

## Impact of periodontal condition for individuals with COVID-19.

Impacto de la condición periodontal para individuos con COVID-19.

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In late December 2019 an outbreak of pneumonia of unknown cause was observed in Wuhan, China. Thereafter, the viral etiology of the coronavirus family was identified by researchers, being named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the condition it causes as coronavirus disease 2019 (COVID-19).

The contamination of health professionals who took care of infected individuals demonstrated the possibility of transmission between humans and the ability to spread of this virus, generating great concern. Since then, we have observed that this virus has spread extremely rapidly around the world. The number of new cases of infection is steadily rising in most countries, as well as the number of deaths due to complications.<sup>1</sup>

The possibility of transmission by asymptomatic individuals seems to contribute to the rapid spread of COVID-19. In addition, many individuals have a mild form of the disease, whose low-intensity symptoms contribute to the maintenance of daily activities and, therefore, the spread of the virus. A significant proportion of contagion is believed to occur before any symptoms appear. Transmission occurs by close contact or by droplets and an incubation time of 3 to 9 days, on average, is observed.

A smaller portion of the population experiences a severe form of the disease. Age over 65 years and the presence of comorbidities such as hypertension, diabetes mellitus and cardiovascular disease increases the risk of more severe disease. The weakening of the immune system due to pre-existing conditions may be the cause of a faster progression of the viral infection. Fever and cough are the most frequent symptoms associated with COVID-19; dyspnea and fatigue are also commonly observed.<sup>2</sup>

SARS-CoV-2 is a single-stranded RNA virus whose genetic material is enclosed within a lipid bilayer. Intracellular invasion occurs through protein binding: The spike-protein (S-protein) binds to the human protein receptor ACE-2, allowing the fusion of the viral lipid layer to the host cell membrane.

This fusion allows SARS-CoV-2 RNA to be introduced into the host cell's cytoplasm with consequent translation of several viral proteins, virus replication and cell death. The ACE-2 receptor used by the virus to invade human cells is found in significant quantities in the lung, heart and kidney.<sup>3</sup>

There is no specific antiviral therapy for COVID-19. Therapeutic protocols for infected individuals consists of supportive measures. Hydration, adequate nutrition, control of fever and cough are actions used for individuals who manifest mild or moderate forms of the disease.<sup>1</sup>

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For more severe cases, oxygen inhalation and mechanical ventilation may be necessary. The main complications associated with COVID-19 are severe acute respiratory syndrome, myocardial injury and co-infections.

The binding of the virus to pulmonary ACE-2 receptors allows the invasion of alveoli, causing serious respiratory impairment in some individuals infected by SARS-CoV-2. It is worth mentioning that the evolution of pulmonary disease can be affected by infectious and inflammatory processes, including periodontitis.

Another complication, co-infection is more often associated with bacteria than with other types of viruses. Bacterial infection has been reported to be responsible for the atypical pneumonia seen in cases of COVID-19.<sup>2</sup> As such, special attention should be given to periodontal diseases, considering the complications associated with COVID-19.

Periodontitis is a common chronic disease of bacterial origin that can lead to the destruction of the connective tissue and bone that support the tooth. Its prevalence increases with age, as well as in the presence of diabetes, groups considered at risk for COVID-19, with greater severity of infection and higher mortality rates.<sup>3,4</sup>

The relationship between periodontitis and several systemic conditions, including respiratory diseases, is due to its infectious and inflammatory profile. Four main mechanisms make the relationship between periodontitis and respiratory diseases plausible. First, oral pathogens aspirated directly into the lungs and consequent infection. Another highlights the role of salivary proteins associated with periodontitis in modifying mucous surfaces in the respiratory tract, favoring bacterial adhesion and colonization.

A third mechanism involves the ability of hydrolytic enzymes, produced by periodontopathogenic bacteria, to destroy the salivary film that protects against pathogenic bacteria.

Finally, cytokines and other active biological molecules, released from periodontal tissues, can alter the respiratory epithelium, promoting colonization by respiratory pathogens.<sup>5</sup> A study by Tan *et al.*,<sup>6</sup> evaluated the relationship between periodontitis and lung function in individuals with chronic obstructive pulmonary disease (COPD).

The results showed that the severity of pulmonary obstruction increased with the worsening of specific periodontal indexes and that *Porphyromonas gingivalis*,

an important periodontal pathogen, showed a significant negative correlation with lung function in individuals with COPD.

Additionally, the study showed the presence of respiratory pathogens in the oral biofilm, emphasizing its role as a reservoir of microorganisms.

A recent systematic review shows that the presence of periodontal infection is associated with an increased risk of developing respiratory diseases, including pneumonia (OR 3.21, 95% CI 1.99 to 5.17), COPD (OR 1.78, 95% CI 1.04 to 3.05) and asthma (OR 3.54, 95% CI 2.47 to 5.07).<sup>7</sup>

Therefore, periodontitis can contribute to the worsening of the serious respiratory failure triggered by COVID-19 and to the development of pneumonia, with an impact on the length of hospital stay, morbidity and mortality associated with this infection.

Additionally, in addressing the respiratory condition caused by SARS-CoV-2, it may be necessary to institute mechanical ventilation.<sup>3</sup> The use of this ventilation apparatus presents the risk of developing a serious hospital infection, that is ventilator-associated pneumonia. This type of pneumonia develops 48 to 72 hours after orotracheal intubation and has a high mortality rate. The reduction in salivary flow coupled with unsatisfactory hygiene and inadequate immune response facilitates bacterial colonization.<sup>5,8</sup>

Again, periodontal bacteria and/or respiratory bacteria present in dental biofilms can play an important role in the development of nosocomial pneumonia in individuals with COVID-19. A current systematic review demonstrated that individuals with periodontitis are more susceptible to the development of nosocomial pneumonia compared with individuals without periodontitis (OR 2.55, 95% CI 1.68 to 3.86).<sup>8</sup>

Taking greater care regarding oral hygiene in this group of individuals can significantly reduce the number of oral bacteria, as well as having a qualitative impact on the oral biofilm. The use of chlorhexidine in the oral hygiene of individuals admitted to intensive care units is a therapeutic option that tends to become a standard in these units. A 0.12% chlorhexidine protocol every 12 hours has been shown to be extremely effective in preventing nosocomial pneumonia.<sup>9</sup>

A study by Araújo *et al.*,<sup>10</sup> compared the periodontal condition of patients admitted to intensive care units and patients not admitted to intensive care units. Additionally, a quantitative microbiological analysis of the subgingival biofilm was performed.

Individuals admitted to the intensive care unit had worse periodontal condition, including a higher prevalence and severity of periodontitis.

A positive correlation was also observed with *P. gingivalis*, *T. denticola* and *A. actinomycetemcomitans*. These results highlight the importance of establishing protocols for oral care in intensive care units.

In this sense, we consider that periodontal infection can negatively impact the evolution of the treatment of

individuals contaminated by COVID-19, contributing to increase the length of hospital stay, the morbidity and mortality associated with this infection. In this moment, when we are preparing for a new world after the decline of COVID-19 rates and the relaxation of isolation measures, changes in behavior will be essential.

These changes added to the imminent risk of new pandemics should culminate in deep discussions about the oral condition of the world's population

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