

COVID-19 and Periodontitis: A Reality to Live with

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ABSTRACT

Background: Coronavirus disease-19 (COVID-19) is a recent pandemic that is advancing at a rapid rate. The future course of the disease includes severe respiratory infection and also leads to death if unattended. Meticulous measures are necessary before attending any patient. The dental operatories and the clinic surroundings must be well sanitized so as to prevent the spread of pandemic.

Aim and objective: This review discusses in brief about the pathophysiology and course of COVID-19. Further, we discussed in detail the management aspects of patients in periodontal perspective and the sanitization procedures required for the dental clinic.

Review results: The SARS coronavirus enters the human circulation via the angiotensin-converting enzyme (ACE) receptors which are also found on the oral mucosal surfaces. Furin and Cathepsin L are the pro-inflammatory molecules released during pathogenesis of periodontitis and mediate the molecular pathways that help the virus invade into the host. The clinic set-up should be modified to best suit the pandemic conditions. This includes the three phases, i.e., phase I: preparatory phase; phase II: implementation phase; and phase III: follow-up. The patient management is explained based on the emergency needs of the patient based on the recent AAP classification of periodontal diseases and conditions 2017 as emergency, urgent, and elective treatment needs which have been explained in detail.

Conclusion: It can be strongly concluded that there is direct relationship between oral health and systemic health. The treatment procedures and sanitization protocols must be definitely modified. Further consensus and systematic reviews help us arriving at a more standardized protocol.

Clinical significance: This review would help clinicians modify the way they treat patients in the clinic and provide better services depending upon the emergency needs of the patient.

Keywords: Coronavirus disease, Pandemic, Periodontitis.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19), the etiologic agent being novel coronavirus SARS-CoV-2 (severe acute respiratory syndrome), began in the Hubei Province of China with first case recorded on December 31, 2019. It was reported as a simple flu and pneumonia-like symptoms. Later, on March 11, 2020, after observing the nature of the virus and its course, the World Health Organization (WHO) announced it as pandemic.¹ There are many speculations about the fatality and mortality rates of COVID-19. According to WHO, as of August 18, 2020, there are a total of 21.8 million recorded cases of COVID-19 of which 77,300 cases showed deaths.

The basic structure of coronavirus is halo spherical comprised of spike proteins and a positive sense single-stranded RNA. The virus is enclosed in multiprotein covering called nucleocapsid which in turn is covered by a glycoprotein layer called as envelope. This virus has six different subtypes of which only two types, i.e., OC43-like and 229E-like, are the ones that belong to or affect humans. The size of the virus ranges between 0.06 and 0.14 μm with the spike protein length varying between 9 and 12 nm. It is this spike protein that interacts with the cell surface receptors (angiotensin-converting enzyme 2) on the human cells.^{2,3}

Experts in the field of airborne respiratory diseases and particles have claimed the evidence of air-borne transmission which can cause losses of many lives.⁴ Infected patients present with common symptoms such as headache, sore throat (pain in the throat), hyposmia or microsmia (reduced ability to smell), hypogeusia (difficulty in sensing taste), dyspnea (difficulty in breathing), diarrhea, and in severe cases pneumonia (inflammation of the alveolar bags), pulmonary edema

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(accumulation of fluid in the respiratory organs), ARDS, multiple organ failure, and death^{5,6}

Since the link between respiratory diseases and periodontal diseases is known, the present review considers the possible link between COVID-19 and periodontal diseases.

PERIODONTAL DISEASE AND COVID-19: AN UNSOLVED LINK?

Periodontal disease, which has an intricate multifactorial pathophysiology with the literature claims of immune-mediated pathogenesis, has been regarded as the silent pandemic since long. Several biochemical studies on gingival tissues have shown

the presence of cells that secrete interleukin 17 in the sera of subjects having both gingivitis and periodontitis when compared to non-affected individuals.⁷ Incidentally, metagenomic analyses often reported high quantities of cariogenic and periodontopathic bacteria in subjects suffering from COVID-19 infection.⁸

There exists a complex microbial community in the mouth. Poor oral hygiene favors an increased amount of pathogenic oral bacteria and an environmental shift to dysbiosis leading to periodontal disease with micro-ulcerations in the sulcular epithelium and thereby damaging the periodontal tissues and rendering the individual more susceptible to bacteremia.⁹ These common pathophysiological pathways of inflammatory response point to a hypothetical link between periodontal disease and COVID-19-related adverse outcomes.

Portal of Entry

SARS-coronavirus-2 expresses high affinity for angiotensin-converting enzyme 2 receptors.¹⁰ The literature has evidence for the presence of these specific receptors even in oral mucosal tissues, such as the tongue, buccal mucous membrane, and the epithelium of gingiva.¹¹ Thus, entry through oral mucosa could be one of the possible routes for SARS-coronavirus-2 infection. Chronic periodontitis has an abundance of proinflammatory mediators being released via the osteopontin signaling, which in turn can operate the p38 mitogen-activated protein kinase pathway (MAPK pathway), stimulating the master bone resorption transcription factor, the nuclear factor-kappa B signaling.¹² Other than furin, cathepsin L is another proinflammatory molecule which is also increased in chronic periodontitis and could be a result of the interleukin 6-mediated activation of the caveolin-1-mediated JNK-AP-1 signaling pathway.^{13,14} Both these mediators individually or together are the important mediators that play a major role in helping the SARS-coronavirus-2 to affect the host gingival fibroblasts. The presence of viruses in the body fluids such as saliva may be due to the direct transfer from infected individuals. Viruses of serious medical infections such as SARS-CoV-2 can be present in saliva in sufficient quantities for transmission from person to person through close (within proximity of 2 m) or intimate contact.^{15,16}

PREDOMINANT ROLE OF PERIODONTAL BACTERIA IN RESPIRATORY DISEASE

Increasing literature evidence suggests that oral infections, particularly periodontitis, may ameliorate the course of respiratory infection. Bacterial-associated pneumonia is a common form of the respiratory ailment that can arise secondary to or as a supra added infection of an underlying viral pneumonia.¹⁷ Treatment of periodontal infection, reducing the bacterial load, and by bringing down the bacterial dysbiosis, the respiratory infections have been reduced to large extent.¹⁸

A number of different oral microflora and other facultative bacteria have been isolated from infected lung fluids such as sputum and pleural fluid, including *P. gingivalis*, *Eikenella corrodens*, *Fusobacterium nucleatum*, *A. actinomycetemcomitans*, *Peptostreptococcus*, *Clostridium*, and *Actinomyces*, most of which, if not all, are the periodontal pathogens that have been implicated as etiologic agents for periodontal disease.

Several plausible reasons that support the contributions of oral bacteria in the causation of a respiratory infection are:¹⁹

- Inhalation of oral microbiota into the alveoli of lungs.
- Periodontitis-associated biomarkers that change the mucosal surfaces to allow for secretions and expression of receptors that create sites for adhesion and colonization of respiratory pathogens.
- Periodontitis-associated enzymes may disrupt the salivary pellicle on bacteria to block their clearance from oral mucosal surfaces.
- Periodontal-associated proinflammatory mediators and other cytokines can potentially alter the respiratory epithelium and promote invasion of respiratory pathogens.

Patient morbidity caused due to pneumonia or a respiratory infection was almost 4-fold higher in subjects with 10 or more teeth with periodontal pocket than in those without periodontal pockets,²⁰ leading a way to a direct relationship between periodontal diseases and aspiration pneumonia.²¹

PERIODONTAL DISEASE AS A RISK FACTOR FOR COVID-19

Reducing the plaque to bare minimum levels is the gold standard way to prevent and control periodontal disease. The fact that good oral care reduces the risk of viral respiratory infections has been confirmed in the literature, one of which is a systematic review that inferred that at least 1 in 10 pneumonia-related casualties in the elderly could be stopped by maintaining oral hygiene²² because periodontopathic bacteria are considered to play role in causing systemic inflammation, bacteremia, and pneumonia.²³

NETosis is one of the important defense mechanisms of periodontal disease. Higher levels of interferon α are released in periodontal disease which in turn stimulate NETosis. Further, it has also been found that the impaired removal of these NETs cause bystander damage.²³ There has been reports of viral-stimulated NETs which undergo unchecked systemic circulation. This starts the expression of proinflammatory cytokines that ultimately leads to inflammation.²⁴

Bronchoalveolar lavage examinations from patients with ARDS and acute COPD have reported the presence of NETs.⁴ Later stages of COVID-19 have showed a hyperinflammatory state, i.e. "cytokine storm" with symptoms seem to be related to elevated serum levels of interleukin-1 beta, 7, 10, 17, 2, 8, 9; granulocyte macrophage colony-stimulating factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF); interferon- γ ; tumor necrosis factor α ; macrophage inflammatory proteins 1A, 1B (MIP); macrophage chemoattractant protein 1; and interferon γ -induced protein 10 (IP 10).²⁵

Improper removal of NETs has caused both these disease forms to spread the state of inflammation. This remains as constant source of harm to the tissues that have been involved. This leads us to a hypothesis that periodontal disease could be a predispose to adverse COVID-19-related outcomes.²⁶

Oral Manifestations of COVID-19

In Italy, dermatologic complications in patients infected by SARS-CoV-2 infection have been reported in the literature.²⁷ A study reported oral signs and symptoms (pain in tongue and palate) in three patients, of which two were suspicious of COVID-19 and one

was confirmed positive case while the case report did not mention about the other two patients. All the three patients reportedly had the symptoms of pain, oral ulcers, or blisters before seeking medical advice where they have been thought to resemble a herpetic recurrent stomatitis or as unilateral ulcers on the palate. There was blister development in internal lip mucosa as well as a desquamative gingivitis. None of the patients had any previous history of herpetic infection.²⁸

PATIENT MANAGEMENT IN COVID-19 PANDEMIC

Although dentist holds the first place for being at high risk, no recorded incidents have been noted in the literature for transmission of COVID during dental procedures. Yet, strict measures should be implemented to prevent the spread of pandemic. According to Ministry of Health and Family Welfare guidelines, the precautions were categorized as:²⁹

- Modifications for dental operatories
- Modifications at patient level screening and examination

Modifications for Dental Operatories

Phase I: Preparatory phase for a dental clinic

Phase II: Implementation phase

Phase III: Follow-up

The preparatory phase includes the management of dental chair, the reception area, triage area, and the patient consultation room. The entrance of the clinic should be equipped with electronic sanitization facilities and triple-layered mouth masks for patients and health workers entering into the clinic. The temperature and the other associated symptoms should be well checked before letting any personnel from entering the clinic. Arrangements should be made in such a way that there should be a plastic or glass shield between the patient and the receptionist. The triage should have patient education aids to create awareness regarding the COVID-19 pandemic. All transactions, if possible, must be made through digital means rather than through cash payments. It should also be made sure that the patients maintain at least 6-feet distance in the patient waiting area.

The implementation phase involves the use of patient disinfection, chair sanitization, proper sterilization of instruments, and appropriate discarding of waste. The patient should be asked to rinse his mouth with 10 mL of 0.5% povidone iodine (diluted in 1:20 concentration with water) for 30 seconds before spitting it out. After appropriate treatment, the dental chair along with other accessory instruments and equipment should be sprayed with 1%

sodium hypochlorite solution by maintaining at least 3-feet distance from the chair. Fumigation should be done on a daily basis before clinic closure so as to prevent spread of infection.

The follow-up phase consists of patient follow-up for at least 7–14 days for any symptoms of COVID-19. In case of any reported COVID symptoms, all the health workers should undergo a RT-PCR test for COVID 19 and should take a prophylactic hydroxychloroquine (200 mg tablet thrice daily for 4 days).

Modifications at Patient-level Screening and Examination

Alharbi et al. in April 2020 have classified the dental treatments as emergency; urgent conditions to be treated without aerosol production; Urgent conditions to be treated with aerosol-generating procedures; non-urgent; and elective procedures.³⁰ In this article, we have tried to modify it by adding the periodontal surgical procedures and by also reconsidering the emergency needs.

The proposed modifications in procedures can be categorized as: (Table 1)

- Those seeking emergency treatment
- Those seeking urgent treatment
- Those seeking elective treatment

The treatment should thus be carved according to the needs of the patient and the category under which the patient falls (unknown for COVID and known for COVID) as shown in the Flowchart 1. All the treatment must be performed with minimum release of aerosols and hand instruments to be used where ever possible. Airborne infection control rooms (AICR) or negative-pressure chambers with high-power suction must be used as treatment chambers to avoid spread of aerosols.

TREATMENT OF PERIODONTAL DISEASES

Similar to the above-mentioned management for general dentistry, the field of periodontology also requires a separate management protocol by classifying the periodontal disease conditions under emergency, urgent, and elective categories. To the best of our knowledge, there is no literature evidence of categorical classification of periodontal diseases and conditions. We have made an attempt to best classify (Table 2) these disease conditions based on the recent AAP Classification system of periodontal diseases and conditions, 2017.³¹ It is intimidating not to classify any of these disease conditions as emergency or elective, as the initial disease process which is considered to be urgent now can lead to an emergency condition with an irreversible damage. So, it is always better to address the

Table 1: Enlisting the various kinds of treatment needs of the patient in general dentistry

<i>Emergency</i>	<i>Urgent</i>	<i>Elective</i>
(1) Road traffic accidents (RTA) or any other trauma involving facial fractures.	(1) Abscess	(1) Crown cementations
(2) Space infections such as Ludwig’s angina.	(2) Oral ulcers	(2) Denture adjustments
(3) An avulsed, luxated or fractured tooth.	(3) Carious teeth	(3) Esthetic corrections (crown lengthening, depigmentation, veneers etc.)
(4) Tooth mobility associated with severe pain.	(4) Orthodontic treatment	(4) Asymptomatic extractions
(5) Uncontrollable postoperative bleeding and	(5) Periodontal surgeries (for gingival recession, periodontal pocket etc.).	(5) Regular scaling and
(6) Any other orofacial condition that can obstruct the airway.	(6) Pericoronitis of 3rd molars and	(6) Follow-up visits.
	(7) Missing teeth (complete dentures, fixed partial denture and implants etc.).	



Flowchart 1: Suggesting the treatment choice for a patient depending upon the severity of the COVID-19 disease

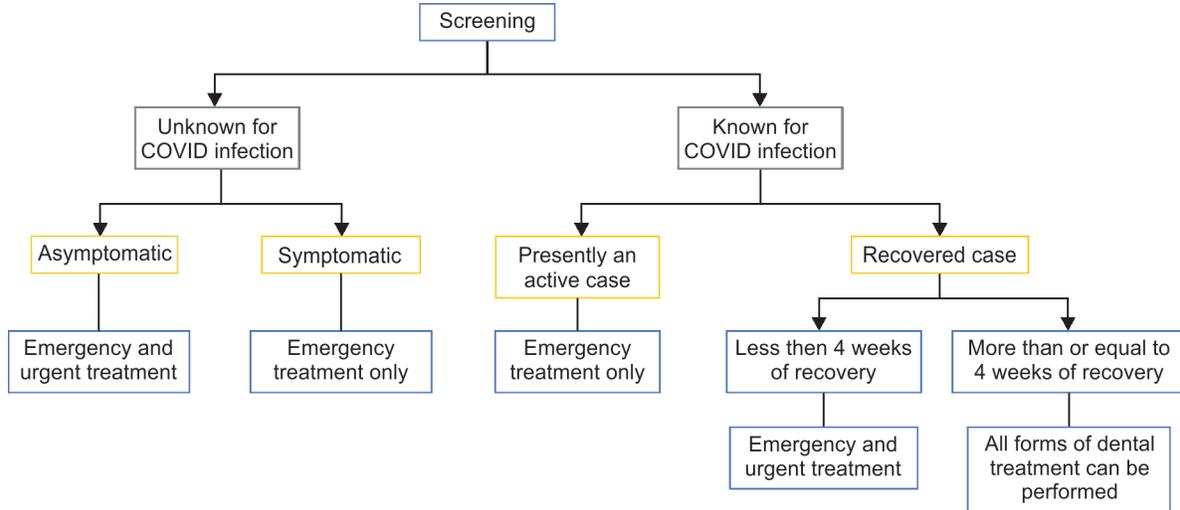


Table 2: Enlisting the various kinds of treatment needs of the patient in periodontal practice

<i>Emergency</i>	<i>Urgent</i>	<i>Elective</i>
(1) Gingivitis with conditions of stage III gingival index according to Loe and Sillness (1963) ³⁸	(1) Gingivitis with conditions of stage II gingival index according to Loe and Sillness (1963) ³⁸	(1) Gingivitis with conditions of stage I gingival index according to Loe and Sillness (1963) ³⁸
(2) Periodontitis—All stages according to Tonetti’s classification ³¹	(2) Mucogingival tissues-related complaints other than esthetic issues.	(2) Routine follow-up visits
(3) Replacement of missing teeth (immediate implant)	(3) Peri-implant mucositis	(3) Depigmentation
(4) Peri-implantitis and related mucogingival conditions	(4) Trauma caused due to occlusal discrepancies	(4) Frenectomy
(5) Necrotizing periodontitis and stomatitis	(5) Necrotizing gingivitis	(5) Vestibular deepening
(6) Abscesses	(6) Prosthesis-related issues	(6) Hopeless teeth extraction
(7) Endo-perio lesions	(7) Replacement of missing teeth (delayed implant)	(7) Esthetic-related issues
(8) Pericoronitis		

minimalistic conditions in a holistic way to prevent the spread of the periodontal disease. Efforts should be made in a way to reduce the aerosol-related procedures.

Gingivitis or a gingival disease is an initial pathologic process that advances to periodontitis. Due to the concept of host susceptibility, different individuals present with different conditions ranging from spontaneous bleeding to minimal erythema. These conditions, after assessing clinically, may require an oral prophylaxis which will arrest the disease condition and can be considered as elective. Treatment should be limited to prescribing astringents, performing oral prophylaxis with hand instruments, and local delivery of antimicrobials.

Periodontitis is an alarming condition that requires immediate attention ranging from scaling and root planning, open flap debridement to advanced regenerative procedures or extractions, and be considered as an emergency. These treatment procedures inevitably involve the release of aerosols, and so the patient is to be given at least a 2-week interval for each appointment so as to assess the patient for any symptoms of COVID.

Implant-related conditions also involve complex procedures such as implant debridement and decontamination and sometimes may even require implant removal followed by a ridge

augmentation procedure. All these procedures are considered to be emergency or urgent depending upon the periodontal destruction. Efforts should be made to perform the initial procedures with plastic or titanium hand instruments.

Other conditions such as pericoronitis, endo-perio lesions, and abscess are very painful conditions and should be considered for emergency procedures. Care should be taken while performing these procedures, as the patient is in deep pain and only a screening procedure is performed before attending these patients, whereas for other non-painful conditions, an RT-PCR test can be performed and then be attended.

Certain procedures such as routine oral prophylaxis, depigmentation procedures, frenectomies, pericoronitis, and follow-up visits can be considered as elective and addressed via telephonic consultation. These patients should be given a later appointment, and priority should be given for emergency and urgent conditions, respectively.

The treatment procedures being performed should be done in three steps according to a recent workshop on treatment of stage I to III periodontitis.^{32–37}

First stage—patient training and education, assessment of risk factors, oral prophylaxis, etc.

Second stage—subgingival instrumentation, host modulation, laser, photodynamic therapy, etc.

Third stage—flap surgeries, resective osseous surgeries, regenerative therapies, extractions, etc.

All these categories are subjective perception of the clinicians writing this review. It is proposed based on the clinical experience, and further analysis may be required for arriving at a standard categorical classification of periodontal disease conditions.

CONCLUSION

The relationship between oral health and overall health is indisputable. With the scanty and inconclusive data available, it can be concluded that there could be connection between periodontal disease and COVID-19 complications which require further investigations for better understanding the outcomes of COVID-19 disease.

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