

# Maintaining Periodontal Health in The Era of COVID-19: Challenges and Strategies

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## Abstract

*In the year end of 2019, a new form of coronavirus that rapidly resulted in severe respiratory syndrome and lethal pneumonia emerged in Wuhan, China. After 3 months, the World Health Organization (WHO) characterized the outbreak as a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which in turn resulted in the pandemic that is coronavirus disease 2019 (COVID-19). On March 11, 2020 the World Health Organization (WHO) declared the novel coronavirus (COVID-19) outbreak a global pandemic, the first ever due to a coronavirus. Severe COVID-19 shares many inflammatory biomarkers with periodontitis. For these reasons, researchers have hypothesized since the early days of the COVID-19 pandemic that there could be an association between the two diseases. This includes two different possible associations, first there is risk of increased initial SARS-CoV-2 infection in individuals with who have periodontitis, and, secondly, the risk of increased COVID-19 severity in those with patients with periodontitis. Therefore, this article will highlight the effect of COVID-19 on periodontium and the protocol to be followed in the periodontal management of patients infected with COVID-19.*

**Keywords:** Coronavirus, Pandemic, Periodontal Management.

## BACKGROUND

In December 2019, an outbreak of pneumonia of unidentified etiology was reported to the World Health Organization (WHO) in Wuhan, Hubei Province, China. On 30<sup>th</sup> January, 2020, WHO declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak.

On February 11, 2020, WHO officially named the current coronavirus disease outbreak coronavirus disease 2019 (COVID-19) and ICTV named the virus SARS-CoV-2.<sup>1</sup> Genealogical studies show that SARS-CoV-2 belongs to the Beta coronavirus genus.

Structurally, coronaviruses are spherical, ranging from 80 to 160 nanometers in diameter, with a lipid bilayer envelope and contain a single-stranded, positive-sense RNA (ssRNA) genome that is 27 to 30 kilobases in length.<sup>2</sup>

## MECHANISMS BEHIND THE ASSOCIATION BETWEEN PERIODONTITIS AND COVID-19

There are five proposed hypotheses linking COVID-19 severity with periodontitis.

These mechanisms can be categorized as direct and indirect:

### 1. Direct Mechanisms:

- **Impact of Periodontal Pathogens on the Respiratory System:** Periodontal bacteria may affect the respiratory system, potentially exacerbating COVID-19 symptoms.
- **Translocation of SARS-CoV-2 via the Bloodstream:** SARS-CoV-2 may enter the bloodstream from the mouth and spread to other organs, worsening disease severity.

### 2. Indirect Mechanisms:

- **Effect on Systemic Inflammation:** Periodontitis could increase systemic inflammation, contributing to a more severe immune response during COVID-19.
- **Effect on Coagulation:** Periodontitis may also influence coagulation pathways, potentially leading to complications in COVID-19 patients.

### 3. Genetic Factors:

Genetic variants might contribute to the development and progression of both COVID-19 and periodontitis, providing another possible link between the two conditions.

## Inflammatory Hypothesis

- 1) **Inflammatory Markers:** Higher blood levels of **C-reactive protein (CRP)** were observed in COVID-19 patients with signs of periodontal disease. Significant associations were also found between increased **serum ferritin** and **HbA1c** with periodontal probing depth in COVID-19 patients.
- 2) **Shared Immune Pathways:** Both periodontitis and COVID-19 are associated with the excessive activation of the **nuclear factor kappa B (NF-κB)** pathway.

## Microbiological Hypothesis

Some studies have suggested that periodontal pathogens could also play a direct role in COVID-19.

- 1) **Oral Microbiome Dysbiosis:** A study with 75 COVID-19 patients observed dysbiosis of the oral microbiome. However, it is unclear whether this microbial imbalance was a cause or an effect of SARS-CoV-2 infection.
- 2) **Fusobacterium nucleatum and ACE2 Expression:** In vitro research demonstrated that **Fusobacterium nucleatum** could increase the expression of **ACE2** in alveolar epithelial cells. This bacterium also elevated the production of pro-inflammatory cytokines **IL-6** and **IL-8** in epithelial cells from the alveolar, bronchial, and pharyngeal regions.
- 3) **Bacterial Cultures from Respiratory Sites:** In a study of 110 COVID-19 patients, bacterial cultures were taken from respiratory sites, such as the lungs. Among the identified bacteria were **Staphylococcus epidermidis** and **Klebsiella pneumoniae**, both associated with periodontitis. Notably, four of the nine patients with positive cultures died, suggesting a potential link between oral pathogens and severe outcomes in COVID-19.

Although these findings point towards a possible role for the oral microbiome in SARS-CoV-2 infection and its complications, more research is necessary to confirm this hypothesis.

## Hypercoagulable State

There are striking parallels between the biomarkers involved in COVID-19 related coagulation issues and those found in periodontitis.

- 1) Coagulation Biomarkers in Periodontitis and COVID-19: In COVID-19 patients found that elevated D-dimer levels correlated with periodontal issues like **gingival recession**, **tooth loss**, and **probing depth** showed positively linked with the severity of periodontitis. And increased levels of **troponin** and **pro-BNP** in COVID-19 patients with more severe periodontitis and higher levels of clinical attachment loss.
- 2) Role of Plasmin in Coagulation and SARS-CoV-2 Infection: Plasmin plays a role in the cleavage processes necessary for SARS-CoV-2 to bind to receptors on infected cells.
- 3) Endothelial Dysfunction as a Link: SARS-CoV-2 also induces endothelial dysfunction, which may exacerbate hypercoagulation, thrombosis, and multi-organ damage in severe COVID-19 cases.

### Genetics

The genetic link between periodontitis and SARS-CoV-2 infection, could explain the increased severity of COVID-19 in patients with periodontal disease.

- 1) Gene Expression and SARS-CoV-2 Infection: Periodontitis has been associated with the **overexpression** of genes that facilitate SARS-CoV-2 infection, such as **ACE2**, **TMPRSS2**, **FURIN**, **CD147**.
- 2) Estrogen Receptor 1 (ESR1) and TMPRSS2: A study using data from the **ChIP-Atlas** and **GEO datasets** found a correlation between the expression of **ESR1**, which is highly expressed in the gingival tissues of periodontitis patients, and **TMPRSS2** expression.
- 3) Transcriptomic Data and Shared Genes: Genes like **DDX56**, **GNAS**, **CA10**, **GRM5**, **CCL5** are involved in important cellular processes like hormone secretion, protein phosphorylation, cell chemotaxis, actin filament assembly, several signaling pathways and immune responses like **rheumatoid arthritis**.
- 4) MYOZ2 Gene: Reduced expression of MYOZ2 could weaken the immune response in both periodontitis and COVID-19, potentially worsening the outcomes of SARS-CoV-2 infection.

### Oral-Vascular-Pulmonary Route

In 2021, Lloyd-Jones et al. proposed termed the **oral-vascular-pulmonary route**. According to this model, the virus may travel from the oral cavity to the pulmonary vessels through the **venous drainage system** of the mouth.

This pathway includes the **jugular veins** in the neck and the **superior vena cava**, ultimately reaching the **right side of the heart** before being pumped to the lungs. This hypothesis offers a plausible explanation for the interaction between oral health and COVID-19 severity.<sup>3</sup>

### PERIODONTITIS AND COVID-19: COMMON RISK FACTORS AND COMORBIDITIES

Several articles identified shared risk factors or comorbidities that might be common between COVID-19 and periodontal diseases. These include diabetes, obesity, and cardiovascular diseases. It is suggested that the cytokine response from periodontitis may contribute to the cytokine storm seen in severe COVID-19 cases.

Additionally, oral bacteria related to periodontal disease may facilitate SARS-CoV-2 entry into cells, especially in older individuals with poor swallowing function, increasing the risk of bacterial aspiration.<sup>4</sup>

## DENTAL PROCEDURES DURING THE COVID-19 PANDEMIC

According to the American Dental Association, dental procedures during the COVID-19 pandemic were divided into two groups: urgent/emergency and routine/elective.

**Urgent dental care:** Includes treatment of conditions requiring immediate attention, such as alleviation of severe pain with or without risk of infection and balancing the patient load in hospital emergency rooms. Such care should be minimally invasive as far as possible.

**Routine/elective or non-urgent dental procedures include:** Initial oral and dental examinations, periodic exams, and follow-up visits which may include periodic x-rays, Cleaning and prophylaxis as a preventive care, Orthodontic procedures unless they may cause acute complications (pain, infection, trauma, etc.), Extraction of asymptomatic teeth, Restorative treatments such as repair of asymptomatic caries and cosmetic dental procedures.

During the COVID-19 pandemic, routine dental procedures were contraindicated and focus was on immediate emergency care only for all patients. Therefore, dentists must first ensure safety of their own health and that of their assistants and then the first step is patient screening, which can be done in two steps.

- **Primary Screening**
- **Secondary Screening**

**Primary screening:** An initial screening should be performed when making an appointment over the phone or online. During this time, patient's status regarding COVID-19 can be determined using a simple questionnaire.

**Secondary screening :** Secondary screening should be carried out when the patient visits the clinic. Primary testing should be carried out before the patient enters the treatment room. In addition, before entering the clinic, patients should be asked to wear a surgical mask and follow respiratory hygiene measures and hands.

**Patient admission and waiting:** It is advisable to schedule patient appointments so that only one patient is waiting in the waiting room. However, three separate waiting rooms for apparently healthy, suspected, and confirmed patients should be considered.

**Operatory room:** Emergency dental treatment should only be performed in negative pressure treatment rooms or isolation rooms to prevent airborne transmission. To improve normal ventilation, the WHO recommends negative pressure rooms with at least 12 air exchanges per hour or 160 liters/second per patient.

**PPE for dentists and clinical staff:** Dentists should strictly follow standard precautions to protect the skin and mucous membranes from infected secretions. According to CDC recommendations, the order of wearing PPE includes washing hands, putting on a hospital gown, mask, hat, goggles, and surgical gloves. The order of removing PPE is reversed, and hand washing is the last step.

**Hand washing:** West China Stomatology Hospital of Sichuan University recommends a hand hygiene policy of two times before and three times after treating a patient.

**Appropriate Masks:** Standard surgical masks, also known as liquid-resistant surgical masks, form a protective barrier over the nose, mouth and airways against droplets, large droplets and other liquids. Masks known as N95 masks and filtering facepieces (FFPs) protect the user from small airborne particles during aerosol-generating procedures.

**Safety glasses or face shields:** COVID-19 can also be transmitted by contact with the conjunctiva, which can be easily contaminated by droplets. It is therefore important to wear goggles or a face shield during treatment and to clean and disinfect after each patient.

**Disinfection of surfaces in the operatory room:** Hospital disinfectants have different recommended concentrations depending on the application. For example, a 1:10 to 1:100 dilution of 5.25 to 6.15% sodium is recommended for decontaminating blood splashes. There is evidence that disinfectants containing 62-71% ethanol or 0.1% sodium hypochlorite for 1 minute can remove coronaviruses from surfaces.

**Use of mouthwashes:** Pre-procedural rinsing with an antibacterial mouthwash has shown to reduce the median viral load in saliva by  $3.3 \times 10^6$  copies per milliliter.

**Dental radiography:** Intraoral x-rays should not be requested as they stimulate saliva production and coughing fits. Intraoral x-rays can be replaced by extraoral x-rays such as panoramic x-rays or cone-beam CT.

**Minimizing the aerosols:** Dentists are encouraged to avoid or minimize, as far as possible, the use of procedures that generate droplets or aerosols, such as the use of three-way syringes, high-speed handpieces, and ultrasonic scalers.

**Dental perspectives in future crises:** Digital dentistry also offers many advantages in terms of infection control. For example, digital intraoral impressions do not require the use of impression trays or dental impression materials, eliminate the risk of contact with a contaminated spoon, minimizing the risk of infection transmission and cross-contamination itself. Recent technological advances have also led to the emergence of robotic dentistry which includes endo micro robots, surgical robots, and robotic dental drilling. The occurrence of events such as the COVID-19 pandemic may therefore prompt dental researchers to focus on novel dental approaches.<sup>5</sup>

### **Pandemic Aftereffects: Periodontal Treatment Needs on the rise**

The COVID-19 outbreak has had a severe impact on healthcare. The cancellation of elective dental treatments has raised concerns about the current prevalence of oral disease, which has devastating effects on oral and overall health. Barriers to resuming regular dental care include financial issues, limited access to treatment, and ongoing concerns about contracting the virus.

## **CONCLUSION**

The impact of low-grade chronic inflammation on COVID-19 and chronic diseases, the systemic impact of untreated periodontitis cannot be underestimated. Increased psychological stress, anxiety and interrupted treatment for people with chronic diseases can impact overall health and wellbeing worldwide.<sup>6</sup>

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