

ORAL INJURIES ASSOCIATED WITH COVID-19

Karina Gomes Canuto Yoshida

Academic in dentistry at the institution:
Centro Universitário ICESP, Brasília-DF
ORCID: 0000-0002-5703-2551

Thaís Calixto Araújo

Academic in dentistry at the institution:
Centro Universitário ICESP, Brasília-DF
ORCID - 0000-0003-3723-4428

Leonardo Araújo Andrade

Professor of surgery at the institution:
Universidade Paulista, Goiânia-GO
ORCID: 0000-0002-4363-5044

Olegário Antônio Teixeira Neto

Professor of periodontics at the institution:
Universidade Paulista, Goiânia-GO
ORCID: 0000-0002-0157-7106

Cláudio Maranhão Pereira

Professor of stomatology and oral pathology
at the institution: Centro Universitário
ICESP, Brasília-DF
ORCID: 0000-0001-5511-0387

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



Abstract: Introduction: The new coronavirus is a highly contagious disease, which promotes great systemic involvement of the infected individual, and which can lead to the emergence of oral manifestations. This is due to the ability of SARS-CoV-2 to bind with angiotensin-converting enzyme (ACE 2) receptors. Which leads to the possibility of the correlation of this virus with the appearance of oral alterations. **Goal:** The purpose of this study is to carry out a literature review in order to present the prevalence and impacts caused in the oral environment, of oral changes possibly associated with COVID-19. **Materials and Methods:** Based on this investigation, the methodology applied for this study was a literature review, with a survey of articles published between 2020 and 2022, which explore the association of covid-19 with oral lesions. The studies were searched on the platforms: SCIELO, Lilacs, and Pubmed, with the search for the following keywords: "covid-19", "oral lesions" and oral manifestations". **Result:** Therefore, as a result of the investigation, it was found that the most prevalent oral manifestations that may be associated with covid-19 are: ulcerative lesions, vesicobullous, xerostomia and gustatory changes, but other lesions may also arise, such as petechiae, dysgeusia, scaly gingivitis, thrush, and herpes simplex virus (HSV-1) infection or reactivation. **Conclusion:** However, it was found that with the current studies it is not possible to determine the causality of oral lesions associated with the new coronavirus. More research is needed in order to specify the action of covid-19 in the oral environment, clarifying its possible causes and effects. **Keywords:** COVID-19; SARS-CoV-2; oral manifestations.

INTRODUCTION

The COVID-19 virus is inserted in a conglomerate called coronavirus, related to problems in the respiratory, intestinal, hepatic and neurological tract, in those individuals, which are infected. It presents a vast disposition in nature, since it can contaminate human beings, as well as different animals, such as cats, pigs, bats, among others (CUI; LI; SHI, 2019).

In view of this, it is believed that SARS-CoV-2 presents itself in all body systems in humans and in different ways. Furthermore, some authors are in agreement and relate the infection of the active virus with oral changes (CARDOSO et al., 2020). That said, the primary form of transmission of COVID-19 occurs through oral and nasal secretions, as well as through contact with infected areas, released by contaminated droplets when an individual has active SARS-CoV-2 and these disperse. There is also the spread of the virus due to aerosols, as well as direct contact with the oral, nasal and ocular mucosa of those patients undergoing dental treatments or who are exposed to interventions in the airways, for example, with orotracheal intubation (BAGHIZADEH FINI, 2020; BRASIL, 2020; UMAKANTHAN et al. 2020).

According to Cardoso et al. (2020), the oral mucosa is classified as one of the main routes of admission of the virus, given that its epithelial cells contain a large amount of enzyme that converts the angiotensin 2 receptor (ACE2), a receptor which the COVID-19 virus 19 binds to infect the human system. As a result of this affinity for the epithelium, it is believed that the salivary glands end up serving as a deposit for SARS-CoV-2.

According to some studies, active COVID-19 can trigger specific symptoms such as fever, cough, anosmia, ageusia, xerostomia, among other manifestations

(BRASIL, 2020). In this context, Halboud et al. (2020) consider that the most common lesions in the oral cavity are ulcerative lesions, as well as vesicobullous and erythematous papules, with the hard palate, dorsum of the tongue and labial mucosa as the most affected regions.

In view of the above, the individual infected by SARS-CoV-2 may present different clinical characteristics, from mild flu-like symptoms to no symptoms, or even manifest more complex conditions when developing critical acute respiratory conditions. However, as it is a new type of coronavirus, more research is important to understand the pathology that this virus causes in humans, although some risk factors exist, such as comorbidities, obesity, older people, which can thus contribute to serious frames. However, a consensus has not yet been reached regarding the fact that people without pre-existing problems present critical situations that can contribute to fatal cases (MACHHI et al., 2020).

Thus, the relevance of approaching the topic emerges here. In view of this, this work aims to carry out a literature review on what COVID-19 is, as well as its origin, in addition to demonstrating the oral impacts caused by the SARS-CoV-2 virus, as well as presenting the prevalence of the main oral changes associated with the disease.

MATERIALS AND METHODS

The present work is a literature review through publications that investigated the main oral manifestations, directly or indirectly associated with the SARS-CoV-2 virus. The research was carried out in the following databases: SCIELO, Lilacs, academic google and Pubmed, using search keywords “covid-19”, “oral lesions” and “oral manifestations”.

Thus, as a selection criterion for studies, the research was directed to articles published

between 2020 and 2022. Integrative review articles, literature review, systematic reviews and clinical case reports were identified and selected for reading, which presented discussions related to the appearance of oral alterations in patients infected with the new coronavirus.

LITERATURE REVIEW

WHAT IS COVID-19 AND ITS ORIGIN

In December 2019, the emergence of a new coronavirus, SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2), was found in Hubei province in China, in a city called Wuhan (OZDEMIR, 2020). This viral infection, which was discovered, appeared to be quite similar to the cases of patients infected with the severe acute respiratory syndrome coronavirus (SARS-CoV), however the disease showed a much higher intensity of contamination (BRASIL, 2020; SANTOS et al., 2020).

Consequently, the new virus quickly spread, due to the flow of people between countries, and became a major global fatality. In view of this, in March 2020 the WHO described the event as a pandemic (LIU & SHIH, 2020; BRASIL, 2020).

Brandao, et. al. (2020) and Santos et. al. (2020) showed that SARS-CoV-2 caused damage to the respiratory tracts and other vital organs. From the contagion, SARS-CoV-2 connects to receptors on angiotensin-converting enzymes 2 (ACE2), so these cells become host for the virus causing inflammation in related tissues and organs. ACE 2 is found in some organs such as lungs, stomach and bladder, and on tissue cell surfaces such as tongue epithelial cells, adipose tissue, uterine epithelial cells, esophageal epithelial cells, among others. (CARVALHO, et. al. 2021; BEYERSTEDT, CASARO E RANGEL, 2021).

COVID-19 has its main form of transmission through the inhalation of

droplets expelled by contaminated people, through coughing or sneezing. However, contamination can also occur through contact with the mouth, nose and/or eyes, droplets of saliva and even through contaminated surfaces or items (BRANDÃO et al.; DIETZ et al., 2020; XU et al., 2020; Chen et al., 2020). In view of this, infected patients present a series of symptoms that can manifest from milder to more severe, namely: fever, cough, sore throat, nasal congestion, diarrhea, abdominal pain, myalgia, shortness of breath, among others. (HUANG, et al. 2020).

When present, the onset of symptoms occurs on average 5 days after infection, determining an incubation period for the virus. These symptoms can lead to complications and impairment of the muscular, respiratory, cardiovascular and neurological systems, potentially evolving into a serious condition. Still, with all these possible symptoms, there are patients who are asymptomatic. (CAPOCASALE 2021; BRASIL, 2020; SILVA, 2022; VASCONCELOS-JUNIOR et al., 2020).

According to MACHHI (2020), even though it is a new virus that needs many studies regarding its actions in the human body, it was observed that there are some risk factors, that is, factors that can lead to more severe cases. They are: advanced age, obesity and patients with comorbidities. Patients with comorbidities, which were associated with worse prognoses, are diabetics, hypertensive patients and those with cardiovascular diseases (KUI et al., 2020; WANG et al., 2020; YANG et al., 2020).

Thus, with the arrival of the new virus, it was necessary to develop preventive measures in order to block its spread. The main measures are: social distancing, hand washing, more frequent cleaning and disinfection of surfaces and objects, use of personal protective equipment, the most used being the mask

(BAGHIZADEH FINI, 2020; BRASIL, 2020).

IMPACTS CAUSED BY COVID-19 ON THE ORAL ENVIRONMENT

It is known that the main routes of transmission of the SARS-CoV-2 virus are through the nose and mouth, when in contact with secretions, as well as with infected surfaces, through the small drops produced by the contaminated person, when coughing or sneezing (BAGHIZADEH FINI, 2020; BRAZIL, 2020;

UMAKANTHAN et al., 2020). This way, the virus present in oral and nasal secretions, brings the alert, in its dissemination, not only to serious respiratory problems, but also to pathological manifestations in the oral environment, of patients affected by COVID-19 (FIDAN; KOYUNCU; AKIN),. 2021).

Even without a consensus on the link between SARS-CoV-2 and oral pathological changes in patients affected by the virus, knowledge of these oral manifestations is necessary. Brandão et al., (2021), reported the importance of understanding these injuries, since they can appear even before specific respiratory problems, and their emergence can precede a serious clinical condition. Thus, it is essential to highlight the role of the dentist during the diagnosis process of COVID-19, as well as in combating the impacts caused in the oral environment associated with the virus, to prevent its proliferation (BRANDÃO et al., 2021).

According to Amorim dos Santos et al., (2020), oral problems (dysgeusia, petechiae, candidosis, ulcers resulting from trauma, herpes simplex, geographic tongue, among others) manifested by a 67-year-old male patient suggested the possibility of these alterations being additional injuries resulting from the affected systemic condition or due to the therapy used against COVID-19.

Fidan, Koyuncu and Akin (2021) found that changes in the oral mucosa are highly likely to be the result of various causes such as anxiety, lack of oral hygiene, systemic conditions or even the indiscriminate use of local antiseptics, especially those that have at their base hydrogen peroxide highly recommended to reduce the volume of viruses in the oral environment.

Brandão et al., (2021) reported that they did not obtain samples of oral manifestations to validate the appearance in tissues injured by aphthous ulcerations and superficial necrosis, however, they found that the advance, as well as the disappearance of these lesions occurred, simultaneously, when the treatment was completed. COVID-19 infection. Thus, they concluded that these oral pathological changes may be directly related to the presence of the SARS-CoV-2 virus in the patients studied or may also occur in the face of the patient's serious condition, but it is not yet decisive.

The appearance of ulcerations and necrosis appear after the infection of oral glandular keratinocytes by SARS-CoV-2, which happens due to the ease of pathogens, of unknown origin, as well as the multiplication of viruses to penetrate the cells lining the oral mucosa. However, due to the insufficient sampling of oral lesions, the authors recommend that in future studies, it is necessary to insert the incisional biopsy and viral exam for SARS-CoV-2 in patients infected with COVID-19 (BRANDÃO et al., 2021).

Dziedzic and Wojtyczka (2021) revealed that hospitalization as well as the medications used for COVID-19 are capable of leading to the appearance of different oral changes. These occur due to the systemic treatment given to the infected patient, with drugs or even through mechanical ventilation, blood oxygenation, among other therapies used in aggravated conditions. Allied to this, changes found in the oral environment have

the potential to cause other complications. In case report articles, in which the oral cavity of three patients infected with COVID-19 was studied, the authors argued the probability of the presence of ulcerations or bullous vesicles in the oral mucosa (FRANCO, A. G. et al). In one of the cases, they could observe the appearance of lesions compatible with erythema multiforme, in the other two, the lesions were similar to those that occur in situations of herpes simplex (CARRERAS-PRESAS et al., 2021). According to the aforementioned authors, there is still a need for further studies to determine the association of oral manifestations with patients infected with the SARS-CoV-2 virus, because in the cases, which they studied and monitored, in the research carried out, biopsy was not performed in the lesions. found, thus, they could not determine whether the lesions are due to COVID-19 infection, whether due to the emotional pressure of the moment experienced or they could not establish this relationship due to the absence of intraoral tests, which may have led to inadequate diagnoses (CARRERAS-PRESAS et al., 2021).

Abu-Hammad, Dar Odeh and Abu-Hammad (2020) argue that caution is necessary when relating COVID-19 to oral lesions, since the therapies used to combat the disease can harm the immune system, consequently, expanding the vulnerability and give rise to a variety of opportune oral alterations, whether viral or fungal.

In another study, in which 26 patients infected with COVID-19 were followed, the authors showed that there was the appearance of ulcerations on the tongue of these patients and directly related to the presence of the SARS-CoV-2 virus, but still, do not disregard the only secondary relationship between the appearance of these oral alterations, due to the fact that the immune system is compromised (RIAD et al., 2020).

PREDOMINANT ORAL CHANGES ASSOCIATED WITH COVID-19

In this context, according to the findings in the research carried out, we were able to verify the existence of the most prevalent alterations, directly or indirectly associated with SARS-CoV-2. Fantozzi et al.,(2020), carried out a study seeking to evaluate xerostomia, olfactory and gustatory dysfunctions associated with patients with covid-19. The study was carried out with 326 patients after hospital discharge. The same concluded that about 45% of the patients presented alterations in the taste, 41.4% olfactory dysfunctions and 45.9% developed xerostomia. According to the author, these three manifestations may be the only manifestations of Covid-19. For some authors, several oral manifestations are associated with contamination by Covid-19, with most cases affected by ulcerations, petechiae, vesicobullous lesions, rash, erythematous lesions, transient linguistic papillitis, xerostomia, glossitis, canker sores and burning mouth syndrome. (BEMQUERER et. al., 2020; CICCARSE et. al., 2020; GONZALEZ et. al., 2021; HALBOUB et. al.,2020; MORTAZAVI et al.et. al., 2020; SANTOS et. al.,2020).

Costa dos Santos Júnior et. al.,(2020), observed that the most relevant oral alterations reported in the literature were infections by fungi, as well as by the HSV-1 virus, as well as unspecified oral ulcerations, drug eruptions, alteration in taste, dry mouth related to the reduction of saliva, as well as the inflammation of the gums, which causes gingivitis. They also highlighted the importance of an adequate and detailed anamnesis, as well as a rigorous intraoral clinical examination, since they are indispensable for the identification and treatment of these probable manifestations (COSTA DOS SANTOS JÚNIOR et al., 2020).

Días Rodrigues et. al., (2020) highlighted that the manifestations with the highest incidence in patients infected with COVID-19 are: oral dryness/xerostomia, vesiculobullous lesions, aphthous lesions, dysgeusia and anosmia, petechiae, candidosis, traumatic ulcers, HSV-1 infection and HZ, geographic tongue, hemorrhagic bullous angina, vascular disorder, nonspecific stomatitis, early ulcerative lesions, initial erythema, multiform lesions, white and erythematous plaques, desquamative gingivitis, lichen planus and necrosis of the oral mucosa (DÍAZ RODRÍGUEZ; JIMENEZ ROMERA; VILLARROEL, 2020; PETRESCU; LUCACIU; ROMAN, 2020; SANTOS et al., 2020).

By associating the manifestations reported in the literature, Carreras et al (2020) state that oral evidence is clinical signs referring to virus contamination or resulting from the treatment performed. The most mentioned alterations are: ageusia, unspecific anosmia and hyposalivation. However, other authors mention the presence of ulcers, desquamative gingivitis, irregular blisters/ulcers on the dorsal surface of the tongue and enlargement of the submandibular glands with an increase in cervical lymph nodes (CARRERAS-PRESAS et al., 2020; PETRESCU; LUCACIU; ROMAN, 2020).

Vieira (2021) reported a study where a report was prepared, which showed all the systemic manifestations of the patients. And then approximately 150 cases were evaluated, where three cases of patients contaminated by COVID-19 presented oral manifestations. The research showed the intraoral manifestations being ulcers with painful symptomatology in the oral mucosa, desquamative gingivitis, blisters, and erythema on the palate and gingival margin the most pertinent.

According to Farid et. al., (2021), with the elaboration of a survey including about

In 19 studies, the following oral clinical findings were found: gustatory alterations (hypogeusia, dysgeusia, ageusia) taste alteration, oral mucosa lesions (ulcers, erosions, blisters, plaque-like lesions, and geographic tongue); ulcers and erosions (single or multiple); vesiculobullous lesions; plates (white and red); reactivation of herpes simplex 1 (HSV 1); bullous angina, gingival changes (generalized erythematous and edematous gums, gingival-paraodontal bleeding, necrotic interdental papillae and desquamative gingivitis); dry mouth; halitosis, pain and swelling in the tongue and masticatory muscles, geographic tongue, papilla hyperplasia associated with changes in taste and macroglossia.

Studies carried out by Santos et. al. show the verification of about 10,228 cases in 19 countries, in which they stated that the lesions considered mild appeared before the onset of respiratory symptoms, and that they were present from 7 to 24 days after the onset of symptoms. The study also reported that oral pathologies can be pointed out as evidence of disease progression. According to the authors, the important clinical findings were: dysgeusia, hypogeusia, white and erythematous plaques, irregular ulcers, bullous lesions, petechiae, desquamative gingivitis; affecting the tongue, palate, lips, gingiva, buccal mucosa.

Wu et. al., (2021) reported a different aspect from other analyzed articles, and benign migratory glossitis was also highlighted. The author also highlighted the following clinical findings associated with coronavirus: Herpes simplex virus infection, candidiasis, anosmia and hyposmia, dysgeusia, ageusia, hypogeusia, xerostomia.

In another study, carried out by Iranmanesh et. al., (2020) indicate that the lesions observed tend to be relatively more severe according to the age of the infected person, that is, the signs and symptoms were

more aggressive in older patients. The study also highlights that lesions may precede systemic symptoms related to COVID-19, being evidenced in the period of 3 to 4 days prior to symptoms, or up to 12 weeks after the first signs and symptoms. The most relevant regions affected by the lesions were: tongue, labial mucosa, palate, gingiva, buccal mucosa, oropharynx and tonsils. And the most notable lesions associated with coronavirus were: ulcers, bullous lesions, vesicles, pustules, tongue fissure, macules, papules, plaques, erythema, halitosis, whitish areas, hemorrhagic crusts, necrosis, petechiae, edema and spontaneous hemorrhage. Given this, Soares et. al.,(2020) present a clinical case study of a 42-year-old patient, gender not mentioned, diagnosed through PCR as infected by SARS-CoV-2. The same has general symptoms such as respiratory and dermatological changes, and oral symptoms such as ulcerations and reddish lesions. To confirm the diagnosis, a biopsy of the ulceration of the patient's oral mucosa was performed. As a result of the microscopic examination, an inflammatory action was observed in the tissue, accompanied by the presence of the microorganism. Thus, a direct action of the virus was declared as the determining agent, responsible for the formation of the lesion.

From a review of 17 studies, Rosa et al.,(2021) stated that the varied lesions associated with the coronavirus appear to be multifactorial. These various lesions include ulcerations, aphthous lesions and macules. Where the main anatomical locations were tongue, lips and palate. In view of this multifactorial nature, the authors highlighted the importance of an approach between physicians, dentists and dermatologists, for the early diagnosis of changes caused by COVID-19, as they are able to recognize lesions that precede changes in the respiratory system.

Favia et. al.,(2021) carried out a study with approximately 123 individuals, who were hospitalized at the University Hospital of Bari. Most individuals had early lesions in the oral and perioral cavity, such as ulcerations. There was greater discomfort in multiple lesions with a diffuse appearance, with an erythematous multiform base, with yellowish fibrins and necrotic areas. They also highlighted the occurrence of late lesions such as: ulcerative, candidiasis, bullous angina, spontaneous oral hemorrhage, petechiae, erythema in papillae, papillary hyperplasia; in addition to necrotic ulcerative gingivitis, which is associated with poor hygiene. These early changes were determined as joint manifestations of systemic changes caused by the coronavirus, observed in the first week and also later in this period. The authors emphasized that the appearance of oral lesions represent physiological determinants, referring to the condition of probable worsening of the disease.

Brandão et al, et. al., carried out a case report study, about 8 cases, where patients were hospitalized and infected with the coronavirus. All cases showed oral manifestations, which appeared soon after the onset of the disease, or after the onset of lack of taste, which ended up harming places such as the tongue, lips, palate and oropharynx. Among the cases presented by Brandão, he reported a case of an 80-year-old patient, who had comorbidities, and who had multiple superficial aphthous ulcers of different sizes, irregular margins and covered by a membrane of purulent secretion, also presented on the lips., superficial necrosis. In view of this, it was observed that there were two more frequent patterns, one in milder cases, in young people, where they had aphthous ulcers and another in more complicated cases of infection and immunosuppressed, in patients with advanced age who had necrotic ulcers of HSV-1. Therefore, the lesions were more severe and disseminated in patients

with advanced age. In general, before the study were found: aphthous, necrotic or hemorrhagic ulcerations, dysgeusia and a certain number of patients tested positive for herpes, expressing that some of the lesions are linked to immunosuppression.

In another review study, carried out by Zarch and Hosseinzadeh (2020), it was observed a total of 170 cases of infected patients with symptoms, aged between 9 and 90 years. It was analyzed that the beginning of the complaint of oral symptoms appeared two days before the general symptoms. The main alterations were: dry mouth, dysgeusia, pseudomembranous fungal structure, ulcerations, myalgia during chewing, edema in the oral cavity and herpetic lesions.

DISCUSSION

There is a consensus on the need for more in-depth studies to determine the association of SARS-CoV-2 with oral changes. However, Brandão et. al.,(2021) highlight the need for knowledge when pathological lesions appear in the individual infected by the virus, because these changes can appear long before the simplest symptoms, as well as precede a more complex problem. This way, the dentist becomes essential in the progress of identifying the disease, including to act in the fight against COVID-19, by identifying these manifestations and preventing their spread (BRANDÃO et al., 2021).

According to Amorim dos Santos et. al,(2020), it was possible to observe that the oral manifestations present in individuals affected by COVID-19 are strongly related to indirect symptoms resulting from the worsening of the patient's systemic situation, as well as from the use of drug therapy. Thus, they emphasize and report the importance of considering that the drugs used to treat the disease can lead to the emergence of oral lesions or even facilitate their appearance.

Costa dos Santos Júnior et. al., (2020) and Amorim dos Santos et. al.,(2020) corroborate that the impacts caused by drugs used in the treatment of COVID-19 cannot be minimized, as there is no consensus as to whether these oral changes occur directly due to the disease or the fragility of the immune system. This is because those who are affected by the virus are more vulnerable to secondary infections, as well as to side effects of medications (COSTA DOS SANTOS JÚNIOR et. al., 2020).

Iranmanesh et. al., (2021) and Riad et. al., (2020) demonstrate that the oral alterations, as well as the first systemic signs of COVID-19 appeared at the same time, and also reinforced the question about the worsening of the disease being directly related to the more complex and diffuse oral manifestations. They also showed that secondary infection can favor the appearance of oral lesions and, according to the systemic health of the individual, these lesions collaborate to worsen the patient's condition, and can lead to death (RIAD et. al., 2020; IRANMANESH et. al, 2021).

In this context, Riyadh et. al., (2020) highlights and ratifies the studies by Brandão et. al.,(2021) on laboratory research, which are essential for a better discernment and understanding of oral alterations present in individuals affected by SARS-CoV-2. Thus, even with evident oral manifestations, Halboub et. al.,(2020) report the need for more in-depth analysis, with biopsies, for example, since these diagnoses were only based on clinical signs, which generates distrust regarding the safe result when associating oral pathology with the disease COVID-19.

CONCLUSION

Oral alterations may manifest without association with the severity of the disease. The most common manifestations in the cases of patients affected by COVID-19 were ulcerative, vesicobullous lesions, taste

disorders and changes in salivary flow, such as xerostomia. They were observed in greater quantity in the buccal mucosa, tongue, palate and gingiva.

Thus, the role and knowledge of the dentist surgeon is extremely important when diagnosing the changes that may be linked to the new coronavirus, as the lesions can precede a serious clinical condition of the disease. In addition to providing preventive protocols and reducing damage to the health of patients.

In this sense, part of the studies relate the oral changes of patients infected by COVID-19, with immunosuppression or the therapy in which the patient is, while other articles associate the coronavirus as the main factor in the emergence of the changes. Therefore, further studies are needed to prove the direct or indirect relationship of the virus with oral manifestations and to associate it with the prognosis of patients.

REFERENCES

1. Abu-Hammad, S.; Dar Odeh, N.; Abu-Hammad, O. *SARS-CoV-2 and oral ulcers: a causative agent or a predisposing factor?* Oral Dis. Dinamarca, v. 28, p. 933-934, 2020.
2. Amorim dos Santos, J.; Normando, A.G.C.; Carvalho da Silva, R.L.; Acevedo, A.C.; De Luca Canto G., et al. *Oral manifestations in patients with COVID-19: a living systematic review.* J. Dent. Res. Washington, v. 100, p. 141-154, 2021.
3. Baghizadeh Fini, M. *What dentists need to know about COVID-19.* Oral Oncol., Oxford, v. 105, p. 104741, 2020.
4. Bemquerer, L.M.; Arruda, J.A.A.; Soares, M.P.D.; Mesquita, R.A.; Silva, T.A. *The oral cavity cannot be forgotten in the COVID-19 era: Is there a connection between dermatologic and oral manifestations?* Journal of the American Academy of Dermatology, v. 84, p. 143-145, 2021.
5. Beyerstedt, S.; Casaro, EB.; Rangel, É.B. *COVID-19: angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-CoV-2 infection.* Eur J Clin Microbiol Infect Dis., v. 40, p. 905-919, 2021.
6. Brandão, T. B. Gueiros, L.A.; Melo, T.S.; Prado- Ribeiro, A.C.; Nesrallah, A.C.F.A, et al. *Oral lesions in patients with SARS-CoV-2 infection: could the oral cavity be a target organ?* Oral Surg. Oral Med. Oral Pathol. Oral Radiol., New York, v. 131, p. e45-e51, 2021.
7. Brasil. Ministério da Saúde. *O que é COVID-19, 2020.*
8. Capocasale, G.; Nocini, R.; Faccioni, P.; Donadello, D.; Bertossi, D., et. al. *How to deal with coronavirus disease 2019: A comprehensive narrative review about oral involvement of the disease.* Clin Exp Dent Res.; v. 7, p. 101- 108, 2021.
9. Cardoso, T.F.; Dias, M.J.L.E.; Chini, M.C.; Pereira, B.LB.; Orrico, S.R.P. et. al. *COVID-19 e a cavidade bucal: interações, manifestações clínicas e prevenção.* ULAKES Journal of Medicine, v. 1, p. 98-105, 2020.
10. Carreras-Pressas, C. M. Sánchez, J.A.; López-Sánchez, A.F.; Jané-Salas, E.; Péres, M.L.S., et al. *Oral vesiculobullous lesions associated with SARS-CoV- 2 infection.* Oral Dis., Dinamarca, v. 27, p. 710-712, 2021.
11. Chen, L; Zhao, J; Peng, J; Li, X.; Deng, X.; et. al. *Detection Of 2019-nCoV in saliva and characterization of oral symptoms in COVID-19 patients.* Cell Prolif., v. 53, p. e12923, 2020.
12. Ciccarese, G.; Drago, F.; Boatti, M.; Porro, A.; Muzic, S. I.; et. al. *Oral erosions and petechiae during SARS-CoV-2 infection.* Journal of medical virology, v. 93, p. 129–132, 2021.
13. Costa dos Santos Junior, J. C.; Souza, M.S.; Santos, V.S.; Carvalho, J.M.S.; Pires, A.L..P.V.P; et al. *Lesões orais em pacientes com COVID-19: uma síntese de evidências atuais.* J. Dent. Public. Health, Salvador, v. 11, p. 224-232, 2020.
14. Cui, J.; Li, F.; Shi, Z.L. *Origin And Evolution Of Pathogenic Coronaviruses.* Nat Ver. Microbiol, v.17, p. 181-92. 2019.
15. Díaz Rodríguez, M.; Jimenez Romera, A.; Villarroel, M. *Oral manifestations associated with COVID-19.* Oral Dis., Dinamarca, v. 28, p. 960-962, 2020.
16. Dietz, L.; Horve, P.F.; Coil, D.A.; Fretz, M.; Eisen, J.A.; et. al. *Novel Coronavirus (COVID-19) Pandemic: Built Environment Considerations To Reduce Transmission.* mSystems, v. 5, p. e00245-20, 2020.
17. Dzidzic, A.; Wojtyczka, R. *The impact of coronavirus infectious disease 19 (COVID 19) on oral health.* Oral Dis Dinamarca, v. 27, p. 703-706, 2021.
- 18- Fantozzi, P.J.; Pampena, E.; Divanna, D.; Pellegrino, E.; Corbi, D.; et al. *Xerostomia, gustatory and olfactory dysfunctions in patients with COVID-19.* Am J Otolaryngol, v. 41, p. 102721, 2020.

19. Farid, H; Khan, M ; Jamal, S; Ghafoor, R. **Oral manifestations of Covid 19-A literature review.** Rev Med Virol., v. 32, p. e2248, 2021.
20. Favia, G.; Tempesta, A.; Barile, G.; Brienza, N.; Capodiferro, S.; et. al. **Symptomatic Patients With Oral Lesions: Clinical and Histopathological Study on 123 Cases of the University Hospital Policlinic of Bari with a Purpose of a New Classification.** J. Clin. Med., v. 10, p. 757, 2021.
21. Fidan, V.; Koyuncu, H.; Akim, O. **Oral lesions in Covid 19 positive patients.** Am. J. Otolaryngol., Estados Unidos, v. 42, p. 102905, 2021.
22. Franco, A.; Eloi, L.J.; Franco, A.B.G; Oliveira B.J. **Associação entre a infecção pelo SARS-CoV-2 e o aparecimento de manifestações orais: uma revisão sistemática.** Research, Society and Development, v. 11, p. e46811125240, 2022.
23. Gonzalez, A.N.; Magaletsky, K.; Carrillo, P.M.; Masdemont, B.L.; Iburguren, A.M.; et al. ¿Son las alteraciones en la mucosa oral un signo de COVID-19? Estudio transversal en un hospital de campaña. Actas Dermo- Sifiligráficas, v. 112, p. 640-644, 2021.
24. Halboub, E.; Al-Maweri, S.A.; Alanazi, R.H.; Qaid, N.M.; Abdulrab S. **Orofacial manifestations of COVID-19: a brief review of the published literature.** Brazilian Oral Research, v. 34, p. 1-10, 2020.
25. Huang, C.; Wang, Y.; Li, X.; Ren, L.; Zhao, J.; et al. **Clinical Features Of Patients Infected With 2019 novel coronavirus in Wuhan, China.** Lancet, v. 395, p. 497-506, 2020.
26. Iranmanesh, B; Khalili, M; Amiri, R; Zartab, H; Afçatoonian, M. **Oral manifestations of Covid 19 disease: A review article.** Dermatol Ther., v.34, p. e14578. 2021.
27. Kui, L.; Fang, Y. Y.; Deng, Y.; Liu, W.; Wang, M. F.; et. al. **Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province.** Chin Med J, v. 24, p. 1025-1031, 2020.
28. Liu, Y.C.; Kuo, R.L.; Shih, S.R. **COVID-19: the first documented coronavirus pandemic in history.** Biomed J, v. 43, p. 328-333, 2020.
29. Macchi, J; Herskovitz, J; Senan, A. M.; Dutta, D.; Nath, B. et al. **The Natural History, Pathobiology, and Clinical Manifestations of SARS-CoV-2 Infections.** J Neuroimmune Pharmacol., v. 15, p. 359-386, 2020.
30. MortazaviI, H.; Rezaeifar, K.; Nassrabadi, N. **Oral Manifestations Of Coronavirus disease-19: a mini-review.** Open Access Macedonian Journal Medical Sciences, v. 8, p. 286-289, 2020.
31. Özdemir, Ö. **Coronavirus Disease 2019 (COVID-19): Diagnosis And Management (Narrative Review).** Erciyes Medicine Journal, v. 42, p. 242-247, 2020.
32. Petrescu, N.; Lucaciu, O.; Roman, A. **Oral mucosa lesions in COVID-19.** Oral Dis., Dinamarca, v. 28, p. 935-936, 2020.
33. Riad, A.; Kassem, I.; Hockova, B.; Badrah, M; Klugar, M.; et al. **Tongue Ulcers Associated With SARS-CoV-2 infection: a case series.** Oral Dis., Dinamarca, v. 28, p. 988-990, 2020.
34. Rosa, G.R.M.L.; Libra, M.; Pasquale, R.; Ferlito, S.; Pedulla, E. **Association of Viral Infections With Oral Cavity Lesions: Role of SARS-CoV-2 Infection.** Front. Med., v. 7, p. 571214, 2021.
35. Santos Júnior, J.C.C.; Souza, M.S.; Santos, V.S.; Carvalho, J.M.S.; Pires, A.L.P.V.; et. al. **Lesões orais em pacientes com Covid 19: uma síntese de evidências atuais.** Journal of Dentistry Public Health, [S.L.], v. 11, p. 224, 2020.
36. Silva, F.F.; Rodrigues, R.C.S.L; Catro, M.L. **Covid-19 e as manifestações na cavidade bucal: revisão de literatura.** JNT - Facit Business and Technology Journal, vol. 2, p. 274- 283, 2022.

38. Soares, C.D.; Carvalho, R.A.; Carvalho, K.A.; Carvalho, M.G.; Almeida, O.P. Carta ao Editor: *Lesões orais em um paciente com Covid-19*. Med Oral Patol Oral Cir Bucal, v. 25, p. e563-e564, 2020.
39. Umakanthan, S.; Sahu, P.; Ranade, A.V.; Bukelo, M.M.; Rao, J.S.; et al. *Origin, transmission, diagnosis and management of corona virusdisease 2019 (COVID-19)*. Postgrad. Med. J., Inglaterra, v. 96, p. 753-758, 2020.
40. Vasconcelos Júnior, F.C.F.; Mouta, A.A.N.; Aragão, R.V.; Barbosa, G.S.L.; Lopes, P.F., et al. *Espectro clínico da infecção por COVID-19 nos organismos humanos: revisão bibliográfica* REAS/EJCH, v. 46, p. e3763, 2020.
41. Vieira, A.R. *Oral manifestations in coronavirus disease 2019 (COVID-19)*. Oral Dis., v.3, p.770, 2021.
42. Wu, Y.H.; Wu Y.C.; Lang, M.J.; Lee, Y.P.; Jin, Y.T.; et al. *Review of oral ulcerative lesions in Covid 19 patients: a comprehensive study of 51 cases*. J Dent Sci., v. 16, p. 1066-1073, 2021.
43. Zarch, E.R.; Hosseinzadeh, P. *Covid 19 from the perspective of dentists: A case report and brief review of more than 170 cases*. Dermatol Ther., v. 34, p. e14717, 2021.