



Periodontal diseases and COVID-19: a literature review

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Abstract

COVID-19 (Sars-COV 2), a disease known worldwide, began in the city of Wuhan, China, and was transmitted through inhalation, ingestion, and/or direct contact with the virus. Due to the pandemic situation, new studies are being carried out on the relationship between COVID-19 and dentistry. In this way, the objective of the study was to carry out a literature review on the relationship between periodontal disease and COVID-19, and how problems in the oral cavity can interfere with the prognosis of patients hospitalized for the disease. It was then concluded that there is a relationship between periodontal disease and COVID-19 and that periodontitis causes COVID-19 cases to be more severe and cause greater sequelae than in patients with healthy gums. It also emphasizes that the dentist, as well as professionals who are on the front line in the care of patients with COVID-19, should be aware of the measures to remove bacterial plaque and oral hygiene, to minimize the sequelae caused to the patient. As COVID-19 is a new and understudied subject, more studies should be developed to confirm the findings of this study.

Keywords: Dentistry. Periodontal Diseases. COVID-19.

Introduction

COVID-19 is a worldwide infection that has challenged the functionality of every aspect of our lives, from healthcare to the economy, from journalism to education. This disease emerged at the end of 2019, in Hubei province, in the city of Wuhan, located in Mainland China. The causative agent of the outbreak has been identified as a beta-coronavirus with a genomic sequence related to the 2003 severe acute

respiratory syndrome (SARS) coronavirus, called SARS-CoV-2, which is likely derived from bats but can be amplified by a host intermediary. The differences are in the efficient way of transmission between humans and how the virus spread across the planet generating a pandemic. Therefore, its propagation speed illustrated a challenge for health care providers, the general population, and the elderly [1,2].

The transmission of the virus occurs by inhalation, ingestion, and/or direct contact of the mucous membranes with droplets of saliva. The coronavirus can cause infection in three different ways present in saliva. The first is the presence of the virus in the lower and upper respiratory tract that can enter the oral cavity, with the fluid droplets exchanged by these organs. The second, when the virus is present in the blood, can access the mouth, via fluid from the gingival sulcus, a specific exudate from the oral cavity, and the third is by infection of the major and minor salivary glands, with subsequent release of particles, in the saliva, through salivary ducts. Thus, we must be aware of the form of transmission as the virus can survive on hands, objects, or surfaces exposed to infected saliva for several days [3,4].

Due to the current pandemic and contagious situation faced worldwide, new studies face their position regarding the interrelationship of various diseases and COVID-19. As for periodontal disease, it is known that there are hypotheses about the connection of cytokines and angiotensin-converting enzymes as a possible correlation between COVID-19 and periodontal disease [5].

Periodontal diseases are a group of pathologies of an inflammatory nature in which a host response is induced by microbial etiological factors that mediate

inflammatory events, which lead to tissue destruction in susceptible individuals [1].

Patients with severe COVID-19 often have an exacerbated immune response, characterized by excessive levels of pro-inflammatory cytokines and widespread tissue damage, the so-called cytokine storm syndrome. Mortality from COVID-19 has been linked to elevated serum levels of interleukin-6 (IL-6), C-reactive protein (CRP), D-dimer, and ferritin suggesting a clear link between disease severity and hyperinflammation. no resolution caused by viruses [6].

Some comorbidities such as hypertension, diabetes, cardiovascular diseases, and obesity were associated with more serious cases of COVID-19, but these factors lead to a worsening of the patient's general clinical status, not being a specific risk factor. Some studies suggest that the oral cavity plays an important role in the transmission and pathogenicity of COVID-19 since in some cases the prevalence of the periodontal disease has been identified as a risk in increasing the severity of the disease, since the change in cytokine profiles observed in periodontal disease may be part of the mechanism responsible for the association between periodontal disease and COVID-19 [5,6].

Thus, the objective of this study was to review the literature on the relationship between periodontal disease and COVID-19, as well as how oral cavity problems can interfere with the prognosis of patients hospitalized for the disease.

Methods

Study Design

The rules of the Systematic Review-PRISMA Platform (Transparent reporting of systematic reviews and meta-analysis-[HTTP://www.prisma-statement.org/](http://www.prisma-statement.org/)) were followed.

Literary Search Strategy

For the present study, a literature review was carried out in the main Pubmed, BVS, and Google academic databases on the subject. The terms used to search for articles were taken from the DeCS (Health Sciences Descriptors). The search strategy used was "Odontology OR Dentistry", "Periodontal Diseases OR Periodontal Diseases", and "COVID-19". The articles were selected in English and Portuguese, the research was carried out from February to March 2022. The review was carried out in an integrative way and the articles were used as needed and relevant to the topic.

Results and Discussion

The COVID-19

COVID-19 is a worldwide infection that has challenged the functionality of every aspect of our lives. This disease emerged at the end of 2019, in Hubei province, in the city of Wuhan, located in Mainland China. COVID-19 is an acute respiratory infection caused by coronavirus 2 (SARS-CoV-2), from the family of single-stranded RNA viruses known as Coronaviridae. The family gets its name from the spicules on the surface that resemble a crown (from the Latin, corona). SARS-CoV-2 is the seventh virus of the β -CoV genus that infects humans and is named for its similarity to SARS-CoV, with which it shares the same host receptor for the human angiotensin-converting enzyme. Its probable natural host is the bat *Rhinolophus affinis*, which has a coronavirus with 96.2% similarity to the SARS-CoV-2 genome, the pangolin would be the intermediate host, with a coronavirus with 99% genomic similarity to SARS-CoV-25. COVID-19 started with a single animal-to-human transmission, followed by sustained human-to-human spread, the latter occurring mainly by respiratory droplets and by contact transmission [1,2,7].

In 2020, the World Health Organization (WHO) declared the spread of the disease caused by SARS-CoV-2 as a pandemic, COVID-19. The risk factors for the development of the most severe symptoms are the elderly and people who have some comorbidity. The main signs and symptoms reported by patients with the virus are usually: fever, dry cough, dyspnea, myalgia or fatigue, nausea, diarrhea, total loss (anosmia) or (hyposmia) of smell, reduction or distortion of taste (dysgeusia), sputum, headache, and sore throat. In more severe cases, severe pneumonia with acute respiratory failure occurs, in which the patient usually requires hospitalization, aggravating their condition, which can lead to organ failure and death [7,8].

The spread is fast due to the form of transmission, which occurs, either by contact with the mucous membranes of the mouth and nose or through inhalation of respiratory droplets and saliva, coming from sneezing or coughing. In addition, some patients are asymptomatic, but they transmit the virus, in these patients the transmissibility occurs from 0 to 10 days, so social isolation measures are necessary during this period, as well as the use of protective masks to avoid contamination [7,9].

Periodontopathic

Periodontal disease is characterized as an infectious disease whose etiological factor is specific microorganisms present in the oral biofilm, which affect the protection and support structures of the teeth,

leading to loss of attachment, bone tissue, and damaging connective tissue and alveolar bone, and eventually the dental element. Thus, for the prevention of periodontal disease, it is necessary to remove the bacterial plaque correctly using brushing and dental floss [10].

The study by Vettore et.al. 2014, which evaluated the SBBrazil 2010 survey, found that the prevalence of "moderate to severe" periodontal disease in adults in Brazil was 15.3%. Regarding the individual variables, periodontal disease was more prevalent among the elderly, men, black individuals, and those with lower income and lower education [11]. And yet the study by Farias et.al. 2021 showed that the prevalence of periodontal disease increased significantly between 30 and 40 years of age [8].

As we have already noted, age is a factor related to periodontal disease, but there are more risk factors related to the disease. The study by Castro et.al. 2010, which evaluated periodontal disease in the elderly, showed that people with periodontal disease are at greater risk of cardiovascular disease than others with healthy gums. And yet the risk factors related to the progression of periodontal disease are age, smoking, and periodontal pathogens [12].

Periodontitis can be affected by some environmental and acquired risk factors such as heredity, smoking, hormonal variation (during pregnancy, menopause), systemic diseases (diabetes, osteoporosis, HIV, neutropenia), stress, nutritional deficiencies, medications (calcium channel blockers, immunomodulatory agents, anticonvulsants) and poor oral hygiene [13].

The relationship between COVID-19 and periodontal problems

As it is an unprecedented disease in the literature, there are still few studies correlating COVID-19 with periodontal disease. Still, several biological indications were observed that consider periodontal disease as a risk factor for respiratory diseases and, as such, may contribute to the development of respiratory complications in patients with COVID-19.

Systemically compromised patients with diabetes mellitus, cardiovascular diseases, hypertension, metabolic syndromes, asthma, cancer, kidney disease, autoimmune diseases, Alzheimer's disease, and viral hepatitis are at high risk of developing periodontal disease. These systemic changes present increased risks and can generate a poor prognosis of COVID-19, which makes possible the association between them [1,8].

In periodontal disease, there is a high expression of cytokines as a response of the body and there are

studies that prove that high levels of these, detected in the inflamed periodontal tissue, reflect on the levels of cytokines in the systemic circulation. As in patients with COVID-19, in which there is an excessive immune reaction of pro-inflammatory cytokines and these are analogous to the cytokines of periodontitis having a common pathway of inflammatory response. Therefore, it is suggested that patients with periodontitis are at higher risk of developing adverse outcomes from COVID-19 [2]. Still in the study by Botros et. al. 2020, in which he proposed to associate the periodontal disease with the increase in the severity of symptoms of COVID-19, it was observed that the secretion of pro-inflammatory cytokines during periodontitis can promote the adhesion of respiratory pathogens in the lung epithelium through the colonization by the respiratory route [14].

Studies also show that angiotensin-converting enzyme-2 (ACE-2) has been thought to be the main receptor for SARS-CoV-2 entry into human cells and is present not only in the lungs (hence the common viral pneumonia) but also in the nasopharyngeal mucosa, salivary gland, and oral epithelial cells. This results in a high viral load in the oral cavity (saliva and crevicular fluid), which has been countered in dental practice by antimicrobial prewashes composed of povidone-iodine, showing promising results in terms of viral killing [1,15].

According to the study by Siddharthan et. al. 2020, it was observed that the oral cavity is an important reservoir for all respiratory pathogens, including *Chlamydia pneumoniae*; and individuals who have periodontal disease have a high chance of developing hospital-acquired pneumonia as well as worsening infection in the lungs. The different mechanisms that explain this condition include aspiration of pathogens present in the oral cavity into the lower respiratory tract, more commonly in high-risk people; surface alteration along the respiratory tract mucosa through salivary enzymes, which leads to colonization of pathogens, and release of pro-inflammatory cytokines along the periodontitis condition, which further stimulates attachment to lung epithelium and colonization of pathogens respiratory [16].

A case-control study was carried out involving 568 patients, taking into account patients who suffered or did not have complications from COVID-19 and their history of periodontal disease. Considering patients who evolved with complications, this risk of COVID-19 was found to be significantly higher among patients with moderate to severe periodontal disease compared with those with milder periodontal disease or without periodontal disease, with a risk of 3.5 times greater for ICU admission, a risk of 4.5 for the need for assisted ventilation and a risk of 9 times greater for death.

Furthermore, blood levels of white blood cells, D-dimer, and CRP were significantly higher in COVID-19 patients who previously had periodontal disease, demonstrating increased blood levels of biomarkers associated with worse coronavirus disease outcomes [17].

In the study by Araújo and Figueiredo 2021, which evaluated the action of interleukin-6 as an inflammatory mediator of periodontal disease and the potential aggravation of COVID-19, it was observed that several hypotheses are being studied to demonstrate the mechanisms responsible for the positive correlation between periodontal disease and COVID-19. Among these hypotheses are the aspiration of pathogenic periodontal bacteria, which could induce a greater release of inflammatory cytokines in the respiratory tract and increase the virulence of COVID-19. Thus, recent studies also reported an increase in serum IL-6 levels in patients with COVID-19 and showed a positive correlation with disease severity, yet it was observed that IL-6 is the cytokine most significantly associated with mortality in patients with COVID-19. Its variations are an important indicator of disease severity [6].

Another important factor that could underline the connection between COVID-19 and periodontitis is age, as can be seen in the study by Martu et. al. 2020 [1]. Periodontal disease affects the elderly, as they have some associated risk factors such as poor oral hygiene, long-term medication, chronic diseases, and, from the point of view of COVID-19, patients over 65 years old represent a higher risk group due to chronic comorbidities and a weakened immune response. The author also points out about smoking, which is the most important risk factor in periodontal disease and affects the progression of the disease. Cigarette smoking impairs the main mechanisms in the fight against periodontal disease and COVID-19 these mechanisms are the host's immune response, the normal activity of periodontal tissues, and a powerful microenvironment to fight pathogens. Furthermore, smoking increases ACE2 expression which is the main receptor for SARS-CoV-2 virus entry and is an additional risk factor in the progression of Covid-19, but more studies are needed to determine the real risk of COVID-19 among smokers [1].

It has been highlighted in most studies that improving oral hygiene aids in the declination of colonization along the oropharyngeal region and reduces the complication of the respiratory system. It was observed that better hygiene in the mouth, oral cavity, and good oral health care lead to a decrease in the development of respiratory diseases, which is more significant in older individuals and ICU patients, as these individuals are more susceptible to acquiring serious complexities associated with COVID-19 [1,6,15,16].

The COVID-19 pandemic has affected the world in every way, dentists must be aware of the interference of this virus in the oral cavity. As studies show COVID-19 is more prevalent in elderly patients and those with comorbidities, these factors are similar to risk factors for the development of periodontal disease. Among these systemic factors, we can highlight some that influence more in the two conditions, which are: diabetes, hypertension, and cardiovascular problems. Therefore, we can infer that there is a relationship between COVID-19 and periodontal disease, as the predisposing factors for both diseases are common [1,8,13,18].

The greatest relationship that we can point out in the relationship between COVID-19 and periodontal disease is concerning cytokines and the presence of the angiotensin-converting enzyme 2 (ACE2), studies indicate that this enzyme is considered the main receptor for the entry of the virus into the body. organism, it is found in human cells, lungs, and mucous membranes of the oral cavity, as well as it can accumulate in the periodontal pocket resulting from periodontitis. Furthermore, the act of smoking increases the expression of the ACE2 enzyme, which further increases the risk factor for the progression of COVID-19 [1,15,19].

Concerning cytokines, which may be present in inflamed periodontal tissue in addition to causing an excessive immune reaction of pro-inflammatory cytokines in COVID-19 patients. Therefore, it is suggested that patients with periodontitis are at greater risk of developing adverse outcomes from COVID-19, as well as being 3.5 times more likely to be transferred to the ICU and 9 times more likely to die. That is, patients who have periodontal disease are at risk of developing a more severe COVID-19 and with greater sequelae than a patient with healthy gums [2,14,17].

Because of this, oral hygiene measures, especially plaque removal, should be highlighted, helping to improve the condition of patients with periodontitis, and even a lower risk for patients with COVID-19. These measures should also be adopted in patients who are in the Intensive Care Units (ICU), as we can observe that the accumulation of plaque causes inflammation of the gum, evolving into periodontal disease, which exacerbates cases of COVID-19, causing a worse prognosis, which can lead to death [1,15,16,20,21].

Conclusion

It was then concluded that there is a relationship between periodontal disease and COVID-19 and that periodontitis causes COVID-19 cases to be more severe and cause greater sequelae than in patients with healthy gums. It also emphasizes that the dentist, as well as

professionals who are on the front line in the care of patients with COVID-19, should be aware of the measures to remove bacterial plaque and oral hygiene, to minimize the sequelae caused to the patient. As COVID-19 is a new and understudied subject, more studies should be developed to confirm the findings of this study.

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Conflict of interest

The authors declare no conflict of interest.

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