

# Correlation between periodontal disease and complications due Covid-19

## Correlación entre enfermedad periodontal y complicaciones por Covid-19

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### Abstract:

COVID-19 became a pandemic that affected all health sectors, both public and private. In the area of dentistry, the main concern is centred on the growing dangers of the production of aerosols by dental procedures in daily practice. In addition to this, the scientific community has recently analysed the direct potential risk of the presence of periodontal disease with the increase in the severity of COVID-19. The objective of this work is to talk about a new SARS-CoV-2 virus, delving into those risk indicators as main elements to understand the role of the virus in the pathogenesis of periodontitis, remembering that periodontitis is the second leading cause of tooth loss in adults. This work aims at updating health professionals, retaking the importance of prevention and control of oral health, as well as of COVID-19. There are few findings in the literature on the direct relationship between both diseases, taking into account the different strains of the virus discovered and its changing symptomatology, scientific and clinical research has had delays in accessing more extensive information regarding this subject; however, one of the main pieces of evidence lies in the role that the oral cavity plays in the periodontal health of the patient's tissues, since these could serve as entrances for the severe acute respiratory syndrome coronavirus SARS-CoV-2, in addition to the pro-inflammatory state subdued by cytokines within periodontal disease that could contribute to the development of severe forms of COVID-19.

### Keywords:

Periodontal disease, periodontitis, complications, COVID-19, SARS-CoV-2

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### Resumen:

La COVID-19 se convirtió en una pandemia que afectó a todos los sectores de salud tanto públicos como privados. En el área de la odontología, la principal preocupación se centra en los peligros crecientes de la producción de aerosoles por procedimientos dentales dentro de la praxis cotidiana. Aunado a esto, recientemente, la comunidad científica analiza el potencial riesgo directo de la presencia de la enfermedad periodontal con el aumento de la gravedad de la COVID-19. El objetivo de este trabajo es hablar sobre un nuevo virus SARS-CoV-2, profundizando en aquellos indicadores de riesgo como elementos principales para entender el papel del virus en la patogenia de la periodontitis, recordando que la periodontitis es la segunda causa de pérdida de dientes en adultos. A través de dicho trabajo se espera poder servir de actualización a los profesionales de la salud, retomando la importancia de la prevención y control de la salud bucodental, así también, de la COVID-19. Se encuentran pocos hallazgos en la literatura sobre la relación directa de ambas enfermedades, tomando en cuenta las diferentes cepas descubiertas del virus y la sintomatología cambiante del mismo, la investigación científica y clínica ha tenido retrasos en el acceso a una información más basta respecto a este tema, sin embargo, una de las principales evidencias radica en el papel que juega la cavidad oral en la salud periodontal de los tejidos del paciente, pues éstos podrían servir como entradas del síndrome respiratorio agudo severo coronavirus SARS-CoV-2, además del estado pro-inflamatorio sometido por citocinas dentro de la enfermedad periodontal que podrían contribuir a desarrollar las formas graves de la COVID-19.

### Palabras Clave:

Enfermedad periodontal, periodontitis, complicaciones, COVID-19, SARS-CoV-2

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### Introduction

Systemic inflammation in response to dysbiosis of the oral microbiome is the main feature of periodontitis. Periodontal diseases are considered as chronic inflammatory diseases, initiated by a bacterium, generating damage in the insertion tissues of the tooth, clinically causing periodontal pockets.<sup>1</sup>

Dental biofilm is the main etiological factor in the development and pathogenesis of periodontal diseases. However, it should not be overlooked that the mouth is also part of the nasal gold complex, that is, the mouth hosts bacteria and viruses typical of the nose, throat and respiratory tract.<sup>2</sup> The pandemic caused by a new coronavirus (SARS-CoV-2) has led to an increase of scientific publications on the main symptoms, the potential for

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virulence, the risk of infection, as well as methods for the treatment and prevention of COVID-19.<sup>3</sup> It is known that COVID-19 infection is related to an exacerbated inflammatory response that can trigger fatal situations for the patient. In addition, there is evidence regarding the severity of COVID-19 infection associated with some comorbidities (e.g., hypertension, diabetes, cardiovascular disease).<sup>4-6</sup> However, the specific risk factors that lead to more fatal clinical outcomes have not been fully defined.<sup>7</sup> The role of the oral cavity in the presence of COVID-19 has been controversial, although it continues to be studied, there is recent evidence where the oral mucosa takes a relevant role in the transmission and progression of COVID-19.<sup>8</sup> In the case of periodontitis it has been shown that it is a multifactorial disease, which is defined as an association between microorganisms and the inflammatory response of the host, resulting in the loss of clinical insertion, this is mainly caused by dysbiosis in the oral microbiome. Also, a release of pro-inflammatory cytokines is observed, generating bone loss in the supporting tissues of the tooth.<sup>9</sup> In current research, it is suggested that an increase in host production of these cytokines may cause a cytokine storm, which is associated with the progression of COVID-19. Another research route is through the periodontal pockets observed clinically in the presence of periodontal disease, as a specific reservoir for SARS-CoV-2. Recalling also that the common transmission routes of the new coronavirus include direct transmission (coughing, sneezing and transmission by inhalation of salivary microdroplets) and transmission by contact (contact with oral, nasal and ocular mucous membranes).<sup>10</sup> In dentistry, the greatest threat of infection in practice is found in the air through aerosols (particles less than 50 µm in diameter) in various dental treatments. That is why the need arises to know and understand periodontal diseases in the patient and the complications that may occur in the presence of COVID-19. The coronavirus and other viral-type infections should be considered important for the dentist, due to the risk of contagion to which the dentist is exposed within his professional practice in the context of the COVID-19 pandemic.

## **COVID-19, THE ORIGIN**

COVID-19 is a new coronavirus that is caused by SARS-CoV-2. The first reports of pneumonia from this virus were presented at the end of December 2019 in Wuhan, Hubei province, China. This condition was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>11</sup> The name coronavirus comes from the Latin "Corona", and this is because this figure can be seen with microscopic sight. These viruses, belonging to the coronavirus family, were found in humans since 1965, mainly causing mild respiratory diseases. The three main outbreaks of coronavirus were SARS COV, found in 2002, first reported in the province of Guangdong, China. This outbreak was considered highly contagious and progressive, had an incubation period of 6 days, the most common symptoms that occurred were: fever, dry cough, chills, headache, and dyspnea. On

pulmonary physical examination there are crackles and dullness to percussion, in paraclinical examinations leucocytosis or moderate leukopenia and lymphopenia are observed.<sup>12</sup> The second outbreak reported was middle east respiratory syndrome (MERS-CoV), discovered in humans in 2012 in Saudi Arabia, the first cases described presented severe pneumonia with respiratory distress and extrapulmonary manifestations. One of the main extrapulmonary manifestations is acute renal failure, which occurs in about 50% of patients with MERS-CoV infection. The average incubation period of the infection has been estimated at 5.2 days, the initial symptoms are nonspecific and correspond to fever, chills, pharyngitis, non-productive cough and dyspnea.<sup>13</sup> Finally, causing one of the most serious pandemics, acute respiratory syndrome (SARS-CoV-2).<sup>14</sup> Although it is known that patients who are considered systemically healthy present the disease with mild COVID symptoms. In 2020, Huang and collaborators<sup>1</sup> found that 14% of patients with this virus develop conditions that require hospitalization and 5% require admission to intensive care. Also, the aggravation in patients by COVID-19, has been related to patients subject to comorbidities such as diabetes, high blood pressure, obesity, cardiovascular diseases.<sup>4-6</sup> The immune response of the host will influence the aggravation or not of COVID-19. Patients with severe COVID-19, usually present an exacerbated immune system, generating a response of excessive levels of pro-inflammatory cytokines and generalized tissue damage, leading to the presence of a cytokine storm, here interleukin 6 (IL-6) will be found at elevated serum levels, as well as Interferon alfa (IFN-alpha) and Interleukin 1 (IL-1). Such systemic inflammatory responses could result in diseases manifesting in the oral cavity, especially in the periodontium area.<sup>15,16</sup> The presence of these cytokines could worsen the clinical picture of the patient with COVID-19. Inflammation is mediated by pro-inflammatory cytokines such as IL-6, IL-8, IL-1, TNF-α, with IL-1 being one of the most studied cytokines with properties relevant to inflammatory diseases, including viral infections.<sup>17</sup>

## **CHARACTERISTICS OF THE NEW COVID-19 VIRUS**

The virus of the coronavirus family are infectious agents for both animals and humans. These coronaviruses have an unsegmented single-stranded RNA genome. To the microscopic view, a rounded form is observed with spicules arranged in a superficial structure, that is why the name, because it resembles a solar corona. The virus contains four structural proteins; the spicule (S spike), the envelope (E), the membrane (M) and the nucleoprotein (N). In the case of non-structural proteins, 16 are recognized and are called nsp1 to nsp16. In the case of SARS-CoV-2 coronavirus, it is the protein that recognizes the cellular protein ECA2 (angiotensin-converting enzyme 2) as the main receptor for host cell fixation. The protein (N) provides protection to the genome and intervenes in the synthesis of viral RNA, while the (M) gives structure and stability to the virion;

the protein (E) forms an ion channel whose function is to give the assembly and output of the virions of the host cell.<sup>18</sup> Xu et al.<sup>19</sup> showed that the mucosa of the oral cavity could express levels of the ACE2 protein, occurring in greater expression on the tongue to differentiate from other oral sites. Interestingly, they found that ACE2 is also expressed in lymphocytes within the oral mucosa, although the proportion of ACE2-positive lymphocytes was quite small. These preliminary findings have led to the understanding that the oral cavity has a potentially high risk for infectious susceptibility to SARS-CoV-2 and provide evidence for the future prevention strategy in dental clinical practice, as well as in daily life.

### TRANSMISSION OF COVID-19 IN HUMANS

Transmission in humans occurs through various routes; that is, by direct transmission, by contact, or through aerosols, coughing, sneezing, inhalation of microdroplets. Salivary, contact of contaminated objects by mouth, turn out to be the most common and rapid routes of contagion for SARS-Cov2.<sup>19</sup> Coronaviruses are capable of infecting humans, but their preferred natural hosts are animal species (mammals, birds), and their human infection must be considered a zoonosis. Previously it is known that the transmission of COVID-19, originated in bats, and this possible transmission to humans may have been intervened by other animals, as it was the case of the seafood market in Wuhan City, Hubei Province, China.<sup>20</sup> The first case in humans was described on December 8, 2019, on January 7, 2020 the Ministry of Health of China identifies a new coronavirus as a possible etiology, by January 24, in China, 835 cases had been reported, of which 534 were reported in Hubei, throughout the weeks it spread to other parts of China. On January 13, the first case was reported in Thailand, on January 19 in South Korea, and then in numerous countries around the world, in Mexico the first case was detected on February 17, 2020. For that reason, the World Health Organization (WHO), declares, as of March 2020, a new global pandemic.<sup>21,22</sup> Regarding dentists, the dental practice exposure to this virus is very high since they work at less than 30 cm away from the patient, with mucous membranes, blood, saliva, other body fluids and the management of sharp instruments. Pathogenic microorganisms can be transmitted in dental settings through the inhalation of airborne microorganisms (aerosols) that can remain suspended for long periods of time. In addition, there are other forms of contagion for the dentist and patients, such as contact of the conjunctival or nasal mucosa with drops and aerosols containing microorganisms generated from an infected individual and propelled at close range, coughing or talking without a mask and indirect contact with contaminated instruments or environmental surfaces.<sup>23</sup>

### SIGNS AND SYMPTOMS OF COVID-19

Undoubtedly, the symptomatologic picture varies according to each patient, this already studied previously, will depend on the response of the host, whether or not there is a systemic commitment to the aggravation of the disease. Clinical features range from mild disease to severe disease with fatal outcome. The main signs of COVID-19 were non-specific and mainly reported fever, cough, and myalgia. Other minor symptoms were sore throat, headache, chills, nausea or vomiting, diarrhea, ageusia, and conjunctival congestion.<sup>19</sup>

### MOST USED METHODS IN THE DIAGNOSIS OF COVID-19

- Nucleic acid screening test (Polymerase chain reaction=PCR)

It is one of the most reliable and fast techniques, evidencing the results within a few hours of the sample, for this test a swab in one of the nostrils to the nasopharynx and will turn the swab 5-10 seconds. Subsequently, it will be placed in a viral or universal transport medium, this technique is based on two consecutive reactions, the first is the conversion of RNA to complementary DNA, by means of a transcription enzyme, the second stage is the amplification of complementary DNA by chain reaction of a limerase. This test is currently considered as the gold standard for the detection of SARS-COV2, mainly due to the ability of the probe to measure the viral genomic parts. The sensitivity of this detection technique for COVID-19 depends on the amount of RNA in each sample. For this test it must be taken into account that the viral load of the nasopharynx rises from the beginning of the incubation period (PI) until day 7 and, subsequently, it decreases gradually, the period of maximum sensitivity of the PCR would be obtained in the first week from the beginning of the symptoms. Both in the first days of the PI and after the resolution of the clinic, the viral load is lower and may not be detected. In this test, patients can be classified as SARS-CoV-2 positive (active case) or SARS-CoV-2 negative depending on the test result.<sup>21</sup> Although this technique is considered the gold standard, it is not exempt from false negatives and positives:

- False negatives (<5-40%): This could occur due to obtaining an insufficient sample or low viral load depending on the stage (asymptomatic, pre-symptomatic or post-symptomatic). An inadequate traffic.
- False positives (infrequent): Cross-contaminations between samples may be related.<sup>22</sup>

- Antibody Detection

An antibody (Ac) is a protein produced by the immune system in response to an antigen, also called immunoglobulins (Ig). Of which five classes are known; IgM, IgD, IgG, IgA and IgE. The antibody test measures the presence and concentration of IgM and IgG levels in blood, serum, plasma samples to determine if the body is struggling with a pathogen. The detection of Ac helps to identify patients who have been infected previously, as well as to diagnose symptomatic recent infection from 3-4 weeks. The optimal point to determine Ac IgM/A would be 8-14 days

after symptoms, while after 15-21 days seroconversion to IgG would be performed. For this test a capillary or blood sample is used, the sensitivity of this method usually depends on the RNA amount in each sample, in addition to the fact that the sensitivity increases after the onset of symptoms, with optimal performance from 3 weeks of more than 90% and with a variable specificity between 90% and 99% depending on the utilized test. Patients can be classified as SARS-CoV-2 positive (active case) or SARS-CoV-2 negative.<sup>21-23</sup>

### GENERAL COMPLICATIONS OF COVID-19

Because most patients develop pneumonia, one of the main complications that occur during COVID-19 is Acute Respiratory Distress Syndrome (ARDS), followed by acute heart injury. Fewer reported cases may result in arrhythmia, shock, acute kidney injury, liver dysfunction and some secondary infections.<sup>24</sup> In most cases, patients who required mechanical ventilation had refractory hypoxemia. In addition, it has been found that the main complications that produced a fatal outcome in patients were ARDS, acute heart injury, and large opacities in the lungs.<sup>25</sup> Patients infected with COVID-19 may have a marked lymphopenia, (low number of lymphocytes in the blood, cells responsible for the body's defense against viruses), as occurs in other respiratory diseases caused by virus. In this regard, it could be mentioned that lymphopenia could be useful as a biomarker, that is, the early recognition of this immunological phenotype could be useful to help quickly identify severe patients. In addition, the low presence of lymphocytes is a sign of poor prognosis for those patients with COVID-19.<sup>26</sup> In the case of the systemic inflammation observed in these patients, viral multiplication increases, alveolo-capillary integrity is compromised and the cells of the pulmonary capillaries are mainly affected, increasing the inflammatory response and a higher concentration of neutrophils, monocytes is observed.<sup>27</sup> Most people who have fallen ill with coronavirus (COVID-19) recover for the most part within a few weeks. But in other cases, even those who presented mild symptoms of the disease, continue to present symptoms after their initial recovery, these patients are described as people with persistent COVID-19, and the conditions are called post-COVID-19 syndrome or "prolonged COVID-19." They are generally considered to be COVID-19 effects that can persist for more than four weeks after a positive diagnosis of COVID-19. The most common signs and symptoms that persist over time include:<sup>28</sup>

- Fatigue
- Shortness of breath or difficulty to breath
- Cough
- Joint pain
- Chest pain
- Problems with memory, concentration, or sleep
- Muscle or headache pain
- Rapid heartbeat or palpitations

- Loss of smell or taste
- Depression or anxiety
- Fever

COVID-19 is considered a disease that mainly affects the lungs, but it can also cause damage to other organs, such as the heart, kidneys and brain. These damages can lead to health complications, after COVID-19 illness. In some reported cases, lingering effects may include long-term breathing problems, heart complications, chronic kidney impairment, stroke, and Guillain-Barré syndrome, a condition that causes temporary paralysis. Some adults and children develop multisystem inflammatory syndrome after having COVID-19. In this condition, it causes some organs and tissues to become severely inflamed.<sup>29</sup> Recently, there have been attempts to relate some COVID-19 complications to periodontitis. COVID-19 is associated with an intense inflammatory response in our body, if this effect adds to the systemic inflammation characteristic of periodontitis, the result can be fatal for the patient who suffers from it, it is also pointed out that patients with periodontitis can inhale oral bacteria and infect the lungs, a risk that is multiplied in those patients who use a ventilator, contributing to their deterioration, and thereby increasing the risk of death. The staff of the hospital or care clinic should identify those patients with COVID-19 and periodontitis in which disinfection strategies can be applied through the use of oral antiseptics to reduce transmission and bacterial load.<sup>30-32</sup>

### PERIODONTAL DISEASE

Periodontal disease (PD) is considered to be one of the leading causes of tooth loss in adults.<sup>33</sup> It can also be defined as a set of infectious and inflammatory alterations that mainly affect the supporting structures of the tooth.<sup>34,35</sup> The onset of periodontal diseases refers to a cluster of bacteria that make up bacterial plaque, currently called "biofilm" or bacterial film, these microorganisms are deposited in the cervical part of the teeth. Therefore, it is said that the destruction of the periodontium happens gradually.<sup>36</sup> The periodontium (*peri: around / odontos: teeth*), is made up of the following tissues: gum, periodontal ligament, root cementum, and alveolar bone (Figure 1). Its primary function is to attach to the tooth.<sup>37</sup>



Figure 1. Anatomy of the periodontium.<sup>38</sup>

The mouth hosts the second largest microbial group in the body, with more than 700 diverse species of bacteria, which colonize the hard surfaces of dental organs, and in turn soft tissues of the oral mucosa. It should be noted that, despite the existence of variations in relation to geographical area, ethnicity or race, the main bacteria found in the process of periodontitis are, *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia* and *Treponema denticola*. *Tannerella forsythia* and *Treponema denticola* are the most pathogenic. The complicated balance that exists between these bacterial species influences the healthy state (symbiosis) or a state associated with disease (dysbiosis).<sup>39</sup> The natural condition of the host's response to the aggression of microbial agents is what establishes the expression and progression of periodontal disease, this response can be modified according to the general health of the host.<sup>40</sup> It is known that the predominance and increase of periodontal diseases are associated with aggregate factors such as genetics, immune status, hormonal alterations, and systemic diseases, all these factors together can trigger the presence of inflammation and periodontal destruction.<sup>41</sup> The PD has been widely studied for its relationship with health, demonstrating that they can present as a secondary manifestation of systemic disorders and influence the etiology of various general diseases, such as cardiovascular diseases, rheumatics, cancer, chronic respiratory diseases, and diabetes. Interestingly, some of these factors have been widely associated with the progression or severity of COVID-19; given that inflammatory and dysbiotic aspects affect systemic health, and it is possible that periodontal status indicates the risk of complication.<sup>42</sup>

**PERIODONTITIS**

Among the main oral diseases, we find caries and periodontal disease, as the most prevalent worldwide, so they are considered one of the biggest problems and with the greatest economic impact on the public health sectors.<sup>14</sup> Periodontitis is the most common representation of periodontal diseases, where there is an increase in circulating systemic cytokines and chemokines, a similar picture within COVID-19. For the diagnosis of this periodontal pathology, a thorough analysis, medical and dental history, intra and extra oral examinations, periapical x-rays, are required as auxiliary methods to identify periodontal disease. The main characteristics of periodontitis is the progressive loss of supporting tissues, generating insertion levels greater than 3mm, and a marked decrease in the bone crest.<sup>42</sup> In an earlier, internationally accepted classification, periodontitis disease was subdivided into chronic periodontitis, aggressive periodontitis, periodontitis in response to systemic diseases, necrotizing periodontal diseases, and periodontal abscesses. In 2018, the new classification of periodontal and peri-implant diseases is published by the American Academy of Periodontology (AAP) and the European Federation of Periodontology (EFP) (Figure 2). In this new classification, stages of the disease are managed, where they will be described as follows. Stages I and II are related to the boundary between gingivitis and periodontitis, the

allocation for each stage varies according to the amount of bone resorption and insertion levels, in stage I, bone loss must be less than 15% in relation to the length of the root, and the level of insertion must be in ranges less than 2 mm. In the case of stage II, the ranges vary minimally, focusing on bone loss of 15 to 33% and insertion levels of 3 to 4 mm. In the case of stage III, bone loss oscillates beyond the middle third of the dental organ, and the level of insertion is greater than or equal to 5 mm, in addition to tooth loss (4 pieces). Stage IV, here is observed an evident periodontal damage, loss of dental organs higher than 5 teeth.<sup>43</sup>

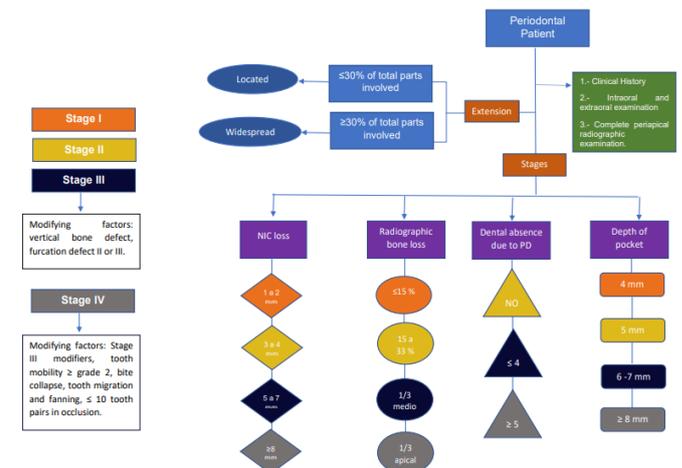


Figure 2. Current classification of periodontal diseases (2018). Diagnostic diagram of periodontitis, according to the new classification of periodontal diseases, which shows the degrees and stages.<sup>43</sup>

**EPIDEMIOLOGY OF PERIODONTAL DISEASE**

Periodontal disease is considered by the World Health Organization (WHO), as one of the main oral conditions worldwide, the distribution has a direct relationship with the higher prevalence in groups with economic and social disadvantages. In addition to bordering other types of conditions such as malnutrition and some psychosocial problems.<sup>44</sup> Periodontal disease, in conjunction with tooth decay, are the most frequent conditions worldwide. In Mexico, according to reports from the SIVEPAB (Epidemiological Surveillance System of Oral Pathologies), in its 2019 report, from a total of 143,995 people studied, 41.7% of the population had a healthy periodontium, it was observed that, in the group between 20 and 34 years old, almost five out of ten patients did not present periodontal disease, while, from the age of 50, the figure decreases to four out of ten. In addition, it was observed that the prevalence of gingivitis is greater than 50% in all age groups.<sup>45</sup> Although oral health is recognized as an integral component of the right to health, there are still gaps in the generation of governmental and intergovernmental health programs. The level of awareness of the general population on this issue remains very low. Too often, periodontal diseases continue to be considered more of an aesthetic problem than a disease. Gingivitis,

considered the mildest form of periodontal disease, occurs in almost all populations, but periodontitis affects approximately 50% of adults in the United States, and advanced periodontitis affects approximately 11% of the world's population.<sup>46</sup> It is well known that PD shares broad risk factors with other conditions. Some of these factors are age, sex, genetics, race, some immunosuppressive diseases such as HIV/AIDS, and other systemic diseases, these factors are not modifiable. However, there are other risk factors that are modified, because it is possible to act on a specific behavior; these are factors that are often related to lifestyle (such as smoking and alcohol), metabolic factors (diabetes and obesity), dietary factors (deficiency in the diet of calcium or vitamin D), or stress. In addition, some local factors can be prevented directly by the dentist; such as plaque levels or calculations, defective restorations and the use of partial prostheses (crowns, bridges).<sup>47</sup>

### INTERACTION BETWEEN PERIODONTITIS AND COVID-19 IN THE LITERATURE

The progression of periodontitis occurs by means of dysbiosis between the host and the oral microbiota.<sup>48</sup> When there is a state of health, most bacterial species generate a symbiotic relationship with the host. For example, potentially cariogenic bacteria or pathogenic periodontium have been detected in health, but at low levels, decreasing the risk of disease. The potential association between periodontitis and the clinical course that COVID-19 may take could be explained through alterations in the expression of cellular receptors that would increase the virulence of COVID-19.<sup>49</sup> Various mechanisms have tried to explain how the condition of COVID-19 can be aggravated, through the pathogens present in the mouth, when they are aspirated into the respiratory tract, this in patients who have required intubation for their recovery (Figure 3). There is an alteration in the surface of the mucosa of the respiratory tract by means of salivary enzymes that lead to a colonization of pathogens in the lung.<sup>50</sup>

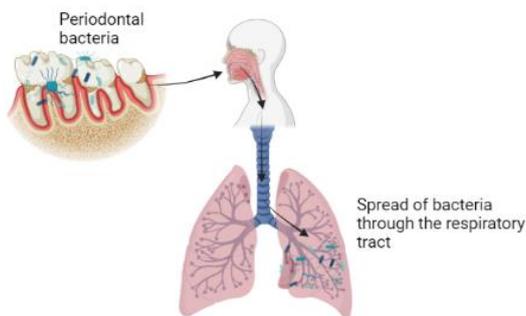


Figure 3. Periodontal bacteria can spread to the lower airways as a result of aspiration of saliva or food, especially in people with endotracheal intubation.<sup>50</sup>

There is also a theory about the possible correlation between these two diseases through periodontal pockets, an important clinical sign in patients with periodontitis, these periodontal

pockets (PP) could act as a niche for SARS-CoV-2 infection, here the virus could find an optimal environment for its replication, by mixing with saliva or migrating systemically through the capillary periodontal complex. Bps as a reservoir of different viruses have been studied on different occasions, among the various dental publications that are available, viruses such as Herpes simplex (HSV), Epstein Barr virus (EBV), and Cytomegalovirus (CMV) have been detected.<sup>51</sup>

In COVID-19, ACE2 has been considered as the main receptor for the entry of SARS-CoV-2 into human cells, these enzymes are not only present in the mucosa of the lungs, but also in the nasopharyngeal mucosa, salivary glands, and in some epithelial cells of the mouth, so the saliva or crevicular fluid of the patient results with high viral load.<sup>36</sup> In addition to the fact that this enzyme is also identified in patients free of SARS-CoV-2, but with periodontal disease, in various cellules such as osteoblast fibroblasts and osteoclasts, which are mainly responsible for the remodelling of the bone and soft tissues that surround the dental organs.<sup>52</sup>

Other studies could indicate that there is a relationship by increasing IL7 (Interleukin 7) produced in gingival tissue in patients with gingivitis and stage II and III periodontitis, this could explain the marked increase of pro-inflammatory cytokines in the circulation in response to inflammatory processes in periodontal tissues.<sup>53</sup>

### BIOLOGICAL LINKS

The multiple bacterial communities present in the oral cavity, make up a mechanism called "Polymicrobial synergy and dysbiosis process". It generates the very relationship between bacteria, and then becomes a dysbiotic community in the process of disease, mainly generating inflammation and tissue damage. According to the literature, three main mechanisms are considered that could promote the development and reproduction of SARS CoV-2 in lung cells in the presence of periodontal pathogenic bacteria, first the senescence induced by *P. gingivalis* is considered, second the exacerbated state of local inflammation in response to SARS CoV-2, and third the decrease in immune surveillance caused by the presence of periodontal bacteria.<sup>54,55</sup> In some articles it is mentioned in summary that in adult patients with a decadent oral hygiene, a greater amount of oral pathogenic bacteria can be generated, bringing with it a greater translocation of pathogens into the respiratory tract.<sup>56,57</sup> And it is that with the COVID-19 pandemic, the SARS CoV-2 virus has received special interest within the scientific and medical community for the behavior it has had, which is why it is believed that the oral cavity can act as one of the main sources of contagion and reproduction of that virus in its active form, this is possibly thanks to the presence of ACE2, facilitating the fixation to the target cells, turning the oral cavity into a source of contagion.<sup>58</sup> Within the hypotheses formulated by some studies, it is observed that 50% of the patients who perished due to serious complications of COVID-19 were related

to secondary infections, mainly systemically compromised patients with various comorbidities mentioned above, in addition to virus. The interactions between the patient's comorbidities, dysbiosis of the oral microbiome has been studied on several occasions, which is why the possible links between COVID-19 and periodontal diseases are of important recognition and understanding.<sup>59-61</sup>

## CONCLUSION

Consequently, improving the oral status of people without age criteria could considerably reduce some of the effects that occur in COVID-19. Poor oral hygiene can increase the risk of bacterial exchanges between the lungs and mouth, increasing in turn, the risk of respiratory infections and potential post-viral bacterial complications, so it is suggested to emphasize the maintenance of good oral hygiene and the control of pre-existing periodontal disease, particularly in that population at risk of developing COVID-19. In addition to promoting as health professionals awareness about gingivitis and periodontitis, as well as their consequences, with great emphasis on the fact that PD is not only an aesthetic problem, but an important health problem. It is important to promote PD prevention, through changes in habits and lifestyles. Although within the literature, the correlation of these diseases seems to have the necessary evidence, more research is needed to obtain a predictive determinant in this relationship. According to the evidence found in relation to these two diseases, it is found that the influence of PD coupled with the presence of other diseases could become critical of the patient's condition. Undoubtedly, the pandemic that occurred in the world due to COVID-19 was a challenge that has passed over all levels and sectors of health. For dental practice was no exception, the complexity of patient care in this pandemic increased because the transmission of the virus is mainly through saliva droplets, having direct contact with natural reservoirs of the virus such as the tongue and mucous membranes of the oral cavity, placing us in an extremely adverse scenario. Being able to identify the mechanisms of interaction between both pathologies can contribute to recognize those patients who are in a line of risk of complications, by containing the problem, making patients aware of the benefits that good oral hygiene brings and in a positive way that it has repercussions at a general level systemically speaking. In addition to generating in the dentist the awareness about the importance of having clean and disinfected offices, personal protection measures for both the dentist and the patient, in order to avoid any type of contagion.

## CONFLICT OF INTEREST

**The researcher declares that there was no conflict of interest during the performance of this work.**

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