

Oral symptoms of patients tested positive for COVID-19 with mild severity- a cross-sectional study

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Abstract

BACKGROUND: The pandemic of Coronavirus disease (COVID-19) has a major effect on the world. It has several signs and symptoms, and the cause of some oral lesions may be related to this virus.

OBJECTIVES: The aim of the study is to determine the proportion and evaluate the different oral symptoms and their time of presentation in patients with mild COVID-19 infection.

MATERIALS AND METHODS: The present study included 55 participants (40% females and (60%) males, with an average age of 38.52 ± 10.46 years.

RESULTS: About 80% (43 patients) had oral symptoms such as Xerostomia, Recurrent Herpes simples, aphthous stomatitis, gingival pain, or other symptoms.

CONCLUSION: COVID-19 has been shown to have some effects on the mouth because a large proportion of COVID-19 patients had oral symptoms.

CLINICAL SIGNIFICANCE: This research showed a high percentage of COVID-19 patients experienced dry mouth, after that the most likely lesions were Herpes; also, other lesions

may occur. In addition, dentists should be conscious of oral manifestation, particularly during the Coronavirus pandemic.

KEYWORDS: COVID-19; Recurrent Herpes; Xerostomia

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Introduction

SARS-CoV-2 was first reported in Wuhan, at the end of 2019, it rapidly became a pandemic disease and spread globally. Many patients with this virus have not exhibited any serious signs or symptoms [1]. This disease is known as COVID-19. The most common clinical symptoms are sore throat, fever, headache, dry throat, dyspnea, cough, abdominal pain, vomiting, and diarrhea [2]. The

virus can transmit between humans by respiratory droplets. The median incubation time typically ranges from four to five days, and it may extend to fourteen days [3].

The severity of COVID-19 in most people is mild (80%), whilst 20% of infected patients have experienced the severe type of this disease, and 5% of patients may become seriously sick with pneumonia or acute respiratory distress syndrome, which

needs ventilation and hospitalization at ICU ward [4]. The mouth forms an entry towards the outer environment and has a significant role in the development of SARS-CoV-2 [5].

Angiotensin-converting enzyme 2 (ACE 2) receptor is found in the lung, liver, gastrointestinal (GI), kidney, and even the epithelial surfaces of sweat glands and endothelium part of dermal papillary vessels [6,7] is a known receptor for SARS-CoV-2. Up

to now, different cutaneous manifestations of COVID-19 disease have been described encompassing varicelliform lesions, pseudochilblain, urticaria form, erythema multiforme (EM)-like lesions, petechiae and purpura, maculopapular, mottling, and livedo reticularis lesions [8].

Although not approved, there may be an association between epithelial expression and localization of the ACE2 protein in the oral and nasal mucosa. It has been shown that the ACE2 protein in the nasopharynx may be the functional receptor for the SARS coronavirus [9]. The virus itself can act as a trigger factor for other virus reactivation thereby leading to oral lesions.

Over activation of T-cells, shown by enhancing of Th17, Lymphocytopenia, and high cytotoxicity of CD8 T- cells were seen and reported in COVID-19 patients [10].

The available data have not yet introduced an efficient and safe pharmacologic treatment against COVID-19 and the potential effects are associated with multiple adverse reactions [11].

Remdesivir, protease inhibitors, hydroxychloroquine, and interferon regimen are introduced as potential drugs for treating COVID-19 which may affect oral health [12].

The most related oral sign of COVID-19 is taste disorders, unspecific oral ulcerations are desquamative

gingivitis, petechiae, and coinfections such as candidiasis, however, these symptoms have not been confirmed yet. These manifestations might be directional signs and clinical patterns of SARS-CoV-2 infection, or they are just consequences of a weak immune system and adverse medication effects [13]. The first recognized oral symptom of COVID-19 which was seen in 38% of patients with mild-moderate severity was Dysgeusia [2].

In this study, we aim to find oral symptoms of COVID-19 patients, then what those symptoms are, and which symptoms are more likely to occur among patients.

Material and Methods

This cross-sectional study was conducted in the west health center of Karaj of Iran country from January 2021 to March 2021 in the middle of the Omicron pandemic. The study was done according to the ethical principles of Helsinki [14]. 55 COVID-19 positive patients, including 22 females and 33 males who were diagnosed by reverse transcription-polymerase chain reaction assay (RT-PCR) from oro-nasopharyngeal swab specimens, were enrolled. The patients had mild to moderate symptoms, due to the latest WHO joint report [15] (mild symptoms consist of every symptom of Covid-19 except shortness of breath and difficulty breathing, furthermore moderate symptoms mean blood oxygen levels remain at 94 percent or higher). All the patients were

informed and signed the consent form.

In this study, Children, patients with any systemic diseases or patients using any medication which can cause oral symptoms or lesions, and also pregnant women were excluded from the study. All the enrolled patients had symptoms of coronavirus disease such as fever, cough, and body pain.

Patient's demographic details were recorded comprising their age, gender, significant previous medical history, and use of any medications. Patient COVID-19 positive infection state was also evaluated. They were enquired about the time when they felt sick and their presenting symptoms. Further, any significant changes within the oral cavity such as burning sensation, loss of taste sensation, changes in saliva flow, dryness of mouth, any redness, difficulty in brushing, swallowing, and maintaining oral hygiene also formed the part of the evaluation. If any complaints were reported, their first appearance and the duration were also recorded. Apart from questioning the patients, oral examination comprising both hard tissue and soft tissue was conducted on all the participants of the study. Any changes in the colour, moistness, continuity of the oral mucosa, flow and thickness of saliva, papilla of the tongue were all clinically examined and recorded. If any changes of significance were observed, their location, size, number, colour, texture and relevant information were

recorded. The oral findings of significance were brought to patients' notice to confirm their appearance during the period of COVID-19 infection. Any oral presentations that were present prior to the infection were excluded. All the patients were followed throughout their treatment period until recovery at regular time intervals. The oral examination was conducted by a fully trained vaccinated dentist, following all the

Table 1. The data of patients.

necessary protocols- complete body

Parameters		
Age (Mean ± SD)		38.52 ± 10.466 years old
Gender	Females	22 (40%) patients
	Males	33 (60%) patients
The average of the first day that the examination of patients began		4.29

protection suit, N95 mask, sterile gloves, and face shield. The oral examination was performed by utilizing sterilized mouth mirrors and probes.

Results

A total number of 55 patients (33 males and 22 females) were enrolled in this cross-sectional study. All the participants had COVID-19 symptoms like fever, shivering body ache, and headache.

The mean age of the patients was 38.52 ± 10.46 years and the average time that they felt sick and were positive for COVID-19 was on day 4.26 of their disease period. The data of patients have shown in Table 1. A week after the oral examination that was done by a dentist, patients were followed and asked about how long their oral symptoms lasted. It was claimed by the patients on average, 6.21 days after the examination day their symptoms disappeared.

A high proportion of the patients had oral symptoms and the most common symptoms were Xerostomia, Recurrent Herpes, (RHL), and concentrated saliva. it was observed that the oral manifestations could present alone or in combination with other oral signs and symptoms (Table 2).

12 participants did not have any oral symptoms, although 9 participants just had Xerostomia. 24 of the participants had Xerostomia with other symptoms such as Recurrent aphthous stomatitis, bitter taste, burning mouth and throat, and concentrated saliva.

In 5 patients, the only symptom was Recurrent Herpes (Figure 1), however, in 8 persons, they had recurrent herpes labialis (RHL) and other oral manifestations which were mentioned before.



Figure 1. Recurrent Herpes in patients with COVID-19 positive infection: A) Herpes lesion on the labial surface of the lower lip; B) Herpes lesions on the labial surface of the lower lip; C) Herpes lesion on the labial surface of the upper; D) Herpes lesions on the hard palate.

7 patients had both RHL and Xerostomia, and 3 of them experienced recurrent aphthous stomatitis (Figure 2).



Figure 2. Aphthous stomatitis in patients with COVID-19 positive infection: A) Aphthous lesion on the labial surface of the lower lip; B) Aphthous lesion on the labial surface of the lower lip.

Table 2. Oral findings in patients tested positive for COVID-19.

The accurate percentage of each item that was observed in the mouth area was mentioned in Table 2. All these symptoms are only observed, and nothing was done for their treatment.

Oral findings	Frequency	Percent	Cumulative Percent
No change	12	21.8	21.8
Recurrent aphthous stomatitis	1	1.8	23.6
bitter taste	1	1.8	25.5
Concentrated salvia	1	1.8	27.3
Recurrent Herpes	5	9.1	36.4
Recurrent Herpes - dry throat	1	1.8	38.2
Loss of taste- concentrated salvia- Recurrent Herpes	1	1.8	40.0
Xerostomia	9	16.4	56.4
Xerostomia - bitter taste	1	1.8	58.2
Xerostomia- Recurrent aphthous stomatitis	1	1.8	60.0
Xerostomia- bitter taste	4	7.3	67.3
Xerostomia- bitter taste- burning throat	1	1.8	69.1
Xerostomia- bitter taste- concentrated salvia- burning gingiva	1	1.8	70.9
Xerostomia- Bitter taste- Recurrent Herpes	1	1.8	72.7
Xerostomia- concentrated salvia	6	10.9	83.6
Xerostomia- concentrated salvia- bitter taste	1	1.8	85.5
Xerostomia- dry throat	1	1.8	87.3
Xerostomia- burning gingiva- Recurrent aphthous stomatitis	1	1.8	89.1
Xerostomia- Recurrent Herpes	3	5.5	94.5
Xerostomia- Recurrent Herpes - bitter taste	1	1.8	96.4
Xerostomia- Recurrent Herpes - concentrated salvia	1	1.8	98.2
Xerostomia- loss of taste- burning gingiva- Recurrent Herpes	1	1.8	100.0
Total	55	100.0	

Discussion

One of the biggest and world-spread pandemics of this century is COVID-19. This contiguous infection has threatened all people all around the

world [16]. It has demonstrated a wide range of symptoms, from asymptomatic to fatal complications [17], but the most common symptoms are coughs, fever, fatigue, and dyspnea [18,19]. There is no

definitive treatment for this infection. The most important management is focused on supportive and palliative care [20]. Until now, June 2022, over 547,512,638 cases have been reported worldwide [21].

In the present study, 55 patients with COVID-19 during their period of the disease have been assessed for their overall and oral symptoms. The results showed that most of the patients had oral symptoms even to a very small extent. For example, 43.2% had Xerostomia with other symptoms. Patients complained about Xerostomia more than other signs. One study showed that SARS-CoV-2 targets ACE2-localizing salivary glands, this virus impairs the secretion function of those glands, resulting in low salivary flow and Xerostomia [22]. However, the most common symptoms seen in the mouth were Recurrent Herpes, and recurrent aphthous stomatitis respectively. Other manifestations such as burning gingiva, bitterness, or loss of taste were observed too. This could be as related to the impaired immune system [23] and immunologic dysregulation and a high level of pro-inflammatory cytokines [24, 25].

It seems that lymphopenia, hyper-inflammatory state, and cytokines all have important roles in the pathology of COVID-19 [26]. Immune cells like macrophages could be part of the disease progression. Macrophages have shown a substantial production of IL-6, suggesting they may help with the excessive inflammation in COVID-19 infection [27]. Because of the T-cell lymphopenia and their decreased function, immunoglobulins delivered by B cells represent the principal arm of the immune system to battle the

virus [28]. Nonetheless, the exact pathophysiologic mechanism of COVID-19 remains still largely unknown. Boosting the immune system to help combat the virus is important [29]. Research showed clinical olfactory and gustatory symptoms are prevalent in COVID-19 patients and mostly emerged in the first three days [30].

The study of Chenghao Qiu et al. on COVID-19 patients showed that olfactory and/or gustatory dysfunction may address early or even the main symptom of SARS-CoV-2 infection in both grown-ups and children. 19% of patients experienced olfactory or gustatory dysfunction preceding some other COVID-19 symptoms, also they considered how long did it take to experience improvement [31]. We measure the time for improvement in our study as well. Healing of the symptoms was seen after a while. A Ganesan et al. found out COVID-19 infection certainly has a significant impact on the oral health of the patients and oral findings are prevalent in the severe form of the disease [32]. In the present study, oral health and manifestations have been assessed in patients with mild to moderate COVID-19 symptoms with no hospitalization history.

Like our study, B Iranmanesh et al. showed which manifestations probably will be occurred in the mouth area. They listed aphthous-like lesions, herpetiform/zosteriform lesions, white/red plaques, EM-like

lesions, necrotizing periodontal disease, and some other lesions in their study. The other subject that they demonstrated was, they saw lack of oral hygiene, stress, immunosuppression, vasculitis, opportunistic infections, and hyper-inflammatory response secondary to COVID-19 are the most important predisposing factors to develop lesions mouth lesions in COVID-19 patients [33].

Amorim Dos Santos et al. reported that taste alterations are the most prevalent oral manifestation in COVID-19 patients and with moderate certainty of evidence it is associated with mild/moderate severity and female sex [8]. Some of the patients in this study reported bitter taste in their mouths along with their sickness. Some research suggested some medications such as corticosteroids and antihistamines for their anti-inflammation effects or antiseptic mouthwash. Palliative drugs, antifungal, and antibacterial therapy may also prescribe. However, other studies have declined to consider any medication or treatment for mild or asymptomatic patients because of the nature of self-healing. NSAIDs may worsen the symptoms of COVID-19, but there is no evidence yet [34].

Carreras-Presas CM et al. Suggested to treat Dysgeusia or taste disorder, Multiple ulcers on the palate and internal lip, desquamative gingivitis, and Pain in the tongue by Valaciclovir 500 mg every 8 h for 10 days, and

topical antiseptics with chlorhexidine and hyaluronic acid; within 7-10 days the symptoms will disappear [35]. Another case report of a 56-year-old woman for treating dry mouth suggested using anti-inflammatory and antiasthmatic drugs such as montelukast, naproxen and acetaminophen for a period of 7 days [36]. Orcina F et al said using Phtalox mouth wash for 12 hours to 4 days could be useful for curing aphthous stomatitis. A few publications indicated that oral lesions are caused by reduced immunity due to viral infection, opportunistic or secondary infection or Covid-19 treatment [35-39].

Many patients with COVID-19 infection may show oral symptoms, and it might be the earliest one. So, dentists should be conscious of these symptoms. It is possible that the patients do not have COVID-19 symptoms, but they have oral signs and symptoms which are related to the virus [39]. These lesions also may be the secondary response to medications. Controlling the infection transmission for community and health care staff and also diagnosis of the asymptomatic COVID-19 makes these findings important. A further clinical study with a larger sample size and based on gender and age groups is recommended to confirm the link between oral lesions and the COVID-19 virus.

Conclusion

Xerostomia, Recurrent Herpes, and recurrent aphthous stomatitis are the three most common symptoms in the evaluated patients of this study. The oral symptoms in patients with COVID-19 infection might be the earliest symptom even if the patient is asymptomatic and he is not aware of his sickness.

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