

Oral Lesions Associated with COVID-19

Subjects: **Infectious Diseases**

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Oral lesions have been reported in patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), raising the possibility that these buccal manifestations are directly related to both the viral infection and the patient's underlying systemic condition. The oral cavity serves as an accessible and immunologically active site, offering a favorable environment for SARS-CoV-2 to interact with mucosal immune components and target epithelial cells.

COVID-19

cavity buccal

oral lesion

1. Oral Manifestations in Patients with COVID-19

Alterations in smell and taste are some early indicators of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and are effective in decision making, and dry mouth is an oral presenting symptom ^{[1][2][3]}, infection of salivary ducts by SARS-CoV-2 has been experimentally confirmed in animal models, which explains the presence of acute sialadenitis, discomfort, pain, inflammation or even improper functioning of the saliva-producing glands ^[4].

Patients with coronavirus disease 2019 (COVID-19) experience fatigue, anosmia, fever, dysgeusia, and dry cough, in which later appeared a generalized erythema on the hard palate and oropharynx with pustules and petechiae on the edge of the soft palate; the suggested diagnosis was enanthem due to COVID-19 ^[5]. Petechiae on the palate, lower lip, and oropharyngeal mucosa due to COVID-19 infection were also observed ^[6]. Pigmentation in the attached and interpapillary gingiva due to increased levels of inflammatory cytokines and arachidonic acid metabolites secondary to the production of basic-fibroblast growth factor (bFGF) and stem cell factor (SCF) from basal layer keratinocytes has been reported in some SARS-CoV-2 patients ^[7]. In a case series reported by Carreras-Presas et al., patients suspected of being infected with SARS-CoV-2 presented fever, halitosis, submandibular lymphadenopathy, and oral lesions ^[8]. The oral lesions were common to that reported by Patel et al. and included erythematous, painful, diffuse, and edematous gingiva with necrosis of the interpapillary areas ^{[8][9]}. In spite of authors suggesting that the oral lesions observed were due to SARS-CoV-2 provokes exanthematic lesions that may resemble other viral processes ^[8], it has also been suggested that the lesions may be associated with bacterial coinfections in conjunction with COVID-19 ^[9]. Many patients with COVID-19 suffer from weakness, present with fever, have episodes of diarrhea, and occasionally have abdominal pain coinciding with the presence of an oral erythematous papular rash; lesions occurring in the oral cavity consist of erosions on the dorsum of the tongue and the mucosa of the mouth, as well as vesicular eruptions ^[10]. **Table 1** lists some of the descriptive

characteristics of representative studies evaluating oral manifestations in patients with COVID-19, including type of lesions, the number of patients (sample), study design, the country, and year in which each study was carried out.

Table 1. Representative studies evaluating oral manifestations in patients with COVID-19.

Design/Reference	Oral Lesions (Percentage, Frequency)	Sample	Country
Case series, Sinadinos, 2020 [11]	Herpetic recurrent stomatitis (n = 2, 67%) Erythema multiform (n = 1, 33%)	3	UK
Cross-sectional study, Mascitti, 2020 [12]	Oral lichenoid lesions (n = 13, 32.5%) Oral enanthem (n = 11, 27.5%) Macroglossia (n = 10, 25%) Herpes (n = 1, 2.5%) Cheilitis (n = 5, 12.5%)	40	France
Case series, Carreras-Presas, 2021 [13]	Herpetic recurrent stomatitis (n = 1, 33.3%) Multiple ulcerations on palate (n = 1, 33.3%) Desquamative gingivitis (n = 1, 33.3%)	3	Spain
Cross-sectional study Katz, 2021 [14]	Aphthous stomatitis (n = 6, 0.67%)	889	USA
Cross-sectional study Halepa, 2021 [15]	Red or swollen lips (n = 23, 48.9%) Strawberry tongue = (n = 5, 10.6%) Other oral manifestation (n = 7, 14.9%)	47	USA
Cross-sectional study Fidan, 2021 [16]	Aphthous-like ulcers (n = 27, 46.6%) Erythema (n = 19, 32.8%) Lichen planus (n = 12, 20.6%)	74	Turkey
Cross-sectional study Favia, 2021 [17]	Geographic tongue (n = 2, 2%) Fissured tongue (n = 3, 2%) Ulcerative lesion (n = 65, 53%) Blisters (n = 19, 15%) Hyperplasia of papillae (n = 48, 39%) Angina bullosa (n = 11, 9%) Candidiasis (n = 28, 23%) Necrotizing ulcerative gingivitis (n = 7, 6%) Petechiae (n = 14, 11%) Spontaneous oral hemorrhage (n = 1, 1%)	123	Italy
Cross-sectional study Falah, 2020 [18]	Oral cavity changes (n = 9, 90%) (unspecified)	10	Pakistan
Case series Cruz Tapia, 2020 [19]	Angina bullosa hemorrhagic-like lesion (n = 2, 50%) Vascular disorder associated with COVID-19 (n = 1, 25%) Mucosal nonspecific localized vasculitis and thrombosis (n = 1, 25%)	4	Columbia, Brazil, and Mexico

Design/Reference	Oral Lesions (Percentage, Frequency)	Sample	Country
Case series Brandão, 2021 [20]	Ulcer (n = 4, 50%) Focal erythema/petechiae (n = 1, 13%) Aphthous-like ulcers (n = 2, 25%) Hemorrhagic ulcer (n = 2, 25%)	5	Brazil
Cross-sectional study Abubakr, 2021 [21]	Ulcerations (n = 117, 20.4%) Xerostomia (n = 273, 47.6%) Oral or dental pain (n = 132, 23%) Pain in jaw joint (n = 69, 12%) Halitosis (n = 60, 10.5%)	665	Egypt
Cross-sectional study Retrospective study Bardellini, 2021 [22]	Oral pseudomembranous candidiasis (n = 2, 7.4%) Geographic tongue (n = 1, 3.7%) Coated tongue (n = 2, 7.4%)	27	Italy

with an

erythematous border on nonkeratinized and keratinized mucosa. The expression of these lesions precedes the systemic symptoms. In one case, geographic tongue appeared after recovery from herpetiform lesions [\[10\]\[11\]\[23\]](#). Clinically, it was observed that the presence of oral ulcerations was very varied, ranging from lesions similar to aphthous stomatitis to the presence of generalized ulcerations with necrosis, some of these oral lesions had a herpetiform pattern, with resemblance to herpes infection, but rendered a negative result to the test for herpes simplex virus (HSV) [\[18\]\[24\]](#). Immunosuppression and stress associated with COVID-19 were suggested as the cause for the appearance of secondary herpetic gingivostomatitis [\[25\]\[26\]](#). Patients suffering from acute COVID-19 infection, together with inadequate therapeutic measures, could contribute to adverse oral health outcomes [\[23\]](#).

1.2. Erosive or Ulcerative Lesions

Erosive or ulcerative lesions appeared as painful lesions with irregular borders on the tongue, labial mucosa, and hard palate [\[27\]\[28\]](#). The lesions appeared after a latency time of 4–7 days before the onset of systemic symptoms. Different factors were suggested as causes for the development of ulcerative and erosive lesions, such as drug eruption, thrombotic vasculopathy secondary to COVID-19, and vasculitis [\[13\]\[29\]](#).

1.3. Red and White Plaques

Red and white plaques have also been reported on the gingiva, dorsum of the tongue, and palate of patients with COVID-19 [\[15\]](#). Candidiasis due to long-term antibiotic therapy, deterioration of general condition, and decreased oral hygiene may be the cause of the red or white plaques [\[7\]](#).

1.4. Erythema-Multiforme-like Lesions

Erythema-multiforme-like lesions appeared as blisters, scaly gingivitis, erosions, and painful cheilitis with hemorrhagic crusting in patients with skin lesions on all four extremities [\[16\]\[30\]](#).

1.5. Angina Bullosa-like Lesions

Some patients confirmed with COVID-19 also had angina bullosa-like lesions as asymptomatic erythematous-purpuric blisters without spontaneous bleeding on the hard palate and tongue [17][19].

Is important to note that patients with COVID-19 who are intubated undergo tracheostomy or assisted external ventilation [31]. These maneuvers cause hyposalivation, which could aggravate the already existing lesions of the oral cavity and could trigger bacterial aspiration pneumonia [32]. The main effect of COVID-19 on the oral mucosa is multifactorial, the prominent role of the immune system is unavoidable, and the certain state of deregulation of this system may lead to infections or the risk of more severe autoimmune conditions through cytokine storm [33]. Some researchers claim that oral lesions contributing to COVID-19 are triggered by an inflammatory response that induces vascular inflammation [34]. Inflammation plays an important role in disease progression and clinical outcomes. Inappropriately increased inflammation causes a cytokine storm, leading to tissue damage, diffuse alveolar damage, myocarditis, renal failure, central nervous system involvement, and multiorgan failure, and is sometimes associated with a poor clinical prognosis. Coronavirus infection causes a release of proinflammatory cytokines, associated with a systemic inflammatory response syndrome (SIRS) [35], resulting in markedly elevated levels of interleukins (IL), which are usually: IL-2, IL-6, IL-7, granulocyte colony-stimulating factor, monocyte chemoattractant protein 1 (MCP-1), macrophage inflammatory protein 1 alpha (MIP1-a), interferon-inducible protein 10-gamma (IP-10), and tumor necrosis factor (TNF)-alpha [36][37][38].

2. Pharmacological Therapy for the Treatment of Oral Lesions in Patients with COVID-19

The use of drugs for the treatment of some oral lesions has been reported, including topical agents such as 2% chlorhexidine for lacerations, hyaluronic acid, tranexamic acid for local bleeding, and miconazole for patients with a cytological diagnosis of candidiasis [17]. Cases have been described of patients with erythema multiforme-like lesions using topical antiseptic medications of 0.2% chlorhexidine solution, in addition to the prescription of vitamin C, B complex, systemic corticosteroids, and panthenol-calcium with pantothenic acid (locally applied tablets); promotion of healing of the labial mucosa in these patients was performed with the typical application of Vaseline [6][39].

Angular cheilitis in most cases has been treated with nystatin, neomycin, and triamcinolone acetonide 0.05%. Xerostomia has been treated with artificial saliva (gels); it has been reported that for burning sensation in the oral cavity the indicated treatment has been triamcinolone acetonide 0.05%, as well as for aphthous lesions [2][14]. In cases of coinfection by herpes simplex virus, systemic acyclovir and some local antiseptics such as panthenol or nystatin have been indicated [34], and if there is also coinfection with candidiasis, intravenous fluconazole, mouthwash with 0.12% chlorhexidine digluconate, mouthwash with 1% hydrogen peroxide, and nystatin have been applied, as well as white plates [23]. Chlorhexidine 0.12% (mouthwash), hyaluronic acid, and prednisolone have been indicated to counteract oral blisters [29]. It has been observed that oral ulcers have healed completely within 10 days after their appearance [40]. When facial nerve paralysis is present, favipiravir and ciclesonide have been reported to improve facial nerve paralysis [41].

Is important to note that many of the pharmacotherapeutics agents used in COVID-19 are also used to treat oral diseases, especially orofacial pain and inflammatory conditions. However, analgesics (paracetamol, nonsteroidal anti-inflammatory agents), antivirals (penciclovir), antibiotics (azithromycin, doxycycline), and immunomodulatory agents (hydroxychloroquine, corticosteroids), have been associated with long-term adverse effects that complicate dental treatment [42]. Treatments involving more than two drugs and invasive therapeutics may cause immune function to be diminished or affected, thus worsening oral conditions, especially when candidiasis is present in the oropharynx [43].

A risk factor for negative outcomes in patients with COVID-19 and associated fungal infection is prolonged antibiotic use in association with immune dysregulation [43]. Perioral pressure ulcers, oral candidiasis, herpetic and hemorrhagic oral ulcer, and acute macroglia were the most commonly complicated health conditions in those patients who presented severe COVID-19 [44]. These oral mucocutaneous conditions were triggered by prolonged prone position and mechanical ventilation equipment in the intensive care unit (ICU) setting, along with the immunosuppressive treatments prescribed to these patients [44].

3. COVID-19: Dental Care and Staff Biosecurity

Dentistry is the profession that deals with the health of the oral cavity in humans, this cavity is undoubtedly the main route of transmission of COVID-19 (small droplets of saliva when coughing or sneezing) [45]; with dental staff and dental offices becoming a focus for the spread of infection, from patients to dentists and from patients to patients, it is important that dentists and dental practices keep up to date with all aspects of COVID-19 [13][46][47]. Adequate guidelines are now in place to protect dentists against SARS-CoV-2 during dental practice and the use of aerosols, although there are guidelines that do not fully prevent transmission caused by aerosols [46][47]. Some statistics show that 0.9% of the surveyed dentists contracted COVID-19 infection, which may indicate that social distancing is an appropriate measure in consultation with dentists to control the spread of SARS-CoV-2 [48]. Although thorough disinfection with chlorine or alcohol-based solutions can inactivate the virus on surfaces, reports indicate that SARS-CoV-2 survives on some surfaces for up to 9 days [49] and is estimated to have an average life of approximately 6–8 h in plastic and 5–6 h in stainless steel [50]. The persistence of SARS-CoV-2 was also detected in surgical masks, where the virus was observed to persist for up to 7 days [51]. Adequate hand washing is essential to combat and control the spread of many diseases [52]. Proper hand washing should be performed for at least 60 s to remove infectious microorganisms, especially if combined with hydroalcoholic solutions that aid in the inactivation of enveloped viruses, including coronaviruses [53]; adequate provision of personal protective equipment is the first and foremost requirement to ensure that healthcare personnel [54]. For proper dental treatment, most dentists prescribed a mouth rinse before starting any procedure. The rinses they recommended using were hydrogen peroxide or chlorhexidine [55][56][57], since the presence of viruses in saliva represents an important risk factor [58][59]. During dental practice, aerosol production should be limited [60][61], limiting the use of handpieces, the use of surgical suction, the four-handed technique, ventilation, and disinfection of surfaces are effective in preventing infections [50][62]. It is considered necessary to consider the recommendations listed in **Table 2** for dental care.

Table 2. Recommendations and procedures that should be performed during dental care throughout the COVID-19 pandemic.

Priority Level Consideration	Description/Recommendation
Priority cases for dental health care	Pericoronitis, pulpitis, abscess, osteitis, localized bacterial infection, dental trauma, extensive caries, broken or defective restorations causing tissue damage or pain, suture removal, adjustments to appliances and prostheses causing damage to oral structures, and replacement of temporary endodontic fillings and patients with presence of pain [63].
Nonpriority dental procedures	Cosmetic dental procedures, orthodontic and orthopedic treatments, replacement of permanent restorations for aesthetic reasons, intentional root canal treatment, elective periodontal care, and nonurgent oral surgery and prosthetics [63].
Regarding location of dental care personnel	It is of vital importance to avoid overcrowding in all areas of circulation of patients and health personnel in addition to waiting rooms; take a distance of not less than 1.8 m within the room or care area of the cases that have been confirmed with COVID-19 [64].
Appointments and schedules	Appointing patients at established times, which must be respected, with a safe time interval between each of the dental consultations, avoiding contact and approach between patients [64].
During the emergency dental consultation	- Evaluate patients suspected of COVID-19 by signs and symptoms, particularly cough and fever [65]. - Attenuate the symptoms that provoke pain and cause inflammation in the dental organs, this can be with analgesics and anti-inflammatory drugs [66]. - Provide information to staff and provide them with the use of personal protective equipment (N95 respirators, safety goggles, clinical gloves, disposable aprons, and hair covers) [67][68]. - Wash hands with soap and water or clean them with 70% isopropanol or 70% ethanol before and after care [63]. - Do not touch the nose, mouth, and eyes without having cleaned hands [69][70]. - Use computed tomography and extraoral radiographs in preference to intraoral radiographs, and avoid the generation of lumps in the areas that trigger coughing and vomiting [71][72]. - Use rubber dam for absolute isolation during the dental procedure and do not use air-water syringe lavage, ultrasonic and sonic scalers, rotary handpieces, and air abrasion units [73].

Priority Level Consideration	Description/Recommendation
	- Do not remove the mask before 30 min in the environment where dental care is performed because it increases the risk of contagion [74]. - Disinfect all surfaces and structures of the dental office and patient care equipment with hospital germicides. Proper sterilization of all dental instruments should be performed according to the biosafety techniques that have been established by the manufacturers of the devices used for sterilization [50]. - Dispose of the remains of all dental procedures in special packages or bags for infected waste [75].

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