

## Research Article

# Persistent Oral Symptoms After Recovery From COVID-19 Infection: A Cross-Sectional Study

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## ARTICLE

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## ABSTRACT

**Background:** To examine the prevalence and severity of persistent oral symptoms in recovered COVID-19 patients and to detect a relationship between oral hygiene, periodontal status, disease severity, and persistent oral symptoms in COVID-19 patients.

**Methods:** A self-administered electronic instrument was distributed online through social media outlets targeting COVID-19 patients in Saudi Arabia from September 1, 2021, to December 30, 2021—adults who had a COVID-19 infection at least two months before the study were included.

**Results:** 301 surveys were analysed. 54% of the participants had recovered from COVID-19 infection for more than six months, and 56.2% had moderate disease severity. 13% of the participants reported experiencing at least one oral symptom during the COVID-19 infection, and 38% said that the oral symptoms persisted after the recovery from the infection. The most common symptoms included: dry mouth (45%), taste and smell alteration or loss (42%), dental pain (29%), mouth ulcers (16%) and gingival bleeding (16%). 61% required pain medication or requested a prescription from the dentist. The presence of oral symptoms was significantly associated with severe COVID cases (OR=6.56) (P<0.001). Persistent oral symptoms were significantly related to the history of gingival inflammation (P=0.001) and gum pain (P=0.006) after adjusting for age, gender, smoking, BMI, and chronic disease.

**Conclusions:** Oral symptoms are common findings with the COVID-19 infection, with many patients having persistent symptoms after recovery. Dentists should be aware of the need for proper assessment and evaluation of patients post-COVID-19.

## 1. INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The most common clinical symptoms are fever, headache, sore throat, dyspnea, dry cough, abdominal pain, vomiting, and diarrhoea (Wang et al., 2020). Most patients will experience mild to moderate respiratory symptoms and recover without treatment. However, some will become severely ill and require medical attention. Older people and those with underlying medical conditions like diabetes, chronic respiratory disease, cardiovascular disease, or cancer are more likely to develop serious illnesses (Jutzeler et al., 2020). Studies have confirmed that the SARS-CoV-2 virus is mainly transmitted through respiratory droplets and contact with an infected person (Aldahlawi & Afifi, 2020).

In the early onset of the pandemic, the literature documented COVID-19 cases that reported oral manifestations associated with the disease. Those manifestations included ulcers in the palatal mucosa, localised erythema

in the palate and margins of the gingiva, oral pain, desquamative gingivitis, and blisters (Galván Casas et al.,

2020; Martín Carreras-Presas et al., 2021). Further research reported alteration or loss of taste and smell, difficulty swallowing, xerostomia, swelling, gingival bleeding and accumulation of dental plaque. In addition, pigmentations, halitosis, whitish areas, hemorrhagic crust, necrosis, petechiae, erythema, spontaneous bleeding, erosions, fissures, or depopulated tongues have been reported (Iranmanesh et al., 2021; Vieira, 2021). Oral lesions either preceded systemic symptoms or appeared simultaneously (Iranmanesh et al., 2021; Wu et al., 2021). The most common sites of involvement were the tongue, labial mucosa, and palate (Amorim Dos Santos et al., 2021). Oral lesions were symptomatic in 68% of the cases and were nearly equal in both genders (Iranmanesh et al., 2021). Patients with older ages and higher severity of COVID-19 disease had more widespread and severe oral lesions (Amorim Dos Santos et al., 2021). Inadequate oral hygiene, opportunistic infections, stress,

immunosuppression, and hyper-inflammatory response secondary to COVID-19 predispose factors to onset oral lesions in COVID-19 patients (Iranmanesh et al., 2021).

Many studies have documented that COVID-19 symptoms may persist after recovery from the acute infection (Davis et al., 2021; Garout et al., 2022; Logue et al., 2021) for a period of up to 6 months after the illness (Logue et al., 2021). The Centers for Disease Control (CDC) use the term “post-COVID” conditions to describe the wide range of health issues that are present four or more weeks after infection with SARS-CoV-2 (CDC, 2021). Studies also showed that post-COVID symptoms were observed in those with mild disease and those hospitalized and older patients with comorbidities (Havervall et al., 2021). A recent meta-analysis reported persistent symptoms associated with poor quality of life and worse mental health (Malik et al., 2022). A high proportion of the patients (47.5–87.4%) reported symptoms like fatigue, headache, myalgia, joint pain, cough, anxiety, sleep disturbance, and neurological/cognitive symptoms (Angelo Carfi et al., 2020; Davis et al., 2021; Garout et al., 2022). Although loss or altered smell and taste sensations and several dermatological conditions were reported (Davis et al., 2021), none of the published literature reported if oral symptoms persisted after recovering from COVID-19 infection.

In this study, we aimed to examine the prevalence and severity of persistent oral symptoms post COVID-19 and detect the relationship between oral hygiene, periodontal status, and disease severity and persistent oral symptoms.

## 2. MATERIALS AND METHODS

A cross-sectional survey was carried out in Saudi Arabia between September 1, 2021, and December 30, 2021, to explore the oral manifestations associated with COVID-19 infection and the continuity of oral symptoms post-COVID infection. Ethical approval was obtained from the Umm Al-Qura University Institutional Review Board, Approval Number (HAPO-02-K-012-2022-01-905). All participants provided their consent to participate in the study at the beginning of the survey.

### 2.1 Data collection and the questionnaire instrument

A self-administered electronic instrument was developed using Google Forms and distributed online through social media outlets targeting COVID-19 patients in Saudi Arabia. Adults over the age of 17 who had a COVID-19 infection at least two months before the study were included. Children and those who did not have a confirmed diagnosis of COVID-19 with PCR were excluded. The instrument was developed based on a literature review (Iranmanesh et al., 2021) and consists of nine sections. Initially, the instrument confirmed if the respondent had a COVID-19 infection and is willing to participate in the study. Also, instructions on filling the instrument and definition of long COVID-19 were included. The first section included demographic data like age, gender, weight, height, medical history, and smoking history. Three sections explored oral hygiene practices and oral health prior

to, during, and after the COVID-19 infection. A history of COVID-19 infection, including PCR tests, disease severity, and duration, was obtained. Disease severity was classified into no symptoms, mild (minor symptoms that did not require medication), moderate (symptoms requiring medication but not hospitalization), severe (hospitalization required), and very severe (ICU admission required). Participants were asked about oral symptoms during COVID-19 and provided with a list to choose from in addition to a free text option. Additionally, the persistence of symptoms after recovering from the COVID-19 infection was explored. Finally, participants were asked about the severity of oral symptoms, what measures they have used to control them, whether they have improved over time, and if they have sought a dental consultation. The instrument was piloted on 20 participants not included in the study sample, and participants' feedback was used to modify the questionnaire.

**2.2 Sampling:** Epitools calculator was used to calculate the sample size required for the study. The sample size is calculated based on 95% CI, 80% power, and a 0.05 margin of error. The required sample size is 300 participants.

**2.3 Statistical analysis:** The data were analysed using SPSS v21. Descriptive statistics, the chi-square test and binary logistic regression, were used to explore associations between periodontal status, oral hygiene measures, and COVID infection severity. Associations were also explored between the presence of oral symptoms, the persistence of these symptoms, and COVID infection severity. The significance level is set at  $P=0.05$ .

## 3. RESULTS

### 3.1 Patient's demographics

A total of 301 surveys were completed and included in the analysis. **Table 1** presents the demographics of the participants. Most of the participants, 138 (45.9%), were in the age group of 31-50 years old. Females were the majority at 231(76.7 %), 104 (34.6%) had a BMI >30, and only 61 (20.1%) were current smokers.

**Table 1: Demographic data of the participants**

	N (%) 301
<b>Age</b>	
<18	27 (9)
18-30	97( 32)
31-50	138(46)
>50	39(13)
<b>Gender</b>	
Male	70 (23.3)
Female	231(77)
<b>BMI</b>	
≥30	104 (34.6)

25-29.9	88 (29.2)
<25	106 (35.2)
<b>Smoking</b>	
Current smoker	61 (20.1)
Former smoker	29 (10)
Never smoked	169 (56.2)

One hundred and sixty-two (54%) participants had recovered from COVID-19 infection more than six months ago; 81 (27%), between 3 and 6 months; and 58 (19%), recovered less than three months ago. In 168 (56%) of the participants, the infection lasted 10-14 days, with 60 (20%) having the symptoms for more than 14 days and 73 (24%) having it for a few days only. The majority, 169 (56.2%), had moderate disease severity (as defined by symptoms that needed medication but not hospitalization). In comparison, 19 (6.3%) had severe to very severe disease that required hospitalization and ICU admission (Table 2). Severe COVID-19 was significantly associated with the older age groups (31-50) (OR=7.39) (P=0.02) and older than 50 years (OR=5.97) (P=0.05).

**Table 2: COVID-19 disease history of the participants**

	N (%) 301
<b>How long ago you had the infection?</b>	
<3 month	58(19.3)
3- 6 month	81 (27)
> 6 months	162(54)
<b>How long was the duration of the infection</b>	
Few days only	73 (24.3)
10-14 days	168(56)
>14 days	60 (20)
<b>Severity of the infection</b>	
Very mild almost no symptoms	36 (12)
Mild: only home care	77 (26)
Moderate: home care and medication	169(56.2)
Severe: hospitalization	15(5)
Very severe: ICU admission	4(1.3)

In terms of chronic systemic diseases, 207 (69%) reported no chronic medical conditions. Out of those who reported chronic medical conditions, hypertension, obesity, asthma, and diabetes were the top reported systemic diseases. Only 3% reported immunological diseases like rheumatoid arthritis (Figure 1). Out of the 94 subjects who reported chronic medical conditions, eleven

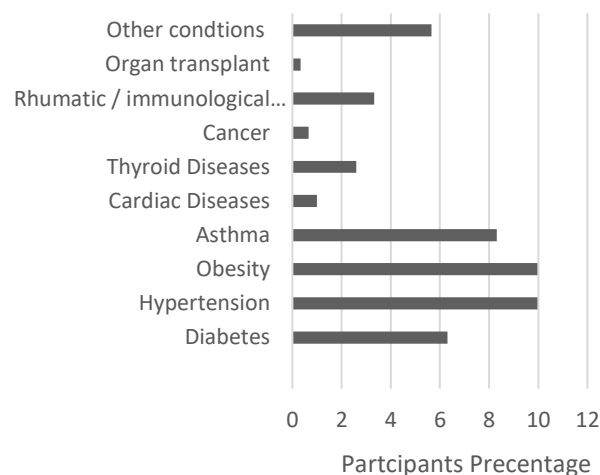
participants (12%) reported having two systemic diseases, and 15 (16%) reported more than 2 systemic diseases.

On dental habits, 194 (65%) admitted irregular visits to the dentist. Dental pain and caries were reported by 93 (31%) and 104 (35 %) of participants, while signs of gingivitis such as gum pain, gum bleeding, and gum inflammation, were reported by 59 (20%), 77 (26%), and 45(15%) respectively. Recurrent mouth ulcers were reported by 49 (16.3%) of the participants.

### 3.2 COVID-19 and oral symptoms

Eighty-two (27%) of the participants reported experiencing at least one oral symptom during the COVID-19 infection, while 263 (87 %) did not have any oral symptoms. Of those who reported oral symptoms, 67 (81.7%) were females; however, a statistically significant relationship was not found between gender and oral symptoms ( $p>0.05$ )

**Figure 1: Percentage of participants who reported chronic systemic disease (N=301).**

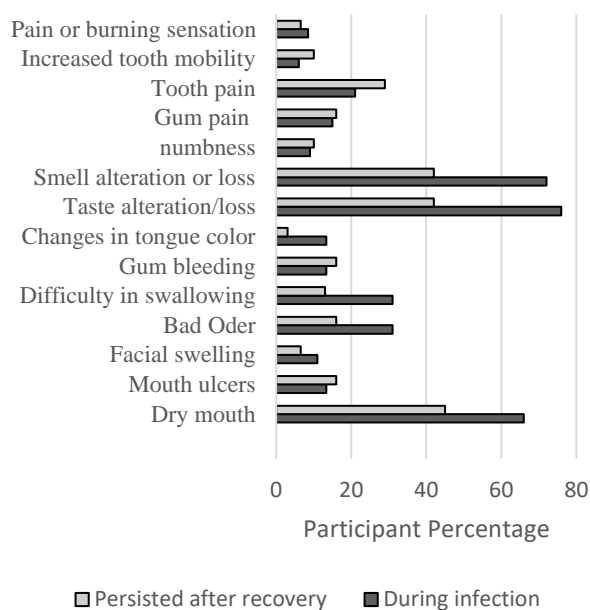


Taste and/or smell loss or alteration were the most reported symptoms (76 and 72%, respectively). Followed by dry mouth (N=54,66%), bad odor (N=26, 32%), difficulty swallowing (N=25, 31%) and tooth pain ((N=12, 21%). More than 10% of participants reported gum pain, bleeding, and increased tooth mobility. Mouth ulcers were also a commonly reported symptom (N=11, 14%) (Figure 2).

The presence of oral symptoms was significantly associated with severe COVID cases (OR=6.56) (P<0.001), adjusting for age, gender, and oral hygiene measures before COVID infection. In addition, the presence of oral symptoms was significantly associated with systemic medical conditions (P=0.04) but not with smoking history (P>0.5). In terms of dental history, history of gingival inflammation and gum pain were significantly associated with oral symptoms during COVID-19 infection (P=0.02, P=0.003) after adjusting for age, gender, smoking, BMI, and chronic disease.

In 24 (29%) participants, the oral symptoms were mild and did not require treatment; however, 61% required pain medication (N=35, 43%) or requested a prescription from the dentist (N=15, 18%).

**Figure 2: Oral symptoms reported during and after the recovery from the COVID-19 infection.**



Thirty-one (38%) participants reported that oral symptoms persisted after recovery from the infection. The leading persistent symptoms were dry mouth (N=14, 45%), tastes and smell alteration or loss (N=13, 42%), dental pain (N=9, 29%), mouth ulcers (N= 5, 16 %) and gingival bleeding (N=5, 16 %) (Figure 2).

Persistent oral symptoms were significantly related to the history of gingival inflammation ( $P=0.001$ ), and gum pain ( $P=0.006$ ) after adjusting for age, gender, smoking, BMI, and chronic disease. Females accounted for 84% (N=26) of those who reported persistent symptoms, and those with chronic medical conditions accounted for 39% (N=12).

In four participants (13%) the severity of the symptoms remained comparable to the severity during the infection, while 25 (83%) reported that the severity of the symptoms had improved over time. None reported worsening of the oral symptoms. However, only 32% visited the dentist regarding their symptoms.

#### 4. DISCUSSION

This study found that a subset of COVID-19 patients has oral symptoms lasting more than 14 days after the infection. The most common persistent symptoms are taste or smell alteration, dry mouth, and dental pain. Gum bleeding, pain, and ulceration were also common findings. Oral symptoms and persistent oral symptoms were associated with gum inflammation, pain, or oral ulceration history. Also, oral symptoms in general during the COVID-19 infection were associated with the severity of the disease and the patient's medical condition.

Several studies examined the endurance of symptoms and complications after SARS CoV-2 infection and showed that 15–76% of such patients might have persistent symptoms six months after severe illness (A. Carfi et al., 2020; Davis et al., 2021; Logue et al., 2021). Evaluating long-term COVID prevalence in Saudi Arabia, Garout et al. (Garout et al., 2022) estimated that 47% of COVID-19 patients had persistent systemic symptoms. This study focused on oral symptoms only, did not evaluate systemic symptoms, and yet reported that 38% of the precipitants stated persistent symptoms. Also, the majority of the participants had a moderate disease that did not require hospitalization; on the other hand, Garout et al. evaluated both hospitalized and non-hospitalized patients (Garout et al., 2022). Similar to this study, a higher proportion of females reported persistent symptoms; however, gender, the severity of illness, and hospitalization were not associated with post-COVID symptoms (A. Carfi et al., 2020; Garout et al., 2022).

The most common long-term COVID-19 symptoms were fatigue, malaise, cognitive dysfunction, sensorimotor symptoms, headaches, and memory issues (Logue et al., 2021; López-Sampalo et al., 2022). Altered taste and smell were among the commonest sensorimotor symptoms reported to affect 57% of patients (Davis et al., 2021). This is in agreement with our findings. However, the literature evaluating oral symptoms in post-acute COVID-19 syndrome is rare. We only found one case report of a 31-year-old female showing parosmia, dysgeusia, and tongue changes that lasted for four weeks after the viral clearance and responded to conservative therapy (Eita, 2021).

Interestingly, a high proportion of the participants in this study reported dry mouth. The presence of ACE2 receptors on the salivary glands and the tongue could suggest that the epithelial cells of the salivary glands and tongue may be involved in COVID-19 infection (Chawla et al., 2022). SARS-CoV-2 and ACE2 interactions might disturb the normal function of oral keratinocytes and therefore result in oral mucosal ulceration and other oral symptoms commonly seen with COVID-19 infections (Brandão et al., 2021).

The study showed that a history of gingival inflammation or pain was associated with oral symptoms or persistent symptoms of COVID-19 infection. Several studies have documented that COVID-19 positive participants who initially reported painful or bleeding gums had a higher risk of mortality from coronavirus disease in 2019 (odds ratio 1.71, 95% confidence interval 1.05-2.72) (Larvin et al., 2020). And after adjusting for potential confounders like age, gender, smoking, BMI, and chronic medical conditions, moderate to severe periodontitis was significantly associated with a higher risk of death or ICU admission for COVID-19 complications (Marouf et al., 2021). The severity of COVID-19 symptoms significantly increased in patients with poor oral health status, and the recovery period was significantly delayed up to six weeks in those with poor oral health (Kamel et al., 2021). In a case-control study, Anand et al. reported that COVID-19 patients had significantly higher plaque scores, gingival bleeding, mobile teeth, and worse probing depth, gingival

recession, and clinical attachment loss compared to controls (Anand et al., 2022).

Periodontal disease and COVID-19 share many risk factors like increased age, smoking, obesity, and chronic medical conditions. Those could act as comorbidities or could have pathological mechanisms linking COVID-19 and periodontitis. Periodontal pockets are known to act as reservoirs for viruses (Aggarwal et al., 2017). SARS-CoV-2 was detected in periodontal tissue biopsies of COVID-19-deceased patients (Zhang et al., 2020). Moreover, SARS-CoV-2 was detected in periodontal pockets and caries lesions in COVID-19 symptomatic and asymptomatic positive patients (Natto et al., 2022). Virus entry into the body could be facilitated either directly through ulcerated pocket epithelium or indirectly by periodontal pathogen-induced upregulation of ACE-2 receptors (Tamimi et al., 2022). Additionally, periodontitis can prime the immune system toward an exacerbated innate response by contributing to systemic inflammation. Which can lead to the cytokine storm that characterizes severe COVID-19 infection (Tamimi et al., 2022). The oral cavity is a known reservoir for respiratory pathogens, especially in patients with periodontal disease and inadequate oral hygiene, and dissemination of periodontal pathogens into the lower respiratory tract can occur through aspiration or during mechanical ventilation (Takahashi et al., 2020). Moreover, perio-pathogens can upregulate the expression of ACE-2 in the lower respiratory tract, leading to excessive cytokine production (Xu et al., 2020).

The result of the study should be interpreted with caution. A limited sample size and the retrospective nature of the study expose the possibility of recall bias, which influences the reliability of symptom prevalence estimates. The lack of clinical examination and details of dental conditions before COVID-19 may result in inconsistencies in reporting symptoms. Also, we did not evaluate the vaccine status of the participants. Vaccinated individuals tend to have a milder illness and fewer severe symptoms (Mohammed et al., 2022). Further research is needed to explore the effect of periodontal treatment on the occurrence of such symptoms. In addition, studies on the impact of vaccination and different virus variants on the development of post-COVID syndromes are needed.

## 5. CONCLUSION AND RECOMMENDATION

Oral manifestations can be present as part of the post-COVID-19 syndrome. There is a deficiency of evidence regarding the risk factors and consequences of post-COVID-19 syndrome. However, dental practitioners should be aware of persisting symptoms in post-COVID-19 patients and should enforce good oral hygiene practices and frequent periodontal maintenance for COVID-19 patients.

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