

Oral manifestations in COVID-19 patients: An observational study

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ABSTRACT

Background: Viral diseases continue to emerge as a threat to mankind and are a serious concern to public health. The latest lethal SARS-CoV-2 or COVID-19 is a highly contagious disease, which propagated quickly across the globe. Similar to other influenza-like viral infections, symptoms such as fever, dry cough, myalgia, arthralgia, headache, diarrhea, dyspnea, and fatigue were reported among COVID-19 patients. Evidence suggests that the oral cavity is affected by this virus either directly or indirectly. **Aim:** The aim of this observational study was to determine the oral manifestations among COVID-19 patients. **Materials and Methods:** A cross-sectional, questionnaire-based study was carried out among COVID-19 recovered patients. A sample of 100 subjects, diagnosed as mild and moderate cases of COVID-19 disease were selected based on inclusion and exclusion criteria. **Results:** The study comprised an almost equal number of male (51%) and female (49%) participants and among them, 48% belong to the health professional group. A total of 54% of subjects were aged above 35 years and 46% below 35 years. Oral manifestations among study subjects during and after the disease illness included xerostomia being the commonest symptom (44%), followed by swallowing difficulty (16%), mouth ulcerations (10%), chewing problem (7%), gum bleeding (6%), and burning sensation (4%). **Conclusion:** Xerostomia, frequent aphthous ulcers, swallowing difficulty, and burning mouth were the most frequently encountered symptoms in study subjects during the disease and post recovery. Early identification of oral symptoms in COVID-19 recovered or suspected cases can help a dentist or a general physician to diagnose high-risk groups, mitigate transmission, and promote overall health.

Keywords: COVID-19, loss of taste, oral manifestations, SARS-CoV-2, xerostomia

Introduction

Viral diseases continue to emerge as a threat to mankind and are a serious concern to public health. In the last millennium, several viral epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV-2) emerged in 2002–2003, H1N1 influenza in 2009, Middle East Respiratory Syndrome Corona-Virus (MERS-CoV) in 2012, and finally, SARS CoV-2

or COVID-19 hit the world in December 2019. Interestingly, in almost all of these pandemics, the causative viruses belong to the same family, Coronaviridae, and have their origin from bats, later moving to mammalian hosts and then finally infect humans, making their dynamics spurious.^[1]

The latest lethal SARS-CoV-2 or COVID-19 is a highly contagious disease that propagated quickly across the globe, declared a Public Health Emergency of International Concern (PHEIC) on January 30, 2020 and a pandemic on March 11, 2020 by the World Health Organization.^[2] Till June 12, 2021, there were 174,502,686 reported cases of COVID-19 disease, resulting in 3,770,361 deaths.^[3]

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Similar to other influenza-like viral infections, symptoms such as fever, dry cough, myalgia, arthralgia, headache, diarrhea, dyspnea, and fatigue were reported among COVID-19 patients. Moreover, generalized body weakness and fatigue are common symptoms even in paucisymptomatic subjects.^[4] However, the frequency, duration, and magnitude of these symptoms depend on an individual's immune competency. As per reports, most of the COVID-19 cases are mild (80%), whereas 20% of infected patients may develop severe disease, and 5% may become critically ill requiring mechanical support due to complications such as pneumonia or acute respiratory distress syndrome (ARDS).^[5-7]

The clinical presentation also involves oral cavity showing signs of chemosensory disorders such as taste alterations, nonspecific oral ulcerations, and aphthous stomatitis, mucositis, drug eruptions, angular cheilitis, hypogeusia, xerostomia, desquamative gingivitis, petechiae, pigmentations, necrotizing periodontal disease, and opportunistic infections such as mucormycosis, candidiasis, aspergillosis, and herpetiform lesions.^[5-11] Reviews by Singh *et al.*^[12] and Farid *et al.*^[13] confirmed ageusia, anosmia, hyposalivation, and mucosal ulcerations to be a common finding in COVID-19 patients.

Sometimes few manifestations pop up late in disease or after patients become seronegative for this virus. As the oral cavity is the mirror of general health, many times it becomes the site for the appearance of inaugural symptoms.^[14] Prevailing knowledge and acquaintance of these oral symptoms can help primary and general care physicians to diagnose asymptomatic, paucisymptomatic, and post-COVID-19 patients with deteriorating immune status.^[15,16] Early diagnosis in these cases can alarm healthcare providers to strictly adhere to preventive protocols and make them explore patients' existing health conditions, which will avoid further worsening of their systemic diseases, the incidence of opportunistic infections such as mucormycosis, and many other post-COVID complications.^[17] High viral concentration was found in the nasal cavity and throat making this route the main source of transmission as well as the preferred site for virus isolation.^[18-20]

Evidence suggests that the oral cavity is affected by this virus either directly or indirectly, but it is still a doubt whether these symptoms are due to direct effects from the virus, impaired immune system, systemic deterioration in this multiorgan disease, or as a response to intense multidrug treatment. Due to the vicious nature of the disease and its varied symptomatology, the present study was aimed to investigate the prevalence of oral manifestations among COVID-19 patients.

Materials and Methods

A cross-sectional, questionnaire-based study was carried out among COVID-19 recovered patients regarding health status, oral hygiene practices, and symptoms in oral cavity during and after the disease illness. Ethical clearance was obtained from the

Institutional Review Board of Panineeya Mahavidyalaya Institute of Dental Sciences and Research Center PMVIDS and RC/IEC/PHD/380-20.

Written consent from all subjects was taken; anonymity and confidentiality were maintained.

A convenient sample of 100 subjects, who were diagnosed as mild and moderate cases of COVID-19 disease was selected by snowball sampling method based on inclusion and exclusion criteria. Data were collected between 2 weeks to 3 months from the date of diagnosis of COVID-19 disease, which was confirmed by positive RT-PCR (real-time reverse transcriptase-polymerase chain reaction) reports.

Inclusion criteria

- 1) Subjects with laboratory-confirmed COVID-19-positive RT-PCR reports.
- 2) Subjects who have recovered from COVID-19 disease either under home isolation or in hospital.
- 3) Mild and moderate cases, who did not undergo any kind of intensive care therapy.
- 4) Subjects who completed a minimum isolation period of 2 weeks.
- 5) Subjects who gave written consent.

Exclusion criteria

- 1) Uncooperative subjects.
- 2) Subjects who submitted the unfilled/partially filled questionnaire.
- 3) Subjects having any common symptoms related to COVID-19 like fever, cough, cold, etc., at the time of interview.
- 4) Subjects who were diagnosed as COVID-19 positive more than 3 months back.

During the survey, data were obtained from study participants by either of the following methods, i.e., through a personal interview, by telephonic interview, or by online survey using Google forms. Majority of subjects gave personal interviews to the examiner and during the interview, all the preventive measures were followed to control disease transmissions such as the use of personal protective equipment, mouth masks, maintenance of hand hygiene, and social distancing. All subjects were interviewed in well-ventilated rooms or open spaces. After the interview, the filled questionnaire was collected in a separate box and reviewed after a rest period for analysis. Oral examination on patients was not performed by the examiner due to risk of disease transmission.

Few subjects who were approached for telephonic interviews were explained regarding the aim of the study and common symptoms found in the oral cavity during and after COVID-19 disease. They preferred to fill questionnaire sent to them in Google forms by referring attached file of clinical pictures showing oral manifestation in COVID-19 patients.

Survey tool

Questionnaire: A close-ended, validated, questionnaire containing 25 questions was used to collect information regarding health status, oral hygiene practices, and symptoms in the oral cavity during and after the disease manifestation.

The following information was gathered from study subjects:

1. Demographic details: age, gender, occupation, history of a previous dental visit, smoking history, oral hygiene practices.
2. Disease-related: date of diagnosis, transmission in family, regarding home isolation and hospitalization, and any other general symptom related to COVID-19.
3. Oral manifestations like xerostomia, chewing and swallowing problems, any mouth ulcerations and burning sensation, gingival and periodontal status, any tooth-related problems, taste alteration, and its duration.
4. Any other unusual symptoms experienced during the disease course.
5. Post-COVID-19 care or any vitamin supplementation.

Statistical analysis

Answers were dichotomized as Yes/No, kept in two categorical variables, and codified. Due to the nature of our survey, we computed descriptive statistics for most of the questions. Answers obtained prior to and during the disease manifestation were compared through the use of the Chi-square test to assess the statistical significance. Statistical significance for different variables was checked by the level of P value < 0.05 . Statistical analysis was performed using SPSS software version 23.0.

Results

Demographic distribution of study subjects shows almost equal participation from all groups [Table 1]. With regards to the oral hygiene practices, though most of the study subjects used tongue cleaner daily (94%), only 27% of them brushed their teeth twice daily. A total of 97% of study participants had more than 20 teeth, and have claimed not having any loose teeth, prosthesis (92%) in their oral cavity. Furthermore, a considerable percentage of subjects visit their dentist regularly (51%).

More than half of study subjects (54%) were on vitamin supplementation during the recovery phase (2 weeks following confirmed infection) and 26% of the patients had general symptoms [Table 2]. With respect to the oral manifestations among study subjects during the disease illness, it was noticed that xerostomia was the commonest symptom (44%), followed by swallowing difficulty, mouth ulcerations, chewing problems, gum bleeding, and burning sensation. Although other symptoms decreased by frequency in the recovery period, burning sensation and frequent mouth ulcerations increased. Around 72% of patients reported altered taste, which lasted for more than a week in 53% of patients. Other oral symptoms reported during the disease were fissured tongue, halitosis, and loss of taste with prevalence of 2% [Table 3].

Table 1: Distribution of study subjects

| Variables | n | % | |
|-------------------------------|---------------------------|----|----|
| Age | >35 | 54 | 54 |
| | <35 | 46 | 46 |
| Gender | Male | 51 | 51 |
| | Female | 49 | 49 |
| Healthcare provider | Yes | 48 | 48 |
| | no | 52 | 52 |
| Smoking | Nonsmoker | 92 | 92 |
| | Yes | 8 | 8 |
| Systemic disease | No | 85 | 85 |
| | yes | 15 | 15 |
| Systemic condition | MI | 2 | 2 |
| | Diabetes | 6 | 6 |
| | Hypertension | 3 | 3 |
| Recovered at | Diabetes and hypertension | 4 | 4 |
| | Home isolation | 82 | 82 |
| Other family members infected | Hospital | 18 | 18 |
| | Yes | 66 | 66 |
| | No | 34 | 34 |

Table 2: Distribution of subjects based on their general symptoms

| Variables | n | % | |
|----------------------|-------------------------|-----|----|
| Presence of symptoms | | | |
| | Yes | 26 | 26 |
| | No | 74 | 74 |
| Symptoms specify | Weakness | 12 | 12 |
| | Fever | 2 | 2 |
| | Loss of smell | 4 | 4 |
| | Body aches | 4 | 4 |
| | Cough | 10 | 10 |
| | Cold | 4 | 4 |
| | Sleep disturbance | 2 | 2 |
| | No | 98 | 98 |
| | Vitamin supplementation | | |
| | | Yes | 54 |
| | No | 46 | 46 |

Presence of general symptoms did not show any significant difference based on variables except for age groups, wherein, subjects aged >35 years had general symptoms such as weakness (8%), cough and cold (4%), and body pain (2%) with P value ($P = 0.004$) during the recovery period. Though a high percentage of males had general symptoms, a significant difference was not observed. Furthermore, no significant difference was noted for vitamin supplements based on age and gender. A significant difference was noticed with respect to the general symptoms based on profession ($P = 0.048$) and comorbidity ($P = 0.005$), wherein health professional subjects and subjects with comorbidity had general symptoms like fatigue/weakness and body pains. There was no significant relationship found between the presence of general symptoms and vitamin supplementation among the healthcare professionals group. Whereas, patients with systemic illness were significantly supplemented with vitamins ($P = 0.00$).

When comparison was done for the presence of oral symptoms based on age and gender, a statistically significant value ($P = 0.042$) emerged only for symptoms like chewing problems, especially in patients aged >35 [Table 4]. In the present study, when variables like profession and presence of comorbidity in subjects were compared with oral symptoms P value was significant ($P = 0.021$) only for swallowing difficulty, which was evident in systemically compromised patients. No significant association was found between the presence of oral symptoms like xerostomia, mouth ulcerations, burning sensation, gum bleeding, and altered taste when compared among healthcare providers and comorbid patients.

Discussion

Due to the rapid infectivity and contagious nature of coronavirus around 66% of our study subjects reported simultaneous infection in their family members and despite taking all

preventive measures the high rate of infectivity was observed among healthcare workers making management of this disease a challenge. But on the positive note, 82% of subjects recovered under home-isolation representing mild-moderate form of severity similar to other research findings.^[5,18]

Xerostomia, swallowing difficulty, mouth ulcerations, and gum bleeding, burning of oral mucosa, and altered taste sensation with different frequency was observed in our study subjects. The data was relevant as it had similarities with other research findings.^[6,15,20-22] The associated possible cause for this may be multidrug therapy, immune-compromised state, chemosensory degradation of cells in COVID-19 patients, and oral/nasal cavity as the main route of infection. Taste disorder, which was the most common outcome seen in our study subjects with a prevalence of 72%, had similarities with previous studies done by Santos *et al.*^[15,71] who reported gustatory impairment with prevalence of 45% in COVID-19 patients. Freni *et al.*^[4] also reported xerostomia, dry eyes, auditory discomfort along with gustatory, and olfactory dysfunction with a prevalence of 70% and 92%, respectively, in their COVID-19 patients. As ACE-2 receptors are in abundance in salivary glands, tongue, and oral mucosa, the neuroinvasive properties of the SARS-CoV-2 virus cause chemosensory degradation leading to various manifestations in oral cavity including altered taste.^[6,11,23,24] A bizarre of oral symptoms were reported in a study done by Iranmanesh *et al.*^[18] like aphthous ulcers, herpetiform lesions, ulcers, erosions, white and red plaques, exanthema-like lesions, necrotizing periodontal disease, xerostomia, erythema multiforme, mucositis, fissured tongue, etc., Likewise, in the present study few subjects had halitosis, aphthous ulcers, swallowing difficulty, fissured tongue, and xerostomia. Furthermore, Presas *et al.*^[8] reported cases of oral ulceration, glossodynia among COVID-19 patients. Few other studies also reported cases of necrotizing periodontal disease, commissural cheilitis, and bilateral atrophy of the tongue as extrapulmonary manifestation in COVID-19 recovered patients.^[9,10]

Table 3: Distribution of subjects based on their oral symptoms

| Variables | During disease n (%) | | After disease n (%) | |
|---------------------------|----------------------|---------|---------------------|-----------|
| | Yes | No | Yes | No |
| Xerostomia | 44 (44) | 56 (56) | 11 (11) | 89 (89) |
| Chewing problems | 7 (7) | 93 (93) | 4 (4) | 96 (96) |
| Swallowing difficulty | 16 (16) | 84 (84) | 2 (2) | 98 (98) |
| Mouth ulcerations | 10 (10) | 90 (90) | 12 (12) | 88 (88) |
| Burning sensation | 4 (4) | 96 (96) | 15 (15) | 85 (85) |
| Gum bleeding | 6 (6) | 94 (94) | 5 (5) | 95 (95) |
| Taste altered | 72 (72) | 28 (28) | 11 (11) | 89 (89) |
| Duration of altered taste | | | | |
| <1 week | | 47 (47) | | |
| >1 week | | 53 (53) | | |
| Other problems specified | | | | |
| Fissured tongue | 2 (2) | 98 (98) | 0 (0) | 100 (100) |
| Halitosis | 2 (2) | 98 (98) | 1 (1) | 99 (99) |
| Loss of taste | 2 (2) | 98 (98) | 0 (0) | 100 (100) |

Table 4: Comparison of study subjects based on the oral symptoms according to variables

| Variables | | Age groups | | | | P | Gender | | | | P |
|-----------------------|-----|------------|----|-----------|----|--------|--------|----|--------|----|-------|
| | | <35 years | | >35 years | | | Male | | Female | | |
| | | n | % | n | % | | n | % | n | % | |
| Xerostomia | Yes | 3 | 3 | 8 | 8 | 0.106 | 7 | 7 | 4 | 4 | 0.526 |
| | No | 51 | 51 | 38 | 38 | | 44 | 44 | 45 | 45 | |
| Chewing problems | Yes | 0 | 0 | 4 | 4 | 0.042* | 4 | 4 | 0 | 0 | 0.118 |
| | No | 54 | 54 | 42 | 42 | | 47 | 47 | 49 | 49 | |
| Swallowing difficulty | Yes | 0 | 0 | 2 | 2 | 0.209 | 2 | 2 | 0 | 0 | 0.495 |
| | No | 54 | 54 | 44 | 44 | | 49 | 49 | 49 | 49 | |
| Mouth ulcerations | Yes | 7 | 7 | 5 | 5 | 1.000 | 4 | 4 | 8 | 8 | 0.230 |
| | No | 47 | 47 | 41 | 41 | | 47 | 47 | 41 | 41 | |
| Burning sensation | Yes | 10 | 10 | 5 | 5 | 0.354 | 6 | 6 | 9 | 9 | 0.115 |
| | No | 43 | 43 | 42 | 42 | | 45 | 45 | 40 | 40 | |
| Gum bleeding | Yes | 3 | 3 | 2 | 2 | 1.000 | 3 | 3 | 2 | 2 | 1.000 |
| | No | 51 | 51 | 44 | 44 | | 48 | 48 | 47 | 47 | |
| Taste altered | Yes | 5 | 5 | 6 | 6 | 0.564 | 4 | 4 | 7 | 7 | 0.323 |
| | No | 47 | 47 | 42 | 42 | | 49 | 49 | 40 | 40 | |

Though more than half of our study subjects used dietary supplements and were on medication, 26% of them reported delayed symptoms like fatigue/weakness and cough even after being seronegative. These findings are in concordance with the findings of Moradian *et al.*,^[25] wherein 19.5% of COVID-19 cases reported symptoms like dyspnea, weakness, and activity intolerance with frequencies of 18.5%, 18%, and 14.5%, respectively. According to research from King's College, London, around 5% of COVID-19 patients experienced long-term symptoms for at least 1 month or more.

Now COVID-19 is recognized as a multiorgan disease and postacute sequelae are seen in pulmonary, hematologic, cardiovascular, neuropsychiatric, renal, gastrointestinal, hepatobiliary, dermatological systems, and few rare incidences of the multisystem inflammatory syndrome in children. The pathophysiological mechanisms behind this may be: direct viral toxicity, endothelial damage and microvascular injury, immune system dysregulation and stimulation of a hyperinflammatory state, hypercoagulability with resultant *in situ* thrombosis, and macrothrombosis, and maladaptation of the angiotensin-converting enzyme 2 (ACE2) pathway.^[14]

With respect to oral symptoms, subjects who were aged and with comorbidities had high pre- and postoral symptoms like xerostomia, chewing and swallowing difficulties, altered taste, and mouth ulcerations. Apparently these findings were supported by Dziejczak and Wejtyc^[17] who linked it to compromised/suppressed immune system and long-term pharmacotherapy in COVID-19 disease. Another cause for xerostomia may be dehydration and atrophy of acinar cells in salivary glands, which is common in viral infections leading to burning mouth and swallowing difficulty as secondary manifestation and intermittent ulcers may be the sign of vitamins deficiency. Production of antibodies against viral infections requires vitamins like vitamin A, B-complex, and E, whereas vitamin C and D act as immune boosters, So their requirement exceeds daily required dietary allowance (9RDA) values. Hence, COVID-19 patients need to continue these supplements during and after the disease along with a good diet.

No significant difference in the presence of general symptoms was observed in our study based on demographic variations. On the other side, subjects who were health professionals and who had underlying systemic conditions had a high prevalence of general symptoms, this might be due to frequent exposure to viral load among professionals and low immune response among subjects with systemic illness.

However, the present study acknowledges certain limitations like the risk of transmission and lack of patient consent for examination, we could not do oral examination among study subjects. Secondly, as most of the findings in our study were self-reported, it might be subjected to reporting bias. Therefore, we tried to minimize this by guiding the participants for self-evaluation of the oral cavity, by producing clinical pictures

of reported oral manifestations, and explaining to them about associated symptoms of COVID-19 disease.

Conclusion

Our study evaluated mild and moderate cases of COVID-19 disease and conspicuous oral manifestations found in them were xerostomia, frequent aphthous ulcers, swallowing difficulty, and burning mouth during the disease and post recovery.

In this present era, when we have started living with this disease, early identification of oral symptoms in COVID-19 recovered or suspected cases can help a dentist or a general physician to diagnose high-risk groups, mitigate transmission, and promote overall health.

Since COVID-19 is a novel infectious disease with insufficient data on pathogenesis and clinical features, a long-term follow-up with a multidisciplinary approach is highly recommended for all COVID-19 recovered patients backed by health informatics data to support further research and prevent many post-COVID-19 complications.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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