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Oral Manifestations in COVID-19 Patients Associated with Oral Hygiene in Aceh, Indonesia: A Literature Review

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Abstract

COVID-19 became a pandemic because of its high-speed transmission via salivary and airborne droplet routes. Viruses can enter host cells through ACE-2 receptors in various human organs, including the oral cavity. The oral manifestations that arise include white plaque, ulceration, burning sensation, oral mucositis, depapillation of the tongue, dry mouth, halitosis, and loss of the sense of taste. Poor oral hygiene, comorbidities, decreased immunity, and stress can exacerbate these manifestations. This review study aimed to report various oral manifestations of COVID-19 related to oral hygiene. Relevant articles were identified from PubMed, ScienceDirect, Elsevier, and Google Scholar. Out of the 60 articles selected, only 36 could be reviewed. The World Health Organization recommends early detection for individuals with suspected exposure to the COVID-19 virus to control its spread, including checking for oral manifestations. Oral hygiene is an important factor affecting the manifestations of the oral cavity of COVID-19 patients, so examination of the condition of oral hygiene is recommended in the medical management of COVID-19 patients. To conclude, oral hygiene is related to the emergence of oral manifestation in COVID-19-infected patients.

Keywords: COVID-19 infection, oral hygiene, oral manifestations

Introduction

Coronavirus disease 2019 (COVID-19) became a pandemic because of its high-speed transmission through close contact between individuals, primarily through saliva droplets and aerosols.¹ One of the complaints most often heard from sufferers of COVID-19 is the loss of their sense of taste and smell. This complaint can be used as an early marker of COVID-19 infection in humans.² Various studies have shown oral manifestations in patients infected with COVID-19. A study in Northern Italy showed 10% and 11% taste and smell disturbances in COVID-19 sufferers quarantined at home.³ Another study showed that 51.9–78.9% of quarantined patients experienced taste disorders due to the presence of angiotensin-converting enzyme 2 (ACE-2) inhibitor receptors, which are commonly found in the oral mucosa and are cellular receptors for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).⁴

Other than impaired sensory function, symptoms of the oral cavity that have also been reported in patients with COVID-19 include atrophy of the tongue, cheilitis, red plaques on the palate, canker sores (ulceration), petechiae, xerostomia, and halitosis.⁵⁻¹⁰ Severe thrombo-

cytopenia also triggers the above phenomena of oral disorders.¹¹ Previous studies found ulcerated lesions on the lower lip in three patients infected with COVID-19 without comorbidities and a history of recurrent ulcers before infection.^{3,10}

Several studies have stated that oral manifestations are also related to poor dental and oral hygiene, opportunistic infections, stress, decreased immunity, and a hyperinflammatory response to COVID-19.¹²⁻¹⁶ Mohammed, *et al.*, stated that each COVID-19 patient could have more than one manifestation of the oral cavity: loss of the sense of taste and dry mouth accompanied by a burning mouth sensation in 8.9% of patients.¹⁷ The number of canker sores experienced by COVID-19 patients varies, as they are triggered by stress and the condition and cleanliness of the patient's oral cavity.¹⁸ As the dentist works on the oral cavity daily, it is more susceptible to COVID-19 infection through a patient's droplets. This condition will contribute to the dental professional sector on detailed intraoral screening before dental treatment and help initiate the best treatment plan for lesions related to COVID-19.¹⁸ This review study aimed to report various oral manifestations of COVID-

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19 described in the literature related to oral hygiene.

Method

This review study focused on oral manifestations in COVID-19 patients associated with oral hygiene statuses. Online articles were searched in PubMed, ScienceDirect, Elsevier, and Google Scholar. Out of the 60 articles selected, 36 met the inclusion criteria (published within the last four years for articles regarding oral lesions related to oral hygiene and within the last three years for those related to COVID-19 keywords and oral manifestations and their relationship to predisposing factors in COVID-19 patients). Articles with irrelevant summaries were excluded. Only review or research articles available for open access were considered. The search terms used in Medical Subject Headings (MeSH) were “COVID-19 and its oral manifestations,” “COVID-19 and its predisposing factors in patients,” and “mouth hygiene status in COVID-19 patients” (Figure 1).

The first three authors independently assessed paper eligibility based on the title and abstract. If necessary, complete papers were obtained to determine eligibility status. Disagreements were resolved through consultation with the fourth and fifth authors. Papers in languages other than English were excluded if translations were unavailable. Full-text papers meeting the eligibility criteria were then evaluated. Study results on oral manifestations in COVID-19 patients and their relationship to oral cavity hygiene were then compiled. Finally, the articles were thoroughly, critically, and objectively reviewed and discussed using the same methods as previous studies.

Results and Discussion

COVID-19 first appeared in Wuhan, China, in December 2019 and was declared a pandemic by the World Health Organization on 11 March 2020.¹⁹ COVID-19 is caused by SARS-CoV-2. This virus is a type of betacoronavirus that causes severe and fatal symptoms in humans. The SARS-CoV-2 resembles SARS and MERS because it has an envelope, is single-stranded, and has monopartite ribonucleic acid.²⁰ Coronaviruses comprise four proteins: spicules, membranes, envelopes, and nucleocapsids. The spicule is composed of a transmembrane trimetric glycoprotein and has two subunits. Subunit one plays a role in the attachment of the virus to the host, while subunit two plays a role in the fusion of the virus into the cell membrane.²¹

The COVID-19 virus is transmitted between individuals via droplets (less than one meter) from infected individuals with coughing and sneezing symptoms. Transmission of these droplets does not have to be through direct contact but can also be through shared objects around the patient.^{22,23} According to the Indonesian Ministry of Health, the symptoms of COVID-19 are di-

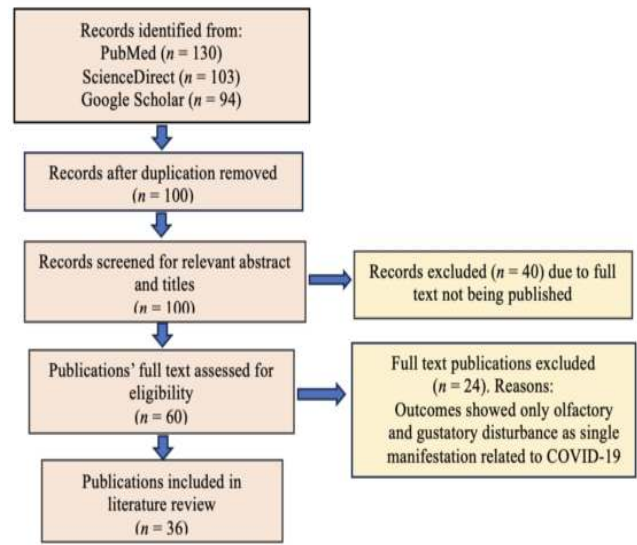


Figure 1. Literature Flow Chart

vided into the following five groups: asymptomatic (without clinical symptoms); mild symptoms: fever, fatigue, impaired smell and taste; moderate symptoms: symptoms of pneumonia (cough, fever, shortness of breath); severe symptoms: symptoms of pneumonia + one of the following features: respiratory rate >30x/minute, severe respiratory distress, or oxygen saturation <93% in room air; critical: acute respiratory distress syndrome, sepsis, or septic shock.²⁴ This severity level is also related to the patient's comorbidities, such as cardiovascular disease, diabetes, cancer, and chronic respiratory disease.¹⁹

Pathogenesis of Oral Manifestations in Patients Infected with COVID-19

The receptor for SARS-CoV-2 in humans is ACE-2, which is widely found in the lungs, heart, ileum, kidneys, and bladder. This process also involves several membrane attachment and fusion proteinase enzymes, such as disintegrin and metalloproteinase domain 17, transmembrane protease serine 2, TNF-converting enzyme, vimentin, and clathrin. The virus enters the cell nucleus through endocytosis, where the virus will enter the cell nucleus to replicate. These viral particles form viral proteins for biosynthesis and are released by the host cell.²⁵ The severe condition in COVID-19 patients is caused by a cytokine storm resulting from a drastic increase in IL-6 and IL-8 production. It triggers severe inflammation throughout the body due to its function as a chemoattractant for neutrophils and T cells.^{26,27}

The ACE-2 receptors can also be found in the oral mucosa and salivary glands. Saliva acts as a solvent and

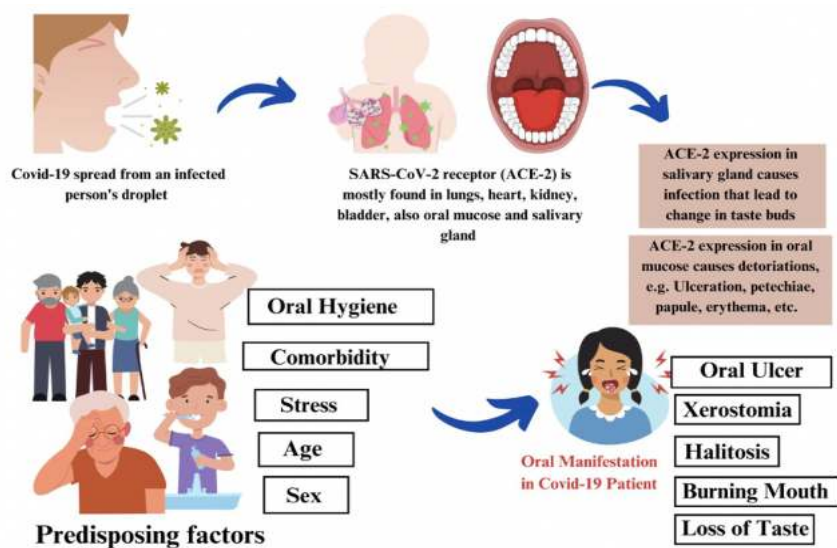


Figure 2. Illustration of Oral Manifestation in COVID-19 Patients and Its Predisposing Factors^{7,17,18,28}

regulates the condition of taste receptors. Infected salivary glands can alter the function of taste buds due to damage to them. ACE-2 is also found in the gingival sulcus, which causes edema and necrosis of the interdental papillae. Expression of ACE-2 in the oral mucosa can also cause other damage, such as ulcerated lesions, plaques, petechiae, erythema, papules, and macules (Figure 2).^{7,28}

The risk of COVID-19 infection increases in the elderly, who have comorbidities (cancer or cardiovascular, kidney, or chronic lung disease), diabetes, immunocompromised conditions, obesity, and sickle cell anemia.²⁹ Some reported results related to oral manifestations in patients infected with COVID-19 are as follows:

- White plaques on the dorsal tongue and yellowish pinpoint ulcers appeared 21 days after the patient was infected with COVID-19. These symptoms may have arisen due to the patient’s systemic condition and treatment while infected with COVID-19.⁷
- Multiple painful ulcers of varying sizes and irregular margins were found on the hard palate and tongue. The first case appeared five days after the initial symptoms, while the second case appeared one week after hospitalization.⁸
- Ulcer/apthous lesions on the lips, tongue, and hard palate six days after the patient was confirmed to have COVID-19, especially with comorbidities.¹⁰
- The sensation of pain, burning mouth, and nonspecific white plaque on the ventral tongue appeared in patients seven days after COVID-19 was confirmed. These symptoms were due to psychological stress during COVID-19 and the patient’s comorbidities. The above symptoms, coupled with the loss of the sense of

taste, are directly related to the COVID-19 infection.¹²

- Oral mucositis with bilateral diffuse erythema, depapillation of the tongue, and dry mouth was found in a patient nine days after COVID-19 was confirmed. This appears to have been caused by mucosal hypersensitivity to COVID-19.¹²
- Ulcer lesions on the tongue and burning mouth sensation due to infection of the salivary glands by COVID-19.¹⁶
- A dry mouth sensation that the patient had never experienced before being infected with COVID-19.²⁹
- Symptoms of dry mouth and damage to the taste buds caused loss of taste buds during infection.³⁰
- Glossitis, depapillation of the tongue, mucositis, and burning mouth sensation.³¹
- Impaired sense of taste in 67.8% of COVID-19 patients on days 10–14 of infection.³²
- Oral cavity lesions were more severe and widespread at older ages, and the severity of the infection was higher. While, gender did not play a role in differences in the appearance of the lesions.³³

Predisposing Factors for Oral Manifestations in Patients Infected with COVID-19

Predisposing factors that increase the severity of oral manifestations are poor oral hygiene, opportunistic infections, comorbid conditions, stress, age, decreased immunity, and the hyperinflammatory response to COVID-19. High exposure to systemic drugs, especially in hospitalized patients, can also affect the gut microbiota and cause oral manifestations.^{12,14,16,22,30-32}

Age and sex characteristics are said to be related to oral manifestations in COVID-19 patients. A study by Binmadi, *et al.*, revealed that oral manifestations in COVID-19 patients are mostly experienced by women aged 45–55 years.¹⁸ However, statistically, there is no relationship between age and sex in the oral manifestations experienced.¹⁸ A previous study also stated that more oral manifestations were proportionately found in older patients infected with COVID-19. This result is associated with decreased immunity in older patients.¹² Several studies also stated no significant difference in oral manifestations among the 20 COVID-19 patients.^{17,18,20}

COVID-19 patients with comorbidities experienced more oral manifestations than patients who did not have comorbidities. A study by Katz, *et al.*, stated that COVID-19 patients with diabetes are 10.54 times more at risk of experiencing recurrent aphthous stomatitis (recurrent canker sores), $p\text{-value} < 0.05$.²⁹ Comorbidities are related to oral manifestations in COVID-19 patients associated with the drugs consumed by individuals with systemic diseases.^{29,30}

Based on the results of the case reports studied, the lesions in the oral cavity that appear in COVID-19 patients are related to the stress they experience.⁸ This is in line with a study conducted by Nwachukwu, *et al.*, showing that the majority of the stress levels experienced by people during the COVID-19 pandemic were moderate and high.³¹ Moderate to high-stress levels in this study were also influenced by the participants' demographic backgrounds, where the most dominant age was 26–45 years, and those participants were productive and predominantly employed.³¹ Kaligis, *et al.*, stated that stressful conditions tended to increase during the productive age during the COVID-19 pandemic because the imposition of restrictions on people's mobility, financial burdens, uncertainty about the end of the pandemic, and fears of contracting or transmitting COVID-19 caused anxiety and stress in some communities.³²

Previous studies showed that oral manifestations during COVID-19 infection could be affected by poor oral hygiene.^{12,20} According to Abubakr, *et al.*, moderate to poor oral hygiene significantly increased oral manifestations in patients infected with COVID-19, such as canker sores and halitosis.¹⁴ A study conducted by Sinjari, *et al.*, supports the results of this study that show there is a decrease in the level of oral hygiene when patients are hospitalized due to COVID-19 infection.²⁰

Kartikha, *et al.*, also stated that the cleanliness of the COVID-19 patient's oral cavity affected the oral cavity symptoms experienced by the patient.⁶ The behavior of maintaining oral hygiene while the patient is infected with COVID-19 needs to be improved, especially in terms of using a toothbrush after breakfast, using floss to clean between the teeth, and visits to the dentist that are

rarely made (less than once every six months). Good oral hygiene prevents plaque formation on the surface of the teeth and mucosa, so there is no disturbance in the balance of the oral microbiota. The condition of a healthy oral mucosa also prevents the occurrence of oral symptoms, such as bad breath, canker sores, and dry mouth, that can disturb the comfort of individuals who experience them.³³

Management of Oral Lesions in COVID-19 Patients

Oral lesions in COVID-19, such as loss of taste, mostly decrease and heal without any treatment intervention.¹²⁻¹⁴ To manage symptomatic lesions such as canker sores, a dental professional should be consulted. Improving oral hygiene by brushing twice daily, interdental flossing, and scrubbing the tongue can help maintain the balance of normal oral microbiota to prevent the emergence of canker sores, dry mouth, and halitosis.^{6,17,20}

Conclusion

Based on the results and discussion, it can be seen that oral hygiene can affect the manifestation of the patient's oral cavity, such as white plaque, ulceration, pain, burning sensation, oral mucositis, depapillation of the tongue, dry mouth, halitosis, and loss of the sense of taste. Since oral hygiene is related to the emergence of oral manifestation in COVID-19 patients, it is suggested that dental professionals give dental education on how to improve oral hygiene adequately. It is also suggested that the dental professional focus more on a detailed intraoral examination before initiating any dental procedure on a confirmed or suspected COVID-19 patient.

Abbreviations

COVID-19: coronavirus disease 2019; ACE-2: Angiotensin-Converting Enzyme 2; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2.

Ethics Approval and Consent to Participate

Not applicable.

Competing Interest

The authors declare that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The authors have full access to all the data in the study and take responsibility for the data integrity.

Authors' Contribution

MH and MA conceptualized, investigated, wrote the manuscript, and validated the study. NN, IS, and SU wrote the main manuscript text, and all authors contributed to interpreting the results.

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