

## Manifestations COVID-19 in the Oral Cavity: A Systematic Review

Adelina Torgomyan<sup>1</sup>, Marina Saroyan<sup>2</sup>, Sergo Hovhannisyan<sup>3</sup>, Mashinyan Karen<sup>4</sup>, Lazar Yessayan<sup>5</sup> and Gagik Hakobyan<sup>6\*</sup>

<sup>1</sup>Associate professor, Department of Physiology, Yerevan State Medical University after M. Heratsi, Armenia.

<sup>2</sup>Senior lecturer, Department of Physiology, Yerevan State Medical University after M. Heratsi, Armenia.

<sup>3</sup>Associate professor, Department of Prosthodontics, Yerevan State Medical University after M. Heratsi, Armenia.

<sup>4</sup>Associate professor, Department of Prosthodontics, Yerevan State Medical University after M. Heratsi, Armenia.

<sup>5</sup>Professor, Head of Dept. of Therapeutic Dentistry, Yerevan State Medical University after M. Heratsi, Armenia.

<sup>6</sup>Professor, Head of Dept. of Oral and Maxillofacial Surgery Yerevan State Medical University after M. Heratsi, Armenia.

### \*Correspondence:

Gagik Hakobyan Mailing address: 0028 Kievyan str. 10 ap. 65 Yerevan, Armenia, Tel: (+37410)271146.

Received: 18 May 2023; Accepted: 15 Jun 2023; Published: 20 Jun 2023

**Citation:** Adelina Torgomyan, Marina Saroyan, Sergo Hovhannisyan, et al. Manifestations COVID-19 in the Oral Cavity: A Systematic Review. *Microbiol Infect Dis.* 2023; 7(2): 1-4.

### ABSTRACT

With COVID-19, along with other organ systems, symptoms can also appear in the oral cavity. COVID-19 can cause a number of pathological conditions in the oral cavity of patients, candidiasis, xerostomia, recurrent herpetic lesions, ulcers, vesicles, desquamative gingivitis have been reported, the tongue, palate, lips, gums and buccal mucosa may be affected, Patients with COVID-19 may have difficulty swallowing, burning sensation, most patients have impaired taste and smell.

However it is still impossible to draw a clear parallel between the manifestations of dental diseases and the severity of the coronavirus infection, since too little statistical data and clinical observations are available therefore needed for further investigation. The goal of this review was to compile a list of COVID-19 symptoms in oral tissues and analyze the potential etiopathogenesis that may influence the development of these oral lesions. The key terms were used to search international databases for information. A total of 50 sources on relevant topics were chosen. These preliminary data explain the underlying mechanism oral lesions in COVID-19, and will help on future preventive strategies in clinical practice and in everyday life.

### Keywords

Coronavirus, Oral cavity, Lesions, Mucosa.

### Introduction

SARS-CoV-2, discovered in 2019, caused the coronavirus illness (COVID-19), and was the cause of the current COVID-19 epidemic that has affected a large part of the world's population [1,2]. Diagnosis of COVID-19 done using PCR, the material is

taken from the pharynx, secretions from the lower respiratory tract [3]. With COVID-19, the most common symptoms are raising temperature, runny nose, cough, fatigue, complicated shortness of breath, taste and smell disturbance, and pneumonia [4].

The oral cavity is one of the main entry routes for SARS-CoV-2, inflammatory enzymes and chemicals accumulate in the gingival sulcus and promote microbial colonization, resulting in mucosal

---

changes [5]. With the above, the purpose of this article is to review pathogenesis and oral manifestations COVID-19.

## Materials and Methods

For the review, 50 sources were selected using the PubMed and Scopus databases. The key terms: SARS-CoV-2 infection, oral manifestations of COVID-19, lesions of the oral mucosa in patients with COVID-19, pathogenesis of COVID-19 in the oral cavity, SARS-CoV-2 in saliva, taste impairment at COVID-19, were used to search for information in international databases.

Due to the presence of ACE2 receptors, the oral mucosa is highly susceptible to SARS-CoV-2 infection. After contact is established to initiate viral entry into the cell, transmembrane serine protease 2 is one of the enzymes required to cleave the binding protein S. The virus, penetrating inside the cell, using the mechanism of the host cell, releases the genetic material and begins to duplicate it [6]. One of the main effects of SARS-CoV-2 infection is formation of an immunological response.

The penetration of macrophages and neutrophils into the affected tissue is accompanied by a strong production of cytokines and a weak interferon response, resulting in a cytokine storm [7,8]. SARS-CoV-2 is thought to have many entry points into human cells [9]. The receptor–protease-mediated mode of entry, on the other hand, is significant because it boosts viral infectivity [10].

Transmembrane protease serine Serine 2 (TMPRSS2) is a key protease in SARS-CoV-2 infection and is a prospective COVID-19 camostat mesylate [11-19]. The spike protein (SP) is involved in binding to the cell membrane, a process that is triggered by certain enzymes such as furin and these proteases is a critical factor in viral infection [20,21]. Immunohistochemical and molecular biological studies in the oral cavity showed higher levels of ACE2 expression in the surface and epithelium and stratum corneum of the tongue than in the gingiva [22,23]. However, ACE2 expression varied between individuals, female hormones [24], salt [25] and smoking [26], among others, alter ACE2 expression. The infectious potential of the tongue may be limited by the surface cells that secrete it [27]. SARS-CoV infected cells remain in the oral cavity and aspiration of these cells may be associated with LRT23 infection [28]. Saliva, on the other hand, contains a large number of protease inhibitors, according to the database analysis. Infected individuals may experience moderate symptoms such as fever, tiredness, myalgia, and a dry cough [29].

In the early stages of COVID-19, symptoms such as altered taste perception, dysgeusia, and burning sensation in the mouth have been found [30], as the disease progressed, patients also developed ulcerative lesions or *Candida albicans* are mostly on the tongue, palate, lip, and cheek [31-33].

One of the symptoms of COVID-19 is altered taste perception, dysgeusia and a burning sensation in the mouth [30], some patients also developed ulcerative lesions, a fungal infection mainly on the tongue, palate, lips and cheeks [31-33].

Dysgeusia (various taste disorders) is one of the symptoms often found in patients with COVID-19. According to this 45 percent overall taste disorder prevalence, 38 percent dysgeusia, 35 percent hypogeusia, and 24 percent ageusia. In the genesis of loss of taste lies neurotropism, an important role is played by the crossing of the olfactory epithelium directly through the lamina cribrosa and reaching the central nervous system [24,25]. Furthermore, when compared to patients who did not have COVID-19 but had similar symptoms, there was a strong link between taste problems and COVID-19 positivity.

Oral mucosal lesions, unlike taste problems, were recorded in only a few case reports, leading to debate over whether this type of illness is caused directly by SARS-CoV-2 or is a later manifestation. Nonetheless, the manifestations included ulcers, blisters, macules, and plaques that varied in amount, color look, and location.

Ulcers were the most common lesions develop as a result of the immunosuppression inherent in COVID-19 disease. According to Kitakawa's observations, ulcerative lesions were most common in moderate to severe COVID-19, and the occurrence of ulcers was linked to herpes [36].

In the immunosuppression inherent in COVID-19, *C albicans* is part of the oral microbiome of a healthy person; may affect mucous membranes. This damage, according to Villarroel-Dorrego et al., is a side effect of COVID-19 and not a direct result of SARS-CoV-23 [37]. Geographic tongue has also been observed in patients with COVID-19, despite the fact that these conditions are very common in the general population [37]. According to Jimenez-Cauhe histological studies, oral lesions may be the result of thrombotic mucosal vessel injury and subsequent vasculitis [38].

COVID-19 patients have also been reported to exhibit enanthem-like lesions Petechiae, erythematous macules, and erythematous-vesicular patterns in the oral mucosa are among these, which are frequently linked with subsequent viral clinical symptoms. In the buccal mucosa of patients, viral infection manifested itself in a variety of ways [39,40].

It is unusual to see a divergent pattern of mucosal lesions caused by a single pathogen [41]. Cox et al. emphasized the importance of coinfection research in severe respiratory diseases [42]. Antibiotics are often given to admitted patients, but little information on bacterial sensitivity is provided [42]. In addition, the majority of patients experienced oral mucosal injury throughout their hospitalization, implying that coinfections, immune compromise, or adverse drug reactions to COVID-19 treatment were to blame. Many fatal COVID-19 cases were found to have bacterial and fungal coinfections, according to studies [43].

These data suggested that the mouth cavity should be considered a high-risk area for COVID-19 infection [44-50]. However, it is still impossible to draw a clear parallel between the manifestations of dental diseases and the severity of the coronavirus infection, since

too little statistical data and clinical observations are available. These preliminary data explain the underlying mechanism oral lesions in COVID-19, and will help on future preventive strategies in clinical practice and in everyday life.

## References

1. Liu X, Liu C, Liu G, et al. COVID-19: progress in diagnostics, therapy and vaccination. *Theranostics*. 2020; 10: 7821-7835.
2. Chung JY, Thone MN, Kwon YJ. COVID-19 vaccines: the status and perspectives in delivery points of view. *Adv Drug Deliv Rev*. 2021; 170: 1-25.
3. Pereira LJ, Pereira CV, Murata RM, et al. Biological and social aspects of Coronavirus Disease 2019 (COVID-19) related to oral health. *Braz Oral Res*. 2020; 34: e041.
4. Wang Y, Li X, Ren L, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020; 395: 497-506.
5. Xiang Z, Koo H, Chen Q, et al. Potential implications of SARS-CoV-2 oral infection in the host microbiota. *J Oral Microbiol*. 2020; 13: 1853451.
6. Hu B, Guo H, Zhou P, et al. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol*. 2021; 19: 141-154.
7. Hu B, Huang S, Yin L. The cytokine storm and COVID-19. *J Med Virol*. 2021; 93: 250-256.
8. Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA*. 2020; 324: 782-793.
9. Mahyuddin AP, Kanneganti A, Wong J, et al. Mechanisms and evidence of vertical transmission of infections in pregnancy including SARS-CoV-2. *Prenat Diagn*. 2020; 40: 1655-1670.
10. Matsuyama S, Ujike M, Morikawa S, et al. Protease-mediated enhancement of severe acute respiratory syndrome coronavirus infection. *Proc Natl Acad Sci*. 2005; 102: 12543-12547.
11. Song H, Seddighzadeh B, Cooperberg MR, et al. Expression of ACE2, the SARS-CoV-2 Receptor and TMPRSS2 in Prostate Epithelial Cells. *Eur Urol*. 2020; 78: 296-298.
12. Kawase M, Shirato K, Van Der Hoek L, et al. Simultaneous Treatment of Human Bronchial Epithelial Cells with Serine and Cysteine Protease Inhibitors Prevents Severe Acute Respiratory Syndrome Coronavirus Entry. *J Virol*. 2012; 86: 6537-6545.
13. Bourgonje AR, Abdulle AE, Timens W, et al. Angiotensin-converting enzyme 2 (ACE2), SARS-CoV-2 and the pathophysiology of coronavirus disease 2019 (COVID-19). *J Pathol*. 2020; 251: 228-248.
14. Darbani B. The Expression and Polymorphism of Entry Machinery for COVID-19 in Human: Juxtaposing Population Groups, Gender, and Different Tissues. *Int J Environ Res Public Heal*. 2020; 17: 3433.
15. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020; 395: 565-574.
16. Wang WK, Chen SY, I-Jung Liu IJ, et al. Detection of SARS-associated coronavirus in throat wash and saliva in early diagnosis. *Emerg Infect Dis*. 2004; 10: 1213-1219.
17. Boöttcher E, Matrosovich T, Beyerle M, et al. Proteolytic Activation of Influenza Viruses by Serine Proteases TMPRSS2 and HAT from Human Airway Epithelium. *J Virol*. 2006; 80: 9896-9898.
18. Tanabe LM, List K. The role of type II transmembrane serine protease-mediated signaling in cancer. *FEBS J*. 2017; 284: 1421-1436.
19. Collin J, Queen R, Zerti D, et al. Co-expression of SARS-CoV-2 entry genes in the superficial adult human conjunctival, limbal and corneal epithelium suggests an additional route of entry via the ocular surface. *Ocul Surf*. 2021; 19: 190-200.
20. Carreras-Presas CM, Sánchez JA, López-Sánchez AF, et al. Oral vesicubullous lesions associated with SARS-CoV-2 infection. *Oral Dis*. 2021; 3: 710-712.
21. Hasan A, Paray BA, Hussain A, et al. A review on the cleavage priming of the spike protein on coronavirus by angiotensin-converting enzyme-2 and furin. *J Biomol Struct Dyn*. 2021; 39: 3025-3033.
22. Coutard B, Valle C, de Lamballerie X, et al. The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in Cov of the same clade. *Antiviral Res*. 2020; 176: 104742.
23. Forner L, Larsen T, Kilian M, et al. Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation. *J Clin Periodontol*. 2006; 33: 401-407.
24. Hamming I, Timens W, Bulthuis M, et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol*. 2004; 203: 631-637.
25. Li Y, Zhou W, Yang L, et al. Physiological and pathological regulation of ACE2, the SARS-CoV-2 receptor. *Pharmacol Res*. 2020; 157: 104833.
26. Wysocki J, Garcia-Halpin L, Ye M, et al. Regulation of urinary ACE2 in diabetic mice. *Am J Physiol Physiol*. 2013; 305: F600-F611.
27. Oakes JM, Fuchs RM, Gardner JD, et al. Nicotine and the renin-angiotensin system. *Am. J. Physiol. Integr Comp Physiol*. 2018; 315: R895-R906.
28. Tu YP, Jennings R, Hart B, et al. Swabs Collected by Patients or Health Care Workers for SARS-CoV-2 Testing. *New Engl J Med*. 2020; 383: 494-496.
29. <https://reviewersmanual.joannabriggs.org/>
30. Cuevas-Gonzalez MV, Espinosa-Cristóbal LF, Donohue-Cornejo A, et al. COVID-19 and its manifestations in the oral cavity: A systematic review. *Medicine*. 2021; 100: e28327.
31. Brandão TB, Gueiros LA, Melo TS, 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*. 2021; 131: e45-e51.
32. Carreras-Presas MC, Amaro Sánchez J, López-Sánchez AF, et al. Oral vesicubullous lesions associated with SARS-CoV-2 infection. *Oral Dis*. 2021; 27: 710-712.
33. Rodríguez DM, Jimenez Romera A, Villarroel M. Oral manifestations associated with COVID-19. *Oral Dis*. 2020.

34. Mahmoud MM, Abuhashish HM, Khairy DA, et al. Pathogenesis of dysgeusia in COVID-19 patients: a scoping review. *Eur Rev Med Pharmacol Sci.* 2021; 25: 1114-1134.
35. Sakaguchi W, Kubota N, Shimizu T, et al. Existence of SARS-CoV-2 entry molecules in the oral cavity. *Int J Mol Sci.* 2020; 21: 6000.
36. Kitakawa D, Oliveira FE, Neves De Castro P, et al. Short report - Herpes simplex lesion in the lip semimucosa in a COVID-19 patient. *Eur Rev Med Pharmacol Sci.* 2020; 24: 9151-9153.
37. Villarroel-Dorrego M, Chac'on L, Rosas R, et al. Oral Findings in Patients with COVID-19. *Actas Dermosifiliogr.* 2021; S1578-S2190.
38. Jimenez-Cauhe J, Ortega-Quijano D, de Perosanz-Lobo D, et al. Enanthem in Patients With COVID-19 and Skin Rash. *JAMA Dermatol.* 2020; 156: 1134-1136.
39. Kahraman CF, Çaşkurlu H. Mucosal involvement in a COVID-19-positive patient: A case report. *Dermatol Ther.* 2020; 33: e13797.
40. Hocková B, Riad A, Valky J, et al. Oral Complications of ICU Patients with COVID-19: Case-Series and Review of Two Hundred Ten Cases. *J Clin Med.* 2021; 10: 581.
41. Galvan Casas C, Catala A, Carretero Hernandez G, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. *Br J Dermatol.* 2020; 183: 71-77.
42. Cox MJ, Loman N, Bogaert D, et al. Co-infections: potentially lethal and unexplored in COVID-19. *Lancet Microbe.* 2020; 1: e11.
43. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet.* 2020; 395: 507-513.
44. Amorim Dos Santos J, Normando AGC, Carvalho da Silva RL, et al. Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations? *Int J Infect Dis.* 2020; 97: 326-328.
45. Farid H, Khan M, Jamal S, et al. Oral manifestations of COVID-19-A literature review. *Rev Med Virol.* 2022; 32: e2248.
46. Kusiak A, Cichońska D, Tubaja M, et al. COVID-19 manifestation in the oral cavity - a narrative literature review. *Acta Otorhinolaryngol Ital.* 2021; 41: 395-400.
47. Biadsee A, Biadsee A, Kassem F, et al. Olfactory and oral manifestations of COVID-19: sex-related symptoms - a potential pathway to early diagnosis. *Otolaryngol Head Neck Surg.* 2020; 163: 722-728.
48. Marouf N, Cai W, Said KN, et al. Association between periodontitis and severity of COVID-19 infection: a case-control study. *J Clin Periodontol.* 2021; 48: 483-491.
49. Maheswaran T, Abikshyeet P, Sitra G, et al. Gustatory dysfunction. *J Pharm Bioallied Sci.* 2014; 6: S30-S33.
50. Vieira LA, Salzano G, Fois AG, et al. Potential pathogenesis of ageusia and anosmia in COVID-19 patients. *Int Forum Allergy Rhinol.* 2020; 10: 1103-1104.