

# Oral Cavity Manifestations in Coronavirus Disease 2019 Patients: A COVID Hospital-based Study

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## Abstract

**Background:** Coronavirus disease 2019 (COVID-19) is an acute respiratory disease caused by novel severe acute respiratory syndrome coronavirus 2. COVID-19 infection presents with mild flu-like symptoms to severe respiratory illness, even respiratory failure. Oral cavity lesions are currently documented in the COVID-19 infections, which increases the morbidity of the patients. **Objective:** The aim of this study is to evaluate the different types of the oral cavity lesions in COVID-19 patient, including its symptoms and signs. **Materials and Methods:** This is a prospective observational study. COVID-19 patients were evaluated for oral cavity manifestations. The age ranges from 18 years to 65 years. All these patients underwent detailed examinations of the oral cavity and oropharynx with the help of headlight, along with wearing personal protective equipment. **Results:** Fifty-six COVID-19 patients showed oral cavity manifestations during their treatment period. The most common clinical entity in this study was gustatory disturbance (26.78%), followed by oral mucositis (14.28%), glossitis (12.50%), and ulcers (8.92%) in the oral cavity of the COVID-19 patients. **Conclusion:** COVID-19 infection significantly affects the oral cavity and salivary glands. Clinicians should keep in mind different lesions in the oral cavity and taste disturbances of COVID-19 patients, which will help the early diagnosis, treatment and avoid the morbidity of the patient.

**Keywords:** Coronavirus disease 2019, dysgeusia, oral cavity, oral ulcer, severe acute respiratory syndrome coronavirus 2

## INTRODUCTION

Coronavirus disease 2019 (COVID-19) infection is a contagious disease that began in Wuhan, China, in early December 2019 and rapidly spread worldwide.<sup>[1]</sup> COVID-19 is an acute respiratory disease caused by the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The common clinical presentations of COVID-19 patients are fever, cough, myalgia, dyspnea, and anorexia.<sup>[2]</sup> The first entry point of the SARS-CoV-2 is the oral cavity before entering into the respiratory tract.<sup>[3]</sup> Currently, the SARS-CoV-2 virus has been detected in the saliva of the COVID-19 patient. It has been confirmed by reverse transcriptase-polymerase chain reaction (RT-PCR), which can be more sensitive than the nasopharyngeal test.<sup>[4]</sup> Furthermore, angiotensin-converting enzyme (ACE)-2 has been detected in the mucosa of the oral cavity and more densely on the dorsum of the tongue and salivary glands relative to the buccal mucosa and palates.<sup>[5]</sup> Certain factors of the patients aggravate the development

of oral cavity lesions, such as older age of the patient, severity of the COVID-19 infection, lack of oral hygiene, stress, opportunistic infection, underlying diabetes mellitus, immunosuppressive medication, immunocompromised disease, and trauma secondary to intubation.<sup>[6]</sup> Currently, there is a very smaller number of literature regarding oral manifestations in COVID-19 patients and these oral cavity lesions almost create more morbidities of the patients. There is a lack of robust epidemiological studies regarding oral manifestations of COVID-19 patients, which indicates that this clinical issue is neglected by patients and clinicians. Here,

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this study aims to evaluate the oral cavity manifestations in COVID-19 patients.

## MATERIALS AND METHODS

This is a prospective observational study conducted at a COVID hospital attached to a tertiary care teaching hospital done between March 2021 and February 2023. This study was approved by our Institutional Ethical Committee (ICE) with reference number IEC/SOA/IMS/22/12.02.2021. We included only adult patients who were diagnosed with COVID-19 positive, and confirmed with RT-PCR. Since it was not feasible to examine all the COVID-19-positive patients clinically, and so we only evaluated those patients who presented with oral cavity manifestations at the COVID hospital. The oral cavity manifestations were documented in patients, such as burning sensations, oral aphthous-like lesions, taste alteration, xerostomia, pain, mucositis/stomatitis [Figure 1], oral candidiasis [Figure 2], commissural cheilitis and tongue depapillation. COVID-19 patients who had an addiction to smoking, chewing pan, gutkha, and alcohol consumption were excluded from this study. We also excluded the patients who had oral lesions before the diagnosis of COVID-19 infection. The symptoms related to the oral cavity lesions were classified into four types. The first category was the gustatory manifestations such as loss of salt sensation, loss of sweetness, and altered food taste. The second category was the symptoms related to salivary gland manifestations such as dry mouth/hyposalivation, pain or swelling in the submandibular gland, pain or swelling in the parotid area, and difficulty in swallowing. The third category of the symptoms in the oral lesions were oral ulcers, redness of the tongue, spots in the mouth, ulcerative lesions of lips [Figure 3], bleeding from gum, and a burning sensation in the mouth. The fourth category of oral manifestations was related to the no symptoms of salivary glands and the oral cavity. The Statistical Package for the Social Science (SPSS) Statistics for Windows, version 20, was used for all statistical analyses (IBM-SPSS Inc., Chicago, IL, USA).

## RESULTS

In this prospective study, 56 (25.45%) patients presented with oral cavity lesions 220 COVID-19-positive patients. The age ranges of the COVID-19 patients who presented with oral manifestations were 18–65 years enrolled in this study. The mean age of the participants was 34.21 years. In this study, there were 34 males and 22 females with male-to-female ratio of 1.54:1. There were 22 (39.28%) patients in the age range of 18–30 years, 18 (32.14%) patients in the age range of 31–50 years and 16 (28.57%) patients in the age range of 51–65 years [Table 1]. All were under treatment at the COVID-19 hospital for COVID-19 infection. They developed oral lesions during their treatment period. Out of 56 patients, 15 (26.78%) presented with loss of taste sensation or dysgeusia, 8 (14.28%) were presented with oral mucositis, 7 (12.50%) presented with glossitis, 5 (8.92%) presented with aphthous

like ulcers, 5 (8.92%) patients presented with dry mouth, 4 (7.14%) patients presented with a burning sensation in the



**Figure 1:** Extensive oral mucositis in a COVID-19 patient. COVID-19: Coronavirus disease 2019



**Figure 2:** Oral cavity showing candidiasis lesions on the dorsum of the tongue in a COVID-19 patient. COVID-19: Coronavirus disease 2019



**Figure 3:** Ulcerative lesion on lips of a COVID-19 patient. COVID-19: Coronavirus disease 2019

mouth and 3 (5.35%) patients with gingival bleeding [Table 2]. All patients with oral manifestations were treated with proper oral hygiene and topical medications to relieve the oral symptoms. All oral manifestations were completely relieved after one 3 weeks to 1 month.

## DISCUSSION

The COVID-19 pandemic is currently evolving and associated with more complications. Currently, several COVID-19 patients are presenting with oral cavity manifestations during their treatment period. The exact etiology of the oral lesions in the COVID-19 patient is still unknown and seems multi-factorial.<sup>[7]</sup> The oral cavity lesions are directly or indirectly associated with SARS-CoV-2.<sup>[7]</sup> However, the direct involvement of SARS-CoV-2 in the development of oral cavity lesions or ulcers remains uncertain. Oral cavity manifestations may occur in COVID-19 patients due to hypersensitivity reactions by certain medications during the treatment of COVID-19 infection. In the case of COVID-19 infections, the cytokines storm and impaired or unregulated immune response may be associated with an increased chance of hypersensitive reactions in the oral cavity followed by ulcerative lesions.<sup>[8]</sup> Moreover, the situations such as stress and anxiety due to restrictions of social life during the COVID-19 pandemic may be the cause for the development of aphthoid ulcers or herpetic recurrences. There are certain drugs used for COVID-19 patients may cause hypersensitivity reactions in the oral cavity and

result in ulcerations or changes in the oral mucosa. At the beginning of the COVID-19 pandemic, it was thought that the absence of the oral lesion was a differentiating feature of the COVID-19 exanthema relative to other viral exanthemas. Currently, the SARS-CoV-2 virus has been found in saliva of the COVID-19 patients and it has been demonstrated that RT-PCR from saliva is more sensitive than samples from nasopharyngeal secretions. SARS-CoV-2 virus infects human cells through ACE 2 receptors, as ACE 2 acts as the primary host cell receptor for this virus.<sup>[9]</sup> SARS-CoV-2 virus binds to ACE 2 with the help of spike-like protein on its surface, whereas ACE2 serves as a cellular portal for entry of the virus which results in COVID-19 infection.<sup>[10]</sup> Therefore the organ which shows high expression of ACE2 can become the target for SARS-CoV-2 infection, and these organs are the lungs, salivary glands, and tongue.<sup>[11]</sup> The involvement of the salivary glands and tongue results in loss of taste sensation and ulcers in the oral cavity because of the destruction of the keratinocytes and oral fibroblasts.<sup>[9]</sup> High viral loads in the salivary glands and nasal secretion can lead to oral changes in COVID-19 infection, which indicates the direct impact of the virus on the tissues of the oral cavity.<sup>[12]</sup> Furthermore, ACE2 has been detected in the oral mucosa, particularly more density over the dorsum of the tongue and minor salivary glands of oral cavity in comparison to the buccal mucosa and palate.<sup>[13]</sup>

There are conflicting reports related to the prevalence of several symptoms and signs in the oral cavity of COVID-19 patients.<sup>[14]</sup> The common clinical manifestations of the COVID-19 patient are fever, sore throat, dry cough, headache, anosmia, dysgeusia, abdominal pain, vomiting, and diarrhea.<sup>[15]</sup> Dysgeusia was the first recognized oral symptom of the COVID-19 patient, which was documented in 38% of the patients, mostly in Europeans and North Americans, females and patients of mild to moderate disease severity.<sup>[16]</sup> There are ulcerative lesions found as multiple shallow ulcers with erythematous halos and yellow–white pseudo membranes at both keratinized and nonkeratinized mucosae. In COVID-19 patients, oral lesions are found simultaneously with systemic symptoms. Recurrent aphthous-like lesions are also found.<sup>[17]</sup> Aphthous-like ulcers without the presence of necrosis are found in younger patients with a mild degree of infection, whereas aphthous-like ulcers with necrosis and hemorrhagic crusts are seen in severe degrees of infection associated with older patients and patients with immunosuppression. The aphthous-like lesions are usually healed after 5–15 days.<sup>[6]</sup> The regression of these oral lesions is usually regressed in parallel with the improvement of systemic diseases. In COVID-19 patients, raised tumor necrosis factor can lead to chemotaxis of the neutrophils to the mucosal layer of the oral cavity and result in aphthous-like lesions. In COVID-19 patients, stress and immunosuppression are also considered aggravating factors for manifesting aphthous-like lesions.<sup>[18]</sup> In this study, 8.92% of patients presented with aphthous ulcers. There are sometimes, red patches or

**Table 1: Demographic profile of coronavirus disease 2019 patient with oral cavity manifestations**

Parameters	n (%)
Gender	
Male	34 (60.71)
Female	22 (39.28)
Age (years)	
18–30	22 (39.28)
31–50	18 (32.14)
51–65	16 (28.57)

**Table 2: Oral cavity manifestations in coronavirus disease 2019 patients (n=56)**

Oral cavity lesions	n (%)
Loss of taste sensation	15 (26.78)
Redness of oral buccal mucosa (mucositis)	8 (14.28)
Redness in the tongue (glossitis)	7 (12.50)
Ulcer	5 (8.92)
Dry mouth	5 (8.92)
Burning sensation (mouth)	4 (7.14)
White patch in mouth/oral thrush	4 (7.14)
Gingival bleeding	3 (5.35)
Difficult to swallow	3 (5.35)
Red spots (petechiae)	2 (3.57)

plaques are found on the dorsum of the tongue, palate, and gingival in confirmed or suspected COVID-19 patients. The whitish lesions are usually candidiasis which is due to long-term antibiotic therapy, reduced general condition or immunity of the body and decreased oral hygiene in COVID-19 patients.<sup>[19]</sup> Oral cavity lesions such as glossitis, cheilitis, and erythematous and swollen tongue (described as strawberry tongue) may be found in COVID-19 patients with Kawasaki-like disease (Kawa-COVID).<sup>[9]</sup> The long period of latency between starting of the systemic symptoms such as respiratory or gastrointestinal) and the onset of the oral or skin manifestations is due to delayed hyperactivation response of the immune symptoms.<sup>[9]</sup> The secondary release of the acute inflammatory cytokines with respect to the direct effects of the virus on the skin and oral mucosa results in the release of the acute inflammatory mediators rather than the direct impact of the viruses on the skin and oral mucosa.<sup>[9]</sup> In some cases of COVID-19 infection, petechiae are seen on the lower lip, palate, and mucosal lining of the oropharynx. The latency time for COVID-19 patients with petechiae is shorter than for patients with both petechiae and macular lesions. In COVID-19 patients, thrombocytopenia due to the SARS-CoV-2 infection or the prescribed drugs during the treatment may be the cause of petechiae formation.<sup>[20]</sup> In this study, 3.57% of patients showed petechiae and 5.35% of patients presented with gingival bleeding. Herpetic form/zosteriform lesions in the oral cavity are seen as multiple painful, yellowish-gray ulcers with erythematous surrounding on both keratinized and nonkeratinized mucosa of the oral cavity.<sup>[21]</sup> Geographic tongue may be detected after recovery of herpetic lesions. Immunosuppression and stress are often associated with COVID-19 infection, which results in the appearance of the secondary type of herpetic gingivostomatitis.<sup>[22]</sup> Some COVID-19-positive patients present with blisters in the lip mucosa, desquamative gingivitis, and skin rashes. Some patients present painful inflammation of the tongue papillae, which may lead to erythematous macules and ulcers.<sup>[23]</sup>

COVID-19 infections often affect the salivary glands, which are reflected in different ways, such as patients complaining of pain or swelling in submandibular or submandibular glands and resulting in dry mouth. In this study, 8.92% of patients presented with dry mouth. These clinical findings reflect the protective role of the saliva, which usually cleans the oral cavity constantly and the antiviral response against COVID-19.<sup>[24]</sup> Hyposalivation is a potential complication of chronic sialadenitis caused by COVID-19 infection. Inflammation of the salivary glands results in fibrosis of the acinic and duct, leading to hyposalivation of the salivary glands. Hyposalivation increases the chance of inorganic salt deposition on the ductal wall, which induces sialolithiasis, which leads to stenosis and dilation of the ducts.<sup>[25]</sup> The incidence of respiratory infection increases by enhancing the adhesion of viruses and colonization and destruction of the oral cavity mucosal linings and airways, resulting in decreased antimicrobial peptides and proteins.<sup>[26]</sup>

The management of oral cavity lesions in COVID-19 patients includes proper oral hygiene and treatment of the exact etiology of the oral lesions. Insufficient oral hygiene of the oral cavity needs regular local antiseptics such as hydrogen peroxide or betadine gargles to reduce viral burdens.<sup>[27]</sup> The stress of the patients during the treatment period of COVID-19 infections should be consulted and managed by a psychiatrist. The current outbreak of COVID-19 infection urges epidemiological and clinical researchers to document sensitive case definitions for tracking all true positive cases where there is emerging evidence of oral cavity lesions.

## CONCLUSION

SARS-CoV-2 can cause oral lesions, and therefore, all COVID-19-positive patients must need a full examination of the oral cavity. Further studies are required for a better understanding of the etiopathology for oral mucosal alteration in COVID-19 patients. The presence of bad oral hygiene, stress, opportunistic infection, and underlying diseases like diabetes mellitus can manifest oral lesions in COVID-19 patients. Clinicians should keep these oral cavity lesions in mind during the examination of COVID-19 patients. Proper management of COVID-19 infections and maintaining oral hygiene will help to improve the oral cavity lesions. The comorbidities of the COVID-19 patients, such as old age, diabetes mellitus, hypertension, and stress, are strongly associated with poor prognosis, which triggers the lesions in the oral cavity. The oral cavity of COVID-19 patients should be evaluated in case of prolonged hospitalization or immunosuppressive status, which may help to patient's recovery.

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## Conflicts of interest

There are no conflicts of interest.

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