REVIEW ARTICLE

POST-COVID ORAL COMPLICATIONS: A REVIEW

Rahul Kumar Raman[1], Vimal Arora[2]

ABSTRACT

Coronavirus disease 2019 (COVID-19) has been testing the world health care system since its arrival. Globalization has introduced the diseases from China to the world and there have different morbidity and mortality rates depending on different regional and personal hygiene protocols. World health Organization (WHO) launched a SOLIDARITY Clinical Trial just to manage the overall mortality, need of assisted ventilation and duration of hospital stay; however it had little or no effect as intended, only corticosteroids were proven effective against severe and critical cases. Hence, much focus has been given to early symptoms and testing. Upon infection, COVID-19, symptomatic cases have demonstrated flu-like symptoms mainly aggravating to fulminant pneumonia and acute respiratory distress in several cases. There are several oral symptoms which have been reported as well. Symptoms of altered taste sensation has been a relatively common finding, while other symptoms that may be caused by SARS-COV-2 infection directly; or indirectly affect the oral mucosa due to debilitating general health and/or use of therapy drugs. These additional symptoms have been reported as dry mouth, oral ulcers, periodontal diseases and superinfection by bacteria and fungi. This review reiterates these symptoms as have been reported in multiple studies.

Keywords: *COVID-19, Coronavirus, SARS-COV-2, Oral manifestations, Post-COVID complications.*

INTRODUCTION

Severe Acute Respiratory Syndrome-Corona Virus 2 (SARS-COV-2) has been the cause of ongoing global pandemic COVID-19.[1] The causative agent, initially named as 2019-nCOV by World Health Organization, was first identified on 7 January, 2020 being responsible for multiple unknown pneumonia cases in Wuhan city in China. Nucleotide sequencing of the viral particle revealed its 79% similarity with Severe Acute Respiratory Syndrome – Corona Virus (SARS-COV), hence due to similarities on clinical case presentation and molecular structure, it was renamed as SARS-COV-2. This virus belongs to genera, Betacononavirus descending from the family of Coronaviridae and subfamily Coronavirinae. It is seventh discovered member of novel human infecting coronaviruses.[2] Other two viruses in this genera are SARS-COV and Middle East respiratory syndrome Coronavirus (MERS-COV), which are similarly zoonotic and fatal in nature and utilize bats as natural reservoir whilst human are the terminal host.[1]

COVID-19 has been highly infectious allowing it to spread throughout the world in short time. The basic reproductive number (R_0) which determines the average secondary infections resulting from a primary case has been variable depending on local and personal safety measures. In India, R_0 was 3.2 in first week of March, then stabilized to 1.3 in few weeks after government regulations took place.[3] As SARS-COV-2 primarily travel through salivary droplets; main mode of transmission of pathogen has been person-person to contact, whether after directly by catching the infected persons moisture while talking, coughing or sneezing or indirectly through fomites that can carry the virus particle and capable to sustain it for 9h to 9days on some surfaces. Hence, maintenance of personal hygiene and social distancing has been very essential to bring down the R_0 and infection rate in the fight against global medical emergency caused by SARS-COV-2.

Once infected, Corona virus travel through the respiratory tract and primarily infect the lungs presenting symptoms of mild flu such as dry cough, fever and tiredness. These symptoms often aggravate to fulminant pneumonia or fatal respiratory distress in some cases.[4] The lower respiratory tract infection has been accompanied by certain oral manifestations such as chemosensory alterations and xerostomia. The possible cause for xerostomia has been attributed SARS-COV-2 using angiotensin-converting enzyme 2 (ACE2) as receptor for its entry into the target epithelial cell and replication.[5] Human salivary glands, particularly the minor salivary gland show high expression of ACE2 thereby promulgating saliva as viable diagnostic marker for COVID-19 over nasopharyngeal swabs.[6]

Mathematic models suggest that 40-81% population of the world may have been infected so far. Infection fatality

1. MDS (Oral Pathology and Microbiology), Consultant, Research & Publication, Clove Dental, India.

2. MDS (Prosthodontics), FDS, RCPS, Chief Clinical Officer, Clove Dental, India.

Corresponding Author
Dr Rahul Kumar Raman
Email: rahulraman2007@gmail.com.

rate, suggestive of chances of death due to infection, has been calculated as 0.27% across 51 locations worldwide.[7] Hence while all the effort has been directed to understand the general health behavior, oral health manifestations have been overlooked and poorly understood. These complications have been direct or residual due to deteriorating general health and supplement treatment modalities. The reported cases have highlighted the development of vesiculobullous lesions, bacterial superinfection, inflammation and acute periodontal lesions.[8]

GUSTATORY IMPAIRMENT

Most commonly reported symptoms with Oral manifestations is alteration in taste sensation: dysgeusia, amblygeusia/hypogeusia or ageusia. High expression of ACE2 in tongue is attributed to possible loss of taste sensation with SAR-COV-2 infection. About 47.2% of cases among 20 patients in Mortazavi *et al*. study showed having amblygeusia. Male and female percentage was found to be 36.5% and 57.1% respectively.[9] Amorim dos Santos *et al*. reported similar results where 45% among the pooled patient data (10,228) were suffering from taste disorders. It was further divided into 38% having dysgeusia, 35% having hypogeusia and 24% having ageusia.[10] Silva Pedrosa *et al*. reported higher 71% (42/59) cases having loss of taste in one of the study.[6] Sinjari *et al*. reported 25% participants with dysgeusia.[5] In a cross-sectional study, Giacomelli *et al*. reported only 10.2% with taste disorders (8.5% with dysgeusia and 1.7% with ageusia) where 91% reported taste alteration before hospitalization.[11] Sighting various studies it is evident that gustatory impairment was invariably seen in several studies with significant number of patient showing altered sensation. Hence gustatory symptoms is considered as a complication with very early signs indicative of COVID-19 related chemosensitive disorder. It may also play a role in early diagnostic marker facilitating early detection and isolation in positive cases.

XEROSTOMIA

Saliva is an essential component that control oral microflora. Reduced salivary flow is likely to assist in other opportunistic infections to flourish. Mortazavi *et al*. reported 46.3% cases (46.2% male, 46.4% female) with xerostomia.[9] While reduced salivary flow can be seen with poor oral hygiene, adverse drug habits, various psychological states and comorbidities like diabetes neural disorders and cardiovascular problems.[5-6] Sinjari *et al*. reported xerostomia in 30% cases during period of hospitalization, where only 15% percent were affected with diabetes, 15% obesity, 25% thyroid disorders and 39% hypertension. According to Sinjari this correlation is very important as rate of xerostomia differ in consideration with patient's medical condition or irrespective of patients therapy modulation.[5] SARS-COV-2 infection of salivary gland speculated due to its association with ACE2 protein as target molecule. ACE2 expression form minor salivary glands has been demonstrated to be higher than lungs in COVID-19. [12] The direct infection of salivary glands via ACE2 proteins can also lead to its inflammation hence reducing salivary flow.[6]

ORAL MUCOSAL LESIONS

COVID-19 has been associated to appearance of oral mucosal lesions in form of irregular ulcers, petechiae, erythematous plaque and small blisters presented on keratinized and non-keratinized mucosal sites of buccal mucosa, tongue, lips, gingiva and palate. While mild COVID cases have presented with oral lesions along with respiratory symptoms, patients under medication and hospitalization developed oral manifestations 7 to 24 days post initial symptoms. Co-infections from Herpes simplex virus, Cytomegalovirus, Treponema pallidum and Epstein-Barr virus were rule out from diagnosis after testing in one study; however, other infections autoimmune and inflammatory disorder were not excluded.[10] Dziedzic and Wojtyczka, suggested that impaired immune response can cause oral ulceration through other factors such as xerostomia, bacterial and viral superinfection.[13] Recurrent Oral ulcers have been reported as possible inaugural symptom of COVID-19. [6] Sinadinos and Shelswell reported 3 cases (1 confirmed, 2 suspected COVID-19) with oral lesions on palate in 2 cases and tongue in 1 case. The palatal lesions resembled herpetic recurrent stomatitis in the absence of previous herpetic infection; lesions resolved with antiseptic treatment in 7d and 10d. The patient with tongue ulcer was hospitalized where oral examination was delayed until patient develop desquamative gingivitis and formed blisters on tongue. Hence authors stated there is possibility of COVID induced oral ulceration; and there is need of early check on oral manifestations for adequate prevention and management.[14] Amorim dos Santos reported one case with persistent white plaque on dorsum of the tongue associated with small ulcers representing late stage herpetic oral lesions, along with geographic tongue and approximately 1 cm nodule on lower lip.[4] Corchuelo and Ulloa reported a 40-year-old female with petechiae on lower lip, canker sores on lateral side of tongue and dark brown pigmentation on attached gingiva of 34. Mortazavi *et al*. reported oral ulcers in few of its studied cases with observation that all reported cases experienced pain in oral cavity and oral mucosal lesions before seeking medical advice.[9] Thus, several authors have affirmed the possibility of oral mucosal lesions arising due to SARS-COV-2 infection that may be primary or due to side effects of drug regime.

PERIODONTAL POCKETS

Sampson *et al*. literature review on oral hygiene and COVID-19 infection signified sharing of ecological community between oral cavity and lung. Pathogenic bacteria from decayed tooth or cytokines such as IL1 and TNF released form compromised periodontal tissue can get aspirated with saliva into the lower respiratory tract provoking infections or inflammation in turn. Thus the authors recommended maintenance of oral hygiene to avoid bacterial superinfections.[2] Jay Patel and Julian Woodley reported a case diagnosed with necrotizing gingivitis in a COVID-19 and made a prediction of spontaneous rise in prevalence of necrotizing periodontal disease with COVID-19. They reasoned with abnormally high occurrence of Prevotella Intermedia along with Streptococci, Fusobacterium, Treponema and Veillonella in such cases suggesting them as major contributing factor for several acute periodontal lesions.[16]

FUNGAL CO-INFECTION

A recent observation from Senior ENT surgeon from Ganga Ram hospital, New Delhi suspected COVID-19 triggered Mucormycosis in 12 cases causing high morbidity and mortality. Thus advising early symptomatic diagnosis and antifungal therapy as remedy measures.[17] De Song *et al*. study on fungal co-infection COVID-19 concluded high chance of such infections due to overall immunocompromised state and pointed to the missed or misdiagnosed opportunity while reporting such cases; hence, they recommended a diagnostic and therapeutic pathway to assist clinicians and laboratory experts.[18]

CONCLUSION

The growing pandemic include patients who are tested and getting required treatment as well as wide number of patients who are asymptomatic and unaware of their infection. Direct complications of SARS-COV-2 is likely to be seen in all kind of patients, but as suspected several complications might be secondary to infection and stewardship strategies. Post-COVID oral complications lies in the midst of possible resulting factor in each case of either neurosensory or chemosensitive disorders, oral mucosal lesions or superinfections. Hence it needs further analysis and observations for definite answers ahead.

BIBLIOGRAPHY

1. **Harapan H, Itoh N, Yufika A, Winardi W, Keam S, Te H, Megawati D, Hayati Z, Wagner AL, Mudatsir M.** Coronavirus disease 2019 (COVID-19): A literature review. Journal of Infection and Public Health. 2020 Apr 8.
2. **Sampson V, Kamona N, Sampson A.** Could there be a link between oral hygiene and the severity of SARS-CoV-2 infections?. British dental journal. 2020 Jun;228(12):971-5.
3. **Marimuthu S, Joy M, Malavika B, Nadaraj A, Asirvatham ES, Jeyaseelan L.** Modelling of reproduction number for COVID-19 in India and high incidence states. Clinical Epidemiology and Global Health. 2020 Jun 30
4. **dos Santos JA, Normando AG, da Silva RL, De Paula RM, Cembranel AC, Santos-Silva AR, Guerra EN.** Oral mucosal lesions in a COVID-19 patient: new signs or secondary manifestations? International Journal of Infectious Diseases. 2020 Jun 9.
5. **Sinjari B, D'Ardes D, Santilli M, Rexhepi I, D'Addazio G, Di Carlo P, Chiacchiaretta P, Caputi S, Cipollone F.** SARS-CoV-2 and Oral Manifestation: An Observational, Human Study. Journal of Clinical Medicine. 2020 Oct;9(10):3218.
6. **Pedrosa MD, Sipert CR, Nogueira FN.** Salivary glands, saliva and oral findings in COVID-19 infection. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2020;20.
7. **Ioannidis J.** The infection fatality rate of COVID-19 inferred from seroprevalence data. medRxiv. 2020 Jan 1.
8. **Patel J, Woolley J.** Necrotizing periodontal disease: Oral manifestation of COVID 19. Oral diseases. 2020 Jun 7.
9. **Mortazavi H, Rezaeifar K, Nasrabadi N.** Oral Manifestations of Coronavirus Disease-19: A Mini-review. Open Access Macedonian Journal of Medical Sciences. 2020 Sep 15;8(T1):286-9.
10. **Amorim dos Santos J, Normando AG, Carvalho da Silva RL, Acevedo AC, De Luca Canto G, Sugaya N, Santos-Silva AR, Guerra EN.** Oral Manifestations in Patients with COVID-19: A Living Systematic Review. Journal of dental research. 2020 Sep 11:0022034520957289.
11. **Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, Rusconi S, Gervasoni C, Ridolfo AL, Rizzardini G, Antinori S.** Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. Clinical Infectious Diseases. 2020 Mar 26.
12. **Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, *et al*.** High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci. 2020;12(1):8. https://doi.org/10.1038/s41368-020-0074-x
13. **Dziedzic A, Wojtyczka R.** The impact of coronavirus infectious disease 19 (COVID 19) on oral health. Oral Diseases. 2020 Apr 18.
14. **Sinadinos A, Shelswell J.** Oral ulceration and blistering in patients with COVID-19. Evidence-based dentistry. 2020 Jun;21(2):49-49.
15. **Corchuelo J, Ulloa FC.** Oral manifestations in a patient with a history of asymptomatic COVID-19: Case report. International Journal of Infectious Diseases. 2020 Nov 1;100:154-7.
16. **Patel J, Woolley J.** Necrotizing periodontal disease: Oral manifestation of COVID 19. Oral diseases. 2020 Jun 7.
17. Express News Service. Doctors flag Covid-linked deadly fungal infection after Ganga Ram hospital sees 12 cases in 15 days. Available From: https://indianexpress.com/article/cities/delhi/covid-19-fungal-infection-black-fungus-mucormycosis-7105025/ [Accessed 22nd December 2020]
18. **Song G, Liang G, Liu W.** Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. Mycopathologia. 2020 Jul 31:1-8.