

COVID-19 and oral implications: An updated review

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Abstract

The emerging (COVID-19) pandemic is a global health disaster, caused by infection with severe acute respiratory syndrome coronavirus-2. The disease spreads at an alarming rate all over the world and presents a range of disease manifestations including asymptomatic, mild, moderate and severe symptoms irrespective of age groups. Most patients with severe symptoms exhibit underlying comorbidities such as diabetes, hypertension and obesity. Alternatively, there is an existing evidence for an association between oral health and nonoral systemic diseases. Since the oral cavity is a significant pool for many respiratory pathogens, patients with oral infections are more likely to develop pneumonia as a complication. Therefore, we emphasize that the oral hygiene status has a great impact on the recession and progression of oropharyngeal and respiratory diseases.

Keywords: Comorbidities, COVID-19, oral health, respiratory complications

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INTRODUCTION

The highly contagious viral disease COVID-19 or the severe acute respiratory syndrome is declared as a global pandemic by the World Health Organization (WHO) on March 11, 2020.^[1] A novel coronavirus was later recognized as the causative agent, provisionally named 2019 novel coronavirus (2019-nCoV). Coronaviruses (CoVs) are a group of viruses belonging to the family called Coronaviridae. The subfamily Coronavirinae consists of three genera, alpha coronavirus, beta coronavirus and gamma coronavirus. The spread of infection of severe acute respiratory syndrome CoV-2 (SARS-CoV-2) is either through direct transmission or inhalation of droplets or due to contact with the oral, nasal and eye mucus membranes.^[2] Genomic sequencing and phylogenetic research methods

have supported that the COVID-19-causing coronavirus is a betacoronavirus that belongs to the same subtypes as SARS virus but exhibits a different variant group. The receptor-binding gene site appears to coincide with that of the SARS-CoV and thus suggesting that the same receptor would be used for entry into the cell.^[3]

COVID-19 manifestations can range from asymptomatic state to acute respiratory distress syndrome and multiorgan dysfunction. Most commonly reported are flu-like symptoms of fever, dry cough, malaise, fatigue, myalgia and diarrhea.^[4] Certain risk factors for COVID-19 disease have been reported by the WHO and the Centers for Disease Control and Prevention (CDC) include diabetes, hypertension, aging, immunodeficiency and cardiovascular

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diseases.^[5] These risk factors are proposed to have a greater impact with the increased severity of COVID-19; however, there are various other comorbidities that could also be involved in affecting the prognosis. Persons with chronic lung disease, bronchial asthma, obesity, chronic kidney disease and liver disease are also at higher risk. A recent study lists hypertension, obesity and diabetes as the three major underlying conditions with the most unfavorable outcomes in COVID-19 patients requiring hospitalization.^[6] Recently, many studies have revealed the association between oral health status and systemic diseases including systemic infections, cardiovascular diseases and respiratory diseases.^[7] In addition, the impact of good oral hygiene on the reduction of risk in viral acute respiratory diseases has been reported in many studies.^[8] This article gives a bird's eye view about the impact of good oral hygiene status on the recession of oropharyngeal and respiratory diseases.

PATHOGENESIS

Recent studies have reported spike in the mortality rate of COVID-19 ARDS approaching 40%–50%.^[9] The rest of the cases have exhibited deterioration due to aggressive counteracting of the immune system, which is termed as “cytokine storm syndrome”. Certain cytokines such as tumor necrosis factor (TNF), interleukin-6 (IL-6) and IL-1 β when released at increased levels damage host cells to some extent and result in localized edema. During this phase, innate cytokine response could be a predictive factor for the disease progression.^[10] These responses may further stimulate the synthesis of inflammatory mediators and lead to multiorgan failures such as the kidneys and heart due to the hazardous complications of vascular permeability. In addition, a serum marker of hyperinflammation named as C-reactive protein (CRP) is generally elevated. Recent studies have revealed that the patients with elevated levels of CRP have been reported to show a poor prognosis with COVID-19 due to acute inflammatory pathogenesis.^[11] Moreover, the virus affects intestinal lymphocytes, hepatic cells, renal cells and T-lymphocytes inducing the apoptosis of T-cells ensuing in complete collapse of the immune system.^[12]

ORAL HYGIENE AND COVID-19 SEVERITIES

The oral cavity is well represented as “the window to general health.”^[13] Certain systemic conditions such as atherosclerosis, pulmonary infections, diabetes mellitus, osteoporosis and kidney diseases are influenced by oral hygiene status. Patients with poor oral hygiene and periodontal infections tend to suffer from recurrent

gingival inflammation and bacteremia, which activate the host inflammatory response.^[14] This chronic inflammatory condition elicits the release of multiple proinflammatory cytokines such as CRP, TNF- α , IL-1 β and IL-6, in association with bacteremia. These responses tend to increase the susceptibility of the vascular endothelium for injury, thus leading to atherosclerosis. The recent studies have established that the periodontal infection and poor oral hygiene have a strong connection with the risk of acute myocardial infarction and coronary heart disease.^[15] Researchers have suggested that periodontal disease ought to be considered as a major impediment of diabetes. There is better evidence to prove that prolonged hyperglycemia has negative effects on the heart, kidneys, eyes and peripheral nerves.^[16] This condition leads to the release of advanced glycation end products which exhibit a systemic impact that results in the prolonged excretion of cytokines causing inflammation and connective tissue loss.^[17]

Increased cytokine release is another important characteristic feature of severe COVID-19 cases, which exhibit an extreme elevation in inflammatory cytokines including IL-1 β , IL-2, IL-6, IL-7, IL-8, IL-10, granulocyte macrophage-colony stimulating factor (CSF), granulocyte-CSF, monocyte chemotactic protein 1, macrophage inflammation protein-1 α , IFN- γ and TNF- α , 2, 3, 12, and 15 establishing a “cytokine storm.”^[18] A spectacular increase in these cytokines levels over a short time period leads to a series of adverse reactions in the human body which initiate viral sepsis and inflammation-mediated lung injury, leading to respiratory distress, organ failure, shock and potentially death.^[19] Furthermore, in severe COVID-19 cases, elevated levels of inflammatory cytokines may result in shock and multiple organ failure. The constant release of increased levels of cytokines such as CXCL10, CCL7 and IL-1RA is related to lung dysfunction as well as poor prognosis, resulting in fatal outcome.^[20] Patients with poor oral hygiene status can elicit such immune responses which may result in the progression of thromboembolic complications. In other words, good oral hygiene and regular dental visits reduce the chances of incidence and progression of pulmonary diseases.

ORAL MANIFESTATIONS IN COVID-19

Literature reveals that the patients with COVID-19 disease have presented features such as ageusia, nonspecific anosmia and hyposalivation.^[21] Few reports have stated the presence of certain intraoral manifestations such as desquamative gingivitis, herpetic form ulcers on attached gingiva and tongue with multiple irregular ulcers on the dorsal surface in the oral cavity.^[22] Besides these,

the enlargement of submandibular glands and cervical lymph nodes have been noticed. The presence of ACE2 receptors on target cells could be the possible reason. These receptors help in the binding of SARS-CoV-2 virus spike proteins to the cells which pave way for consequent infections.^[23] The presence of ACE2 expressing cells in large numbers in the epithelial cells of the oral and nasal mucosa attributes to ageusia and anosmia, respectively.^[24] The oral conditions presented by some patients in few studies support the hypothesis that they are extremely indicative of secondary lesions ensuing due to the deterioration of systemic health or due to therapeutic measures for COVID-19. In COVID-19 patients, the presence of some oral manifestations including ageusia, traumatic ulcers, petechiae, candidiasis, HSV-1 infection and geographic tongue need to be considered. Various associated therapies in COVID-19 infection could perhaps contribute to adverse consequences regarding oral health such as unexplained oral ulcerations, recurrent oral herpes simplex virus (HSV-1) infection, opportunistic fungal infections, fixed drug eruptions, ageusia and xerostomia as a result of the altered immune system and its responses.^[25]

Among the opportunistic fungal infections, mucormycosis though rare yet is the rising fungal infection in COVID-19 cases. The causative fungi belong to Mucorales. Manifestations include cutaneous, mucosal, sinusitis, pulmonary, gastrointestinal or sometimes dissemination. These fungi affect the immunocompromised patients those that are on high-dose glucocorticoids, hemodialysis and uncontrolled diabetes mellitus.^[26] In a healthy individual, the spores and hyphae are attacked by immune cells and destroyed by monocytes, macrophages and polymorphonuclear phagocytes. When patients exhibit diminished immune status with low phagocyte count, altered phagocyte function or uncontrolled diabetes mellitus, they become progressively susceptible to the invasive type of mucormycosis.^[27]

OROFACIAL ADVERSE EFFECTS FOLLOWING COVID-19 VACCINES

Certain medication-related events such as adverse drug reactions (ADRs) are possibly life-threatening consequences due to the usage of medicines as well as vaccines. Hence, it is significant to recognize the adverse events on time to reduce the conceivable harm.^[28] Therefore, health professionals including dentists should be primed to diagnose orofacial ADRs probably being drug induced. The clinical trials and the development of effective vaccines against SARS-CoV-2 virus have been extremely progressing.^[29] At present, two RNA-based COVID-19 vaccines have

been permitted for emergency use and authorized for marketing by the regulatory agencies in Europe and America and are being used all over the world. Of late, another vaccine (AZD1222, Oxford–AstraZeneca) has been granted for use in the UK. Recent literatures have revealed the data on preliminary efficacy and safety for both BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines.^[30] As several billion doses of vaccination need to be administered, it is possible that an ample number of adverse events to be reported. The knowledge of the dentist regarding orofacial manifestations will enhance the diagnosis, management and reporting of vaccine-related adverse events. Recent study shows that COVID-19 vaccines have possible yet rare orofacial side effects including anaphylaxis associated with facial swelling, Bell's palsy and swelling of the face, lips or tongue. In addition to orofacial manifestations and systemic ADRs with anaphylaxis, both of the vaccines were seen associated with acute peripheral facial paralysis. It has been reported that there were two serious adverse events regarding facial swelling seen only with respect to mRNA-1273 vaccine recipients. The onset of the adverse event was reported 2 days after vaccine administration and was probably related to vaccination according to MHRA (UK).^[31] Finally, it has been concluded that both BNT162b2 and mRNA-1273 COVID-19 vaccines are associated with ADRs including orofacial manifestations with heterogeneity expression all over the world.

CONCLUSION

Patients with COVID-19 exhibit a range of disease manifestations including asymptomatic, mild, moderate and severe symptoms and high cytokine levels, which can be considered potential biomarkers for disease progression. The specific immune responses of COVID-19 tend to establish cytokine storm and thromboembolic complications which can further lead to multiple organ dysfunctions. In addition to this, compromised immune status leads to the rise of certain opportunistic infections such as mucormycosis which is rare yet extremely exhibit fatal outcome. On the other hand, poor oral hygiene can contribute to altered immune responses. Therefore, improving oral hygiene and reducing gingival and periodontal inflammation may reduce the risk of complications arising due to COVID-19 disease. Since knowledge about this concept and orofacial adverse effects due to vaccination is brainstorming, further researches are required to report cases of COVID-19 seen associated with oral diseases to add to the pool of knowledge on a comprehensive level.

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Conflicts of interest

There are no conflicts of interest.

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