

# Oral Lesions in Patients with SARS-CoV-2 Infection - Pilot Study

M. Ramishvili<sup>1</sup>, G. Gobadze<sup>1</sup>, A. Machavariani<sup>1</sup>, G. Menabde<sup>1</sup>, M. Zurmukhtashvili<sup>2</sup>

## ABSTRACT

### Background

The rapid spread of the new coronavirus since December 2019 has posed a new challenge to the world. Studies demonstrated that cells that are highly susceptible to ACE2 expression will be target cells that are easily and severely damaged by SARS-CoV-2 infection. High expression of ACE2 receptors is usually observed in the epithelial cells of the oral mucosa and especially in the epithelium of the tongue, which should lead to the manifestation of symptoms in the oral cavity.

### Aim

The aim of our pilot study was to preliminary evaluate the statistical data about incidence of oral manifestations in post-covid period.

### Methods

20 patients (10 women and 10 men) who had recovered from COVID-19, aged 21 to 63 years were examined and screened for specific oral manifestations of COVID-19. Only symptomatic patients with different degrees of severity of COVID-19 were included in the pilot study. Examination methods included collection of patient complaints and anamnesis information from patient and clinical examination. Patients included in the study were asked to fill a special questionnaire developed by our group. Dental examination of patients was carried out according to the generally accepted scheme

### Results

The observed patients complained of various rashes, defects, the appearance of plaques, and cracks in the oral cavity. Loss of taste was observed in 17 patients, halitosis in 12 patients, dryness of mouth in 6 patients, mouth ulcers, aphtae and petechiae in 4 patients.

### Conclusions

The results obtained from oral cavity examination patients who have undergone COVID-19 demonstrate a variety of dental manifestations. However, it is still uncertain whether these manifestations could be a typical clinical pattern resulting from the direct SARS-CoV-2 infection or a systemic consequence, given the possibility of coinfections, impaired immune system, and adverse reactions of medical treatment. To clear this question more extensive research is needed.

**Keywords:** COVID-19, oral manifestation, dental manifestations, oral screening

## Introduction

The rapid spread of the new coronavirus since December 2019 has posed a new challenge to the world. The pandemic has had a severe impact on the health sector and economy in more than 200 countries. By the end of June 2021, more than 4 million people had been killed by the diseases caused by this new virus (1).

One of the three main criteria for diagnosing a new coronavirus is the detection of viral nucleic acids in a nasopharyngeal smear.

In addition, there are data on the detection of these proteins in other body fluids, including saliva (2). In addition, according to the results of various studies, viruses such as SARS and MERS have been found in saliva (3). However, solid evidence for the identification of SARS-CoV-2 virus in saliva is not yet available and requires further large-scale studies.

Analysis of angiotensin-converting enzyme enzyme II (ACE2) single-cell RNA sequence data and serological analysis of patient samples showed that ACE2 may be a SARS-CoV-2 cell receptor, hence cells that are highly susceptible to ACE2 expression (4). There will be target cells that are easily and severely damaged by SARS-CoV-2 infection. High expression of ACE2 receptors is usually observed in the epithelial cells of the oral mucosa and especially in the epithelium of the tongue, which should lead to the manifestation of symptoms in the oral cavity

From the <sup>1</sup>Faculty of Medicine, Iv.Javakishvili Tbilisi state University;  
<sup>2</sup>European University  
 Received September 09, 2022; accepted September 21, 2022.  
 Address requests to: Zurmukhtashvili Marika  
 Copyright © 2022 Translational and Clinical Medicine-Georgian Medical Journal

(5, 6). Several studies have also confirmed the expression of ACE2 receptors by salivary epithelial cells, which should be the basis for salivary gland damage and changes in salivary flow and salivary composition (7-9).

Saliva is one of the most important biological fluids. It often reflects changes in the blood and important molecular markers of various pathologies are found. It can therefore be hypothesized that an infectious agent such as SARS-CoV-2 can cause a number of changes in the composition of saliva and various markers in it (10,11). However, the latest scientific evidence to support or refuse this hypothesis is scarce.

Since in the oral cavity there are several tissues with ACE2 expression, the oral cavity can be the target organ for SARS-CoV-2 and oral lesions can be observed in patients with COVID-19. Therefore, the aim of pilot study was to evaluate most prevalent oral manifestations during COVID-19 and in post COVID period.

**METHODS**

On the basis of University Clinic “Dentex-95”, the Department of Oral and Maxillo-facial Surgery of Iv. Javakhishvili Tbilisi State University within the framework of the advisory council on periodontal and oral mucosa diseases, 20 patients (10 women and 10 men) who had recovered from COVID-19, aged 21 to 63 years have been examined and screened for specific oral lesions. Only symptomatic patients without hospitalization were included in the pilot study. According to severity of disease, duration of recovery period and duration of isolation period patients have been examined at different time points. Mild symptomatic patients without hospitalization have been examined on 16th -21st day after they've been tested positive for COVID-19. Unfortunately, at the current stage of our pilot study we excluded patients during the height of the disease and hospitalized patients due to the high risk of infection, since the virus is transmitted by airborne droplets. There is also a lack of statistical observations regarding the fact whether dental disease is the primary symptom in coronavirus infection or should be considered as a secondary manifestation against the background of infection or medication.

Before inclusion in pilot study each patient has signed informed consent about participation in study. Patient informed consent form, study design and patient questionnaire used in study were approved by the local ethic committee of the University Clinic Dentex-95. Study was conducted in full compliance with the Declaration of Helsinki of the World Medical Association and the national legislation of Georgia on the protection of patient rights and the conduction of medical research.

Examination methods included collection of patient complaints and anamnesis information from patient and clinical examination. Patients included in study were asked to fill a special questionnaire developed by our group (Fig.1).

**Figure 1. COVID-19 Oral symptoms questionnaire**

1. \_\_\_\_\_  
(Name, Surname)

2. COVID 19 confirmation date \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_

3. Hospitalization                      yes /  no   

4. Disease

asymptomatic  
 symptomatic

<p><b>General</b></p> <p><input type="checkbox"/> Temperature</p> <p><input type="checkbox"/> Swollen lymph nodes</p> <p><input type="checkbox"/> Loss of smell</p> <p><input type="checkbox"/> cough</p> <p><input type="checkbox"/> Diarhea</p> <p><input type="checkbox"/> Difficulties in breathing</p> <p><input type="checkbox"/> Muscle pain</p> <p><input type="checkbox"/> Back pain</p> <p><input type="checkbox"/> Head ache</p> <p><input type="checkbox"/> sore throat</p> <p><input type="checkbox"/> pneumonia</p> <p>  <u>  </u></p> <p>  <u>  </u></p>	<p><b>oral cavity</b></p> <p><input type="checkbox"/> Dry mouth</p> <p><input type="checkbox"/> burning sensation</p> <p><input type="checkbox"/> ulcer</p> <p><input type="checkbox"/> rash</p> <p><input type="checkbox"/> crack</p> <p><input type="checkbox"/> bleeding gums</p> <p><input type="checkbox"/> loss of taste</p> <p>other: _____</p> <p>_____</p>
---	---

5. Medicaments

\_\_\_\_\_

\_\_\_\_\_

6. Had you any complaints in oral cavity before Covid?

Yes    *Oral mucosa*                      *Gums*                      *tongue*

no

7. Had you complaints in oral cavity during Covid?

Yes    *Oral mucosa*                      *Gums*                      *tongue*

no

8. Had you complaints in oral cavity after Covid?

Yes    *Oral mucosa*                      *Gums*                      *tongue*

no

9. Have you recieved any treatment for oral symtoms?

yes    *medications*                      *mouth wash*                      *ointment*

no

Dental examination of patients was carried out according to the generally accepted scheme, including examination of the oral mucosa (color, moisture, presence and localization of lesions) and assessment of the condition of the teeth (lack of oral hygiene, presence of dental plaque, presence and quality of orthopedic structures).

To identify concomitant pathology, patients were recommended to consult a therapist, endocrinologist, gastroenterologist, immunologist. Based on the results of the examination, the patients were prescribed complex pathogenetic and etiotropic treatment, taking into account the principles of an individual approach. The patients were advised to sanitize the oral cavity with professional hygiene.

Study results were statistically assessed by non-parametric statistics (Chi2-test) for normality of data distribution. Null hypothesis was rejected at  $p < 0.05$ . For statistical analysis software SPSS Statistics 22.0 (IBM® USA) was used.

## RESULTS AND DISCUSSION

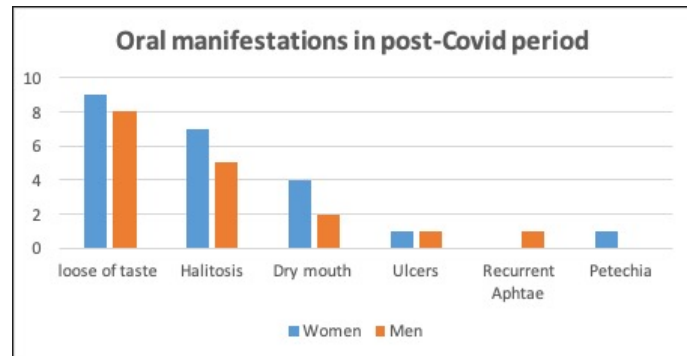
The Patient's questionnaire revealed presence of concomitant diseases in two cases: one patient with diabetes mellitus and one patient with cardio-vascular diseases. Seven patients took different medications mostly to easy COVID-19 mild symptoms: Ibuprofen 400mg P.O. every 12 hours (3 patients), Paracetamol 500mg P.O. every 8 hours (2 patients). One patient took Captopril 25mg P.O. every 24 hours for treatment of concomitant cardiovascular disease and one patient Metformin 1000mg P.O every 12 hours.

The observed patients complained of various rashes, defects, the appearance of plaques, and cracks in the oral cavity. At the same time, a clear boundary was not noted regarding the time of occurrence of certain pathological elements in the oral cavity, whether they formed during the height of the COVID-19 disease or appeared after treatment.

It is known that coronavirus infection leads to temporary disturbances in taste and olfactory sensitivity (11). In our observations disturbances in taste and olfactory sensitivity were present in 85% of cases (Fig.2). It should be noted that violations of smell and taste are absolute and relative. All patients noted the recovery of taste at various times after recovery, while 12% of patients reported a decrease in their sense of smell after recovery.

Second most common oral manifestation observed in our study was halitosis. Prevalence of this symptom was 60%. Respiratory infections can be the probable cause of halitosis. Pneumonia (gram-negative infections), which is one of the leading complications of COVID-19, produces an unpleasant odor. At the same time, men were less likely to report halitosis in relation to females (Fig.2).

**Figure 2 Oral manifestations in post-Covid period**



Two patients noted the appearance of ulcers on the oral mucosa. In one patient oral ulcers appeared on the soft palate (Fig. 3) and in the second case – on the attached gingiva in the maxillary premolar region (Fig.4). At the same time, the patients complained of pain when eating, talking, chewing and swallowing. One of the most common oral diseases in patients who have had coronavirus infection is chronic recurrent aphthous stomatitis (HRAS) (12-14). Diagnosis of this pathology does not cause difficulties. It can be assumed that the etiological factor of the onset of the development of the disease is a violation of cellular and humoral immunity, both local and general (15). The leading factor in etiopathogenesis is modulation of the cross-immune response, as a result of which aphthae are formed in the oral cavity. One patient out of 2 presented with oral ulcers developed recurrent ulcers after 5 months from first manifestation.

**Figure 3**



**Figure 4**



In one patient petechial changes occurred. Localization of enanthem was noted only on the hard palate (Fig. 5). The patients' erythematous rash varied in appearance. In the latter case, millimeter petechiae without erythema on the background of non-inflamed mucous membrane were noted on the hard palate.

**Figure 5**



Also, patients noted dryness in the mouth (30%) (Fig.6). Xerostomia can be caused by taking medications or under the influence of systemic diseases. More than 500 medicines can cause xerostomia. The presence of dryness in the oral cavity affects the development of diseases caused by periodontal pathogenic factors, and infectious lesions of the oral cavity by the type of candidiasis. In such patients, their lips are cracked. Also, patients complain about the adhesion of the lips to the teeth, sometimes there are epithelial particles adhering to the vestibular surfaces of the

anterior group of teeth.

**Figure 6**



It should be noted that patients had periodontal disease in 95% of cases. Depending on the patient's age, the severity of the coronavirus infection, the different forms of gingivitis and periodontitis were observed. Oral hygiene was unsatisfactory, with copious amounts of soft plaque, supra- and subgingival calculus. Development / exacerbation of periodontal diseases can be caused by an imbalance of microorganisms in the oral cavity.

Statistical analysis of results demonstrated significance of observed oral lesions only for halitosis and dryness in the mouth (Fig.7). Statistical analysis did not show association between comorbidities and oral lesions as well. This fact can be caused by the low number of evaluated patients. Small sample size can be considered a limitation of our study.

Figure 7 Results of statistical analysis

Results of statistical analysis

Test Variable	Observed		%	Chi2	p
	Yes/no	number			
<b>Disturbances in taste and olfactory sensitivity</b>					
	No	3	15.0%	9.80	.002
	Yes	17	85.0%		
<b>Halitosis</b>					
	No	8	40.0%	.80	.371 (NS)
	Yes	12	60.0%		
<b>Ulcers</b>					
	No	18	90.0%	12.80	.000
	Yes	2	10.0%		
<b>Chronic recurrent <u>aphthous stomatitis</u></b>					
	No	19	95.0%	16.20	.000
	Yes	1	5.0%		
<b><u>Petechia</u></b>					
	No	19	95.0%	16.20	.000
	Yes	1	5.0%		
<b>Dryness in the mouth</b>					
	No	14	70.0%	3.20	.074 (NS)
	Yes	6	30.0%		
<b>Comorbidities</b>					
	No	18	90.0%	12.80	.000
	Yes	2	10.0%		
<b>Medications</b>					
	No	13	65.0%	1.80	.180 (NS)
	Yes	7	35.0%		

## CONCLUSION

The results obtained from oral cavity examination of patients who have undergone COVID-19 demonstrate a variety of oral lesions. Because of the limitation of our study – small sample size - currently, no evidence can be demonstrated that the root cause of complications in the oral cavity during and after coronavirus infection is the virus itself or the drugs that patients receive during pharmacotherapy. Therefore, it is also still uncertain whether these lesions could be a typical clinical pattern resulting from the direct SARS-CoV-2 infection or a consequence of such systemic conditions as coinfections, impaired immune system and adverse reactions of medical treatment. To clear this question more extensive research is needed.

However, oral lesions observed in the patients with COVID-19 can substantiate the advisability of including a dental examination in this category of patients after their clinical recovery. The task of a dentist is to timely diagnose different conditions in patients who have undergone coronavirus infection and select the most adapted algorithm for their treatment. The issue of carrying out and prescribing therapeutic and prophylactic measures in order to prevent the development of pathology and its complications also remains open at the moment.

## References

1. WHO Weekly epidemiological update on COVID-19 - 29 June 2021. Available from: <https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---29-june-2021>
2. To KK, Tsang OT, Yip CC, Chan KH, Wu TC, Chan JM, Leung WS, Chik TS, Choi CY, Kandamby DH, Lung DC, Tam AR, Poon RW, Fung AY, Hung IF, Cheng VC, Chan JF, Yuen KY. Consistent Detection of 2019 Novel Coronavirus in Saliva. *Clin Infect Dis.* 2020 Jul 28;71(15):841-843. doi: 10.1093/cid/ciaa149.
3. Williams E, Bond K, Zhang B, Putland M, Williamson DA. Saliva as a Noninvasive Specimen for Detection of SARS-CoV-2. *J Clin Microbiol.* 2020 Jul 23;58(8):e00776-20. doi: 10.1128/JCM.00776-20
4. Bourgonje AR, Abdulle AE, Timens W, Hillebrands JL, Navis GJ, Gordijn SJ, Bolling MC, Dijkstra G, Voors AA, Osterhaus AD, van der Voort PH, Mulder DJ, van Goor H. Angiotensin-converting enzyme 2 (ACE2), SARS-CoV-2 and the pathophysiology of coronavirus disease 2019 (COVID-19). *J Pathol.* 2020 Jul;251(3):228-248. doi: 10.1002/path.5471. Epub 2020 Jun 10.
5. Brandão TB, Gueiros LA, Melo TS, Prado-Ribeiro AC, Nesrallah ACFA, Prado GVB, Santos-Silva AR, Migliorati CA. 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 Feb;131(2):e45-e51. doi: 10.1016/j.oooo.2020.07.014. Epub 2020 Aug 18.
6. Díaz Rodríguez M, Jimenez Romera A, Villarroel M. Oral manifestations associated with COVID-19. *Oral Dis.* 2020 Jul 22;10.1111/odi.13555. doi: 10.1111/odi.13555. Epub ahead of print. PMID: 32697005; PMCID: PMC7404436.
7. La Rosa GRM, Libra M, De Pasquale R, Ferlito S, Pedullà E. Association of Viral Infections With Oral Cavity Lesions: Role of SARS-CoV-2 Infection. *Front Med (Lausanne).* 2021 Jan 14;7:571214. doi: 10.3389/fmed.2020.571214.
8. Cruz Tapia RO, Peraza Labrador AJ, Guimaraes DM, Matos Valdez LH. Oral mucosal lesions in patients with SARS-CoV-2 infection. Report of four cases. Are they a true sign of COVID-19 disease? *Spec Care Dentist.* 2020 Nov;40(6):555-560. doi: 10.1111/scd.12520
9. Paradowska-Stolarz AM. Oral manifestations of COVID-19: Brief review. *Dent Med Probl.* 2021 Jan-Mar;58(1):123-126. doi: 10.17219/dmp/131989.
10. Iranmanesh B, Khalili M, Amiri R, Zartab H, Aflatoonian M. Oral manifestations of COVID-19 disease: A review article. *Dermatol Ther.* 2021 Jan;34(1):e14578. doi: 10.1111/dth.14578.
11. Iranmanesh B, Khalili M, Amiri R, Zartab H, Aflatoonian M. Oral manifestations of COVID-19 disease: A review article. *Dermatol Ther.* 2021 Jan;34(1):e14578. doi: 10.1111/dth.14578.

12. Katz J, Yue S. Increased odds ratio for COVID-19 in patients with recurrent aphthous stomatitis. *J Oral Pathol Med.* 2021 Jan;50(1):114-117. doi: 10.1111/jop.13114. Epub 2020 Oct 26.
  13. Riad A, Kassem I, Stanek J, Badrah M, Klugarova J, Klugar M. Aphthous stomatitis in COVID-19 patients: Case-series and literature review. *Dermatol Ther.* 2021 Jan;34(1):e14735. doi: 10.1111/dth.14735.
  14. Dominguez-Santas M, Diaz-Guimaraens B, Fernandez-Nieto D, Jimenez-Cauhe J, Ortega-Quijano D, Suarez-Valle A. Minor aphthae associated with SARS-CoV-2 infection. *Int J Dermatol.* 2020 Aug;59(8):1022-1023. doi: 10.1111/ijd.15004. Epub 2020 Jun 18. PMID: 32557570; PMCID: PMC7323002.
  15. 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.* 2021 Apr;27 Suppl 3:710-712. doi: 10.1111/odi.13382. Epub 2020 May 29. PMID: 32369674; PMCID: PMC7267423.
  16. Diaz-Guimaraens B, Dominguez-Santas M, Suarez-Valle A, Pinedo-Ortega C, Selda-Enriquez G, Bea-Ardebol S, Fernandez-Nieto D. Petechial Skin Rash Associated With Severe Acute Respiratory Syndrome Coronavirus 2 Infection. *JAMA Dermatol.* 2020 Jul 1;156(7):820-822. doi: 10.1001/jamadermatol.2020.1741.
- Jamshidi P, Hajikhani B, Mirsaedi M, Vahidnezhad H, Dadashi M, Nasiri MJ. Skin Manifestations in COVID-19 Patients: Are They Indicators for Disease Severity? A Systematic Review. *Front Med (Lausanne).* 2021 Feb 16;8:634208. doi: 10.3389/fmed.2021.634208