

TRABAJO DE FIN DE GRADO
GRADO EN ODONTOLOGIA

**ORAL LESIONS IN PATIENTS WITH
COVID-19**

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Abstract

In December 2019, a new virus called the coronavirus (SARS-CoV-2) was detected and has ever since then had a huge impact on the world. The virus is believed to have originated from Wuhan, China and has rapidly spread throughout the whole world. As of today 136 million cases have been confirmed and the total number of deaths due to the virus has risen up to 2.9 million. It's believed that the virus invades the human cells through a receptor called the angiotensin-converting-enzyme 2 (ACE2). Whenever these cells gets invaded by the virus, it generates an inflammatory response which causes certain signs and symptoms such as fever, dysgeusia, dry cough, myalgia, sore throat, diarrhoea, breathing difficulties and respiratory complication (shortness of breath) to appear in the host. The receptor ACE2 is normally present in almost all organs, however the number of ACE2 receptors differs from organ to organ. It's believed that the salivary gland and the tongue contain more ACE2 receptors than many other organs, which is why one of the main symptoms of this disease is ageusia and dysgeusia.

In this study, we have highlighted 7 different cases, where 7 different patients all of whom are COVID-19 positive have presented different oral lesions and have received different treatments to combat the infections and to heal from the oral lesions that they have presented. We have highlighted a numerous number of different oral lesions and syndromes that have been found in COVID-19 patients. But the question is, what causes the presence of these oral lesions? Are they directly associated to SARS-CoV-2 (coronavirus) or could their presence be due to an opportunistic infection or is it maybe due to an adverse reactions coming from the medical treatment that the patients received in order to combat the infection?

Resumen

En diciembre de 2019, se detectó un nuevo virus llamado SARS-CoV-2 o comúnmente coronavirus (causante de la COVID-19) y desde entonces ha tenido un gran impacto en el mundo. Se cree que el virus se originó en Wuhan, China y se ha extendido rápidamente por todo el mundo. Hasta hoy se han confirmado 136 millones de casos y el número total de muertes ha aumentado hasta 2,9 millones. Se cree que el virus invade las células humanas a través de un receptor llamado enzima convertidora de angiotensina II (ACE2). Cuando estas células son invadidas por el virus, se genera una respuesta inflamatoria que provoca ciertos signos y síntomas como fiebre, disgeusia, tos seca, mialgias, dolor de garganta, diarrea, dificultad a respirar y complicación respiratoria (disnea) en el anfitrión. El receptor ACE2 normalmente está presente en casi todos los órganos, sin embargo, el número de receptores ACE2 difiere de un órgano a otro. Se cree que la glándula salival y la lengua contienen más receptores ACE2 que muchos otros órganos, por lo que uno de los principales síntomas de esta enfermedad es la ageusia y la disgeusia.

En este estudio, hemos destacado 7 casos diferentes, donde 7 pacientes todos COVID-19 positivos han presentado diferentes lesiones orales y han recibido diferentes tratamientos para combatir las infecciones y curar las lesiones orales que han presentado. Hemos destacado una gran cantidad de diferentes lesiones y síndromes orales que se han encontrado en pacientes con COVID-19. Pero la pregunta es, ¿qué causa la presencia de estas lesiones bucales? ¿Están directamente asociadas al SARS-CoV-2 (coronavirus) o su presencia podría deberse a una infección oportunista o quizás a una reacción adversa proveniente del tratamiento médico que recibieron los pacientes para combatir la infección?

Introduction

In December of 2019 a new virus called the Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) or better known as the coronavirus emerged from Wuhan, China. The virus is believed to have most likely originated from bats. From the bats it continued spreading to certain intermediate hosts such as dogs, snakes and pangolins and eventually through contaminated meat products it made its way to humans as well (1)(3). The virus spread itself very rapidly throughout the whole world and by March, 2020 the World Health Organisation (WHO) declared this disease as a global pandemic. At that point a total number of 118.000 people in 114 countries had been infected by this virus. Out of the 118.000 cases, 4.291 people had lost their life due to the coronavirus. As of today, according to the WHO, a total of 136 million cases have been identified and the total number of deaths are a bit over 2.9 million. Many countries have been severely affected by this virus and one of the countries that has been affected the hardest is Spain. Due to the rapidly growing number of cases, in March of 2020, Spain went into a lockdown. The majority of the dental clinics and university clinics closed down their businesses and didn't re-open until the following fall. At the time when everything closed down, no regular treatments were carried out, all pending non-emergency treatments was put on hold. The only treatments carried out were emergency treatments (2).

The coronavirus is believed to be spread through person-to-person contact, where an infected person (symptomatic or asymptomatic) either coughs, speaks or sneezes and thereby spreads the disease to other people that are in the vicinity of the infected person (1)(3). The incubation time from when a person contracts the virus until they start showing clinical symptoms ranges anywhere between 2-14 days (4)(11).

The clinical symptoms of COVID-19 vary from case to case. Some people infected by SARS-CoV-2 risk developing serious life-threatening conditions like acute cardiac damage, acute renal failure, gastrointestinal complications, dysgeusia, dysomnia and even neurological symptoms such as Guillain Barré syndrome (6). However, these are exceptional cases and these are usually affecting people that have a history of asthma, diabetes, people with weak immune-system, people with heart conditions, etc (1)(7)(8). The majority of the SARS-CoV-2 cases are usually mild and do not cause any serious life-threatening complications (1)(4). The typical signs and symptoms related to COVID-19 are fever, dry cough, myalgia, sore throat, diarrhoea, breathing difficulties and respiratory complications (shortness of breath), symptoms that are typical for any severe acute respiratory syndrome (1)(8)(10). It is believed that 20% out of all the infected patients develop severe diseases and only 5% of these cases become critically ill developing serious symptoms like pneumonia or acute respiratory distress syndrome which requires a mechanical ventilation and intensive care treatment in the hospital (5).

Research that has been carried out on the route of transmission of the SARS-CoV-2 virus has shown that the virus invades the human cells by binding to the angiotensin-converting enzyme (ACE2) receptor on the cell and then starts replicating. Cells with ACE2 receptors may therefore become host cells for the coronavirus and cause an inflammatory response in the related tissues and organs (5)(23). The ACE2 receptor can normally be found in the cell membrane of the lungs, kidneys, liver, skeletal muscles, the nervous system, the upper respiratory tract and especially in the epithelial cells of the tongue and salivary glands (6), which explains why so many patients suffer from gustatory impairment when contracting the virus.

Even though it's well known today that SARS-CoV-2 can be identified in the saliva and in the oropharyngeal secretions, but apart from that not much is known about its route of transmission through the oral mucosa (6).

Early studies indicated that the oral signs and symptoms related to SARS-CoV-2 were taste and smell chemosensory disorders. It was reported that these two symptoms were the initial and only signs of the disease in a fraction of the patients (10). However, in more recent studies, other oral lesions such as unspecific oral ulceration, desquamative gingivitis, petechiae and co-infections like candidiasis have been manifested amongst COVID-19 patients (20).

Developing a good understanding about the oral lesions associated to COVID-19 is of high importance and can be very beneficial for both the early detection of the disease and in order to prevent the spreading of it as well. However the question still remains, are the oral lesions found amongst the COVID-19 patients directly associated to the coronavirus? Or could it be as a result of an opportunistic infection due to a lowered immune response in these patients? Or could it maybe be due to adverse reactions coming from the medical treatment that the patients receive?

Objectives

Primary objective: to highlight the different oral lesions presented in patients with COVID-19

Second objective: to analyse if the oral lesions found in patients with COVID-19 are directly related to the SARS-CoV-2 virus itself or is it related to something else

Third objective: to analyse if SARS-CoV-2 has any further impact on the oral health of the patients

Materials and Methods

Electronic databases such as Medline, PubMed, Google Scholar, ResearchGate and Dulce Chacón Library at the UEM were searched in order to find articles related to oral lesions in patients with COVID-19.

Searches were made using the following words: "oral lesions in patients with covid-19", "covid-19", "oral lesions covid 19", "SARS-CoV-2 oral lesions", "2019-nCov", "2019-nCov oral lesion".

The articles found have been selected through an inclusion and exclusion criteria in order to ensure that only relevant information will be used for this project.

Articles written in English have been selected for this project and has been included only if they were relevant to the subject of oral lesions in patients with COVID-19

All of the selected articles are from 2020 and onwards

Results

One of the first recorded cases of oral lesions related to COVID-19 was recorded by Dr. Carmen Martin Carreras-Presas and other colleagues from Madrid, Spain. They presented 3 cases where three different patients presented different oral lesion, related to SARS-CoV-2 (ulcer, vesicle, desquamative gingivitis)(2).

Case 1:

Patient is a healthy 56 year old male, with no previous medical history. The patient suspected that he had an infection of SARS-CoV-2 due to having some of the typical COVID-19 symptoms. The patient had fever and asthenia for 2 days and decided therefore to self-isolate himself. He also presented hyposmia, dysgeusia and enlargement of a lymph-node. The symptoms that this patient presented were not severe enough to the



Figure 1: Multiple orange ulcers with erythematous halo and symmetric distribution on the right hard palate. Sourced by: Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, Jané-Salas E, Somaçarrera Pérez ML. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. Oral Dis. 2020;00:1–3.

grade that he was allowed to do a COVID test at the time. The patient complained about pain in his palate and having a sore throat at the time of the symptoms and through tele-consultation he sent photographs of the lesions (Figure 1).

The lesions seen on the photos resembled a herpetic recurrent stomatitis and it was the first time this patient ever came across this lesion. To treat this, he was prescribed valaciclovir 500 mg every 8h for 10 days as well as topical antiseptics with chlorhexidine and hyaluronic acid. The treatment was successful and the patient presented a full recovery of the oral lesions (2).

Case 2:

58 year old male, with a history of diabetes and hypertension complained about pain on his palate. The patients spouse had been diagnosed with SARS-CoV-2 so both of them decided to self-isolate. At first the patient thought that the pain was coming from a bacterial infection of a tooth. Through tele-communication, the patient sent images of his palate, where multiple small ulcers could be seen on his palate with a unilateral affection (figure 2). The patient had no previous history of any herpetic infections. To treat this, the patient was prescribed topical antiseptic mouthwash and within 1 week the pain and the lesions were gone (2).



Figure 2: Multiple pinpoint yellowish ulcers with an erythematous halo on the left hard palate of the patient. Sourced by: 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;00:1–3.

Case 3:

A 65 year old female patient with a history of obesity and hypertension had high fever, diarrhoea and pain on the tongue. The patients hypertension was controlled by taking ACE inhibitors and diuretics. A week after developing these symptoms the patient all of a sudden collapsed and was then rushed to the hospital. At the hospital she was diagnosed with bilateral pneumonia as a result of SARS-CoV-2 infection. She was then treated with antibiotics, corticosteroids and antiviral drugs (lopaniavir 200 mg, ritonavir 50 mg and hydroxychloroquine 200 mg). A few weeks later she Sida 10 av 61



Figure 3: The patient presented 3 blisters on the inner lip mucosa. The blister located closer to her right commissure was intact and tense. The bulla located on the left appeared to be broken. The lesions were affecting both intra- and extraoral mucosa, and the patient developed crusts on the external lip mucosa 3 days after this photograph was taken. Sourced by: 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;00:1–3

started developing a rash on her skin, under her chest and in her genital area. She was seen by a dermatologist after this and the dermatologist decided to do a biopsy on her and also prescribe antifungals again. After this, she started developing desquamative gingivitis and blisters in her internal lip mucosa (figure 3). To treat these lesions she was prescribed chlorhexidine mouthwash, hyaluronic acid and prednisolone 30 mg per day. After 3 days, the lesions started disappearing. The result of the biopsy showed "non-specific morphological findings with some criteria suggestive of viral exanthema or urticariform dermatitis with discrete blood extravasation" (2).

Case 4:

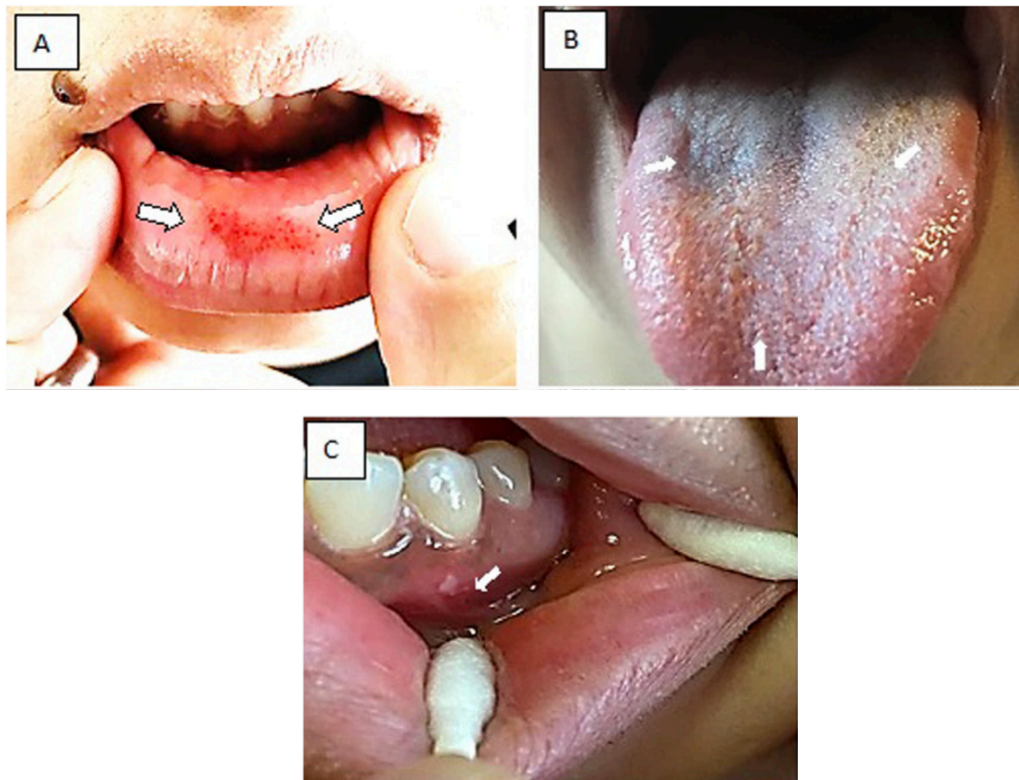


Figure 4: A, B and C. A: multiple petechiae can be seen in the mucosa of the lower lip. B: the posterior area of the tongue has more of an intense whitish colour and in the anterior area it's slightly more diffuse which suggests a mild case of *C. albicans*. C: in this image an aphthous ulcerative lesion can be seen below the lower left first premolar Sourced by: Corchuelo J, Ulloa F. Oral manifestations in a patient with a history of asymptomatic COVID-19: Case report [Internet]. PubMed. 2020 [cited 20 November 2020]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7462545/>

A 40 year old female living in New York, USA who had tested positive for COVID-19, attends a tele-consultation presenting several different oral lesions which could or could not be related to the

COVID-infection. She shows reddish plaque lesion on her lower lip and dark brown pigmentation in the gum which has progressed for 8 days (Fig 4A). The patient also presents a whitish area on the back of the tongue which is also accompanied by bacterial plaque in the middle third of the tongue (Fig 4B). At the level of the premolar on the left side of her mouth, she's showing thrush/canker sores lesions (Fig 4C). A well defined brown band can also be seen in the attached gingiva. At the time of the tele-consultation it had been 3 weeks since the patient tested positive for COVID-19 (SARS CoV 2 AB IGG Positive). The patient was also asked several questions associated to the presence of the lesions, when the lesions started appearing, whether the lesions were painful, whether she smoked or consumed any alcoholic beverages, if she was experiencing any dry mouth symptoms and whether she could taste or smell food. The patient described the lesions that she had as being painless except for one lesion, which was the aphthous ulcer that she presented in the gum. She was not a smoker, didn't drink any alcohol. She did feel that her mouth was more dry than normal but she did not have any loss or decrease in the sense of smell or taste (3).

Case 5:

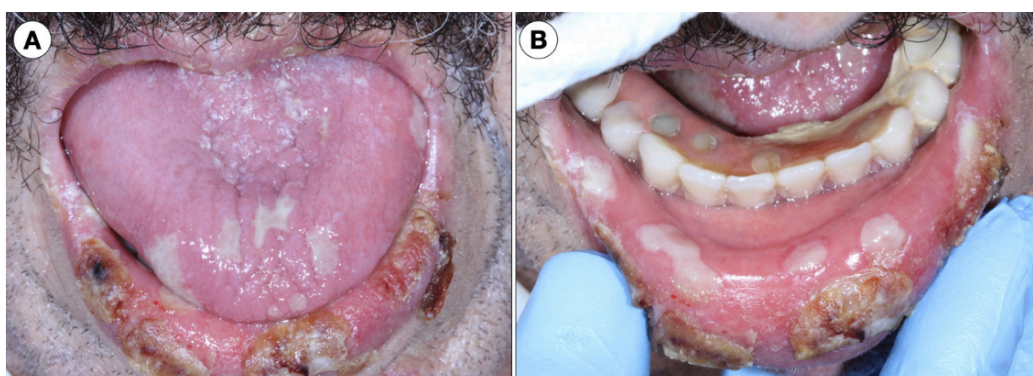


Figure 5A shows images of clustered ulcers covered with crusts on the lower lip and ulcerative lesions on the anterior part of the tongue. Figure 5B: ulcers on the lower lip mucosa Sourced: Brandão T, Gueiros L, Melo T, Prado-Ribeiro A, Nesrallah A, Prado G et al. Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ? [Internet]. PubMed. 2020 [cited 20 November 2020]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7434495/>

A 81 year old man from Sao Paulo, Brazil, presented progressive chest tightness and cough for 10 days. The patient had a history of well-controlled hypertension and chronic obstructive pulmonary

disease. The patient had come in contact with a family member who had tested positive for COVID-19 back in March, 2020. A few days later the patient developed dry cough and mild dyspnea. His body temperature went up to 37.7°C. The patient was eventually hospitalised and was treated with azithromycin and ceftriaxone for 7 days. Oral examination showed multiple aphthous-like ulcers of varying sizes and irregular margins covered with mucopurulent membrane, suggesting a superficial necrosis in both the upper and the lower lip, as well as the anterior dorsal side of the tongue (fig 1A and 1B). The lesions were painful upon palpation and it's believed that they had been developed during the days that the patient had been in the hospital. While performing a PCR-test at the hospital, Herpes simplex virus (HSV-1) was detected in the saliva of the patient. The patient was then immediately put on a course of acyclovir 150 mg/m², 3 times a day for 10 days.

The treatment showed no clinical improvement, so in order to alleviate the pain, the patient was given photobiomodulation therapy (PBTM) for 10 days. 2 days after the PBMT, the pain caused by the ulcers started to alleviate and after 11 days, the lesion resolved completely (6).

Case 6:

A female patient, 71 years old from Sao Paulo, Brazil with a history of hypertension, diabetes, obesity and renal failure was admitted to the hospital due to symptoms of SARS-CoV-2. She had developed cough, dysgeusia, fever and mild dyspnea. The patient's fever at the time of the hospitalisation was 38.5°C. The patient was put on a treatment with azithromycin (20 days) and ceftriaxone (3 days). During the intraoral examination of this patient, small hemorrhagic ulcerations on the upper and the lower lips was found,



Figure 6: focal ulcerative lesions can be seen on the anterior part of the tongue and hemorrhagic ulcerations on the upper and lower lip Sourced: [Brandão T, Gueiros L, Melo T, Prado-Ribeiro A, Nesrallah A, Prado G et al. Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ? \[Internet\]. PubMed. 2020 \[cited 20 November 2020\]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7434495/>](#)

as well as focal areas of shallow necrosis on the anterior dorsal part of the tongue (fig 6). When performing a PCR-test in the hospital, it was detected that the patient had Herpes simple virus (HSV-1). The patient was immediately put on a course of acyclovir 250 mg/m², 3 times a day for 7 days. However this didn't show any improvement of the clinical symptoms and due to the intense pain that the patient was feeling due to the ulcers, she was then treated with PBMT for 10 days. After 10 days of PBMT therapy the intraoral lesion regressed, however the ulcers on the lip did not respond to this treatment (6).

Case 7:



Figure 7A: painful ulcer seen on the right lateral border of the tongue. Figure 7B: Focal erythema/petechiae and a shallow necrotic area on the hard palate. Sourced: Brandão T, Gueiros L, Melo T, Prado-Ribeiro A, Nesrallah A, Prado G et al. Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ? [Internet]. PubMed. 2020 [cited 20 November 2020]. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7434495/>

A 83 year old female with severe obesity was admitted to a hospital in Sao Paulo, Brazil due to signs and symptoms of abdominal distension and mild dyspnea. She has previously had a history of Parkinson disease, hypertension, pancreatitis and chronic obstructive pulmonary disease. Upon arrival to the hospital, the patient had a fever of 37.5°C. On the intraoral examination an ulcer was identified on the right lateral border of the tongue and petechia in the anterior part of the hard palate (fig 7A and 7B). She described both lesions as being painful. Upon her arrival to the hospital a PCR-test was performed, which showed no signs of HSV-1. To alleviate the painful oral lesions, she was put under a PBMT-therapy. 5 days into the PBMT treatment, the pain was completely gone (6).

TABLE 1 Clinical and laboratory characteristics of patients with oral manifestations

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Verdoni ²⁸	7/5 (2/9-16)Y	M = 7 F = 3	-	MP Acral swelling	NA	-	Lip Oral cavity (80%)	-	Fever Diarrhea Conjunctivitis Meningeal sign Lymphadenopathy	-	20% + (PCR) 80% (IgG) 30% (IgM)	Kawasaki-like	-	-
Jones ²⁹	6 M	F	-	MP Acral swelling	Cracked lip Prominent papilla in tongue	-	Lip Tongue	-	Fever Conjunctivitis Tachypnea	2	+ (PCR)	Kawasaki-like	IVIG ASA	Increased levels of CRP, ESR Hypoalbuminemia
Pouletty ³⁰	10 (4/7-12/5)Y	M = 8 F = 8	Over weight Asthma	Rash	Cracked lip (87%)	-	Lip	-	Fever Respiratory & GI symptom Anosmia	-	69% + (PCR)	Kawasaki-like	IVIG CS ANTI IL1, IL6 HCH	Increased levels of cardiac markers Increased levels of CRP, ESR Lymphocytopenia
Singh ¹⁹	44Y	M	DM HTN	Non blanch able erythema Necrosis	Extensive mucosal damage	-	Lip Tongue	-	Malaise Dyspnea	4	-	Vascular inflammation Ischemic reperfusion injury	-	-
Chiotos ³¹	5Y	F	-	-	Fissured lip	-	Lip	-	Fever Diarrhea Conjunctivitis	-	-	Kawasaki-like	IVIG	Thrombocytopenia Increased levels of cardiac marker
Chiotos ³¹	9Y	F	-	-	Fissured lip Straw berry tongue	-	Lip Tongue	-	Fever Diarrhea Conjunctivitis	-	+ (PCR)	Kawasaki-like	IVIG ASA CS	Increased levels of CRP, ESR
Chiotos ³¹	12Y	M	-	-	Fissured lip	-	Lip	-	Fever Abdominal pain Diarrhea	-	(-) (PCR)	Kawasaki like	IVIG Milrinone	Increased levels of Cardiac marker Increased levels of CRP, ESR
Chiu ³²	10Y	M	-	-	Cracked lip Erythema	-	Lip Oropharynx	-	Fever Cough Diarrhea Conjunctivitis	-	+ (PCR)	Kawasaki-like	Dopamine	Leukocytosis Lymphocytopenia Increased levels of CRP, ESR, D- dimer, Procalcitonin Increased levels of Cardiac markers
Mazzotta ²⁴	9Y	M	-	Urticaria Angioedema Acral edema	Glossitis Cheilitis	Painful	-	-	Fever Cough Diarrhea Conjunctivitis	28-84	+ (Ig G)	Kawasaki-like	CS	-

TABLE 1 (Continued)

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Indu ¹³	NS	M	-	-	Ulcer	Burning Itching Painful	Lip Tongue	10	Fever	-4	+ (PCR)	Zosteriform	-	-
Tajkun ²⁵	61Y	F	-	Nodules	Minor aphthous ulcer	-	Hard palate Buccal	-	Fever Fatigue Myalgia Arthralgia	-	+ (PCR)	Atypical Sweet syndrome	AZT HCH Oseltamivir Tocilizomab Favipiravir	Increased levels of CRP, ESR, D-dimer Leukocytosis
Taşlıdere ²⁴	51Y	F	-	-	Swollen lip Fissured tongue	-	Lip Tongue	-	Malaise Unilateral Facial paralysis Facial edema	Coincident	-	MRS	HCH AZT CS	Increased levels of CRP Negative Serology for HSV, CMV,EBV, coxsackie Ground glass opacity in CT scan
Brandio ⁷	28Y	M	-	-	Aphthous-like Ageusia	-	Lip Tongue	6	Fever Cough Headache Myalgia Chills Anosmia	8	+ (PCR)	-	Mouthwash	-
Brandio ⁷	29Y	M	-	-	Aphthous-like Ageusia	Painful	Tongue	5	Cough Dyspnea Fever Malaise Headache Anosmia	8	+ (PCR)	-	Ipratropium bromide Fenoterol hydrochloride	-
Brandio ⁷	35Y	M	-	-	Aphthous-like	-	Tonsil	8	Fever Malaise Sore throat Cough Hyposmia Ageusia Odynophagia	6	+ (PCR)	-	-	-
Brandio ⁷	32Y	F	-	-	Aphthous-like	-	Tongue	5	Dysgeusia Fever Cough Headache Anosmia	10	+ (PCR)	-	Dipyron	-

(Continues)

TABLE 1 (Continued)

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Brandão ⁷	72Y	M	HTN DM	-	Aphthous-like Necrosis Hemorrhagic ulcer	painful	Lip	7	Fever Dyspnea	5	+ (PCR)	-	P/T AZT Ceftriaxone Acyclovir PBM	Increased levels of CRP Lymphocytopenia Positive PCR for HSV
Brandão ⁷	83Y	F	HTN COPD Obesity Parkinson Pancreatitis	-	Aphthous-like Petechiae Necrosis	painful	Tongue Hard palate	5	-	2	+ (PCR)	-	Ceftriaxone PBMT P/T	Negative PCR for HSV Lymphocytopenia
Brandão ⁷	71Y	F	HTN DM CRF Obesity	-	Aphthous-like Hemorrhagic necrosis Ulcer	painful	Tongue Lip	15	Fever Cough Dyspnea	4	+ (PCR)	-	AZT Ceftriaxone Acyclovir PBMT	Positive PCR for HSV
Brandão ⁷	81Y	M	HTN COPD	-	Aphthous-like Necrosis Hemorrhagic ulcer	painful	Lip Tongue	11	Dry Cough Dyspnea Fever Chills Dysgeusia	5	+ (PCR)	-	AZT Ceftriaxone Acyclovir PBMT	Increased levels of CRP Ground glass opacity in CT scan Positive PCR for HSV
Mali ⁸	38Y	M	-	MP	Erythema Aphthous-like	Painful	tonsil	-	Fever Fatigue Myalgia Loss of taste and smell	3	+ (PCR)	-	Acetaminophen	-
Labé ²²	3Y	M	-	Exanthema Palmar edema	Cheilitis Glossitis Stomatitis	-	Lip Tongue Oral cavity	-	Fever Asthenia Cervical LAP	-	-	Kawasaki-like	IVIg	Increased levels of CRP Leukocytosis Ground glass opacity in CT scan
Labé ²²	6Y	M	-	Target lesions	Erosion Cheilitis Hemorrhagic crust	painful	Lip Gingiva	21	Loss of appetite	7	+ (PCR)	EM like	-	Negative serology for mycoplasma Negative PCR for HSV
Aghazadeh ⁹	9Y	F	-	Papule Plaque	Vesicles Erosions	-	Lip Tongue Buccal	7	Fever Weakness Loss of appetite Abdominal pain Diarrhea	Coincident	+ (PCR)	Herpetiform	Acetaminophen	Bilateral ground glass opacity

TABLE 1 (Continued)

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Kämmerer ¹⁰	46Y	M	HLP CAD	-	Multiple ulceration covered by yellow gray membrane	Painful	Oral cavity Gingiva	-	Fever Fatigue Dry cough Respiratory distress LAP submandibular	5 days after intubation	+ (PCR)	Secondary herpetic Gingivostomatitis	AZT Meropenem Acyclovir	Increased levels of CRP, IL6, Eosinopenia Positive PCR for HSV Positive serology for HSV(IgM) Bilateral ground glass opacity in CT scan
Cruz Tapia ²³	42Y	M	-	-	Macules	Burning	Hard palate	7	Fever Malaise Dysgeusia Headache	14	+ (PCR)	Mucositis due to vasculitis and thrombosis	Acetaminophen Mouthwash CS	-
Cruz Tapia ²³	55Y	F	-	-	Tongue enlargement Purple blister	-	Tongue	5	Fever Headache Nasal congestion	2	+ (PCR)	Angina bullosa-like	Acetaminophen	-
Cruz Tapia ²³	51Y	F	HTN	-	Vascular-like purple macule nonbleeding Purple plaque	-	Palate	-	Fever Malaise Dysgeusia Arthralgia	-	+ (PCR)	Vascular disorder	CS AZT NSAID	-
Cruz Tapia ²³	41Y	F	-	-	Erythematous blister	-	Hard palate	-	Fever Malaise Dysgeusia Hyposmia	-	+ (PCR)	Angina-bullosa-like	Acetaminophen Fexofenadine	-
Diaz Rodríguez ⁶	78Y	F	-	-	Dry mouth Atrophy of surface of tongue White & red patches Fissured tongue	-	Tongue Hard Palate Soft palate Lip	15	-	-	+ (PCR)	Pseudomembranous candidiasis Angular cheilitis due to Stress Immunosuppression	Artificial saliva Nystatin Neomycin CS	-
Diaz Rodríguez ⁶	53Y	M	-	-	Angular cheilitis	Burning	Lip	10	Dysgeusia Anosmia	Few days after discharge	+ (PCR)	Cheilitis due to stress and immunosuppression	Nystatin CS Neomycin, Mouthwash	-
Diaz Rodríguez ⁶	43Y	F	-	-	Multiple ulcer covered by yellow-gray membrane Lingual depapillation	Burning	Tongue	10	Fever Malaise Dysgeusia Anosmia Diarrhea Pneumonia	14	+ (PCR)	Aphthous-like due to stress and immunosuppression	Mouthwash CS	-

(Continues)

TABLE 1 (Continued)

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Chérif ²⁷	35Y	F	-	Macule	Chapped lips Ulcer Hypogeusia	-	Tongue Lip	10	Fever Myalgia Dyspnea Dry cough Vomiting Diarrhea	-	+	Kawasaki-like (PCR)	HCH AZT Cefuroxime	Thrombocytopenia Anemia Neutrophilia Lymphopenia Increased levels of liver and cardiac markers Increased levels of CRP, LDH, ferritin
Ansari ¹⁸	75Y	M	HTN	-	Irregular ulcer in erythematous background	Painful	Tongue (anterior)	7	Hypoxia	7	+	Mucosal ulcer due to COVID-19	AZT, Mouthwash	Negative Serology for HSV 1-2
Ansari ¹⁸	56Y	F	DM	-	Irregular ulcer in erythematous background	Painful	Hard palate	7	Fever Dyspnea	4	+	Mucosal ulcer due to COVID-19	Remdisivir AZT	Negative Serology for HSV 1-2
Bladsee ⁹	36.25Y	NS	HTN DM Hypothyroidism Asthma	-	Plaque bleeding Swelling Xerostomia Dysgeusia	-	Tongue Palate Gingiva	-	Fever Cough Myalgia Sore throat Anosmia GI symptoms	-	+	(PCR)	-	-
Olsova ¹¹	12Y	F	-	Purpura Macule	Swollen, Irritated Pronounced lingual papilla	-	Tongue	3	Fever Fatigue Headache	3	+	(PCR)	Paracetamol	Increased levels of ESR, CRP
Tomo ²⁶	37Y	F	-	-	Erythema Depapillation of tongue	Painful	Tongue (border)	14	Fever Asthma Dysgeusia Anosmia	9	+	Mucositis due to hypersensitivity to SARS-CoV-2	CS Dipyron Mouthwash	-
Ciccarese ¹⁷	19Y	F	-	Macules Papules Petechiae	Erosion Ulcer Hemorrhagic crust Petechial	-	Lip Palatal Gingival Oropharynx	5	Fever Fatigue Hyposmia Sore throat	7	+	Thrombocytopenia due to COVID-19 and cefixime	IVIg CS	Thrombocytopenia Leukocytosis Increased levels of liver markers and LDH
Sakaida ¹⁶	52Y	F	-	MP Petechiae	Erosion	-	Lip Buccal	-	Fever Dyspnea Dry cough	-3	+	Drug eruption (PCR)	NSAID Clarithromycin SAM Levofloxacin Cs	Leukocytosis Lymphopenia Neutrophilia Increased level of CRP

TABLE 1 (Continued)

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Dominguez-Santas ³⁷	19Y	M	-	-	Minor aphthous	-	Lip	-	Fever Headach Anosmia Malaise dyspnea	0	+	Cytokine storm due to COVID-19	-	Lymphocytopenia Negative PCR for HSV Negative serology for syphilis, HIV, EBV, CMV, HBV, HCV
Dominguez-Santas ³⁷	37Y	M	-	-	Minor aphthous	-	Tongue	-	-	5	+	Cytokine storm due to COVID-19	-	Lymphocytopenia Negative PCR for HSV Negative serology for syphilis, HIV, EBV, CMV, HBV, HCV
Dominguez-Santas ³⁷	33Y	M	-	-	Minor aphthous	-	Mucogingivl junction	-	Pneumonia Fever Malaise	3	+	Cytokine storm due to COVID-19	-	Lymphocytopenia Negative PCR for HSV Negative serology for syphilis, HIV, EBV, CMV, HBV, HCV
Dominguez-Santas ³⁷	43Y	F	-	-	Minor aphthous	-	Buccal	-	Bilateral pneumonia Fever Malaise	4	+	Cytokine storm due to COVID-19	-	Lymphocytopenia Negative PCR for HSV Negative serology for syphilis, HIV, EBV, CMV, HBV, HCV
Putra ⁵	29Y	M	-	Papule	Aphthous Stomatitis	-	-	-	Fever Myalgia sore throat Dry cough	6	+	Enanthema due to COVID-19	Paracetamol AZT HCH Oseltamivir Vitamin C Vitamin D	Increase level of CRP
Martin Carreras-Presas ¹²	65Y	F	HTN Obesity	Rash	Desquamative gingivitis	Painful	Tongue Gingiva	28	Fever Diarrhea	25	+	EM-like (serology)	Antibiotic CS HCH HA L/R	-

(Continues)

TABLE 1 (Continued)

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Martin Carreras-Presas ¹²	58Y	M	DM HTN	-	Unilateral multiple small ulcers	Painful	Palate	7	-	-	-	Herpetiform	Mouthwash	-
Martin Carreras-Presas ¹²	56Y	M	-	-	Dysgeusia, Herpetiform Stomatitis	Painful	Hard Palate	10	Fever Asthenia LAP	2	NP	Herpetiform	Val acyclovir Mouthwash HA	-
Jimenez-Cauhe ²¹	60Y	M = 2 F = 4	-	EM-like	Macule Petechiae	-	Palate	-	-	19	-	Enanthema due to COVID-19	AZT HCH L/R	-
Jimenez-Cauhe ²¹	40Y	-	-	Purpura EM-like	Petechiae Macule Petechiae	-	Palate Palate	-	-	2 24	-	Enanthema due to COVID-19 Enanthema due to COVID-19	AZT HCH AZT T CS L/R HCH AZT Tocilizomab CS	Thrombocytopenia High D-dimer High D-dimer
Jimenez-Cauhe ²¹	50Y	-	-	-	-	-	-	-	-	-	-	-	-	-
Jimenez-Cauhe ²¹	60Y	-	-	EM-like	Macule Petechiae	-	Palate	-	-	19	+	Enanthema due to COVID-19 (PCR)	L/R HCH AZT	High D-dimer
Jimenez-Cauhe ²¹	60Y	-	-	Papule Vesicle	Petechiae	-	Palate	-	-	-2	+	Enanthema due to COVID-19 (PCR)	L/R HCH AZT	High D-dimer
Jimenez-Cauhe ²¹	40Y	-	-	purpura	Macule	-	Palate	-	-	12	+	Enanthema due to COVID-19 (PCR)	L/R HCH	Thrombocytopenia High D-dimer
Patel ³³	35Y	F	-	-	Bleeding Halitosis Generalized edematous erythematous gingiva Necrosis	Painful	Gingiva	5	Fever LAP submandibular	3	NP	Bacterial co-infection	Metronidazole Mouthwash	-
Chaux-Bodard ¹⁴	45 Y	F	-	Patch	Ulcer	Painful	Tongue (dorsal)	10	Asthenia	-	+	Vasculitis (PCR)	-	-

TABLE 1 (Continued)

First name author	Age	Sex	Underlying disease	Cutaneous	Oral	Oral Symptom	Site	Duration (days)	Systemic manifestations	Latency (days)	COVID-19	Suggested etiology	Treatment	Lab tests
Soares ¹⁵	42Y	M	DM HTN	Petechiae Vesicle Blister	Ulcer Macules	Painful	Buccal Tongue Lip Hard Palate	21	Fever Cough Dyspnea	-	+	Thrombotic vasculopathy due to SARS-CoV-2 (PCR)	CS Dipyron	IHC: negative for other viral and treponema palladium
dos Santos ⁴	67Y	M	CAD HTN PCK RT	-	White plaque Multiple yellowish ulcer Geographic tongue Erythema Hypogeusia	-	Tongue Palate Tonsil	14	Fever Diarrhea Dyspnea	24	+	Herpetiform lesions secondary to determination of systemic health and treatment (PCR)	Mouthwash Fluconazole Nystatin AZT Ceftriaxone HCH Meropenem T/S	Positive Culture for +Saccharomyces cerevisiae
Corchuelo ²⁰	40Y	F	-	-	Petechiae Whitish area Brown pigmentation	Painful	Tongue Lip Gingiva	20	LAP of neck	-	+	Candidiasis Thrombocytopenia due to ibuprofen (IgG) PIH	Ibuprofen Vitamin D AZT Mouthwash Nystatin	-
Jimenez-Cauhe ³⁵	66.7(58-77)Y	F = 3	-	EM-like	Petechiae Macule	-	Palate	14-21	-	19.5 (16-24)	-	EM-Like	AZT Ceftriaxone Cs HCH L/R	Increase levels of CRP High D-dimer Lymphocytopenia Negative serology for syphilis, M. Pneumonia and other viral
Cebeci Kahraman ³⁴	51Y	M	-	-	Large erythematous Petechiae Pustules	Painful	Hard palate Oropharynx Soft palate Agusia	A few days	Fever Fatigue Dry cough Sore throat Anosmia	10	+	Enanthema due to COVID-19 (IgM)	Clarithromycin	-

Abbreviations: AZT, azithromycin; CAD, chronic arterial disease; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; DM, diabetes mellitus; HCH, hydroxychloroquine; HLP, hyperlipidemia; HTN, hypertension; L/EX, lower extremity; M, month; MP, maculopapular; MRS, Meikerson-Rosenthal syndrome; P/T, piperacillin/tazobactam; PCK, polycystic kidney; PIH, postinflammatory hyperpigmentation; RT, renal transplantation; SAM, ampicillin sulbactam; T/S, trimethoprim/sulfamethoxazole; Y, year.

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The following table shows the different oral manifestations that have been detected on patients with COVID-19. This is a conglomeration of all the different cases and oral lesions that have been reported by different health professionals around the world. Oral lesions such as ulcers, erosions, bullas, vesicles, fissured or depapillated tongue, macule, papule, plaque, pigmentations, halitosis, whitish areas, hemorrhagic crust, necrosis, petechiae, swelling, erythema and spontaneous bleeding. These are all different oral manifestations that has been found during intraoral examinations of patients with COVID-19. Some of the diagnosed lesions have been aphthous stomatitis, herpetiform lesions, candidiasis, vasculitis, cheilitis, atypical sweet syndrome and Melkeson-Rosenthal syndrome. The most frequent site that the lesions have been discovered on is in the tongue. However, other oral sites such as the labial mucosa and the palate are also sites where some lesions have presented itself. The gingiva, buccal mucosa, oropharynx and tonsils has also manifested some lesions, but at a far less degree compared to the tongue, labial mucosa and the palate

- Tongue (38%)
- Labial mucosa (26%)
- Palate (22%)
- Gingiva (8%)
- Buccal mucosa (5%)
- Oropharynx (4%)
- Tonsils (1%)

The lesions had a healing time of anywhere between 3-28 days from the day of its appearance and has been treated with several different methods, including chlorhexidine, nystatin,

photobiomodulation therapy (PBMT), systemic or local corticosteroids, systemic antibiotics, acyclovir and artificial saliva (22).

The following oral lesions have been discovered in patients with COVID-19. According to the table above we see many different types of oral lesions that has presented itself in patients with either confirmed COVID-19 or patients with COVID-19 symptoms.

Angina bullosa hemorrhagica-like lesions

Angina bullosa is a benign subepithelial blister filled with blood. These type of lesions were presented in two confirmed cases of COVID-19. In both cases these lesions were asymptomatic, erythematous, purple blisters with no spontaneous bleeding. They were presented on the tongue and on the hard palate (22).

Aphthous-like lesions

The aphthous-like lesions are lesions that appear as multiple shallow ulcers with an erythematous halo and a yellow-white pseudomembrane found on keratinised mucosa as well as non-keratinised mucosa (22).

Atypical sweet syndrome

A 61 year old female patient presented fever, fatigue, arthralgia, myalgia and several erythematous nodules on her trunk, extremities and her scalp. Her PCR-test came back positive and confirmed a SARS-CoV-2 infection. In the intraoral examination minor aphthous ulcers was found in the buccal mucosa and on the hard palate. A skin biopsy was taken which showed diffuse neutrophilic infiltration in the upper dermis with granulomatous infiltration in the lower dermis and subcutaneous area that was compatible with erythema nodosum-like Sweet syndrome (22).

Erythema Multiforme-like lesions

These lesions appeared between 7-24 days after the onset of the systemic symptoms. These type of lesions appeared as blisters, desquamative gingivitis, erythematous macules, erosions and painful cheilitis with hemorrhagic crusts in patient with cutaneous lesions in their extremities. The recovery time for these lesions was 2-4 weeks (22).

Herpetiform/zosteriform lesions

Herpetiform lesions constitute another type of oral lesion that have been identified in patients with COVID-19. It has been understood that these lesions can either precede the systemic symptoms, coincide with the systemic symptoms or present themselves following after the presentation of the systemic symptoms. Herpetiform lesion can be very painful, they're round, yellowish-gray ulcers and unilateral with an erythematous rim. They are presented both on keratinised mucosa and non-keratinised mucosa (22).

Kawasaki-like disease

Kawasaki disease normally presents alterations in the lips and the oral cavity. Patients with Kawasaki disease normally presents erythema, dryness, fissuring, dryness of the lips, peeling, cracking and also something called a "strawberry tongue", where the tongue turns completely red. It has been reported that some patients infected by COVID had developed the same oral signs as in the Kawasaki disease: cheilitis, glossitis, erythematous and swollen tongue (red strawberry tongue).

Melkersson-Rosenthal syndrome

A 51 year old woman with a history of Melkersson-Rosenthal syndrome from 4 years ago presented unilateral lip swelling, facial edema, malaise, fissured tongue and facial paralysis. Her laboratory data demonstrated high levels of CRP and her CT-scan showed ground-glass opacities in

both lungs. The patient was put on a course of hydroxychloroquine, azithromycin and corticosteroids and after the treatment the patient cured completely from this syndrome.

Necrotizing periodontal disease

Necrotizing periodontal disease manifests itself by causing necrosis and ulceration in the gingival margins and the interdental papilla of the oral mucosa. Patients with necrotizing periodontal disease usually suffer from a lot of pain, halitosis, spontaneous gingival bleeding, malaise and sometimes they get fever as well. The etiology for NPD is usually immunodeficiency, smoking, malnutrition, stress and poor oral hygiene

One patient, female 35-years old presented with fever, submandibular lymphadenopathy, halitosis and oral lesions. The oral lesions that this patient presented were painful, diffuse erythematous with necrosis of the inter-papillary areas. The presumptive diagnosis that was made on this was necrotizing periodontal disease due to a bacterial co-infection associated with SARS-CoV-2 infection (22).

Non-specific lesions (mucositis)

Another type of oral lesions that have been presented in patients with COVID-19 are erythematous-violaceous macules, patches, papule and plaques that have presented themselves on several locations in the mouth. The tongue, the lip mucosa, hard palate and oropharynx.

Petechiae

Some studies reported that in patients with COVID-19, during intraoral examination petechiae were found. These lesions was located in the lower lip, in the palate and in the mucosa of the oropharynx. The difference between patients just presenting petechiae and patients presenting both petechiae and macular lesions is that the latency period was shorter in patient presenting just petechiae.

Post-inflammatory pigmentation

There's one case that has been reported about a patient developing post-inflammatory pigmentation. A 40 year old woman started developing a colour alteration or a pigmentation in the attached and the inter-papillary gingiva (22).

Ulcer and erosion

Ulcers and erosive lesions is another type of lesion that has been identified on the tongue, on the hard palate and on the labial mucosa of the patients. Ulcers are very painful lesions and in most cases they've appeared somewhere between 4-7 days after the onset of the systemic symptoms. However in one case the lesions appeared 3 days before the onset of the systemic symptoms.

Vesicles and pustules

Two patients COVID-19 positive who have presented vesicles and pustules in their intraoral examination. One patient was a 9 year old female who presented fever, weakness, abdominal pain and diarrhoea. Her PCR test came back positive for COVID-19. She was treated with acetaminophen and the lesions cured after 1 week.

The other patient was a 51 year old male who had a positive serology test for COVID-19. Patient was complaining about fever, fatigue, dry cough, dysgeusia and anosmia. This patient also presented a widespread erythema on the hard palate and the oropharynx with petechiae and pustules on the border of the soft palate. The presumptive diagnosis for this patient was enanthema due to COVID-19. He was treated with clarithromycin and after a few days the lesions disappeared (22).

White/red plaques

These lesions has been reported on the dorsum of the tongue, gingiva and palate of patients with either confirmed- or suspected COVID-19 infection.

Discussion

COVID-19 has had a severe impact on all businesses and professions. Every single profession has been affected by this disease and it has led to drastic measures being taken in order to save businesses. Nevertheless, most businesses have been negatively impacted by this disease and will most likely suffer in the long-term as well from this. One of the potential long-term effects that COVID-19 will have on dentistry is that it will eventually increase the cost of the dental treatments due to several reasons. One reason being that the dentist will need additional resources like personal protective equipment (PPE), another reason will be increased waiting times due to the need for segregation in the waiting area, which then results in a decreased number of patients visiting the clinic and therefore higher treatment costs in order to be able to save the clinic (1). E-consultation will become more frequent due to the fact that we don't want patients coming into the clinic unless they really have to and because technology has evolved so much during the last 15 years, we can many times diagnose the patients without them actually having to be physically present in the clinic. Many of the following studies and treatments have been carried out through tele-consultation where symptomatic/asymptomatic COVID-19 patients have presented oral lesions (3).

The corona virus has different ways of being transmitted, it can be transmitted directly through cough, sneeze, inhalation of the virus-containing droplets or it can be transmitted through contact with the oral, nasal and eye mucous membranes (1).

Many studies suggest that the transmission of SARS-CoV-2 can also be airborne, usually occurring during aerosol-generating procedures (AGP). Taking into consideration all the different routes of transmission, it would be safe to assume that the health professionals are the ones that have the highest risk of contracting COVID-19 while working.

The corona virus has a multi-organic manifestation with a variable severity of complications.

Numerous studies has shown that the virus invades the human cells through a receptor called angiotensin-converting enzyme 2 (ACE2). This means that the cells with ACE2 receptors becomes host cells for the virus and whenever a patient gets infected by the SARS-CoV-2 virus, that cell causes an inflammatory response(5)(23).

ACE2 receptor is present in almost all organs, but the number of ACE2 receptors differs from one organ to another organ. According to some scholars we have a higher number of ACE2 receptors in the oral mucosa, especially the tongue and the salivary glands, than we have in most other organs. We can find more ACE2 receptors in the epithelial cells of the salivary glands than in the lungs for example, which explains why gustatory impairment is one of the main symptoms that this disease causes (6). Also another thing that has to be taken into consideration when it comes to the signs and symptoms related to COVID-19 is that different lifestyles plays a huge role in the ACE2 expression in people, i.e. people in Spain may present a higher number of a certain sign or symptom of COVID-19 compared to what people in China presents. People in China might present higher number of another typical sign or symptom of COVID-19 compared to what people in the United States presents (5). However, after a lot of investigation on the signs and symptoms of COVID-19 it is safe to say that the most common oral manifestation that SARS-CoV-2 infection causes is gustatory impairment, either ageusia or dysgeusia (5)(11). Approximately 45% of the total number of COVID-19 cases has caused some type of gustatory impairment amongst the patients (5). What happens is that when the virus (SARS-CoV-2) enters the cell through the ACE2 receptors, it starts damaging the glands and the ducts. As a result of this, an immediate healing process mediated by fibroblasts commences. The fibroblasts starts forming fibrous connective tissue in order to heal the damaged gland and duct. This mechanism is the cause for the manifestation of sialadenitis which is accompanied by both pain and tremor in the parotid and the submandibular glands and that leads to patients usually losing their sense of taste (11).

The oral manifestation that has been related to COVID-19 are many, taste disorder, various number of oral lesions such as ulcers, desquamative gingivitis, petechiae and as well as co-infections like candidiasis (20). However the question still stands whether these manifestation are a typical sign of the SARS-CoV-2 virus, is it as a result of systemic infections that normally impairs the immune system and increases the risk of co-infections or could it be due to the adverse effects of the medical treatment that has been given to the patients?

It's regarded as uncommon to find a divergent mucosal lesion related to a single viral, which would indicate that there are other factors behind the presentation of the oral lesions that has been reported (5). A lot of times high levels of stress and fatigue, which this disease many times can cause can be associated to the manifestation of certain oral lesions, i.e. reactivation of herpes simplex virus (HSV), which some patients have presented (11). Same thing can be said about some of the other lesions that has been shown as well. Erythema multiforme for example has been associated with several different viruses such as adenovirus, enterovirus and herpes virus (11). Approximately 70% of viral infections by either adenovirus, enterovirus or herpes virus causes an oral manifestation of oral lesions (11).

Something similar happens in the Kawasaki-like disease, where one of the most reported risk factors for this disease is a viral infections by Adenoviruses, Enteroviruses, Influenza A and Parainfluenza type 3 (11).

However several diseases present an oral manifestation as a first sign or even as an only sign in some cases, which means that in order to confirm confirm the association between the different oral lesions and SARS-CoV-2 more tests have to be done.

Angina bullosa hemorrhagica-like lesions

These lesions are not found very commonly. It's usually not associated to any systemic disorders or any hemostatic defects. Its pathogenesis has not been discovered yet but it's assumed that it's multifactorial. One of its main aetiologies is believed to be due to trauma or due to the use of steroid-inhalers (22).

Apthous-like lesions

One possible etiology of the apthous-like lesions can be due to the stress and immunosuppression that an infection like COVID-19 can bring to a person. For one patient the apthous-like lesion appeared simultaneously with the systemic symptoms. For other patients the presentation of these lesions took somewhere between 2-10 days.

One of the patients presenting this lesion, had a history of getting recurrent apthous stomatitis and in two other patients, it was found out that their PCR-test showed them having herpes simplex virus (HSV). This type of lesion was presented in both younger and older patients. Younger patients with mild infections presented apthous-like lesions without any necrosis, older patients with immunosuppression and severe infection however showed these type of lesions but with necrosis accompanying it and hemorrhagic crusts.

The healing of these lesions was associated with the improvement of the systemic disease itself.

The healing time was somewhere between 5-15 days (22).

Atypical sweet syndrome

Atypical sweet syndrome is quite an unusual disease. In the rare cases that it does appear it's usually associated to malignancies, inflammatory bowel disease, autoimmune disorders, drugs and infection. The etiology of this disease can many times be due to an immune reaction against certain drugs. Biological agents and tumours can initiate a cytokine cascade which results in the onset of the atypical sweet syndrome. This syndrome can many times lead to patient suffering from fever, myalgia, arthralgia, leucocytosis.

So far only case has been reported about a patient having atypical sweet syndrome, whilst suffering from the coronavirus. In this case no other cause apart from SARS-CoV-2 infection could be determined to have caused the atypical sweet syndrome. However, not many cases (if any) apart from this one has reported about a patient with COVID-19 presenting atypical sweet syndrome, so we can't conclude that this is a sign or a symptom of COVID-19 (25).

Erythema Multiforme-like lesions

Erythema multiforme is normally a type of an acute allergic reaction, caused by an infection most of the time. Infections that usually leads to the appearance of erythema multiforme lesions are infections by viruses such as herpes simplex, which causes cold sores and genital herpes, but they can also be caused by bacterial infections or fungal infections. In the case of bacterial infections it usually ends up with lung affectation and the fungal infection results in histoplasmosis (22)

Herpetiform/zosteriform lesions

Similar to the aphthous-like lesion, a possible etiology for these lesions can be the high level of stress and the immunosuppression that an infection like COVID-19 brings to the patient (22).

Kawasaki-like disease

When the pandemic first hit, one of the issues of interest was the potential association between COVID-19 and the Kawasaki disease. A study done in Bergamo, Italy reported that when the pandemic first hit, the number of Kawasaki disease cases in one month was 30 times higher than the monthly incidence in the previous 5 years.

The duration time between the appearance of the systemic symptoms that comes with a COVID-19 infection (respiratory and gastrointestinal) and the onset of the oral and cutaneous symptoms was very long in this case. However a possible explanation for that could be that the oral manifestation was delayed due to the response of the immune system releasing acute inflammatory cytokines rather than the direct effect of the SARS-CoV-2 virus on the oral mucosa.

A more in depth study needs to be carried out on this matter in order to find potential differential diagnosis between the two diseases and in order to be able to perform early diagnosis. According to a study done in Bergamo, Italy, when the pandemic started the number of Kawasaki disease cases increased (26).

Melkersson-Rosenthal syndrome

Melkersson-Rosenthal syndrome is a very rare disorder that usually presents three different symptoms, orofacial edema, fissured tongue and facial paralysis. The etiology for the Melkersson-Rosenthal syndrome is unclear at the moment but some researchers believe that it can be triggered by viral infection such herpes simplex virus, Epstein Barr virus, varicella zoster virus and cytomegalovirus. COVID-19 has previously not been considered as an etiology for Melkersson-Rosenthal syndrome. However, more research needs to be carried out in order to see if there is an association between both diseases (27). As of right now there's no standardised treatment developed for Melkersson-Rosenthal syndrome, but certain treatments such as local triamcinolone injections, antibiotics, surgical interventions, TNF alpha blockers and exclusive enteral nutrition has been proven to be effective. Because this syndrome is so rare it's hard to find a treatment that works in all cases of treating this syndrome. But this case can potentially show a breakthrough in the chase of treating this syndrome (22).

Necrotizing periodontal disease

The treatment for NPD usually depends on the presence of pain and gingival necrosis, this patient had both so she was treated with a metronidazole mouthwash. 5 days into the treatment, the lesions had regressed (22). Necrotizing periodontal disease can many times be appear due to a subsequent bacterial co-infection (29).

Non-specific lesions (mucositis)

Some studies has reported about COVID-19 patients presenting mucositis. Mucositis presented in these patient can come from several different aetiologies, one of them being thrombotic vasculopathy, vasculitis or hypersensitivity that is associated to COVID-19. It's believed that mucosal hypersensitivity secondary to COVID-19, thrombotic vasculopathy and vasculitis may be the possible origin for mucositis in COVID-19 patients (22).

Petechiae

The etiology for these oral lesions is thought to be due to thrombocytopenia caused by COVID-19 infection or the drugs that has been prescribe to the patient to combat the COVID-19 infection (22).

Post-inflammatory pigmentation

It's believed that this occurred as a result of increased levels of inflammatory cytokines (including interleukin-1 [IL-1], tumour necrosis factor [TNF]- α) and arachidonic acid metabolites (prostaglandins) secondary to the production of stem cell factor (SCF) and basic-fibroblast growth factor (bFGF) coming from keratinocytes of the basal layer of the gingiva. This is believed to have lead to a post-inflammatory pigmentation (22).

Ulcer and erosion

Ulcerative lesions are the most commonly presented oral lesions of COVID-19 patient. It's believed that different factors like drug eruption, vasculitis or thrombotic vasculopathy secondary to COVID-19 infection could be the cause for the development of the ulcerative and erosive lesions (22).

Vesicles and pustules

In the case of the 9 year old girl who presented vesicles and pustules in the intraoral examination, a differential diagnosis was made which included hand-foot-mouth disease (HFMD), atypical herpes simplex infection, mycoplasma-induced rash and mucositis, erythema multiforme (EM) and drug eruption. HFMD was disregarded because HFMD characteristically presents elongated greyish vesicles on the palmar and plantar surfaces and in this case the patient showed none of that. Erythema multiforme was disregarded due to the lack of classical targetoid lesions that EM presents. The patient received only acetaminophen for pain relief and no other antiviral or antibacterial drugs was given to her, which disregards drug eruption as an etiology. A PCR test for herpes simplex virus or enterovirus was not performed, so in this case that can't really be disregarded as an etiology for the vesicles and pustules (30)

White/red plaques

The cause for these oral lesions can be candidiasis due to long-term antibiotic therapy, bad oral hygiene or an overall deterioration of the general status of the patient (22).

Conclusion

Because of the novelty of the disease, there is still not enough evidence on the effects of SARS-CoV-2 on the oral cavity. Some studies have shown different oral lesions in patients with COVID-19 but further investigation on the matter is needed. In many occasions the first sign of an infection and sometimes the only sign of an infection can present itself in the oral mucosa (6)(14).

Oral lesions can many times precede a typical respiratory infection and at the same time, worsening of the oral lesions may precede an even more serious clinical scenario (6)(22). Based on this it's very important that a lot more studies are carried out on the effect that COVID-19 might have on the development of oral lesions. Dentists can play a critical role in the battle against COVID-19 by recognising its oral manifestations and thereby detecting possible future cases. It would be highly advisable that from now the anamnesis of the patients visiting the dental clinic included "recent onset of taste disturbance" or "oral ulcers" as well as a thorough oral examination should be performed on suspected cases of COVID-19 (11).

From the studies that have been carried out, the most prevalent oral manifestation related to COVID-19 is without a doubt the gustatory impairment where as much as 45% of the total number of COVID patients have reported about having some type of taste alteration upon contracting the virus. Based on this, dysgeusia is considered as the first oral manifestation directly related to SARS-CoV-2 (5).

When it comes to oral lesions and the effect that SARS-CoV-2 has on them, there's not as much certainty as there is for its effect on taste. Many studies suggest that the etiology of the lesions that have been presented in these cases can either be due to co-infections, immunity impairment or adverse effects from the drug therapy against the infection, rather than being an oral mucosa infection directly caused by SARS-CoV-2.

Since there hasn't been any standard treatment developed for COVID-19 or no vaccine was created until very recently, a concoction of several different drugs has been administered to the patients in order to fight the infection. This in turn can lead to several adverse effects and eventually the manifestation of the different oral lesions that have been presented in these different cases.

Another possible factor for the presence of the oral lesions seen in these patients can be due to the acute condition that SARS-CoV-2 causes in people. People infected by SARS-CoV-2, especially in the beginning of the pandemic got very stressed and felt very fatigued. This can certainly take its toll on the immune system and can therefore lead to other opportunistic infections such as Herpes simplex and candidiasis presenting itself (11)(12).

Social Responsibility

The aim of this study is to highlight the different oral lesions that has been identified in patients with COVID-19 and try to find out what their etiology is?

COVID-19 is a rather new disease and therefore there hasn't been a ton of research carried out on this topic. Even less when it comes to the oral signs and symptoms that this disease might manifest.

The importance of finding out if SARS-CoV-2 can present any oral lesions can be vital for the battle against this virus, because as we already know, many times oral lesions precedes a respiratory infection, so if we can figure out what oral signs this virus presents, we can take faster action and try to halt this disease from developing even further.

Apart from all the deaths that this disease has caused, it has also had a huge economic impact on today's society. The cost of keeping businesses open have increased by a big margin, the amount of clients that a clinic or a restaurant/bar have been able to take in has decreased drastically due to the new rules and regulations that every business has to follow in order to comprehend with the new reality that we are facing. This in turn has led to a lot of businesses being forced to shut down and a lot of people losing their jobs.

A lot more research and studies needs to be carried out on this disease and its oral manifestation which can be regarded as a prodromal signs of the infection.

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dentistry journal



Review

Novel Coronavirus (COVID-19) and Dentistry–A Comprehensive Review of Literature

Poyan Barabari¹ and **Keyvan Moharamzadeh**^{2,*}

¹ Eastman Dental Institute, University College London, London WC1X 8WD, UK; p.barabari@ucl.ac.uk

² School of Clinical Dentistry, University of Sheffield, Sheffield S10 2TA, UK

* Correspondence: k.moharamzadeh@sheffield.ac.uk; Tel.: +44-114-215-9328; Fax: +44-114-2665-326

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Abstract: The novel coronavirus (COVID-19) pandemic has become a real challenge for healthcare providers around the world and has significantly affected the dental professionals in practices, universities and research institutions. The aim of this article was to review the available literature on the relevant aspects of dentistry in relation to COVID-19 and to discuss potential impacts of COVID-19 outbreak on clinical dentistry, dental education and research. Although the coronavirus pandemic has caused many difficulties for provision of clinical dentistry, there would be an opportunity for the dental educators to modernize their teaching approaches using novel digital concepts in teaching of clinical skills and by enhancement of online communication and learning platforms. This pandemic has also highlighted some of the major gaps in dental research and the need for new relevant knowledge to manage the current crisis and minimize the impact of such outbreaks on dentistry in the future. In conclusion, COVID-19 has had many immediate complications for dentistry of which some may have further long-term impacts on clinical practice, dental education and dental research.

Keywords: coronavirus; COVID-19; SARS CoV-2; dentistry; dental practice

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SHORT COMMUNICATION

ORAL DISEASES | WILEY

Oral vesiculobullous lesions associated with SARS-CoV-2 infection

Carmen Martín Carreras-Presas¹ | Juan Amaro Sánchez² |
Antonio Francisco López-Sánchez³ | Enric Jané-Salas⁴ | Maria Luisa Somacarrera Pérez¹

¹Adult's Dentistry Department, Oral Medicine, Universidad Europea de Madrid, Madrid, Spain

²Master in Periodontics, Universidad Rey Juan Carlos, Madrid, Spain

³Head of Master in Periodontics, Universidad Rey Juan Carlos, Madrid, Spain

⁴Dentistry Department, Universidad de Barcelona, Barcelona, España

Correspondence: Carmen Martín Carreras-Presas, Adult's Dentistry Department, Oral Medicine, Universidad Europea de Madrid, Urb. El Bosque, Tajo Street, 28670 Villaviciosa de Odón, Madrid, Spain.
Email: carmen.martin2@universidadeuropea.es

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Case Report

Oral manifestations in a patient with a history of asymptomatic COVID-19: Case report



Jairo Corchuelo^{a,b,*}, Francisco Chavier Ulloa^c

^aSchool of Dentistry, Universidad del Valle, Colombia

^b21st Century Pacific Research Group, Colombia

^cUniversidad del Valle, Colombia

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ABSTRACT

The pandemic situation has led to public health measures that have forced patients with and without the SARS-CoV-2 virus to remain isolated and take steps to prevent the spread. Many of these patients have been unable to attend the control of medical-dental services, which in many cases complicates their situation. This study reports on the oral manifestations of an asymptomatic COVID-19 patient treated interdisciplinary by teleconsultation due to the sudden appearance of lesions in the oral mucosa. Lesions are diagnosed, therapeutic measures are taken, and improvement is shown. This case shows that the problems that arise in the oral mucosa in patients with suspected or confirmed SARS-CoV-2 infection can be monitored through interdisciplinary teleconsultation during the pandemic with the support of information technology currently available worldwide. It also decreases the risk of transmission of SARS-CoV-2 between patients and health professionals.

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REVIEW ARTICLE



A Review of Coronavirus Disease-2019 (COVID-19)

Tanu Singhal¹

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Abstract

There is a new public health crises threatening the world with the emergence and spread of 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus originated in bats and was transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei province, China in December 2019. There have been around 96,000 reported cases of coronavirus disease 2019 (COVID-2019) and 3300 reported deaths to date (05/03/2020). The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 d. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, malaise among others. The disease is mild in most people; in some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction. Many people are asymptomatic. The case fatality rate is estimated to range from 2 to 3%. Diagnosis is by demonstration of the virus in respiratory secretions by special molecular tests. Common laboratory findings include normal/ low white cell counts with elevated C-reactive protein (CRP). The computerized tomographic chest scan is usually abnormal even in those with no symptoms or mild disease. Treatment is essentially supportive; role of antiviral agents is yet to be established. Prevention entails home isolation of suspected cases and those with mild illnesses and strict infection control measures at hospitals that include contact and droplet precautions. The virus spreads faster than its two ancestors the SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), but has lower fatality. The global impact of this new epidemic is yet uncertain.



Keywords 2019-nCoV · SARS-CoV-2 · COVID-19 · Pneumonia · Review

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Clinical Review

Oral Manifestations in Patients with COVID-19: A Living Systematic Review

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J. Amorim dos Santos¹, A.G.C. Normando^{1,2}, R.L. Carvalho da Silva¹,
A.C. Acevedo¹, G. De Luca Canto³, N. Sugaya⁴, A.R. Santos-Silva² ,
and E.N.S. Guerra¹ 

Abstract

This living systematic review aims to summarize evidence on the prevalence of oral signs and symptoms in patients with COVID-19. The review was reported per the PRISMA checklist, and the literature search was conducted in 6 databases and in gray literature. Studies published in any language mentioning oral symptoms and signs in patients with COVID-19 were included. The risk of bias was assessed by the Joanna Briggs Institute appraisal tools. The certainty of evidence was evaluated through GRADE assessment. After a 2-step selection, 40 studies were included: 33 cross-sectional and 7 case reports. Overall, 10,228 patients (4,288 males, 5,770 females, and 170 unknown) from 19 countries were assessed. Gustatory impairment was the most common oral manifestation, with a prevalence of 45% (95% CI, 34% to 55%; $I^2 = 99\%$). The pooled eligible data for different taste disorders were 38% for dysgeusia and 35% for hypogeusia, while ageusia had a prevalence of 24%. Taste disorders were associated with COVID-19 (odds ratio [OR], 12.68; 95% CI, 6.41 to 25.10; $I^2 = 63\%$; $P < 0.00001$), mild/moderate severity (OR, 2.09; 95% CI, 1.25 to 3.49; $I^2 = 66\%$; $P = 0.005$), and female patients (OR, 1.64; 95% CI, 1.23 to 2.17; $I^2 = 70\%$; $P = 0.0007$). Oral mucosal lesions presented multiple clinical aspects, including white and erythematous plaques, irregular ulcers, small blisters, petechiae, and desquamative gingivitis. Tongue, palate, lips, gingiva, and buccal mucosa were affected. In mild cases, oral mucosal lesions developed before or at the same time as the initial respiratory symptoms; however, in those who required medication and hospitalization, the lesions developed approximately 7 to 24 d after onset symptoms. Therefore, taste disorders may be common symptoms in patients with COVID-19 and should be considered in the scope of the disease's onset and progression. Oral mucosal lesions are more likely to present as coinfections and secondary manifestations with multiple clinical aspects (PROSPERO CRD42020184468).

Keywords: gustatory dysfunction, coronavirus infections, meta-analysis, oral-systemic disease(s), systematic reviews, evidence-based medicine

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Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ?



Thaís Bianca Brandão, DDS, PhD,^{a,b} Luiz Alcino Gueiros, DDS, PhD,^c Thayanara Silva Melo, DDS, MSc,^c Ana Carolina Prado-Ribeiro, DDS, PhD,^{b,d} Ana Cristina Froelich Alo Nesrallah, DDS,^a Gladys Villas Boas Prado, MD, PhD,^c Alan Roger Santos-Silva, DDS, PhD,^d and Cesar Augusto Migliorati, DDS, PhD^f

Several viruses transmitted through saliva, such as herpes simplex virus, cytomegalovirus, and Zika virus, are capable of infecting and replicating in the oral mucosa, leading to painful oral ulcers. Few studies have described the oral manifestations of coronavirus disease 2019 (COVID-19). There is growing evidence that angiotensin-converting enzyme 2 (ACE2), the main host cell receptor of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is highly expressed on the epithelial cells of the tongue and of the salivary glands, which may explain the development of dysgeusia in patients with COVID-19. Hence, it is important to understand if SARS-CoV-2 can infect and replicate in oral keratinocytes and fibroblasts, causing oral ulcerations and superficial necrosis. Here, we report a series of 8 cases of COVID-19 infection, with oral necrotic ulcers and aphthous-like ulcerations which developed early in the course of disease after the development of dysgeusia and affected the tongue, lips, palate, and oropharynx. A short review of the literature regarding the important role of ACE2 in SARS-CoV-2 cellular entry is also provided, bringing new insights into oral keratinocytes and minor salivary glands as potential targets. (Oral Surg Oral Med Oral Pathol Oral Radiol 2021;131:e45–e51)

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Oral mucosal lesions in patients with SARS-CoV-2 infection. Report of four cases. Are they a true sign of COVID-19 disease?

Roberto Onner Cruz Tapia¹ | Alberto Jose Peraza Labrador² |
Douglas Magno Guimaraes³ | Luciano Hermios Matos Valdez⁴

¹ Department of Oral and Maxillofacial Pathology, Postgraduate and Research Division, Universidad Nacional Autónoma de México, Mexico City, Mexico

² Department of Oral and Maxillofacial Pathology, Universidad El Bosque, Bogota, Colombia

³ School of Dentistry, Centro Universitario do Estado do Para, Belem, Brazil

⁴ Faculty of Dentistry, Postgraduate Unit, Universidad Nacional Mayor de San Marcos, Lima, Peru

Correspondence
Luciano Hermios Matos Valdez, Faculty of Dentistry, Postgraduate Unit, Universidad Nacional Mayor de San Marcos, Lima 01, Peru.
Email: lmatosv@unmsm.edu.pe; diagnoctubercal@gmail.com

Abstract

Background: Vesiculobullous and macular lesions in the oral mucosa have been reported in patients positive for SARS-CoV-2 infection. Nonetheless, the significance and physiopathology of oral manifestations have not been clearly established in the clinical progression or outcome of the infection.

Aim: To describe the clinico-pathological oral mucosal lesions in four patients with confirmed SARS-CoV-2 infection.

Methods and Results: Four patients with COVID-19 disease and confirmed by polymerase chain reaction (PCR) presented angina bullosa hemorrhagica-like lesion, vascular disorder, and nonspecific stomatitis, one patient with histological analysis demonstrated perivascular reactive lymphocytic infiltrate, focal capillary thrombosis, and hemorrhage. According to the discrimination of other local and systemic conditions and the synchronous onset of oral and systemic symptoms, the diagnosis of oral lesions probably associated with COVID-19 was established.

Conclusion: Infection with SARS-CoV-2 may result in oral manifestations with various clinical presentations, which presumably support the hypothesis of thrombi formation and vasculitis; nevertheless, these findings need more evidence and a long-term follow up of patients to accurately establish the significance of the oral mucosa affection in the COVID-19 disease.

KEYWORDS

case reports, COVID-19, oral manifestations, SARS-CoV-2

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Comprehensive review of coronavirus disease 2019 (COVID-19)



Shaylika Chauhan*

Department of Internal Medicine, Geisinger Commonwealth School of Medicine, PA, USA



Dr. Shaylika Chauhan

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ABSTRACT

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first identified in December 2019 in Wuhan, the capital of China's Hubei province and has rapidly spread all over the world. The World Health Organization (WHO) declared the outbreak to be a Public Health Emergency of International Concern on 01/30/2020 and recognized it as a pandemic on 03/11/2020. The number of people diagnosed with COVID-19 worldwide crossed the one million mark on 04/02/2020; two million mark on 04/15/2020; three million mark on 04/27/2020 and the four million mark on 05/09/2020. Despite containment efforts, more than 187 countries have been affected with more than 4,178,346 cases in the world with maximum being in USA (1,347,936) followed by 227,436 in Spain and 224,422 in United Kingdom as of May, 2020. COVID-19 is the latest threat to face mankind cutting across geographical barriers in a rapidly changing landscape. This review provides an update on a rapidly evolving global pandemic. As we face the threat of emerging and re-emerging infectious diseases, this is a stark reminder to invest in population health, climate change countermeasures, a global health surveillance system and effective research into identifying pathogens, their treatment and prevention and effective health delivery systems.

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Evidence-Based Dentistry

Nature Publishing Group

Oral ulceration and blistering in patients with COVID-19

Angela Sinadinos and Jonathan Shelswell

[Additional article information](#)

Abstract

Design Case series.

Introduction The most common signs and symptoms of SARS-CoV-2 infection include headache, sore throat, hyposmia, hypogeusia, diarrhoea,

dyspnoea and pneumonia. Dermatological manifestations have also been reported but few authors have documented oral signs and symptoms.

Methods Three cases are reported where oral ulceration or blistering is found in patients with confirmed or suspected COVID-19.

Results One patient had serologically confirmed COVID-19, whilst the remaining two cases were only suspected. Two patients reported pain from the palate, whilst the third reported in the tongue. The first two patients had lesions affecting keratinised tissue consistent with herpes simplex lesions but with no history of herpetic infection. The third patient had lesions compatible with erythema multiforme.



Conclusions The authors suggest a link between COVID-19 and oral ulceration and blistering, but acknowledge these signs may often go undetected due to a lack of intraoral examination during hospital admission.

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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.

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

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 sialadenitis 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.

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REVIEW ARTICLE

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How to deal with coronavirus disease 2019: A comprehensive narrative review about oral involvement of the disease

Giorgia Capocasale¹  | Riccardo Nocini² | Paolo Faccioni¹ | Dario Donadello¹ | Dario Bertossi¹ | Massimo Albanese¹ | Francesca Zotti¹

¹Section of Dentistry and Maxillofacial Surgery, Department of Surgical Sciences, Paediatrics and Gynaecology, University of Verona, Verona, Italy

²Section of Ears, Nose and Throat (ENT), Department of Surgical Sciences, Dentistry, Gynecology and Pediatrics, University of Verona, Verona, Italy

Correspondence

Giorgia Capocasale, Department of Surgical Sciences, Paediatrics and Gynaecology, University of Verona, Policlinico G. B. Rossi, Piazzale L. Scuro n.10, 37134 Verona, Italy.
Email: capocasalegiorgia@gmail.com

Abstract

Objectives: The aim of this narrative review was to collect all findings from literature about oral signs and symptoms of COVID-19, in order to draw a picture of oral involvement of this challenging viral infection, to help oral professionals in a better triage and early diagnosis.

Material and methods: The search for international literature was made including articles written in English and reporting about oral manifestations in patients with a diagnosis of COVID-19. The publication time was limited to 2019 and 2020, up to May 20, 2020. A narrative review was performed.

Results: Twenty-three articles were included in this review. Three different oral manifestations were found: taste alteration, oral blister and ulcers, and oral lesions associated with Kawasaki-like diseases (erythema, bleeding of lips, "strawberry tongue"). The higher expression of Angiotensin-converting enzyme 2 in the oral cavity and in endothelial cells might be responsible for oral manifestation and the major report of signs and symptoms in the occidental countries.

Conclusions: Detecting oral signs and symptoms of COVID-19 could be useful to perform a better preliminary triage in dental setting, and in recognizing possible early manifestations of the disease. However, considering the outbreak of COVID-19 and the consequent difficulty of undergoing oral examinations, the oral manifestations might be misdiagnosed; then, we would encourage oral professionals to perform other studies about this topic.

KEYWORDS

COVID-19, dysgeusia, oral blister, oral disease

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Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations?



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ABSTRACT

Some oral manifestations have been observed in patients with coronavirus disease 2019 (COVID-19). However, there is still a question about whether these lesions are due to coronavirus infection or secondary manifestations resulting from the patient's systemic condition. Thus, this article aims to report an additional case of an oral condition in a patient diagnosed with COVID-19. Our patient, a sixty-seven-year-old Caucasian man, tested positive to coronavirus and presented oral manifestations such as recurrent herpes simplex, candidiasis, and geographic tongue. We support the argument that some oral conditions could be secondary to the deterioration of systemic health or due to treatments for COVID-19. The present case report highlights the importance of including dentists in the intensive care unit multi-professional team to improve oral health in critical patients, not only COVID-19 patients, but also, to contribute to evidence-based and decision-making in managing infectious diseases.
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Letter to the editor

Social media and telemedicine for oral diagnosis and counselling in the COVID-19 era



Letter to editor

Over the last years, there has been a significant improvement in the survival rate of patients with critical oral diseases, and this result is directly correlated to stage at initial presentation [1,2]. The early diagnosis is the most effective way of reducing the individual burden of the disease, decreasing morbidity, and mortality and improving quality of life. For this to happen, health professionals need to be close to their patients. How to do it in the COVID-19 era?

During this COVID-19 pandemic, a known program has achieved even more focus, the telemedicine. The care to have the least in-person contact between people to prevent the spread of the virus (self-quarantine), defended by international authorities, has made electronic consultations gain even more visibility [3,4]. Besides helping patients to control chronic diseases and to give an early diagnosis, the telemedicine can "forward triage" people with possible symptoms of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This approach allows patients to be efficiently screened as well as avoid the spreading of the virus among patients, health professionals, and exposed community.

The obstruction here is about the existence of just a few telemedicine systems. Since no telemedicine program can be created suddenly, an alternative adopted by different patients is to use the instant messaging applications from social media. Mobile applications based on text messaging and images can be useful with instant communication and quick decisions. Even with some limitations, this alternative also helps people to rule out oral lesions, have an early diagnosis and correct follow-up. Similarly, such an alternative helps to rule out SARS-CoV-2 symptoms quickly and avoid long lines in hospitals and emergency care, which is really great to reduce the virus spreading.

Rather than expected, all the recommendations regarding COVID-19 in-person care places, these programs enable us to refer only patients with oral lesions of greater severity and to high-risk patients to triage lines of COVID-19 and even allows patients to schedule a medical consultation by video. After this automatic flow, these patients may be isolated from others with positive COVID-19 when they arrive at in-person care places, avoiding either their contamination or, in case they are positive COVID-19, spreading it to the others.

We can illustrate a usefulness for this strategy using a model case. Here in Brazil, we are on social isolation since this middle March, and many specialized oral health care services are closed to the public.

Despite this situation, patients are still looking for urgency services, and general clinics are communicating with reference professionals. This last week, a general dentist looked for assistance due to pinky-purple symptomatic nodule lesions affecting the oral mucosa, with few days of onset, associated with purple spots on skin on a 49 years-old female patient with controlled diabetes. The dentist sent images and a brief description by WhatsApp (Fig. 1). She was advised to order a blood examination due to suspected Idiopathic Purpura. The exam result showed severe thrombocytopenia, and the patient was referred to the hospital unit in order to be treated by the use of systemic steroids. The procedure had an outstanding response.

Thus, although telemedicine programs or similar will not solve all the health problems, they are well suited for scenarios like the one we are experiencing with the COVID-19. In this case, it may be a virtually perfect solution, and the in-person visits should become the second, third, or even last option for meeting patient needs, as Duffy and Lee said in 2018 [5].

Authors' contributions

R.A. Machado contributed to conception, design, data acquisition and interpretation, drafted and critically revised the manuscript. N.L. de Souza, R.M. Oliveira, H. Martelli Júnior, and P.R.F. Bonan contributed to conception, design, data acquisition and interpretation and critically revised the manuscript. All authors gave their final approval and agree to be accountable for all aspects of the work.

Declaration of Competing Interest


The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Covid-19 and oral diseases: Crosstalk, synergy or association?

Daniela A. Brandini¹ | Aline S. Takamiya¹ | Pari Thakkar² | Samantha Schaller² | Rani Rahat² | Afsar R. Naqvi² 

¹Department of Diagnosis and Surgery, School of Dentistry, São Paulo State University (UNESP), Araçatuba, São Paulo, Brazil

²Mucosal Immunology Lab, College of Dentistry, University of Illinois at Chicago, Chicago, Illinois, USA

Correspondence

Afsar R. Naqvi, Department of Periodontics, College of Dentistry, University of Illinois at Chicago, 561B Dent MC 859, 801 South Paulina, Chicago, IL 60612, USA.
Email: afsarr@uic.edu

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Summary

The coronavirus disease 2019 (Covid-19) is a viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that clinically affects multiple organs of the human body. Cells in the oral cavity express viral entry receptor angiotensin-converting enzyme 2 that allows viral replication and may cause tissue inflammation and destruction. Recent studies have reported that Covid-19 patients present oral manifestations with multiple clinical aspects. In this review, we aim to summarise main signs and symptoms of Covid-19 in the oral cavity, its possible association with oral diseases, and the plausible underlying mechanisms of hyperinflammation reflecting crosstalk between Covid-19 and oral diseases. Ulcers, blisters, necrotising gingivitis, opportunistic coinfections, salivary gland alterations, white and erythematous plaques and gustatory dysfunction were the most reported clinical oral manifestations in patients with Covid-19. In general, the lesions appear concomitant with the loss of smell and taste. Multiple reports show evidences of necrotic/ulcerative gingiva, oral blisters and hypergrowth of opportunistic oral pathogens. SARS-CoV-2 exhibits tropism for endothelial cells and Covid-19-mediated endotheliitis can not only promote inflammation in oral tissues but can also facilitate virus spread. In addition, elevated levels of proinflammatory mediators in patients with Covid-19 and oral infectious disease can impair tissue homeostasis and cause delayed disease resolution. This suggests potential crosstalk of immune-mediated pathways underlying pathogenesis. Interestingly, few reports suggest recurrent herpetic lesions and higher bacterial growth in Covid-19 subjects, indicating SARS-CoV-2 and oral virus/bacteria interaction. Larger cohort studies comparing SARS-CoV-2 negative and positive subjects will reveal oral manifestation of the virus on oral health and its role in exacerbating oral infection.

KEYWORDS

Covid-19, cytokines, inflammation, oral diseases, SARS-CoV-2

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Kawasaki Disease and COVID-19

Athanasios Gkoutzourelas¹ , **Dimitrios P. Bogdanos¹** , **Lazaros I. Sakkas^{1,2}** 

¹Department of Rheumatology and Clinical Immunology, Faculty of medicine, School of Health Sciences, University of Thessaly, Larissa, ²Faculty of Medicine, School of Health Sciences, University of Thessaly, Larissa, Greece

ABSTRACT

The recent passing away of Dr. Tomisaku Kawasaki, who first described what is now known as Kawasaki Disease (KD), and recent reports of a multisystem inflammatory disease in children associated with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (MIS-C), makes a review on KD and MIS-C timely. Kawasaki Disease is a systemic vasculitis with predilection for coronary arteries occurring mostly in early childhood. The main features are high fever, extensive skin rash, cheilitis with red, cracking, bleeding lips and strawberry tongue, conjunctivitis, erythema and induration of hands and feet, subsiding with periungual peeling, cervical lymphadenopathy, and coronary artery dilation/aneurysms. Treatment consists of intravenous (IV) immunoglobulin (Ig) plus acetylsalicylic acid. MIS-C is considered a cytokine storm with high fever, inflammation, multi-organ dysfunction, that shares features with KD, toxic shock, and macrophage activation syndrome. Many children require admission to paediatric intensive care units for circulatory support. Bacterial sepsis, staphylococcal toxic shock syndrome, and enterovirus-causing myocarditis should be excluded. Treatment is not standardized and includes IVIg, IV methylprednisolone and IL-6 and IL-1 inhibitors.

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Keywords: Atypical Kawasaki disease, Kawasaki-like disease, Kawasaki-COVID-19, paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2, macrophage activation syndrome, myocarditis, toxic shock syndrome

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Oral symptoms and lesions in SARS-CoV-2 positive patient

Running title: Oral manifestations of SARS-CoV-2 infection

Keywords: oral symptoms; oral lesions; herpes simplex virus; SARS-CoV-2

Ana Glavina¹, Dolores Biočina-Lukenda¹, Marinka Mravak-Stipetić², Jasenka Markeljević³

¹University of Split, School of Medicine, Department of Oral Medicine and Periodontology, Dental Clinic Split, Split, Croatia

²University of Zagreb, School of Dental Medicine, Clinical Department of Oral Medicine, University Dental Clinic, University Hospital Center Zagreb, Zagreb, Croatia

³University of Zagreb, School of Medicine, Department of Clinical Immunology, Pulmonology and Rheumatology, Department of Internal Medicine, Clinical Hospital Center „Sestre milosrdnice“, Zagreb, Croatia

Correspondence:

Ana Glavina, DMD

University of Split, School of Medicine, Department of Oral Medicine and Periodontology, Dental Clinic Split, Šoltanska 2, Split, Croatia

Email: glavina20014@gmail.com

Telephone no. (+385 98 9375302)

Dear Editor-in-Chief Professor Lodi,

we would like to contribute to the oral manifestations of SARS-CoV-2 infection due to the small number of case reports described and confusing data from the available literature. Previous data from the literature describe heterogeneous signs and symptoms on the oral mucosa: dysgeusia or ageusia, desquamative gingivitis, erythema exudativum multiforme (EEM), salivary gland infections, xerostomia, necrotizing periodontal disease (NPD), nonspecific erythematous lesions, recurrent herpes simplex virus (HSV) infection, vesiculobullous lesions (Martín Carreras - Presas et al., 2020; Galván Casas et al., 2020; Jimenez-Cauhe et al., 2020; Sinadinos et al., 2020; Patel et al., 2020; Petrescu et al., 2020; Al-Khatib, 2020; Passarelli et al., 2020; Abu-Hammad et al., 2020; Chaux-Bodard et al., 2020). Such results should be interpreted with caution so as not to create unnecessary concern among physicians, dentists, and patients. A short communication by Martín Carreras - Presas et al., 2020 described oral lesions in patients with suspected SARS-CoV-2 infection, so it is not possible to draw conclusions about a causal relationship. To date, acute ageusia is the most significant symptom in the oral cavity that can raise suspicion of early SARS-CoV-2 infection.

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Oral lesions of herpes zoster in COVID-19 patients or truly associated to the disease?

In response to the report of Martín Carreras-Presas, Amaro Sánchez, López -Sánchez, Jané -Salas, and Somacarrera Pérez (2020) in which they present 3 cases with vesicobullous oral lesions associated with SARS-Cov-2 infection and with very interesting findings, however, we cannot consider the possibility that findings be intrinsically related to COVID-19 disease. The first two cases presented did not have laboratory confirmation of COVID-19 infection, but the authors reported that these patients had compatible signs and symptoms. The presented oral lesions with the diagnostic hypothesis of recurrent herpetic stomatitis are more consistent with the oral manifestations of herpes zoster, due to the unilateral lesions on the palate in keratinized mucosa and complaint of pain. In addition, these patients never had these lesions before and are in the sixth decade of life.

Varicella-like skin lesions are also reported by Tang et al. (2020), as may indicate a correlation between the findings by Martín Carreras-Presas et al. (2020), contributes with hypothesis of herpes zoster (herpes varicella-zoster-HVZ3) is implied in both infections (Cohen, 2013). As the clinical manifestations of COVID-19 are very variable and can occur from asymptomatic cases (most of the cases), to cases with rapid and severe evolution with important disorders, mainly in the respiratory system, we believe that most patients were not fully evaluated in terms of oral mucosa. Due to the severity of the disease, we agree that such an assessment becomes a difficulty for clinicians, and often without painful symptoms, patients end up not reporting lesions in the mouth.

Given the above, there are some questions: Is the clinical manifestation of lesions compatible with herpes zoster an initial manifestation or herpes zoster is a disease strongly associated with COVID-19? Another very interesting point is if the lesion is a manifestation related to the stress of the pandemic situation itself, also commented by Martín Carreras-Presas et al. (2020). Latest, it could be a truly clinical manifestation of COVID-19 itself, being a herpes zoster-like lesion. Although we do not consider that the symptoms of chickenpox and herpes zoster are caused only by COVID-19, the development of symptoms can promote by the expression of VZV in COVID-19.

In this pandemic moment, there is a search for an increasing understanding of the disease, mainly in the matter of signs and symptoms. Most often, the absence of taste and smell has been strongly associated as one of the symptoms that may be associated with the

disease (Vaira, Salzano, & De Riu, 2020). Finally, we need to be very precise regarding new signs and symptoms that may appear, including from the oral region, we as clinicians are always attentive to the reports of patients with COVID-19.

CONFLICT OF INTEREST


The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

Luis Felipe das Chagas e Silva Carvalho: Conceptualization; Data curation; Formal analysis; Resources; Supervision; Validation; Visualization; Writing-original draft; Writing-review & editing. **Dárcio Kitakawa:** Conceptualization; Formal analysis; Investigation; Resources; Supervision; Validation; Writing-review & editing. **Luiz Antonio Guimarães Cabral:** Supervision; Writing-original draft.

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Luis Felipe das Chagas e Silva de Carvalho^{1,2} 
Dárcio Kitakawa²
Luiz Antônio Guimarães Cabral³

¹Universidade de Taubaté, Taubaté, Brazil

²Centro Universitário Braz Cubas, Mogi das Cruzes, Brazil

³Instituto de Ciência e Tecnologia-UNESP, São José dos Campos, Brazil

Correspondence

Luis Felipe das Chagas e Silva de Carvalho, Universidade de Taubaté. R. dos Operários, 09 - Centro, Taubaté - SP, 12020-340.

Email: luisfelipecarvalho@hotmail.com

ORCID

Luis Felipe das Chagas e Silva de Carvalho  <https://orcid.org/0000-0003-1063-4624>

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LETTER TO THE EDITOR | [Free Access](#) |

Oral manifestations associated with COVID-19

Milagros Díaz Rodríguez ✉, Amelia Jimenez Romera, Mariana Villarroel

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LETTER TO THE EDITOR | [Free Access](#) |

Oral mucositis in a SARS-CoV-2-infected patient: Secondary or truly associated condition?

Saygo Tomo ✉, Glauco Issamu Miyahara, Luciana Estevam Simonato

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COVID-19 Pandemic: Oral Repercussions and its Possible Impact on Oral Health

Panmella Pereira Maciel¹, Hercílio Martelli Júnior^{2,3}, Daniella Reis Barbosa Martelli², Renato Assis Machado^{4,5}, Priscila Victor de Andrade⁶, Danyel Elias da Cruz Perez⁷, Paulo Rogério Ferreti Bonan¹

¹Department of Clinical and Social Dentistry, School of Dentistry, Federal University of Paraíba, João Pessoa, PB, Brazil.

²Oral Diagnosis, School of Dentistry, State University of Montes Claros, Montes Claros, MG, Brazil.

³Center for Rehabilitation of Craniofacial Anomalies, School of Dentistry, Unifenas, MG, Brazil.

⁴Department of Oral Diagnosis, School of Dentistry, University of Campinas, Piracicaba, SP, Brazil.

⁵Hospital for Rehabilitation of Craniofacial Anomalies, University of São Paulo, Bauru, SP, Brazil.

⁶Medicine School, State University of Montes Claros, Montes Claros, MG, Brazil.

⁷Department of Clinical and Preventive Dentistry, School of Dentistry, Federal University of Pernambuco, Recife, PE, Brazil.

Author to whom correspondence should be addressed: Panmella Pereira Maciel, Rua José Simões de Araújo, 611, Bessa, João Pessoa, PB, Brazil. 58035-070. Phone: +55 83 981240358. E-mail: panmellamaciel@hotmail.com.

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Abstract

Many viral infections cause oral manifestations, including disorders in odontogenesis, resulting in dental malformations. In this review, based on current knowledge, we will discuss the likely dental and oral consequences of COVID-19. In this article, we review currently available data associated with vertical transmission of COVID-19 and odontogenesis, oral manifestations, and the impact of COVID-19 pandemic on a diagnosis of oral diseases. Owing to the severity of the pandemic, the population's anxiety and fear of becoming infected with COVID-19 may underestimate the signs and symptoms of serious illnesses, besides discourage patients from seeking health, medical or dental services to determine the diagnosis of oral lesions. Thus, the COVID-19 pandemic could be an additional and aggravating factor for the delay of serious illness diagnosis, such as oral squamous cell carcinoma resulting in higher morbidity and worse prognosis. Several changes and oral lesions have been described as oral manifestations of COVID-19, such as dysgeusia, oral ulcers, petechiae, reddish macules, desquamative gingivitis, among others. Besides, it can cause major systemic changes and predispose opportunistic infections. As with other viral infections, oral manifestations, including dental anomalies, can occur as a direct result of SARS-CoV-2 infection. However, further studies are needed to guide and clarify possible oral changes.

Keywords: Coronavirus, Odontogenesis, Tooth Abnormalities, Infectious Disease Transmission, Vertical.

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The impact of coronavirus infectious disease 19 (COVID-19) on oral health

Arkadiusz Dzedzic¹  | Robert Wojtyczka² 

¹Department of Conservative Dentistry with Endodontics, Medical University of Silesia, Katowice, Poland

²Department of Microbiology and Virology, School of Pharmacy and Division of Laboratory Medicine in Sosnowiec, Medical University of Silesia, Sosnowiec, Poland

Correspondence

Arkadiusz Dzedzic, Department of Conservative Dentistry with Endodontics, Medical University of Silesia, Pl. Akademicki 17, 41-902 Bytom, Katowice, Poland.
Email: adzedzic@sum.edu.pl

Abstract

Health services across the world face an unprecedented situation as a result of a global COVID-19 outbreak. Urgent joined research efforts regarding the SARS-CoV-2 rapid tests, accurate diagnosis, especially early recognition, and effective treatment of life-threatening complications would be highly desirable for humanity and medical workforce all over the world that try to combat a current global pandemic threat. Due to indirect complex effect, intensified COVID-19 therapies and multi-drug treatment, it is believed that some oral conditions could be aggravated by COVID-19 disease, particularly those with autoimmune aetiology, linked to compromised immune system or long-term pharmacotherapy.

KEYWORDS

COVID-19, immunopathology, oral health, oral medicine, SARS-CoV-2 coronavirus, therapy

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Oral manifestations of COVID-19 disease: A review article

Behzad Iranmanesh¹  | Maryam Khalili¹  | Rezvan Amiri¹ | Hamed Zartab¹ | Mahin Aflatoonian² 

¹Department of Dermatology, Kerman University of Medical Sciences, Kerman, Iran

²Leishmaniasis Research Center, Afzalipour Hospital, Kerman University of Medical Sciences, Kerman, Iran

Correspondence

Mahin Aflatoonian, Leishmaniasis Research Center, Afzalipour Hospital, Kerman Medical University, Kerman, 761614111, Iran.
Email: maafatoonian@gmail.com

Abstract

Dysgeusia is the first recognized oral symptom of novel coronavirus disease (COVID-19). In this review article, we described oral lesions of COVID-19 patients. We searched PubMed library and Google Scholar for published literature since December 2019 until September 2020. Finally, we selected 35 articles including case reports, case series and letters to editor. Oral manifestations included ulcer, erosion, bulla, vesicle, pustule, fissured or depapillated tongue, macule, papule, plaque, pigmentation, halitosis, whitish areas, hemorrhagic crust, necrosis, petechiae, swelling, erythema, and spontaneous bleeding. The most common sites of involvement in descending order were tongue (38%), labial mucosa (26%), and palate (22%). Suggested diagnoses of the lesions were aphthous stomatitis, herpetiform lesions, candidiasis, vasculitis, Kawasaki-like, EM-like, mucositis, drug eruption, necrotizing periodontal disease, angina bullosa-like, angular cheilitis, atypical Sweet syndrome, and Melkerson-Rosenthal syndrome. Oral lesions were symptomatic in 68% of the cases. Oral lesions were nearly equal in both genders (49% female and 51% male). Patients with older age and higher severity of COVID-19 disease had more widespread and severe oral lesions. Lack of oral hygiene, opportunistic infections, stress, immunosuppression, vasculitis, and hyper-inflammatory response secondary to COVID-19 are the most important predisposing factors for onset of oral lesions in COVID-19 patients.

KEYWORDS

aphthous, COVID-19, gingivostomatitis, manifestation, oral

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Oral lesions in COVID-19 infection: Is long-term follow-up important in the affected patients?

Dear Editor,

It is still not well-established if SARS-CoV-2 infection is the direct cause or a predisposing factor for the onset of oral lesions (Rodríguez, Romera & Villarroel, 2020). Important aspects, such as systemic health deterioration, acute onset, and multidrug therapy may contribute in this process (Martín Carreras-Presas, Amaro Sánchez, López-Sánchez, Jané-Salas & Somacarrera Pérez, 2020) (Putra et al., 2020) (dos Santos et al., 2020). Therefore, it is plausible that the COVID-19 immunological scenario favors the occurrence of secondary oral ulcers (dos Santos et al., 2020) since SARS-CoV-2 could induce a similar immune response as observed in other viral infections (Russel et al., 2020). Besides, COVID-19 may cause an inflammatory immune response overactivation, leading to a cytokine storm and immune exhaustion (Putra et al., 2020) (Paces et al., 2020). Thus, most of the reported lesions were present during the COVID-19 infection period. We present a case of a patient with late oral ulcers after COVID-19 onset.

A 33-year-old male patient sought medical assistance with headache, myalgia, fever, shortness of breath, anosmia, and ageusia. His wife presented the same symptoms. Under COVID-19 hypothesis, he was treated with ivermectin and azithromycin. PCR examination was not performed because it was restricted to severe cases. Seventy days after the initial symptoms, hyposmia and dysgeusia were still present, and painful mouth ulceration emerged in the floor

of mouth. The lesion remitted in 10 days with topical application of corticosteroids. After twenty days, the patient still reported hyposmia and dysgeusia, and two other crateriform ulcers with a necrotic background emerged in the retromolar region and lip mucosa, both on the left side (Figure 1a,b). The patient did not report any similar oral lesions before, no episodes of recurrent aphthous ulceration (RAU) nor previous trauma at the site, and only secondary trauma due to feeding difficulties after the lesion's onset. Treatment included topical application of triamcinolone acetonide and the use of 0.12% chlorhexidine digluconate mouthwash for 7 days. Serologic assay detected IgG COVID-19 antibodies. Oral ulcerations remission occurred in 7 days. The patient reported persistent hyposmia and remains in clinical follow-up.

Ulcerated oral lesions are usually caused by trauma, infection, immunological dysregulation, and neoplasia (Fitzpatrick et al., 2019). We considered traumatic ulcer, herpetic stomatitis, and RAU as the main differential diagnosis in this case. Interestingly, we did not observe the presence of an erythematous halo surrounding the ulcerated area, as expected for RAU. In addition, the patient reported no previous episodes and no associated trauma. It is possible that the COVID-19 systemic immune deregulation that leads to the deterioration of systemic health may bring a more prolonged immune imbalance, which could predispose these late secondary oral lesions.

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Oral manifestations of COVID-19 related multi-system inflammatory syndrome in children: a review of 47 pediatric patients

Steven Halepas, DMD, Kevin C. Lee, DDS, MD, Aaron Myers, DDS, Richard K. Yoon, DDS, Wendy Chung, MD, PhD, Scott M. Peters, DDS



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COVID-19 Presenting with Atypical Sweet's Syndrome

[Banu Taşkın](#),^{1, 2} [Seçil Vural](#),¹ [Elif Altuğ](#),³ [Cüyan Demirkesen](#),⁴ [Emek Kocatürk](#),¹ [İrfan Çelebi](#),⁵ [Burhan Ferhanoğlu](#),⁶ and [Sibel Alper](#)^{1, 2}

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Abstract

On March 11, 2020, the first case of the novel coronavirus 2019 disease (COVID-19) was officially confirmed in Turkey. The disease continues to spread, and the number of patients has risen to 120,000 by the end of April. In this observation, we report an atypical presentation of COVID-19 in a patient with indurated painful nodules. A 61-years-old woman with a one-week history of fever (axillary 38°C) and nodules on the cheek was admitted to the hospital with fatigue, arthralgia and myalgia.

Keywords: COVID-19, Sweet's syndrome, acute febrile neutrophilic dermatosis, SARS-CoV-2

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An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study

Lucio Verdoni, Angelo Mazza, Annalisa Gervasoni, Laura Martelli, Maurizio Ruggeri, Matteo Ciuffreda, Ezio Bonanomi, Lorenzo D'Antiga

Summary

Background The Bergamo province, which is extensively affected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic, is a natural observatory of virus manifestations in the general population. In the past month we recorded an outbreak of Kawasaki disease; we aimed to evaluate incidence and features of patients with Kawasaki-like disease diagnosed during the SARS-CoV-2 epidemic.

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Melkersson-Rosenthal Syndrome Induced by COVID-19



Bahadır Taşlıdere ^{a,*}, Liljana Mehmetaj ^a, Ayşe Büşra Özcan ^a, Bedia Gülen ^a, Nazan Taşlıdere ^b

^a Department of Emergency Medicine, Bezmialem Vakıf University School of Medicine, Istanbul, Turkey

^b Department of Dermatology, Bezmialem Vakıf University School of Medicine, Istanbul, Turkey

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ABSTRACT

Melkersson–Rosenthal syndrome is a rare condition characterized by a triad of orofacial edema, facial paralysis, and fissured tongue. Histopathological examination of the disease has demonstrated areas of inflammation involving mast cells. Activated mast cells also play a part in the pathogenesis of COVID-19 infection, as they release cytokines in the lungs. We present a case of a female patient presenting with edema. We present a case of a female patient presenting with edema. Her examination revealed edema in the right lower lip, right facial paralysis, and fissured tongue. COVID-19 may be associated with which was not previously included in the etiology of the disease.

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Considerations on oral manifestations of COVID-19

Fernando Augusto Cervantes Garcia de Sousa [✉] ¹ and Thaís Cachuté Paradella ¹

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Abstract

Since the first confirmed cases in the end of 2019 in the city of Wuhan, Hubei province in China, COVID-19 has spread around the world, totaling, until July 25th, 2020, 15.785.641 confirmed cases and 640.016 deaths^[1].

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Keywords: COVID-19, Oral manifestations, SARS-COV-2

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Necrotizing periodontal disease: Oral manifestation of COVID-19

[Jay Patel](#)¹ and [Julian Woolley](#)²

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We read with interest the series of cases reported by Martín Carreras-Presas, Amaro Sánchez, López-Sánchez, Jané-Salas, and Somacarrera Pérez (2020). We believe that the described oral vesiculobullous manifestations were suggestive of coronavirus disease 2019 (COVID-19) co-infections, which, at present, are overlooked and poorly understood (Cox, Loman, Bogaert, & O'Grady, 2020). Increased disease severity and mortality among individuals with respiratory viral infections are often attributed to subsequent bacterial co-infections, accounting for approximately 95% of deaths during the 1918 Spanish flu pandemic (Morens, Taubenberger, & Fauci, 2008).

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Oral vesicles and acral erythema: report of a cutaneous manifestation of COVID-19

[Nessa Aghazadeh MD](#), [Mona Homayouni MD](#)✉, [Julio C. Sartori-Valinotti MD](#)

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Dear Editor,

Dermatologic manifestations of COVID-19 are emerging, which include a wide range of presentations from exanthema, urticaria, livedo, and petechiae to vasculitis and vasculopathic skin eruptions. Acro-ischemic, pernio-like eruptions have been reported in children and adolescents. Herein, we report a 9-year-old girl presenting with fever, a vesicular oral eruption, and acral erythematous papules and plaques preceding the development of respiratory symptoms of COVID-19. The pneumonia and skin eruption favorably improved over the course of a few weeks with supportive therapy. Clinicians should consider COVID-19 within the differential of oral vesicular eruptions, especially in children.

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Mucosal involvement in a COVID-19-positive patient: A case report

Filiz Cebeci Kahraman ✉, Hülya Çaçkurlu

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Dear Editor,

The novel coronavirus disease (COVID-19) first surfaced in the Chinese city of Wuhan on 1 December 2019 and quickly turned into a global issue. On 11 March 2020, the World Health Organization (WHO) declared this outbreak a pandemic.¹ COVID-19 can affect different organ systems, probably including the oral mucosa. Although cutaneous involvement has been defined for COVID-19, there are no studies that report oropharyngeal involvement. To the best of our knowledge, this is the first case report of oropharyngeal involvement in COVID-19 describing oral lesions in detail.

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Letter to Editor: Oral lesions in a patient with Covid-19

[Ciro Dantas Soares](#),^{1,4} [Rejane Andrade de Carvalho](#),² [Kalline Andrade de Carvalho](#),³ [Maria Goretti Freire de Carvalho](#),⁴ and [Oslei Paes de Almeida](#)¹

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The coronavirus disease 2019 (COVID-19) is a global pandemic burden caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection with variable clinical outcome. The symptoms of this disease include headache, sore throat, fever, and dyspnoea. About 10% of the patients develop severe acute respiratory syndrome and 1-2 %, particularly elderly, die (1,2). Possible oral-related symptoms include hypogeusia, xerostomia and chemosensory alterations (3).

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Special Care Dentistry and COVID-19 Outbreak: What Lesson Should We Learn?

Arkadiusz Dzedzic 

Department of Conservative Dentistry with Endodontics, School of Medicine with the Division of Dentistry in Zabrze, SUM, Medical University of Silesia in Katowice, Pl. Akademicki 17, 41-902 Bytom, Poland; adziedzic@sum.edu.pl

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Abstract: The recent outbreak of coronavirus disease 2019 (COVID-19) caused by the emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the declaration of pandemic by the World Health Organization have made an enormous impact on medical and dental care across the world. The current COVID-19 situation may teach dental teams a better approach and optimal ways concerning the management of patients with special needs, by bringing people together to discuss and optimize standards of care, as often happens in challenging situations. We can always learn new things that turn out to be valuable and useful even in exceptionally difficult times, and in addition, dental services can benefit from enabling positive attitudes and introducing constructive changes. Clinicians just need to keep in mind that adjustment to a new future reality appears inevitable for both patients and professionals who provide care.

Keywords: special care dentistry; COVID-19; coronavirus SARS-CoV-2; service provision