰ Although its pathogenesis is multifactorial, it could be correlated with exacerbated cytokine storm induced inflammation along with thrombocytopenia caused by a direct viral attack to bone marrow, and the use of medicines may further reduce the platelet count.

A limitation of our research is that we were not able to quantitatively analyze oral manifestations and disease patterns due to vast amounts of unprovided and incomparable data.

6 | CONCLUSION

In conclusion, our review outlined the clinical characteristics of oral manifestations in patients with COVID-19 and their potential mechanisms. The oral symptoms often appeared after general symptoms such as fever and asthenia, but can still be the initial or only sign of COVID-19. Thus, a careful clinical intraoral examination must be performed on COVID-19 positive patients and equally on any patients who need dental care thoroughly and systematically to ensure that no parts are missing and to obtain further clinical data, which could pave the way for further studies.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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