Critical Review
Oral Pathology

Orofacial manifestations of COVID-19: a brief review of the published literature

Esam HALBOUB[a]
Sadeq Ali AL-MAWERI[b]
Rawan Hejji ALANAZI[c]
Nashwan Mohammed QAID[d]
Saleem ABDULRAB[e]

[a]Jazan University, College of Dentistry, Department of Maxillofacial Surgery and Diagnostic Sciences, Jazan, Saudi Arabia.

[b]AlFarabi College of Dentistry and Nursing, Department of Oral Medicine and Diagnostic Sciences, Riyadh, Saudi Arabia.

[c]AlFarabi College of Dentistry and Nursing, Department of Oral Medicine and Diagnostic Sciences, Riyadh, Saudi Arabia.

[d]AlFarabi College of Dentistry and Nursing, Department of Restorative Dental Sciences, Riyadh, Saudi Arabia.

[e]Primary Health Care Corporation, Madinat Khalifa Health Center, Doha, Qatar.

Declaration of Interests: The authors certify that they have no commercial or associative interest that represents a conflict of interest in connection with the manuscript.

Corresponding Author:
Sadeq Ali Al-Maweri
E-mail: sadali05@hotmail.com

https://doi.org/10.1590/1807-3107bor-2020.vol34.0124

Submitted: July 9, 2020
Accepted for publication: September 28, 2020
Last revision: October 7, 2020

Abstract: Coronavirus disease 2019 (COVID-19) has spread exponentially across the world. The typical manifestations of COVID-19 include fever, dry cough, headache and fatigue. However, atypical presentations of COVID-19 are being increasingly reported. Recently, a number of studies have recognized various mucocutaneous manifestations associated with COVID-19. This study sought to summarize the available literature and provide an overview of the potential orofacial manifestations of COVID-19. An online literature search in the PubMed and Scopus databases was conducted to retrieve the relevant studies published up to July 2020. Original studies published in English that reported orofacial manifestations in patients with laboratory-confirmed COVID-19 were included; this yielded 16 articles involving 25 COVID-19-positive patients. The results showed a marked heterogeneity in COVID-19-associated orofacial manifestations. The most common orofacial manifestations were ulcerative lesions, vesiculobullous/macular lesions, and acute sialadentitis of the parotid gland (parotitis). In four cases, oral manifestations were the first signs of COVID-19. In summary, COVID-19 may cause orofacial manifestations that might be the initial features in several cases. However, the occurrence of orofacial manifestations in COVID-19 seems to be underreported, mainly due to the lack of oral examination of patients with suspected and/or confirmed COVID-19. Oral examination of all suspected and confirmed COVID-19 cases is crucial for better understanding and documenting COVID-19-associated orofacial manifestations.

Keywords: COVID-19; Coronavirus; Oral manifestations, Review.

Introduction

Caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the novel coronavirus 2019 disease (COVID-19) has caused an unprecedented global healthcare crisis. By the time of this writing, over 19 million people have been infected, and approximately 728,013 have lost their lives worldwide.[1] While most cases are either asymptomatic or affected with mild symptoms, a considerable fraction of cases develop severe respiratory symptoms, leading to acute severe respiratory distress (ASRD) and sometimes multiple organ failure.[2]

The most commonly reported manifestations include fever, cough, sore throat, myalgia, arthralgia, headache, dyspnea, and sputum production.[2] However, an increasing number of atypical clinical presentations have been reported, such as gastrointestinal symptoms, dermatological manifestations, and chemosensory dysfunctions.[2,3,4] Interestingly, some studies have found that taste and smell chemosensory dysfunctions were the initial and only signs of the disease in a considerable fraction of patients.[3,5] Additionally, more recent studies have reported clinical orofacial manifestations in COVID-19-positive patients, including oral ulcerative lesions,[6] vesiculobullous lesions, and acute sialadenitis.[7,8,9] Understanding the orofacial manifestations of COVID-19 by dentists is extremely important for the early detection of the disease and prevention of transmission. Although a number of studies have reported on orofacial manifestations in patients with COVID-19, no attempt has been made thus far to review the available literature in this context. Therefore, the present review sought to summarize the available literature and provide an overview of the potential orofacial manifestations of COVID-19, as well as to highlight the implications for dental practitioners.

Methodology

Literature search and eligibility criteria

A literature search was conducted in the PubMed and Scopus databases for all relevant studies published up to June 2020. The search was updated in July 2020 for any additional studies. A combination of the following keywords was used: ("oral manifestations" OR "oral lesions" OR "oral findings" OR "orofacial findings" OR "orofacial manifestations" OR "orofacial lesions" OR "dental manifestations" OR "gingival findings" OR "gingival manifestations" OR "periodontal findings" OR "periodontal manifestations" OR "salivary glands" AND "COVID-19" OR "Coronavirus" OR "SARS-CoV-2" OR "novel coronavirus disease"). The full-text articles of all potential studies were obtained and evaluated for inclusion. The reference lists of the relevant studies were also manually searched for additional studies. All studies that reported orofacial manifestations in patients with laboratory-confirmed COVID-19 were included. Studies with suspected COVID-19 cases were excluded.

Data extraction

The following information was extracted and tabulated: author, country of the study, number of cases with orofacial manifestations, age, sex, orofacial manifestations, onset of the orofacial manifestations, any special investigations performed, treatment of oral lesions, and signs and symptoms of COVID-19.

Results

General characteristics of the included studies

Out of the 370 retrieved studies, only 16 articles fulfilled the inclusion criteria.[4,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20] The 16 included studies (10 case reports and six case series) comprised 25 patients with laboratory-confirmed COVID-19.[4,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20] A full description of the included cases is provided in Table 1. The number of cases in the included studies ranged from one to four. Most of the studies were published during May and June 2020. The age of the participants ranged from 6 to 77 years. Over half of the cases (61.1%) were females. With reference to COVID-19 diagnosis, all included cases in this review were confirmed with PCR; suspected COVID-19 cases were excluded. Approximately half of the subjects had one or more systemic diseases, e.g., diabetes mellitus, hypertension, or kidney problems. Orofacial manifestations were the first clinical signs of COVID-19 in four cases;[10,12,16] in the remaining cases, the reported onset of orofacial manifestations in relation to COVID-19 general symptoms ranged from 3 to 31 days (Table).

Orofacial manifestations

The orofacial manifestations were highly variable. The most common presentations were ulcerative lesions, vesiculobullous lesions, macular erythematous lesions, and acute parotitis. The most commonly affected intraoral site was the hard palate, followed by the dorsum of the tongue and labial mucosa. The diagnosis of oral mucosal lesions was based on clinical features in most of the included studies, with only three studies[6,7,14] having performed biopsies to confirm the diagnosis.

Table. Characteristics of patients with COVID-19 with oral manifestations.

Author/Year	Cases (country)	Sex, age (General health)	Oral manifestations/site (Onset relative to COVID-19)	Differential diagnosis	Special investigation	Treatment of oral lesions (Resolution time)	Coronavirus symptoms and treatment
Ansari et al., 2020[7]	Case 1 (Iran)	F, 56 ys (DM)	Several painful irregular ulcers varying in size, on a red background of the whole hard palate Onset: After day 5	Aphthous ulcer	Histopathology: diffuse edema with mucosal desquamation, along with granulation and ulceration with invasion of mono-nuclear cells. Serology: negative for herpes antibodies	Topical of: diphen-hydramine, dexamethasone, tetracycline, and lidocaine (after one week)	Symptoms: fever, shortness of breath Treatment: remdesivir, azithromycin, and supportive treatment
	Case 2 (iran)	M, 75 ys (Hypertension)	Several small painful ulcers, with irregular margins on red back-ground on the anterior tongue Onset: After one week	Aphthous ulcer	Histopathology: identical to the first case. Serology: negative for herpes antibodies	Diphenhydramine, dexamethasone, tetracycline, lidocaine (after one week)	Symptoms: hypoxia Treatment: azithromycin and supportive treatment
Chaux-Bodard et al., 2020[12]	Case 1 (Frace)	F, 45 ys (Healthy)	Irregular, nonpainful ulcer on the dorsum of the tongue Onset: First sign	NM	None	NM (after 10 days)	Symptoms: mild asthenia Treatment: NM
Martín Carreras-Presas et al., 2020[8]	Case 1 (Spain)	F, 65 ys (Hypertension)	Blisters on the labial mucosa and desquamative gingivitis Onset: After 31 days	Viral enanthema	None	Hyaluronic acid and CHX MW, Prednisolone 30 mg tab (within 3 days)	Symptoms: fever, diarrhea Treatment: lopinavir 200 mg, ritonavir 50 mg, hydroxychloroquine 200 mg
Putra et al., 2020[9]	Case 1 (Indonesia)	M; 29 ys (Healthy)	Intraoral ulcer along with skin lesions Onset: After day 7	Hand-foot-mouth disease, Aphthous stomatitis,	None	Typical oral hygiene care (resolved on day ten)	Symptoms: fever, myalgia, sore throat and dry cough, skin lesions Treatment: paracetamol 500 mg, azithromycin, hydroxychloroquine, oseltamivir, vitamins
Cebeci Kahraman et al., 2020[11]	Case 1 (Turkey)	M, 51 ys (Healthy)	Large erythematous surface in the oropharynx, and 1-3 mm size petechiae on the hard and soft palate Onset: After 10 days	Viral enanthema	None	Clarithromycin 500 mg (after few days of antibiotic therapy)	Symptoms: sore throat, fever, fatigue, dry cough, ageusia, anosmia, and skin rash Treatment: clarithromycin 500 mg

Continue

Continuation

Author/Year	Cases (country)	Sex, age (General health)	Oral manifestations/site (Onset relative to COVID-19)	Differential diagnosis	Special investigation	Treatment of oral lesions (Resolution time)	Coronavirus symptoms and treatment
Santos et al., 2020[18]	Case 1 (Brazil)	M, 67 ys (Hypertension, CKD)	White plaque, multiple pinpoint yellowish ulcers on the dorsum of tongue Onset: After 24 days	RHU, Candidiasis, Geographic tongue	Tongue scrape culture	IV fluconazole, oral nystatin, CHX MW, and 1% H2O2 (after 2 weeks)	Symptoms: fever, dyspnea, diarrhea, hypogeusia Treatment: hydroxychloroquine ceftriaxone sodium 2 g, azithromycin 500 mg, sulfamethoxazale
Jimenez-Cauhe et al., 2020[14]	Case 1 (Spain)	F, 63 ys (NM)	Palatal macules and petechiae on the hard palate along with skin rash Onset: After 19 days	EM	Histopathology of the skin lesions.	Systemic corticosteroids (NM)	Symptoms: NM Treatment: lopinavir, hydroxychloroquine, azithromycin, corticosteroids, ceftriaxone
	Case 2 (Spain)	F, 77 ys (NM)	Palatal macules and petechia along with skin rash Onset: After 16 days	EM	Histopathology of the skin lesions Microbial: negative for CMV, VZV, HSV, syphilis	Systemic corticosteroids (NM)	Symptoms: NM Treatment: lopinavir, hydroxychloroquine, corticosteroids, azithromycin
	Case 3 (Spain)	F, 58 ys	Palatal macules and petechia along with skin rash Onset: After 24 days	EM	Histopathology of the skin lesions	Systemic corticosteroids (NM)	Symptoms: NM Treatment: lopinavir, hydroxychloroquine, corticosteroids, azithromycin, and ceftriaxone
	Case 4 (Spain)	F, 69 ys (NM)	Palatal macules and petechiae Onset: After 19 days	EM	Histopathology of the skin lesions. Microbial: negative for CMV, VZV, HSV, syphilis	Systemic corticosteroids (NM)	Symptoms: NM Treatment: lopinavir hydroxychloroquine, and azithromycin
Sakaida et al., 2020[17]	Case 1 (Japan)	F, 52 ys(NM)	Erythematous lesions and erosions on lips and buccal mucosa Onset: Couple of days prior to systemic signs	NM	Histopathology of the skin lesions.	Prednisolone (NM)	Symptoms: In the first 4 days, no symptoms except skin rash; on day 5, fever, cough, chills, shortness of breath

Continue

Continuation

Author/Year	Cases (country)	Sex, age (General health)	Oral manifestations/site (Onset relative to COVID-19)	Differential diagnosis	Special investigation	Treatment of oral lesions (Resolution time)	Coronavirus symptoms and treatment
Soares et al., 2020[6]	Case 1 (Brazil)	M, 42 ys (Hypertension, DM)	Painful ulcer in buccal mucosa and multiple reddish macules varying in size on buccal mucosa, hard palate, tongue and lips along with skin vesiculobullous lesions Onset: NM	NM	Histopathology: severe vacuolization and occasional exocytosis of the epithelium; a diffuse chronic inflammatory infiltrate; blood vessels were obliterated with thrombi. HSV, CMV, EBV, and syphilis were negative	NM (after 3 weeks)	Symptoms: cough, shortness of breath, high fever, and skin lesions Treatment: dipyrone, dexamethasone
Labe et al., 2020[15]	Case 1 (France)	M, 6 ys (healthy)	Severe erosive cheilitis with diffuse gingival erosion and thick hemorrhagic crusts on the lips Onset: After 2 weeks	EM	HSV and *Mycoplasma pneumoniae* tests were negative	(after 2 weeks)	Symptoms: fever, anosmia, rash extremities and target lesions, and conjunctivitis Treatment: NM
Lechien et al., 2020[16]	Case 1 (Fance)	F, 23 ys (Healthy)	Unilateral, ear pain and retromandibular swelling with no pus discharge. Onset: First sign of the disease in two patients; day 3 in the third.	Acute parotitis	MRI: Intraparotid, lymphadenitis	Paracetamol 1 g (10 days)	Symptoms: Headache, sore throat, myalgia, fatigue, nasal obstruction anosmia and ageusia Treatment: paracetamol 1 g
	Case 2 (Fance)	F, 27 ys (Healthy)	Ear pain, retromandibular edema	Acute parotitis	MRI: Intraparotid lymphadenitis	Paracetamol 1 g (3 days)	Symptoms: anosmia, fever, headache, malaise, and dyspnea Treatment: paracetamol 1 g
	Case 3 (Fance)	F, 31 ys (Healthy)	Ear pain, retromandibular edema, sticky saliva, pain during chewing	Acute parotitis	MRI: Intraparotid lymphadenitis	Paracetamol 1 g Vitamins (15 days)	Symptoms: cough, arthralgia, fatigue, diarrhea, headache, abdominal pain Treatment: paracetamol 1 g
Fisher et al., 2020[20]	Case 1 (USA)	F, 21 ys (Healthy)	Left-sided facial and neck swelling associated with malocclusion and trismus	Acute parotitis	CT of the neck showed a diffuse asymmetric enlargement of the left parotid gland	Amoxicillin/ clavulanate	Symptoms: fever, cough, and dyspnea, decrease in oral intake Treatment: NM

Continue

Continuation

Author/Year	Cases (country)	Sex, age (General health)	Oral manifestations/site (Onset relative to COVID-19)	Differential diagnosis	Special investigation	Treatment of oral lesions (Resolution time)	Coronavirus symptoms and treatment
Capaccio et al., 2020[10]	Case 1 (Italy)	M, 26 ys (Healthy)	Discrete painful swelling of left parotid, with no purulent discharge Onset: First sign	Acute parotitis	Ultrasonography CMV and paramyxovirus antibodies were negative	NM (after 2-3 days)	Symptoms: fever, myalgia, hyposmia, and ageusia Treatment: NM
Ciccarese et al., 2020[13]	Case 1 (Italy)	F, 19 ys (Healthy)	Erosions, ulcerations and blood crusts on the inner surface of the lips; palatal and gingival petechiae Onset: 5 days	NM	None	NM (day 10)	Symptoms: fever, myalgia, hyposmia, sore throat, skin rash and petechial rash Treatment: methyl-prednisolone; immune globulins
Hedou et al., 2020[4]	Case 1 (France)	NM	Oral ulcer	Herpetic-like ulcer	None	NM	The patient was in the intensive care unit
Dominguez-Santos, 2020[19]	Case 1 (Spain)	F, 43 ys (Healthy)	Single oral ulcer in right buccal mucosa Onset: 4 days	Minor aphthous ulcer	Serology test: negative for syphilis, hepatitis B, hepatitis C, HIV, and Epstein-Barr virus	NM	Symptoms: anosmia, fever, headache, malaise, and dyspnea
	Case 2 (Spain)	M, 33 ys (Healthy)	Single aphthous ulcer in the superior mucogingival junction Onset: 3 days	Minor aphthous ulcer	Serology test: negative for syphilis, hepatitis B, hepatitis C, HIV, and Epstein-Barr virus	NM	Symptoms: anosmia, fever, headache, malaise, and dyspnea
	Case 3 (Spain)	M, 37 ys (Healthy)	Seven aphthae on the ventral right side of the tongue Onset: 5 days	Minor aphthous ulcer	Serology test: negative for syphilis, hepatitis B, hepatitis C, HIV, and Epstein-Barr virus	NM	Symptoms: anosmia, fever, headache, malaise, and dyspnea
	Case 3 (Spain)	M, 19 ys (Healthy)	Four clustered aphthae on the right side inferior labial mucosa Onset: At the onset of symptoms of COVID-19	Minor aphthous ulcer	Serology test: negative for syphilis, hepatitis B, hepatitis C, HIV, and Epstein-Barr virus	NM	Symptoms: anosmia, fever, headache, malaise, and dyspnea

M: male; F: female; ys: years; DM: diabetes mellitus; CKD: chronic kidney disease; NM: not mentioned; EM: erythema multiform; RHU: recurrent herpes ulcers; HSV: herpes simplex virus; CMV: cytomegalovirus; VZV: varicella zoster virus; CHX MW: chlorhexidine mouthwash; MRI: magnetic resonance imaging.

The management of oral mucosal lesions included one or more of the following: topical or systemic corticosteroids, diphenhydramine, mouthwashes, and antibiotics. Six studies[6,10,12,13,15,19] did not provide any information about the treatment of the lesions. In all cases, the reported orofacial manifestations completely resolved within a couple of days (range: 3-21 days) from the day of diagnosis.

Ulcerative lesions

Ulcerative lesions were the most commonly reported orofacial manifestations of COVID-19. Seven studies from France, Spain, Brazil, Iran, Spain, and Indonesia reported oral ulcerative lesions among patients with COVID-19.[4,6,7,9,12,18,19] In five studies,[4,6,9,12,19] the patients presented with single ulcers, while in some cases, the patients presented with several small painful ulcers.[7,18,19] In one study,[13] the patient presented with severe erosions, ulcerations, and blood crusts on the labial mucosae along with gingival and palatal petechia.[13] The site of ulcers varied greatly across the studies, but the dorsum of the tongue was the most frequently affected site, followed by the hard palate and the buccal mucosa. Interestingly, in one study,[12] oral ulcers were the first sign of the disease. Three studies performed laboratory investigations and showed negative herpes antibodies.[6, 7, 19]

Vesiculobullous/macular lesions

Five studies reported oral vesiculobullous/macular lesions in patients with COVID-19.[8,11,14,15,17] The clinical presentations varied greatly, ranging from blisters, to erythematous lesions, to petechial and erythema multiform-like lesions. Of these, erythema multiform-like lesions were the most common presentation, being reported in 5 cases, and were accompanied by skin target lesions.[14,15] Most of the cases with vesiculobullous/macular manifestations were associated with cutaneous lesions.

Acute parotitis

Five patients with COVID-19 presented with acute parotitis.[10,16,20] Capaccio et al.[10] was the first to report parotitis in the context of COVID-19. The authors reported a 26-year-old patient with COVID-19 who presented with painful swelling of the left parotid gland, with no purulent discharge upon parotid massage. Strikingly, acute parotitis was the first clinical sign of COVID-19, which was then followed by other symptoms such as fever, myalgia, hyposmia and ageusia. Serological tests showed negative results for cytomegalovirus and paramyxovirus antibodies. Based on the clinical, serological and ultrasonographic findings, acute nonsuppurative parotitis related to COVID-19 was diagnosed.[10] In another study, Lechien et al.[16] reported three COVID-19 cases with acute parotitis; strikingly, parotitis was the initial sign of COVID-19 in two of these cases.[16] The three cases were females (aged between 27 and 33 years) and presented complaints of unilateral ear pain and retromandibular swelling. Clinically, there was no pus discharge upon massaging the gland. Based on clinical findings, a diagnosis of parotitis was made. All patients underwent magnetic resonance imaging (MRI), which showed intraparotid lymphadenitis.[16] Additionally, Fisher et al.[20] reported COVID-19-associated parotitis in a 21-year-old female who presented with unilateral left-sided facial and neck swelling. The manifestations resolved within a few days after the diagnosis in all of these cases.

Discussion

Recognition of disease signs and symptoms is critical for early detection, prompt treatment and hence better prognosis. This applies to COVID-19 cases. Dental practitioners can play an important role not only in the prevention of COVID-19 transmission but also in the early recognition and referral of affected patients. A number of reports have documented various orofacial manifestations associated with COVID-19.[7,8,10,11] However, to the best of our knowledge, no attempt has been made to review the available literature in this context. Therefore, this review aimed to summarize the literature and provide an overview of COVID-19-associated orofacial features. Overall, there are limited published studies on this topic, and the reported orofacial manifestations are highly heterogeneous, including multiple oral ulcers, vesiculobullous lesions, erythematous lesions, and acute parotitis, among others. Notably, the actual prevalence of orofacial manifestations in patients

with COVID-19 must have been underestimated, mainly due to the lack of documentation owing to the absence of oral examination in this group of patients for various reasons.[21]

Essentially, SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) receptors to access cells, mainly those of the lower respiratory system.[22,23] In its route to that destination, SARS-CoV-2 may infect nasal and oral mucosal cells,[22] which may explain the occurrence of smell and taste dysfunctions early in the course of the disease.[23] This also suggests the potential development of other oral lesions. There are two mechanisms that may explain the development of such lesions: directly through the effects of the replicating virus, where these lesions will be SARS-CoV-2-specific; and indirectly through COVID-19-associated physical and psychological stress or secondary to the drugs used for its treatment.[7,8,16]

In the present review, painful oral ulcers were the most common orofacial manifestations in patients with COVID-19. Seven studies reported oral ulcerative lesions among patients with COVID-19.[4,6,7,9,12,18,19] Interestingly, in one of these studies, oral ulcer was the first sign of COVID-19, suggesting that oral ulceration might be COVID-19-related.[12] Additionally, the site (keratinized mucosa), shape and pattern of ulcers in the aforementioned studies indicate viral infections. In two of these studies (that reported oral ulcers), serological tests were performed and showed negative results for herpes antibodies (common causative agent of oral ulcerations), ruling out the role of this virus[6,7] and suggesting that these ulcers are COVID-19-associated. However, due to the lack of clear temporality as well as the small sample size (being case reports) and heterogeneous clinical pictures, it is unclear whether these lesions are COVID-19-specific or developed as a result of COVID-19-associated stress and/or are related to its treatments. Therefore, more large-scale observational studies are required to better understand the pathogenesis of these lesions in patients with COVID-19.

Vesiculobullous and macular lesions were also common in patients with COVID-19, although with highly variable clinical presentations. Notably, oral vesiculobullous lesions were accompanied by cutaneous lesions in most cases, substantiating previous studies that suggested an association between cutaneous lesions and COVID-19.[24]

Another important orofacial presentation of COVID-19 is acute inflammation of the parotid salivary gland. Four patients with COVID-19 presented with acute parotitis.[10,16] Strikingly, this was the first sign of the disease in three patients, suggesting that sialadenitis may be a possible clinical manifestation of the COVID-19 disease spectrum. As mentioned earlier, SARS-CoV-2 uses ACE2 receptors to gain access to the cells. Evidence has shown that ACE2 receptors are highly expressed in salivary glands, rendering them potential targets for SARS-CoV-2.[23,25] Similar to what happens elsewhere, it is hypothesized that SARS-CoV-2 attaches to ACE2 receptors on the epithelial cells of the salivary glands, gets endocytosed inside these cells where it replicates, and causes lysis of the cells, ultimately resulting in inflammation and swelling of the major salivary glands.[23,25] In line with this hypothesis, other studies reported xerostomia in a large proportion of patients with COVID-19.[5,23]

One major challenge to define orofacial manifestations in patients with COVID-19 is the lack of temporal dimension, and thus, it is not clear whether these alterations are real, direct manifestations of COVID-19, or indirect manifestations as a result of other factors such as stress, immunosuppression, and/or medications.[4,7,14,26] Additionally, the scarcity of studies on this topic is another evident limitation, as the present review relied merely on a limited number of published case reports/case series. Hence, large-scale observational studies are highly recommended to document the oral manifestations of COVID-19. Another weakness is the lack of definitive diagnosis of oral mucosal lesions in most of the included cases, with only very few studies that have biopsied the lesions to confirm the diagnosis.[6,7,14] However, despite these shortcomings, this review has its own strengths worth noting. First, this is the first review that summarized the oral manifestations of COVID-19. Second, this review included only laboratory-confirmed COVID-19 cases.

Conclusion

Patients with COVID-19 manifest with certain orofacial features that may help clinicians identify

suspected cases. These include oral ulcers, vesiculobullous lesions, erythematous macules, and acute parotitis. However, it seems that oral manifestations of this disease are underreported, mainly due to it being a novel disease with no more than 9 months elapsing since the first case was reported and the lack of oral examination of patients with COVID-19 owing to the lockdown and the carelessness of patients regarding other manifestations that might be less serious compared to the typical COVID-19 manifestations.[21,27] Therefore, a thorough oral examination should be routinely performed for all suspected COVID-19 cases. Indeed, dentists can play a pivotal role in the battle against COVID-19 through recognition of its oral manifestations. Hence, dentists should be familiar with all potential orofacial manifestations of COVID-19. Additionally, further studies employing large cohorts of patients with COVID-19 are highly recommended to document all COVID-19-associated orofacial manifestations.

References

1. World Health Organization – WHO. Coronavirus disease (COVID-19) pandemic: advice for the pubic: country and technical guidance. Geneva: World Health Organization; 2020 [cited 2020 Aug 11]. Available from: https://www.Who.Int/emergencies/diseases/novel-coronavirus-2019
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in china. N Engl J Med. 2020 Apr;382(18):1708-20. https://doi.org/10.1056/NEJMoa2002032
3. Aziz M, Perisetti A, Lee-Smith WM, Gajendran M, Bansal P, Goyal H. Taste changes (dysgeusia) in Covid-19: a systematic review and metaanalysis. Gastroenterology. 2020 Sep;159(3):1132-3. https://doi.org/10.1053/j.gastro.2020.05.003
4. Hedou M, Carsuzaa F, Chary E, Hainaut E, Cazenave-Roblot F, Masson Regnault M. Comment on "Cutaneous manifestations in covid-19: a first perspective " by Recalcati S. J Eur Acad Dermatol Venereol. 2020 Jul;34(7):e299-300. https://doi.org/10.1111/jdv.16519
5. Biadsee A, Biadsee A, Kassem F, Dagan O, Masarwa S, Ormianer Z. Olfactory and oral manifestations of covid-19: sex-related symptoms: a potential pathway to early diagnosis. Otolaryngol Head Neck Surg. 2020 Oct;163(4):722-8. https://doi.org/10.1177/0194599820934380
6. Soares CD, Carvalho RA, Carvalho KA, Carvalho mg, Almeida OP. Letter to editor: Oral lesions in a patient with covid-19. Med Oral Patol Oral Cir Bucal. 2020 Jul 1;25 (4):e563-4. https://doi.org/10.4317/medoral.24044
7. Ansari R, Gheitani M, Heidari F, Heidari F. Oral cavity lesions as a manifestation of the novel virus (COVID-19): a letter-to-editor. Oral Dis. 2020;odi.13465. https://doi.org/10.1111/odi.13465
8. Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, Jané-Salas E, Somacarrera Pérez ML. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. Oral Dis. 2020 May;odi.13382. https://doi.org/10.1111/odi.13382
9. Putra BE, Adiarto S, Dewayanti SR, Juzar DA. Viral exanthem with "spins and needles sensation" on extremities of a covid-19 patient: a self-reported case from an indonesian medical frontliner. Int J Infect Dis. 2020 Jul;96:355-8. https://doi.org/10.1016/j.ijid.2020.05.020
10. Capaccio P, Pignataro L, Corbellino M, Popescu-Dutruit S, Torretta S. Acute parotitis: a possible precocious clinical manifestation of sars-cov-2 infection? Otolaryngol Head Neck Surg. 2020 Jul;163(1):182-3. https://doi.org/10.1177/0194599820926992
11. Cebeci Kahraman F, Çaşkurlu H. Mucosal involvement in a COVID-19-positive patient: a case report. Dermatol Ther. 2020 Jun;e13797. https://doi.org/10.1111/dth.13797
12. Chaux-Bodard AG, Deneuve S, Desoutter A. Oral manifestation of covid-19 as an inaugural symptom? J Oral Med Oral Surg. 2020;26(2):18. https://doi.org/10.1051/mbcb/2020011
13. Ciccarese G, Drago F, Boatti M, Porro A, Muzic SI, Parodi A. Oral erosions and petechiae during SARS-CoV-2 infection. J Med Virol. 2020 Jun;jmv.26221. https://doi.org/10.1002/jmv.26221
14. Jimenez-Cauhe J, Ortega-Quijano D, Carretero-Barrio I, Suarez-Valle A, Saceda-Corralo D, Moreno-Garcia Del Real C, et al. Erythema multiforme-like eruption in patients with COVID-19 infection: clinical and histological findings. Clin Exp Dermatol. 2020 May;45(7):892-5. https://doi.org/10.1111/ced.14281
15. Labé P, Ly A, Sin C, Nasser M, Chapelon-Fromont E, Ben Saïd P, et al. Erythema multiforme and kawasaki disease associated with covid-19 infection in children. J Eur Acad Dermatol Venereol. 2020 Oct;34(10)):e539-41. https://doi.org/10.1111/jdv.16666
16. Lechien JR, Chetrit A, Chekkoury-Idrissi Y, Distinguin L, Circiu M, Saussez S, et al. Parotitis-like symptoms associated with covid-19, france, march-april 2020. Emerg Infect Dis. 2020 Sep;26(9):26. https://doi.org/10.3201/eid2609.202059

17. Sakaida T, Tanimoto I, Matsubara A, Nakamura M, Morita A. Unique skin manifestations of COVID-19: is drug eruption specific to COVID-19? J Dermatol Sci. 2020 Jul;99(1):62-4. https://doi.org/10.1016/j.jdermsci.2020.05.002
18. Santos JAD, Normando AGC, Silva R, Paula RM, Cembranel AC, Santos-Silva AR, et al. Oral mucosal lesions in a covid-19 patient: new signs or secondary manifestations? Int J Infect Dis. 2020 June 8. https://doi.org/10.1016/j.ijid.2020.06.012
19. Dominguez-Santas M, Diaz-Guimaraens B, Fernandez-Nieto D, Jimenez-Cauhe J, Ortega-Quijano D, Suarez-Valle A. Minor aphthae associated with SARS-CoV-2 infection. Int J Dermatol. 2020 Aug;59(8):1022-3. https://doi.org/10.1111/ijd.15004
20. Fisher J, Monette DL, Patel KR, Kelley BP, Kennedy M. COVID-19 associated parotitis: a case report. Am J Emerg Med. 2020 Jun;S0735-6757(20)30549-0. https://doi.org/10.1016/j.ajem.2020.06.059
21. Al-Maweri SA, Halboub E, Warnakulasuriya S. Impact of COVID-19 on the early detection of oral cancer: a special emphasis on high risk populations. Oral Oncol. 2020 Jul;106:104760. https://doi.org/10.1016/j.oraloncology.2020.104760
22. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. Sars-cov-2 viral load in upper respiratory specimens of infected patients. N Engl J Med. 2020 Mar;382(12):1177-9. https://doi.org/10.1056/NEJMc2001737
23. Chen L, Zhao J, Peng J, Li X, Deng X, Geng Z, et al. Detection of 2019-ncov in saliva and characterization of oral symptoms in covid-19 patients. SSRN. 2020 Mar 19. https://doi.org/10.2139/ssrn.3557140
24. Marzano AV, Cassano N, Genovese G, Moltrasio C, Vena GA. Cutaneous manifestations in patients with COVID-19: a preliminary review of an emerging issue. Br J Dermatol. 2020 Sep;183(3):431-42. https://doi.org/10.1111/bjd.19264
25. Wang C, Wu H, Ding X, Ji H, Jiao P, Song H, et al. Does infection of 2019 novel coronavirus cause acute and/or chronic sialadenitis? Med Hypotheses. 2020 Apr;140:109789. https://doi.org/10.1016/j.mehy.2020.109789
26. Patel J, Woolley J. Necrotizing periodontal disease: oral manifestation of COVID-19. Oral Dis. 2020 Jun;odi.13462. https://doi.org/10.1111/odi.13462
27. Halboub E, Al-Maweri SA, Al-Soneidar WA. Utilization of COVID-19 testing for opportunistic screening of oral cancer. Oral Oncol. 2020 Jul;106:104775. https://doi.org/10.1016/j.oraloncology.2020.104775