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Original Research

# An Analytical Cross-Sectional Investigation into Oral Manifestations Associated with COVID-19 Infection

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***ABSTRACT:***

**Introduction-** The current COVID-19 pandemic has created a huge impact across the globe. Recent literature has reported the occurrence of varied oral lesions in COVID-19 patients in the form of sporadic case reports. This analytical cross-sectional study was carried out to gauge and understand the pattern of oral lesions in qualitative RT-PCR-confirmed COVID-19 patients. **Materials and Methods-** This observational cross-sectional study enrolled all individuals aged 18 and above who received treatment for COVID-19. A meticulous oral examination was conducted using sterilized mouth mirrors and probes, following stringent aseptic precautions. . Exclusions comprised the paediatric population and individuals with systemic conditions affecting the oral mucosa. **Results-** The present cross-sectional study included a total of 600 RT-PCR-confirmed COVID-19 patients, comprising 450 males and 150 females. - The mean age of the patients was 52 years. Among the participants, 120 were asymptomatic, 175 exhibited symptoms of Influenza-Like Illness (ILI), and 105 presented symptoms of Severe Acute Respiratory Infection. **Conclusion-** Patients with severe COVID-19, particularly those with Severe Acute Respiratory Infection (SARI), exhibit a higher likelihood of experiencing oral health issues. This increased probability may stem from the direct impact of the disease, the body's immune response, and a potential decrease in motivation for personal hygiene measures among individuals with more severe cases.

**Keywords**- Covid-19, pandemic, severe acute respiratory disease

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## INTRODUCTION

Corona viruses (CoVs) belong to the subfamily Orthocoronavirinae in the family Coronaviridae, Order Nidovirales. There are four genera within the subfamily Orthocoronavirinae, namely Alphacoronavirus (α-CoV), Betacoronavirus (β-CoV), Gammacoronavirus (γ-CoV) and Deltacoronavirus (δ-CoV) [1,2]. The CoV genome is an envelope, positive-sense, single-stranded RNA with a size varying between 26 kb and 32 kb, the largest genome of known RNA viruses. Both α- and β-CoV genera are known to infect mammals, whilst δ- and γ-CoVs infect birds. Two recent outbreaks of viral pneumonia caused by β-CoVs are severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). In 2002, an outbreak of SARS was first reported in China and then spread quickly worldwide, resulting in hundreds of deaths with an 11% mortality rate.[3] In 2012, MERS first emerged in Saudi Arabia and subsequently spread to other countries, with a fatality rate of 37% . In both of these epidemics, the viruses likely originated from bats and then infected humans through other intermediate animal hosts, e.g. the civet (*Paguma larvata*) for SARS-CoV and the camel for MERS-CoV.[4,5]Human-to-human transmission of the virus via respiratory droplets has already been established. The median incubation time generally ranges from 4 to 5 days and can extend for maximum up to 14 days.[6,7] There are various symptoms associated with COVID-19 infection which includes influenza-like illness (ILI) and severe acute respiratory infection (SARI). These symptoms include fever, dry cough, sore throat and respiratory rate more than 30 cycles per min and $SpO_2$ less than 90%

Involvement of oral cavity by COVID-19 may be suggested to have multifactorial aetiology with different compounding mechanisms. The oral cavity forms a gateway to the external environment and plays a major role in the spread of SARS-CoV-2. Extensive

research has identified the role of a metallopeptidase enzyme, i.e. angiotensin-converting enzyme 2 (ACE-2) as a functional receptor for SARS-CoV-2.[8,9] Apart from localisation in the other parts of the body, ACE-2 expression is found extensively in the basal layer of the non-keratinizing squamous epithelium of nasal and oral mucosa as well as nasopharynx .The psychological impact of COVID-19 leads to panic behaviour with feelings of hopelessness and negative outcomes, and there is a complete shift of focus from daily hygiene maintenance further worsening the oral health. Drugs therapy used in the treatment of the COVID-19 like remdesivir, hydroxychloroquine, protease inhibitors and interferon regimen was also postulated as reasons although they have reported minimal effect on oral health, except Lopinavir which may cause taste alteration. An analytical cross-sectional study was designed to comprehensively assess the oral condition of individuals with COVID-19 and to establish correlations with the severity of the disease.

## MATERIALS AND METHODS

This observational cross-sectional study enrolled all individuals aged 18 and above who received treatment for COVID. The study excluded the paediatric population and patients with any other systemic conditions. A meticulous oral examination was conducted using sterilized mouth mirrors and probes, following stringent aseptic precautions. All COVID patients aged 18 and above who underwent treatment were included in the study. Exclusions comprised the paediatric population and individuals with systemic conditions affecting the oral mucosa.

The examination involved recording detailed findings using a comprehensive performa, encompassing both soft tissue and hard tissue assessments. Patients were queried about their perception of xerostomia (dry mouth), followed by a soft tissue examination to identify signs of inflammation, spontaneous bleeding, erythema, petechiae, and ulcers. Hard tissue examination involved assessing the presence of exposed or necrosed bone and any pus discharge. A rigorous clinical examination was preceded by a thorough history to confirm that only new lesions appearing in the prodromal and disease phases of COVID-19 patients were considered. Symptom-positive patients underwent additional verification, with those having a previous history of oral lesions strictly excluded. Positive findings were documented in the Performa without further attempts to categorize them.

## RESULTS

The present cross-sectional study included a total of 600 RT-PCR-confirmed COVID-19 patients, comprising 450 males and 150 females. The mean age of the patients was 52 years. Among the participants, 120 were asymptomatic, 175 exhibited symptoms of Influenza-Like Illness (ILI), and 105 presented symptoms of Severe Acute Respiratory Infection (SARI). A majority of the patients reported no deleterious habits related to tobacco consumption (98), while the remaining individuals had habits such as consuming smokeless tobacco (35) in various regional forms of pan and supari (17), gutkha chewing (18), and bidi/cigarette smoking (32). The oral examination was conducted at an average of 7 days from the date of testing positive for COVID-19. As such there was no significant correlation found between age, gender or habit history with the oral manifestations of COVID-19.

## DISCUSSION

This observational cross-sectional study enrolled all individuals aged 18 and above who received treatment for COVID. The study excluded the paediatric population and patients with any other systemic conditions known to affect the oral mucosa. A meticulous oral examination was conducted using sterilized mouth mirrors and probes, following stringent aseptic precautions. All COVID patients aged 18 and above who underwent treatment were included in the study. Exclusions comprised the paediatric population and individuals with systemic conditions affecting the oral mucosa. Understanding the pattern of oral manifestations of COVID-19 infection is of utmost importance, as oral lesions can compromise the nutrition of the patients, their psychological well-being, quality of life and final outcome, and it may also work as a diagnostic-screening tool due to easy accessibility of the oral cavity to health care workers.

In this study, the prevalence of taste alteration was notably higher compared to other manifestations. In cases where both taste and olfactory disturbances coexist, the primary etiology is presumed to be an underlying olfactory disturbance. According to research, the SAR-CoV-2 virus binds to angiotensin-converting enzyme 2 (ACE2) receptors, which are highly expressed in the epithelial cells on the tongue. Consequently, the alteration in taste perception could be linked to the inactivation of ACE2 receptors present on the taste buds.[12]

Xerostomia was found in patients who could be attributed to either poor hydration, prolonged antibiotic course or an existing Candida infection. Atypical erythematous lesions on the buccal mucosa adjacent to the molar region were isolated, solitary ulcers resembling minor aphthae. Initially, these lesions are asymptomatic and begin as inconspicuous isolated erythematous areas, which then progresses to a diffuse erythematous area with irregular borders. Some patients complained of burning sensation localized to the erythematous region. The burning sensation could be attributed to the persistent inflammatory processes or alterations in the immune response or frequent use of antibiotics. Although the recent literature which included mainly case reports mentioned about the COVID-19-infected patients with oral manifestations, none of the studies till date has

supported or has sufficient evidence to correlate the exact cause of such manifestations.[11,6] These lesions could be a result of direct viral replication process or could be because of increased probability of opportunistic injuries caused by products of systemic deterioration. According to Ciccarese et al. 2020, the presence of cutaneous or oral mucosal petechiae could be possibly related to SARS-CoV-2-induced thrombocytopenia.[10]

The study observed prevalent oral manifestations, with the buccal mucosa being the most affected by erythematous patches, ulcers, and white patches, followed by the labial mucosa and palate. Another common occurrence was depapillation of the tongue or atrophic glossitis in the study population. While histopathological confirmation was lacking, a plausible hypothesis suggests an association with Candida. Given its status as an oral commensal, Candida may act as an opportunistic pathogen in immunocompromised patients.[13] The administration of antibiotics to patients might contribute as an additional factor to atrophic glossitis with a potential candidal origin. Notably, research by Petrescu et al. (2020) highlighted a high expression of ACE2 in the epithelial cells of oral mucosa, suggesting an increased susceptibility to early infections.[14,15]Inflammation was seen at the ductal orifice, specifically in Stensen's ducts .Additionally, there were instances of inadvertent tooth mobility in hard tissues. Notably, none of the patients exhibited vesiculobullous lesions, pus discharge, or clear indications of osteomyelitis. Oral lesions were most frequently observed on the tongue in this study, followed by the buccal mucosa, labial mucosa, palate, and least commonly in the gingiva.

In this study, asymptomatic COVID-19 patients were less likely to exhibit oral manifestations compared to patients with ILI or SARI. Furthermore, among patients with ILI, the odds of developing oral lesions were lower than those with SARI. This suggests a correlation between the severity of the disease and the likelihood of presenting with oral findings. When comparing disease severity among the three groups, alterations in taste, xerostomia, and ulcers showed similar occurrences. This may be attributed to factors such as intubation, prolonged hospitalization, and compromised oral hygiene observed in individuals with SARI. Until now, there has been a notable absence of studies with a large and diverse sample size encompassing varying severity levels among COVID-19 patients. Existing literature has primarily consisted of case reports. The objective of our cross-sectional study was to examine the oral manifestations in COVID-19 patients. However, ethical considerations, financial constraints, and the strain on healthcare systems prevented further attempts at histopathological diagnosis of the observed lesions. A more robust confirmation of the lesions as part of SARS-CoV-2 infection could have been achieved through swabs taken from the lesion site and subsequent evaluation using RT-PCR.

## CONCLUSION

Patients with severe COVID-19, particularly those with Severe Acute Respiratory Infection (SARI), exhibit a higher likelihood of experiencing oral health issues. This increased probability may stem from the direct impact of the disease, the body's immune response, and a potential decrease in motivation for personal hygiene measures among individuals with more severe cases.

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