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The effect of severe acute respiratory syndrome coronavirus 2 on the health of oral tissue: A survey-based study

Duygu Goller Bulut PhD[1], *Nursat Turker Dt.*[2], *Sema Serin Dt.*[2], *Gulbahar Ustaoglu PhD*[3]

Original Article

Abstract

BACKGROUND AND AIM: The aim of this survey study was to determine the possible effects of coronavirus disease 2019 (COVID-19) on oral tissues and to investigate the relationship between changes in oral tissues and COVID-19.

METHODS: In this study, 200 volunteers who had COVID-19 in their anamnesis were included. After the routine clinical examination in the Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Bolu Abant Izzet Baysal University, Bolu, Turkey, the volunteers were asked to fill out a 33-item questionnaire created on "Google Forms" to determine the changes occurred in the oral tissues during and after COVID-19. Data were analysed using descriptive statistics in SPSS software and the statistical significance level was determined using the chi-square test and McNemar's test.

RESULTS: The study population consisted of 75 men and 125 women. While suffering from COVID-19, 53.0, 21.0, 16.0, and 17.5% of the subjects reported that they had taste loss, halitosis, pain in the chewing muscles, and pain in the temporomandibular joint (TMJ), respectively. Pain and wound in the oropharynx were the variables that more affected the possibility of halitosis ($P < 0.001$, Odds ratio = 4.749). Xerostomia was observed in 38.0% of the patients during the disease. In 27.6% of the patients who had xerostomia during the disease, the complaint associated with this complication continued after recovery ($P < 0.001$).

CONCLUSION: Xerostomia and loss of taste were the most common symptoms in the oral area during COVID-19. Further studies including clinical studies are needed to determine the relationship between changes in oral tissues and COVID-19.

KEYWORDS: Coronavirus Disease 2019; Halitosis; Oral Manifestation; Severe Acute Respiratory Syndrome; Xerostomia

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The coronavirus disease 2019 (COVID-19), which started in Wuhan, China, quickly turned into a public health crisis and spread exponentially to many parts of the World.[1] This novel coronavirus belongs to the Coronaviridae family of single-stranded ribonucleic acid (RNA) viruses,[2] which is known to be zoonotic. These viruses include the severe acute respiratory syndrome coronavirus (SARS-CoV), first identified in 2002, and the Middle East respiratory syndrome coronavirus (MERS-CoV), first identified in 2012.[3] SARS-CoV-2 is a coronavirus that was first identified in 2019 and is known to infect humans.[4] The most commonly reported clinical symptoms of the COVID-19 disease are fever, dry cough, and myalgia.[5] In some patients, headache, nasal congestion, runny nose, sore throat, decreased sense of smell (hyposmia) and diarrhea have been reported.[5,6] However, this disease can cause acute respiratory distress syndrome, heart and kidney failure, and even

1- Associate Professor, Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Bolu Abant Izzet Baysal University, Bolu, Turkey
2- Research Assistant, Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Bolu Abant Izzet Baysal University, Bolu, Turkey
3- Associate Professor, Department of Periodontology, Faculty of Dentistry, Bolu Abant Izzet Baysal University, Bolu, Turkey
Address for correspondence: Duygu Goller Bulut PhD; Associate Professor, Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Bolu Abant Izzet Baysal University, Bolu, Turkey; Email: duygugoller@hotmail.com

death in older ages (> 70 years of age), in the presence of hypertension, diabetes mellitus (DM), cardiovascular diseases (CVDs), lung diseases, chronic kidney diseases, and immunosuppressive conditions.[7]

There are few scientific studies in the literature describing the oral symptoms that can be caused by SARS-CoV-2.[8] Although there are many studies on clinical symptoms in COVID-19 patients, most of them did not provide information on patients' oral symptoms.[9] Possible oral symptoms have been reported to be taste loss, abnormal taste sensation (dysgeusia), and dry mouth (xerostomia).[10] The cause of xerostomia in patients with COVID-19 is thought to be due to the neuroinvasive and neurotrophic potential of SARS-CoV-2.[8] Some oral symptoms of viral infection may play an important role in the early diagnosis of the disease.[5] Recent studies have shown that loss of taste and smell may be the first sign of the disease.[11] Angiotensin-converting enzyme 2 (ACE2) has been reported to be the early target of SARS-CoV-2 in rhesus macaques in the epithelial cells of the salivary gland in the patients affected by COVID-19.[12] The ACE2 receptor, a membranous protein found in the salivary glands and oral epithelium, is used as a binding mechanism for SARS-CoV-2.[13] In a cross-sectional survey of 108 patients with COVID-19 in China, 46% of the patients reported xerostomia.[12,14] Bodard et al.[15] and Martin Carreras-Presas et al.[16] reported that COVID-19 positive and suspected patients had ulcerative and vesiculobullous lesions in the oral region. Cruz Tapia et al. reported that COVID-19 disease can cause xerostomia through reduced saliva flow, thus, leading to more bad breath.[17]

In the light of these data in the literature, this survey study aimed to determine the possible effects of COVID-19 on oral tissues and to investigate the relationship between changes in oral tissues and COVID-19.

Methods

This study was performed on 200 volunteers who referred to the Department of Oral, Dental and Maxillofacial Radiology, Faculty of Dentistry, Bolu Abant Izzet Baysal University between September 2020 and March 2021 and reported that they had COVID-19 in their anamnesis. In this observational study, the volunteers were asked to fill out a 33-item questionnaire created on Google Forms and their answers were recorded. After a literature review, the survey items were formed considering the study hypothesis. The survey aimed to collect information about the patients' demographic characteristics such as gender, age, and general health, oral habits, and symptoms in the oral cavity. The questionnaire forms were filled out after the routine clinical and radiographic examinations of the patients were completed. Before starting the study, the applicability of the questionnaire was tested on 15 patients. Each question was evaluated separately in the study. An overall score was not obtained.

The questions were answered by the patients under the supervision of a dentist. The patients received help from the dentist in order to give the correct answer to the questions they could not understand. For example, for the question of whether they had xerostomia, it was asked whether one or more of the symptoms such as feeling of dryness in the throat, increased thirst, feeling of stickiness in the mouth, difficulty in swallowing and speaking, etc., were observed, and if these symptoms were observed, it was stated that it would be appropriate to mark “Yes” to the question of xerostomia. In addition, brief descriptions of lesions such as aphthous ulcers and herpes were included in the questionnaire. Despite the explanations, the patients received help from the dentist in the case of not understanding the questions.

Individuals under the age of 18 years were excluded from the study. Some of the answers were as binary variables (e.g., Yes/No responses) or general categorical variables (e.g., multiple-choice tests).

The data were analysed using descriptive statistics and were expressed as number, percentage, and frequency. The chi-square test was used to evaluate the statistical significance, and the McNemar's test was used to compare the responses given during and after recovery. The odds ratio was calculated to evaluate the effect of parameters on each other. Statistical analysis was performed using SPSS (version 23, IBM Corporation, Armonk, NY, USA) at the statistical significance level of $P < 0.050$.

Results

The demographic data of the patients are given in table 1.

Table 1. Demographic characteristics of the patients

Characteristics		Value
Gender	Men	75 (37.5)
(n = 200)	Women	125 (62.5)
Age (year)	20-30	89 (27-62)
(number of	31-40	65 (22-43)
male-female)*	41-50	27 (13-14)
	51-60	15 (11-4)
	61-70	4 (2-2)
Marital status	Married	114 (57.0)
	Single	80 (40.0)
	Other	6 (3.0)
Tooth brushing	Once a day	63 (31.5)
frequency	Twice a day	97 (48.5)
	Three times a day	16 (8.0)
	Not brushing regularly	24 (12.0)
How much	1-2 weeks before	59 (29.5)
before did	2-4 weeks before	40 (20.0)
she/he recover?	1-2 months before	59 (29.5)
	2-4 months before	25 (12.5)
	> 4 months	17 (8.5)
Presence of	Absent	175 (87.5)
symptom	Present	25 (12.5)
Hospitalization[x]	Yes	23 (11.5)
	No	177 (88.5)
If yes, duration	1-3 days	10 (43.5)
of hospitalization	3-7 days	5 (21.7)
(n = 23)	7-10 days	2 (8.7)
	>10 days	6 (26.1)

Values are presented as n (%), unless otherwise is indicated.
[8]Significant difference between genders based on the chi-square test.

75 (37.5%) patients were women and 125 (62.5%) were men; a total of 200 COVID-19 survivors were included. Most of the patients aged 20-30 years (44.5%) and 31-40 years (32.5%). The majority of the patients who had the disease between the ages of 51-60 years were men ($P = 0.019$). 29.5% of the patients had the disease and completed the isolation period 1-2 weeks before referring to the dental examination. In 29.5% of the subjects, this period was between 1 and 2 months. 61.7, 12.3, 16.9, 7.1, 5.2, and 5.2, of the patients were respectively using antiviral drugs, hydroxychloroquine, anticoagulant injection, antiaggregant, dexamethasone, and antibiotics, and 27.9% did not use any medication. The majority (87.5%) had the disease with symptoms and 10.5% of the patients were hospitalized. The most reported hospitalization period was 1-3 days (43.5%). The results of analysis of the answers given by gender showed that the percentage of the hospitalized patients was higher in men ($P = 0.030$). 88.5% of the patients continued to brush their teeth with the same frequency and method as they used to brush during the active period of the disease, and 24.5% used mouthwash during this period.

The changes observed in the oral region during the active period of the disease included taste loss (53.0%), halitosis (21.0%), oropharyngeal wound and pain (18.0%), pain in temporomandibular joint (TMJ) (17.5%), pain in the chewing muscles (16.0%), aphthous ulcer (14.5%), sensitivity and/or pain in teeth (12.0%), herpes labialis (8.5%), and burning in the tongue (7.5%), respectively. Analysis of the answers given by gender showed no significant difference in terms of oral findings ($P > 0.050$) (Table 2).

It was revealed that 17.5% of the patients had complaints of gum bleeding during the disease. In addition, 13.0, 3.5, 10.5% of the subjects had gingival bleeding at the same degree as the pre-disease period, more complaints of gingival bleeding compared to the previous period, and the same severity of gingival bleeding after recovery, respectively. Xerostomia was observed in 38.0% of the patients during the disease period.

Table 2. Oral manifestations observed during the disease

Symptoms	Men (n = 75) (% within Gender)	Women (n = 125) (% within Gender)	Total (n = 200) (% of Total)
Herpes labialis	6 (8.0)	11 (8.8)	17 (8.5)
Aphthous ulcer	8 (10.7)	21 (16.8)	29 (14.5)
Burning tongue	3 (4.0)	12 (9.6)	15 (7.5)
Loss of taste	34 (45.3)	72 (57.6)	106 (53.0)
Pain and wound in oropharynx	10 (13.3)	26 (20.8)	36 (18.0)
Halitosis	20 (26.7)	23 (18.4)	43 (21.5)
Tooth pain or sensitivity	6 (8.0)	18 (14.4)	24 (12.0)
Pain in the chewing muscles	8 (10.7)	24 (19.2)	32 (16.0)
Pain in TMJ	11 (14.7)	24 (19.2)	35 (17.5)

Based on the chi-square test, the variables did not differ in terms of gender (P > 0.050).
TMJ: Temporomandibular joint.

In the patients who had xerostomia during the disease period (76 patients), 27.6% continued to have it after recovery (P < 0.001). Although the complaints of pain in the gums of both male and female patients did not reduce after recovery (P = 0.263), the complaint of xerostomia significantly reduced (P < 0.001) (Table 3).

The patients who were hospitalized gave more "No" answers to the question "whether they continued to brush their teeth" (P = 0.004) (Figure 1). However, the responses to gingival bleeding, halitosis, xerostomia, and other oral symptoms were similar to those received home treatment (P > 0.050). The relationship between tooth brushing, dry mouth, wound complaints in the oropharyngeal area, and halitosis is shown in table 4. Considering the odds ratios, the risk of halitosis is 4.749 times higher in the case of a wound or pain in the oropharyngeal area compared to those without a wound or pain. Wound or pain in the oropharyngeal area is the variable that most affects the possibility of halitosis. Other variables are xerostomia and tooth brushing.

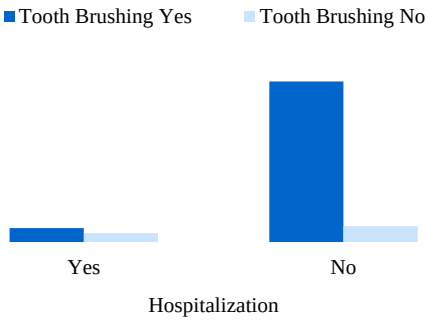

Figure 1. Diagram showing hospitalized patients responded "No" to the question of tooth brushing at a higher rate than those receiving home treatment (chi-square test; P = 0.004)

Table 3. Xerostomia and gingival manifestations during disease and after recovery

Symptoms	Answers	Men (n = 75) (% within Gender)	Women (n = 125) (% within Gender)	Total (n = 200) (% of Total)
Gum bleeding	Yes	9 (12.0)	26 (20.8)	35 (17.5)
	No	66 (88.0)	99 (79.2)	165 (82.5)
If yes, degree of bleeding	Same as before	6 (8.0)	20 (16.0)	26 (13.0)
	More than before	0 (0.0)	3 (2.4)	3 (1.5)
	Lower than before	3 (4.0)	3 (2.4)	6 (1.5)
Gum bleeding after recovery	Increased	0 (0.0)	2 (1.6)	2 (1.0)
	Decreased	5 (6.7)	7 (5.6)	12 (6.0)
	Same	9 (12.0)	12 (9.6)	21 (10.5)
Pain in gum*	Yes	6 (8.0)	10 (8.0)	16 (8.0)
	No	69 (92.0)	115 (92.0)	184 (92.0)
Pain in gum after recovery*	Yes	6 (8.0)	16 (12.8)	22 (11.0)
	No	69 (92.0)	109 (87.2)	178 (89.0
Xerostomia**	Yes	31 (41.3)	45 (36.0)	76 (38.0)
	No	44 (58.7)	80 (64.0)	124 (62.0)
Xerostomia after recovery**	Yes	10 (13.3)	14 (11.2)	24 (12.0)
	No	65 (86.7)	111 (88.8)	176 (88.0)

*Given the McNemar's test, there was no significant change in gingival pain complaints for both genders after recovery (P = 0.263).
**Given the McNemar's test, the complaints of xerostomia in both genders decreased significantly after recovery (P < 0.001).

Table 4. Data of the factors affecting xerostomia

Features		Halitosis [n (%)]		Odds Ratio (%95 CI)	P
		No	Yes		
Tooth brushing	No	12 (52.2)	11 (47.8)	4.154 (1.683-10.250)	0.003
	Yes	145 (81.9)	32 (18.1)		
Xerostomia	No	109 (87.9)	15 (12.1)	4.239 (2.077-8.649)	< 0.001
	Yes	48 (63.2)	28 (36.8)		
Pain and wound in oropharynx	No	138 (84.1)	26 (15.9)	4.749 (2.183-10.329)	< 0.001
	Yes	19 (52.8)	17 (47.2)		

CI: Confidence interval

Discussion

In the presented study, oral lesions observed in the patients with COVID-19 during the active period of the disease were evaluated and the changes observed in the perioral region during and after the disease were compared. There are various studies about COVID-19 in the literature, and the idea that this disease may cause interrelated pathological changes in the perioral region has been supported by many studies.[5,8,18] In the present study, taste loss and xerostomia were the most common complications in the disease period, and also, oral mucosal lesions such as aphthous ulcer, herpes labialis, burning feeling on the tongue, and oropharyngeal wound and pain were observed at various rates in patients during the disease.

In a study conducted by Liu et al.,[19] it was reported that ACE2 receptors in epithelial cells of salivary glands would be an initial target for the SARS coronavirus; and in the light of this information, Zhou et al.[20] reported that based on the phylogenetic similarity between SARS-CoV and SARS-CoV-2, taste disturbance may occur in patients with COVID-19 and the presence of xerostomia should be evaluated in these patients.

In their survey study conducted on 20 cases, Sinjari et al. reported xerostomia, loss of taste, and burning sensation respectively in 30, 25, and 15% of the patients during the disease.[8] Biadsee et al. in their study on 128 patients, reported that 52% of the patients had a change in their sense of taste and more than 50% had xerostomia, and xerostomia did not differ between genders.[5] In this study, although the rates of complications differ numerically due to the population size and racial reasons, the loss of taste sensation was found in 53.0% of the patients and xerostomia in 38.0% of them, and there was no difference in these findings between genders.

In a case report by Martin Carreras-Presas et al. on 3 patients in which oral findings related to COVID-19 were presented, a 56-year-old male patient with multiple orange-colored ulcers on the hard palate, a 58-year-old male patient with multiple-point yellowish ulcers on the hard palate, and a 65-year-old female patient with three blisters on the inner mucosa of the lip were reported.[16] In a case series presented by Brandao et al., an 81-year-old male patient with clustered ulcers (1-1.5 cm) on the lower lip vermilion border and painful ulcerative lesions in the anterior dorsum of the tongue, a 71-year-old female patient with hemorrhagic ulcers on the lower and upper lips and tongue, and an 83-year-old female patient with painful ulcers on the lateral tongue and focal erythema anterior to the hard palate were presented. Moreover, aphthous ulcers were observed in 5 cases with ages of 28-72 years.[18] Similarly, Cruz Tapia et al.[17] reported vesiculobullous lesions in 4 cases and Bodard et al.[15] reported an ulcerative lesion in the tongue dorsum in a 45-year-old female patient. In the present study, respectively 8.5, 14.5, 18.0% of the patients reported that they had herpes labialis, aphthous ulcers, and pain and wound in oropharynx during the disease.

It has been reported that SARS-CoV-2 can target the oral mucous membranes[21] and these lesions healed with the healing of the disease, and therefore, the lesions may be

caused by viruses.[18] On the contrary, studies have reported that these lesions were observed incidentally during the disease period. Furthermore, Abu-Hammad et al. reported that lesions in the oral region may be due to the stress triggered by the disease or by immunosuppression caused by COVID-19 and the drugs used in its treatment.[22] Ponce et al. suspected that the herpes simplex virus (HSV) lesions observed during the COVID-19 disease may have contributed to immunosuppression and potentially to the reactivation of HSV.[23] In the literature, a joint decision has not been concluded on the relationship between COVID-19 and lesions observed in the oral region, therefore, more comprehensive studies are needed on this subject.

One of the common symptoms of COVID-19 is myalgia, and studies on this subject have reported that myalgia continued for an average of 23 days after viral infectivity was stopped.[24] Lechien et al. reported that more than 50% of patients had myalgia.[25] Biadsee et al. reported that 11% of the patients experienced pain in the muscles during chewing. In this study, 16.0% of the patients reported pain in the chewing muscles, and 17.5% complained of pain in TMJ.[5] These results suggest that COVID-19 may cause a decrease in function by causing a pain in the maxillofacial area, as well as general body weakness and myalgia symptoms.

It has been reported in the literature that the COVID-19 acute infection may lead to various opportunistic fungal infections, xerostomia, ulcerations, and gingivitis depending on the drugs used, and these conditions may cause halitosis.[26] Riad et al. reported that the COVID-19 disease adversely affects health-related behaviors and may cause halitosis indirectly through impaired oral hygiene.[27] In this study, 21.5% of the patients had halitosis, and according to the odds rates, pain and wound in oropharynx were the variables that mostly affected the probability of halitosis. This suggests that the infection in the tonsils and the soft palate may lead to the accumulation of bacteria and fungi, causing halitosis.

The limitation of this study was using a small sample size group. In addition, the changes observed in the oral region could not be evaluated by the dentist because the patients could not be examined due to quarantine conditions during the period of COVID-19.

Conclusion

This study suggests that there may be a relationship between the COVID-19 disease and symptoms observed in the oral and perioral tissues. Based on the analysis of the data obtained, it is difficult to distinguish whether the symptoms reported by the patients are caused by the SARS-CoV-2 virus or by the immunosuppression state caused by the disease and treatment. Although the cause of xerostomia in patients can be explained by the effect of the SARS-CoV-2 virus on the salivary glands, the exact cause is yet unknown. The most common symptoms of loss of taste and xerostomia in patients indicate that these symptoms may be a warning sign for the COVID-19 disease. Further studies including clinical and histological data are needed to reveal the relationship between changes in oral tissues and COVID-19. Nevertheless, patients are suggested to be motivated about oral care during and after COVID-19.

Conflict of Interests

Authors have no conflict of interest.

Acknowledgments

The study protocol, including all changes and revisions, was carried out in Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Bolu Abant İzzet Baysal University, according to the principles outlined in the Declaration of Helsinki (DoH). Ethical approval was obtained from Clinical Research Local Ethics Committee of Bolu Abant İzzet Baysal University for the study (Ethical code: 2021/15).

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