

Future Challenges of Covid-19 and Oral Manifestations in Daily Dental Practice: A Literature Review

Grecia Riofrio¹, Stephanny Castillo¹, Gabriela Salcedo¹, Daniel Alvez-Temoche¹, Romel Watanabe², Frank Mayta-Tovalino³

¹Academic Department, ²Department of Rehabilitative Stomatology, Faculty of Dentistry, Universidad Nacional Mayor de San Marcos, Lima, Peru, ³CHANGE Research Working Group, Postgraduate Department, Faculty of Health Sciences, Universidad Científica del Sur, Lima, Peru

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ABSTRACT **Objective:** Some patients reportedly present with oral manifestations of coronavirus disease 2019 (Covid-19). It is unknown if this is due to the virus itself or a side effect of treatment; however, severe acute respiratory syndrome coronavirus 2 has been shown to have a predilection for angiotensin-converting enzyme receptors that are present in the respiratory tract, oral mucosa, tongue, and salivary glands, causing alterations in taste and smell. Therefore, the objective of this review was to present the future challenges of Covid-19 and oral manifestations in daily dental practice through a literature review. **Materials and Methods:** Scientific evidence in the databases Scopus and PubMed was searched using the Boolean operators. Articles published in Spanish and English between January and December 2020 were included. **Results:** Of the 89 articles found in Scopus, 69 were of the open access type and 20 were in the “others” category; only 22 scientific articles were found in PubMed. **Conclusion:** It is important to take into account these clinical manifestations such as loss of taste and smell in order to detect the disease. Good oral hygiene is also recommended as a preventive measure to reduce viral load, which considerably reduces the probability of infecting other people who are in contact with the infected patient.

KEYWORDS: Covid-19, dentistry, oral manifestation

INTRODUCTION

In the city of Wuhan, China, coronavirus disease 2019 (Covid-19) was registered for the first time in December 2019 as an unknown respiratory disease.^[1] The World Health Organization indicated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as the cause of Covid-19, and Covid-19 was also named “the first pandemic of the 21st century.”^[2-4] As of May 2020, the average number of confirmed cases was 4,789,205, with more than 318,789 deaths.^[5-7]

Within the genealogy of the coronaviruses is the SARS-CoV-2, with a high degree of pathogenicity. This virus belongs to a family of single-stranded RNA viruses^[2,8] and presents projections that come out of the surface of the virion, which give it a solar corona appearance.^[2,9,10] Transmission of the virus occurs through contact with

an infected person when they cough, sneeze, or talk, and indirectly, through fomites.^[11,12] The elderly and children have a higher risk of mortality^[2,13]; this risk is further aggravated in individuals with co-morbidities, such as hypertension; diabetes; cardiovascular, pulmonary, and chronic renal diseases; and immunosuppression or having undergone recent surgery.^[2,14,15]

The general symptoms of Covid-19 are fever, fatigue, cough, myalgia, dyspnea, headache, and sore throat.^[11,16-19] In severe cases, patients present with pneumonia,^[16] and there have been reports of oral

Address for correspondence: Dr. Frank Mayta-Tovalino, Academic Department, Faculty of Health Sciences, Universidad Científica del Sur, Av. Paseo de la República 5544, Miraflores 15074, Lima, Peru.
E-mail: fmaytat@cientifica.edu.pe

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clinical manifestations, which have currently generated great interest. Therefore, this literature review aims to describe the oral manifestations of Covid-19 in the mucous membrane and salivary glands and alterations due to the disease in the olfactory and gustatory systems. Through this review, we aim to present the future challenges and oral manifestations of Covid-19 seen in daily dental practice.

MATERIALS AND METHODS

A non-systematic narrative review was conducted because the literature was relatively scarce. In addition, scientific evidence in the databases Scopus and PubMed was searched using the Boolean operators OR, AND, and NOT and keywords “oral manifestations” [MeSH Terms], “COVID-19” [All Fields], and “dentistry” [All Fields]. Articles published in Spanish and English between January and December 2020 were included. Bibliographic reviews, descriptive and analytical studies, randomized controlled clinical trials, and systematic reviews in Spanish and English were included. The following search formula was used:

Oral manifestations: “oral manifestations” [MeSH Terms] OR (“oral” [All Fields] AND “manifestations” [All Fields]) OR “oral manifestations” [All Fields]

Covid-19: “severe acute respiratory syndrome coronavirus 2” [Supplementary Concept] OR “severe acute respiratory syndrome coronavirus 2” [All Fields] OR “ncov” [All Fields] OR “2019-nCoV” [All Fields] OR “COVID-19” [All Fields] OR “SARS-CoV-2” [All Fields] OR “coronavirus” [All Fields] OR “cov” [All Fields]

Dental care: “dental care” [MeSH Terms] OR (“dental” [All Fields] AND “care” [All Fields]) OR “dental care” [All Fields]

Dentistry: “dentistry” [MeSH Terms] OR “dentistry” [All Fields] OR “dentistry’s” [All Fields]

The data were obtained by the following PICO question:

P (Population): Patients with Covid-19

I (Intervention): Dental care protocol

C (Comparison): None

O (Outcome): Oral Manifestations

Exclusion criteria were

Studies not related to dentistry

Animal studies

Studies published before or after 2020

Studies in languages other than English and Spanish

Risk of bias

As this study is a narrative review, it is pertinent to consider the risk of bias in the collection of information; however, it provides rapid identification of the main oral manifestations of Covid-19.

RESULTS

ORAL MANIFESTATIONS

Oral lesions in Covid-19 could be a direct manifestation of the infection, a manifestation of systemic deterioration, or an adverse reaction to the treatment.^[20] They include dysgeusia, ulcerations, gingivitis, petechiae, or opportunistic infections, such as candidiasis; however, they cannot be accepted as a clinical pattern of the disease.^[21] Early detection of the manifestations of Covid-19 is important to prevent the spread of the disease, perform rapid isolation, and assist frontline teams, such as physicians and nurses, in fighting this pandemic.

TASTE AND SMELL ALTERATIONS

The most common symptoms are alteration of taste^[11,17,18,21] and smell, presenting as anosmia, which is considered a marker of Covid-19 because it is among the first manifestations and can help reduce the spread of the virus, even in asymptomatic patients.^[22] In a meta-analysis, 52.73% and 43.93% of the patients presented with alterations in smell and taste, respectively.^[23] Furthermore, in another study, 38%, 35%, and 24% of the patients presented with dysgeusia, hypogeusia, and ageusia, respectively.^[21] In yet another study, a questionnaire was administered to 140 patients; of them, 77 (52%) showed changes in taste sensation.^[24] The molecules used to diagnose Covid-19 are angiotensin-2 converting enzyme (ACE 2) receptor and TMPRSS2, which are located in the taste buds and are believed to help in the invasion of SARS-CoV-2. They can also be found in the sulcular epithelium of periodontal pockets; it is a thin and permeable lining and is a focal point of the infection.^[25] In Europe, 70% of the patients with Covid-19 showed olfactory and taste alterations. These manifestations could help in predicting the prognosis during the disease. Neurosensory recovery is rapid and complete in a large percentage of patients.^[19]

SALIVA AND COVID-19

SARS-CoV-2 requires ACE 2 receptor as a receiver to enter the target cells.^[26] ACE 2 receptor is expressed in several organs, which may indicate possible routes of infection.^[16] In addition, the salivary gland and oral epithelium also express this receptor (18). This is how the saliva plays a fundamental role by allowing SARS-CoV-2 to penetrate the cells^[5]; however, saliva proteases have been found to inhibit or diminish viral entry.^[25]

SIALOADENITIS AND XEROSTOMIA

As mentioned earlier, Covid-19 binds and fuses to ACE 2 receptors in the epithelium of salivary glands; when it replicates in the salivary ducts, they can be damaged, causing inflammation and inducing signs and symptoms, such as swelling, discomfort, and pain in the salivary glands; or chronic obstructive sialadenitis when the salivary glands are repaired by proliferation of fibroblasts and connective tissue. Dilatation of the ducts can be increased by hyperplastic fibrous scarring, which affects the function of lubrication and washing of the ductal system by saliva. This may cause a retrograde infection through the ductal orifices and the deposition of inorganic salts in the ductal wall, which blocks the excretion of saliva and aggravates the obstruction.^[26]

In a study conducted in Italy, in 326 patients positive for Covid-19, 45.9% reported xerostomia with a dry mouth score of 5 in a range of 0–10. A total of 76.5% stated that it was the first time they felt a dry mouth. A total of 19.6% reported xerostomia as the first symptom correlated with the virus, with an average onset time of 7 days before the definitive diagnosis of Covid-19. Of the patients who had xerostomia, 39.2% also had difficulty swallowing, 27.5% had difficulty swallowing dry food, and 37.3% needed fluids to swallow.^[27]

KAWASAKI DISEASE (KD) AND COVID-19

KD is a systemic vasculitis that mainly damages the coronary arteries and is common in early childhood.^[28-30] The etiological factor of this disease is not yet known, but it is accepted that viral agents can act as trigger.^[28,30-33] Chang *et al.*^[34] conducted a study, wherein a statistically significant association was found between Coronaviridae and KD; more than half of the patients positive for KD simultaneously presented with a viral infection affecting the respiratory tract.

The literature indicates that children positive for Covid-19 usually present symptoms similar to those presented by adults but milder^[35]; however, some studies have reported that Covid-19-positive pediatric patients have symptoms very similar to KD,^[36,37] which can manifest itself at the same time or after the resolution of Covid-19 infection.^[38,39] Despite this, not all the symptoms manifested by pediatric patients are consistent with the American Heart Association Kawasaki guide; for that reason, the World Health Organization attributed the name of multisystemic inflammatory syndrome to this set of symptoms^[37,40] caused by a storm of cytokines triggered by SARS-CoV-2, in which the number of inflammatory markers is high.^[28,41] Multisystemic inflammatory syndrome has also been called a Kawasaki-like disease, or Kawa-Covid-19, as it shares

clinical, pathogenic, and laboratory characteristics with KD, as well as with toxic shock syndrome and macrophage activation syndrome.^[28,42-44]

Oral manifestations reported in the literature of Kawasaki-like disease include alterations in the oral cavity, such as dryness, peeling, fissures, cracking and bleeding of the lips, and erythema of the oral and pharyngeal mucosa.^[32,33,37,45,46] Verdoni *et al.*^[33,46] conducted an observational study of 10 pediatric patients reported to be Covid-19-positive with KD conditions; among them, 80% presented with alterations of the lips or oral cavity, in addition to non-exudative conjunctivitis. Similarly, Falah *et al.*^[39] reported that of the 10 pediatric patients with Covid-19 and Kawasaki-like disease, 90% presented with conjunctival and oral cavity changes as the most common manifestations.

Therefore, the study of this disease can be useful for dental professionals since it determines possible differential diagnoses, facilitates early diagnosis,^[33] and maintains a preventive attitude. Therefore, this study suggests considering all pediatric patients and their parents as possible carriers of Covid-19 during dental consultation, unless proven otherwise.^[35]

DISCUSSION

Vascular lesions in Covid-19-positive patients could be due to a direct action of the virus on endothelial cells; this involves immune or autoimmune reactions, such as thrombocytopenic purpura or cytokine storm, leading to microvascular dysfunction, increased vasoconstriction, organ ischemia, and inflammation.^[25,26] These reactions could also alter the oral keratinocytes and salivary gland ducts, leading to increased permeability of cell walls to pathogens replicating in oral cells.^[23]

For instance, a 40-year-old patient diagnosed with Covid-19 was found to have lesions in the oral mucosa, including petechiae on the lower lip, aphthae on the tongue and gum, and whitish spots on the back of the tongue and ventral area diagnosed as candidiasis, due to decreased salivary flow.^[11] In another study, an 81-year-old patient with Covid-19 was found to have multiple superficial aphthous ulcers of various sizes with irregular margins, covered with a mucopurulent membrane, with pain on palpation. Another 71-year-old patient, on intraoral examination, was observed to have small hemorrhagic ulcers on the lips with areas of superficial necrosis on the anterior dorsum of the tongue. All patients received daily treatment with photobiomodulation therapy for 10 days. In a 32-year-old patient, circular ulcers with a whitish center

surrounded by a 3–4 mm erythematous halo were found on the lateral edges and apex of the tongue; they regressed after 8 days.^[23]

People with systemic diseases may have a weak immune system and are more likely to be infected with Covid-19, which, in addition to poor oral health, may contribute to the presence of oral ulcerations that can be aggravated by the presence of opportunistic microorganisms.^[27] These intraoral lesions are often misdiagnosed by the lack of intraoral examination owing to a fear of contracting Covid-19.^[17]

An effective drug therapy to combat Covid-19 or its adverse effects has not yet been established, so the associated medication may cause side effects in the oral cavity. Therefore, oral manifestations cannot yet be considered a specific clinical pattern of Covid-19. Studies are needed to determine whether the oral manifestations could be due to the presence of co-infections or systemic deterioration caused by the drugs used for treatment.^[21,47,48]

Studies have been conducted on different pharmacological regimens used for the treatment of COVID-19. Many of these affect the oral cavity; these could be oral adverse effects or possible complications affecting subsequent dental treatment. For example, Sinjari *et al.*^[49] proposed that xerostomia may be associated with drug therapy of Covid-19. For this reason, dental personnel should be part of the healthcare team, handling updated information on SARS-CoV-2, with main emphasis on the transmission and treatment of this disease.^[50]

Pereira *et al.*^[1] se han mencionado diferentes cambios en la mucosa oral como manifestaciones orales de COVID-19, como; disgeusia, petequias, úlceras, máculas eritematosas, etc. Sin embargo, al igual que el presente estudio consideramos que se necesitan mas estudios para establecer fehacientemente estas alteraciones en la mucosa oral. Por otro lado, otra implicancia importante en la cavidad oral es que el COVID-19 puede ser diagnosticado mediante la saliva, debido a que es un nicho ecológico fundamental para la colonización y multiplicación viral.^[5]

Oral health is directly related to global health. Several studies claim that cytokines or microbial pathogens are released systemically as a result of oral infection, cause inflammation in different organs, and aggravate systemic disease. In the oral cavity, respiratory pathogens that cause pneumonia, such as *Chlamydia pneumoniae*, are found, and patients with periodontitis are at the greatest risk of developing this disease.^[51-53] Oral pathogens and the release of proinflammatory

cytokines in periodontitis can cause colonization of the lower respiratory tract.^[52,54,55] Studies have shown that oral health care decreases the risk of respiratory diseases such as Covid-19; therefore, good oral hygiene decreases oropharyngeal colonization and respiratory complications, particularly in older adults and intensive care patients. The relationship between good oral hygiene and the severity of Covid-19 disease is evident; however, further investigations are needed.^[52]

The main limitation of this literature review was that the studies are recent and have not established a causal relationship between the long-term symptoms of Covid-19 in the oral cavity. Therefore, the exact time that these signs and symptoms last is still unknown. However, the current literature shows that this disease has important oral manifestations that the professional must take into account for an accurate diagnosis.

CONCLUSIONS

Within the scope of this literature review, there are indications of alteration or changes in saliva due to the viral load that occurs during the infection process. Furthermore, the principal oral manifestations of Covid-19 are dysgeusia, anosmia, and ulcers, which may be associated with the patient's systemic diseases or the administration of drugs. Although more research is needed on the relationship and pathogenesis of these manifestations of Covid-19, they should be considered for an early diagnosis. Finally, it has been shown that people with periodontal disease have a higher risk of dying.

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The authors declare that this review was carried out with our own resources.

CONFLICTS OF INTEREST

None to declare.

ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT

Not applicable.

PATIENT DECLARATION OF CONSENT

Not applicable.

DATA AVAILABILITY STATEMENT

Not applicable.

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