

Periodontal Disease: A Threat to Covid-19 Severity

Research Article

Bushra Ijaz^{1*}, Farzeen Tanwir^{1,2,3,4}, Chander Kumar³, Saima Mazhar¹, Syeda Natasha Zaidi¹, Sarah Moideen^{2,4}, Areeba Dilshad⁵, Hira Ejaz⁶¹ Department of Dentistry, Bahria University Dental College, Pakistan.² Department of Dentistry, Fatima Jinnah Medical and Dental College, Pakistan.³ Department of Dentistry, Dow University Health Sciences.⁴ Department of Pharmacology, Fatima Jinnah Medical and Dental College, Pakistan.⁵ Management Trainee officer, Department of Quality Assurance, Memon Medical Institute Hospital, Pakistan.⁶ Malir Shed Hospital, Karachi, Pakistan.

Abstract

PD is an inflammatory illness affecting tissues that surrounds teeth. Co morbidities linked with PD are age, smoking, diabetes, hereditary, poor oral hygiene. These factors have been linked with severity of COVID-19, caused by virus namely corona virus "SARS-CoV-2." As dysbiotic, inflammation and comorbidities disturb general well-being, it is probable that "periodontal status indicates the risk of complication of COVID-19". Patients with COPD have a higher risk of provocation with COVID. Pregnancies can be complicated with co infection of SARS-CoV-2 with periodontal disease. Diabetic people also have PD probably because they are more prone to contract infections and higher chances to develop COVID-19 can also be increased with obesity and its consequences. Researchers have proved that aging is linked with PD and severe COVID-19 along with these factors. Smoking is the major risk factor in PD which leads to increase in enzyme ACE2; it's an important element for development of covid-19. Chronic inflammation of airways had showed a relation between periodontal disease and asthma with enhanced ACE2 and TMPRSS 2 expression, increased SARS COV-2 infection susceptibility and Covid19 morbidity. Rheumatoid arthritis and liver disease also correspond to the development of covid-19 along with periodontitis. Patients who had history of liver disease have more chances to get SARS-COV-2 by means of the ACE-2 receptor. Degree of immunosuppression is thought to play a part in the vulnerability to SARS-CoV-2 infection. Hence, knowing the link between periodontal disease and COVID-19 severity, can aid in identifying the risk groups and create recommendation. The goal of the this review paper is to explain in detail the co-relation between periodontal disease and covid19.

Keywords: Corona Virus; Periodontal Disease; Risk Factors; Covid19 Pandemic.

Introduction

"Periodontal disease" also referred to as "gum disease". It is a set of inflammatory illnesses distressing the tissues that surrounds the teeth. In its initial stage, which is called gingivitis the gums turn out to be red, swollen and might start bleeding. Its signs and symptoms include: soreness or bleeding of gums while cleaning teeth, bad breath, after brushing spitting out blood, swelling of gums or formation of pockets between gums and teeth, in some cases teeth may become mobile in later stages [1]. Periodontal disease consists of gingivitis and periodontitis, the most common disease of mankind. Its extreme form is distinguished by periodontal ligament loss and destruction of adjacent alveolar bone.

Global prevalence of periodontal disease increased by 57.3% from 1990 to 2010 [2]. Risk factors of periodontal disease include diabetes, hereditary, and stress, poor oral hygiene, smoking, medication, age [3].

Covid-19 disease is caused by a virus called novel "corona virus", SARS-CoV-2, it was found in Wuhan, China. Globally the prevalence of patients infected with SARS-Cov-2 has exceeded 83,652 on 28 February 2020, and also number of mortality cases of Covid-19 that is 2858 has been reported. On March 11, 2020, COVID-19 was professed a pandemic by the World Health Organization (WHO). As of 27 March, 2020, a total of 103,942 confirmed cases with 1689 deaths in the United States reported

***Corresponding Author:**

Bushra Ijaz,
Department of Dentistry, Bahria University Dental College, Pakistan.
E-mail: bushraijazz96@gmail.com

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Figure 1. An outline of Covid-19 infection. COVID-19 is more evident in people with co morbidities such as cardiovascular disease, periodontitis, obesity and diabetes. It triggers uncontrolled cytokine production (cytokine storm) and inflammation by inducing oxidative stress. The chances of morbidity and mortality rate increases in vulnerable populations [4].

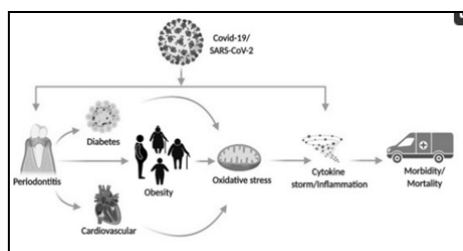
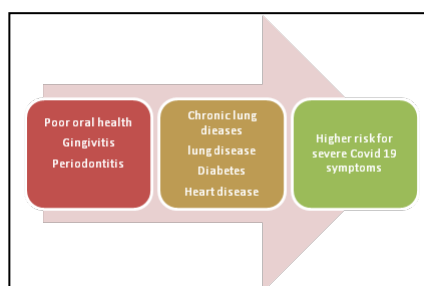


Figure 2. These events lead to poor oral health and intensify covid-19 symptoms [9].



globally, 27,324 expiries have been reported amongst 595,800 confirmed cases [5]. Uptillnow 85 403 patients in 57 territories/ countries are effected by Covid-19 and 2924 deaths in 9 countries are reported. Comparatively death and illness and cases are more reported in china than other countries. Evidence has reported in Current epidemiological reports the transmission of Covid-19 is form person to person in family and also in hospital facility, the death ratorate was highest 4.47% in Wuhan. A public health emergency of international concern was constituted by WHO when they declare SARS-COV-2 outbreak [6]. Initial signs and symptoms at incubation period, include: cough, fever, myalgia and fatigue, however those who have lung disease, asthma ranging moderate to severe, stern obesity, CKD (chronic kidney disease), diabetes, and liver disease are as well at increased risk for severe symptoms of COVID-19 [7]. The studies have shown that those having chronic respiratory disease, diabetes, hypertension, has higher risk of covid-19. In addition, age can be a risk factor [8]. The goal of this article is to study Covid-19 and periodontal disease at individual level and to assess the link between these two. The importance of this review paper that periodontal disease, its risk factor can be associated with Covid-19 severity. This paper explain SEVERE COVID-19 ILLNESS AND PERIODONTAL DISEASE SHARED RISK FACTORS that are Mouth-Covid Connection, Chronic obstructive pulmonary disease (COPD), Pregnancy, Inflammatory Markers, Diabetes, Obesity, Aging, Hypertension and Cardiovascular, Oral dysbiosis- ETHIOPATHOGENIC, Smoking, Asthma, Gender, Rheumatoid arthritis, Liver Disease ended with HIV.

Hypothesis

“It is hypothesized that Periodontal disease can be associated with increased risk of COVID-19 severity.”

COVID-19 patients, who also have other co morbidities and risk factor, also exacerbate the risk of periodontal disease. Until now, evidence on oral health history counting periodontal status in patients with intense COVID-19 infection has not been reported [9].

Severe Covid-19 Illness And Periodontal Disease Shared Risk Factors

Mouth-Covid19 Connection

According to researcher, in Covid19 patient's interleukin-6 is associated with pulmonary consequences. Systemically and locally cytokines are increase due to periodontitis, it also linked with respiratory condition, lung function, pneumonia, and COPD. Therefore, there is connection between covid-19, periodontitis and IL6 for this alliance the mechanism can be due to endothelial function, gut dysbiosis, inflammation, and disturbance in IL-6 gene, which also aggravate the inflammatory response, elevated levels of pro inflammatory cytokines, such as IL-6, have been related to periodontitis. In periodontal disease IL-6 is a known mediator. In the dental literature, to reduce cytokine levels the ability of nonsurgical periodontal therapy has been recognized. As a result, periodontal disease can potentially protect COVID-infected individuals by lowering IL-6 levels and inflammation. In adults the frequency of periodontal disease is higher and the link between respiratory problems, periodontal treatment IL-6 levels and COVID-19 can be significant. In periodontal tissues, saliva, GCF and serum in periodontitis patients, increase IL-6 levels have been reported. The relationship between periodontitis and COVID-19 has various biological mechanisms. The pulmonary endothelium and gut microbiome can be influence by periodontal disease because of the dental bacterial load and systemic inflammation it causes. Oral pathogens via aspiration of oral bacteria may also enter the respiratory tract and boost the severity of the disease by interrelate with the SARS-CoV-2 virus [10].

Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease is persistent Lung disease is caused by revelation to gases or elements that are toxic, in urbanized states smoking being a major risk feature. COPD and PD are associated as per different studies on the other hand; different

factors can confound this link such as smoking. Or age lately, it was suggested that in older patients severe periodontitis has more chances for COPD mortality or causality, the molecular mechanism is unknown. It was stated that patients, when they present COPD have a higher risk of provocation with COVID-19 and those patients have a 4-fold greater risk to build up COVID-19 illness severely with preexisting COPD. It was proposed that patients with chronic obstructive pulmonary disease ACE-2expression are increased leads to increased risk. Hence, to recognize risk groups to develop severe COVID-19, the link of PD with COPD could be useful, as the risk of this affection importantly increased by COPD [7].

Pregnancy

Pregnancy leads to many physiological changes, and to allow gestational growth by suppressing the mother's immune system. It was reported in studies that in pregnant women the susceptibility of PD is because of exaggerated inflammatory response over the last few years. In addition, it has been established that the gingival response is triggered by high progesterone levels and leading to dysbiosis. High periodontal pathogens development occurs in this way, leading to medical manifestations in the protective and supporting tissues of teeth. While, the connection among pregnancy and PD is debatable, along with PD and pregnant women as they may have complications during premature delivery or pregnancy, some risk has been suggested. As long as worldwide the novel coronavirus SARS-CoV-2 is increasing, some cases in pregnant women of COVID19 have been confirmed. Although, women with pregnancy are predispose to respiratory infectious disease due to estrogen levels, high progesterone and immunosuppression, only fewer than 10% prone to severe COVID-19 disease. But, prenatal

events such as, premature breakage of the membrane, preeclampsia, low birth weight can be complicated by infection or it can even cause death cases of COVID-19 with Vertical transmission are not completely confirmed. Although the association between periodontal disease and pregnancy is not clear, stating the fact. Pregnancies in pregnant women can be complicated with coinfection of SARS-CoV-2 with periodontal disease [7].

Inflammatory Markers

In Covid-19 infection anosmia and Aguesia are common finding of patient however 20% of the patients develop serious illness with 6% mortality rate which is mostly related with systemic diseases, older age and immunosuppressant. Patients have elevated levels of serum pro-inflammatory cytokines also chemokine including IL1RA,IL1-b, IL2, IL6,IL7 IL8, IL9, IL10, MCP1 – 1a, FGF2, GMCSF, GCSF, IFNc, TNFa and IP10, that lead to stimulate infection severity. Dental specialists can get diseased easily due to their straight revelation to blood and saliva [11].

During periodontitis, Low serum CD133+/KDR+ levels appear to be associated with the likelihood of evolving forthcoming endothelial dysfunction and CVD threat. Interestingly, these provocative features of the host and disrupted immune-regulation in PD have been extensively linked with development or severe corona virus illness (COVID-19) [12].

Diabetes

In older age, presence of hypertension, Diabetes Mellitus and stern obesity (BMI 40 kg/m²) enhance illness and death in patients of COVID-19 [5]. It can be difficult to treat diabetic patients with

Figure 3. The illustration explain biological link between corona virus disease, respiratory problems and periodontitis. The significance of this evaluation lies in the awareness that on the COVID-19 pandemic, dental experts can have a key impact through periodontal health promotion, taking in account the benefits of hindrance and treatment of periodontal disease on general well-being, with the prevention of complications resulting from the corona virus [10].

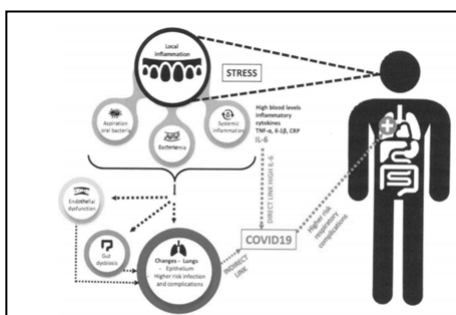


Figure 4. Some common systemic diseases and chronic periodontitis segments links with numerous chronic inflammatory illness. Proinflammatory cytokines, important immune-related mediators are additional elements, involved in the disease pathogenesis. Only the most shared noncommunicable illnesses and pregnancy difficulties were illustrated, even though others (neurodegenerative disorders, rheumatoid arthritis, etc.) show links with chronic periodontitis [13].

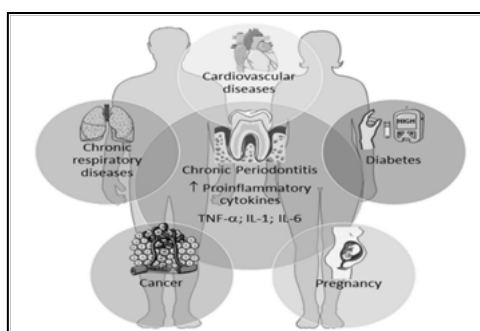
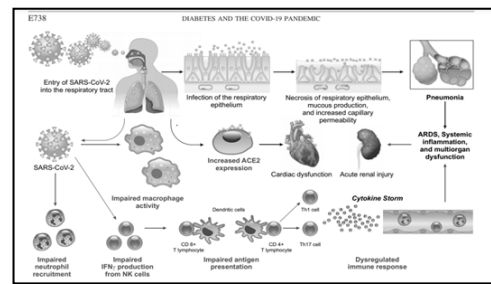


Figure 5. Diabetes and Covid-19 [5].

viral infection due to variations in plasma glucose levels because of two reasons. Firstly, if the defensive system is compromised, it is problematic to combat the infection and leading to prolonged recovery period. Secondly, if levels of blood glucose are high the virus may grow, similar to other respiratory disease; COVID-19 is transmitted through air-droplets that are scattered when person who is infected sneezes, cough and talks. Depending on the ecological conditions the virus can continue to exist from a few hours up to a few days [14]. Mechanisms that may enhance the liability for COVID-19 patients with DM contain: 1) decreased viral clearance, 2) existence of CVD, 3) advanced affinity cellular binding and efficient virus access 4) reduced function of T cell 5) enlarged susceptibility to hyper infection and cytokine storm syndrome [5].

Individuals with diabetes are expected to have periodontal disease PD, probably because they are more prone to contract infections. It is considered a complication of diabetes. Those people whose diabetes is not controlled are at risk. It was reported that diabetes and periodontal disease are linked. PD makes it harder for individuals who have diabetes to control their levels. Extreme periodontal infection can expand glucose, adding to expanded timeframes when the body capacities with a high glucose. This puts individuals with diabetes at danger for periodontal difficulties [15].

Obesity

With increasing prevalence yearly, almost 50 percent of the population is obese or over weight. It is counted as an utmost risk factor for developing periodontal disease after smoking. Alteration of microbial composition of periodontal can occur with Obesity and is linked with an increase in periodontal pathogens. A systemic inflammation state is the main consequences of obesity in individuals if PD is established and accompanied by the proinflammatory cytokines and bacterial products dissemination [16]. The threat to progress severe COVID-19 disease can be increased with obesity and its consequences. Factors drawn in this could be functional capacity, reduced expiratory reserve capacity, and respiratory system acquiescence. Moreover, reported in obesity the augmented inflammatory factors could contribute to intensify the development of severe COVID-19 and the response of the patient [17]. Periodontal Disease, by dissemination of bacterial products could add to the intensification of a complete inflammatory response and as a cause of inflammatory cytokines in individuals with COVID-19, consequently leading to the disease aggravation. Furthermore, the people with PD and obesity have a bigger threat of developing extreme COVID-19 possibly [7].

Aging

Adults are more prone to periodontal disease because of additional risk factors, presence of chronic diseases, delayed dental treatment, poor oral hygiene and use of medication. Smoking can also amend gingival micro biota and cause periodontal disease and respiratory tract infection [18-20]. Above 65 years of age, people are likely to have severe COVID-19 illness [7]. Other factor which is important is immunity and that is not as strong as young ones [21]. Hence it is proved that aging factor is linked with PD and severe COVID-19.

Hypertension and Cardiovascular

In PD, Chronic inflammatory response is induced by bacterial species that lie in sub gingival bio film by encouraging the production of cytokines "IL-1, IL-6, IL-8 and TNF-a" [22]. Which increase and regulate levels of (CRP) C-reactive protein. High density CRP is a marker present in cardiovascular diseases and also in periodontitis where it is increased by large production of cytokines [23-25]. Hypertension represents one of the main comorbidities to the COVID-19 patients. CVD is also an important risk factor; epidemiological studies have established a link between periodontitis, cardiovascular disease and hypertension [26].

Oral dysbiosis - ETHIOPATHOGENIC

When the bacteria of oral micro biota are imbalanced it is called oral dysbiosis [4]. It is also associated with oral disease like periodontitis, candidiasis etc. whereas, oral microbes including Porphyromonas gingivalis, Salmonella, Prevotella intermedia and others involved in periodontitis [26]. Impaired oral health is reported in patients who are hospitalized with severe Covid-19 illness or on some lifesaving mechanism or intubation. Moreover other factors like, lack of oral hygiene, use of drugs that attack the SARSCoV-2 virus, and other comorbidities can produce dysbiosis and could trigger oral diseases like periodontal disease [21]. In oral mucosa levels of ACE2 are increased in covid-19 patients due to presence of fusibacterium, Prevotella hence it proved the link between Covid-19 severity and periodontitis [26].

Smoking

In periodontal disease smoking is the major risk factor, because of which periodontal treatment is also affected, smoking impedes host immune response, periodontal tissue activity and powerful microenvironment to combat against pathogen. Whereas expression of angiotensin converting enzyme ACE2 is increased by

smoking and it is also a major factor for development of covid-19, being more probable about 1.4 times to have severe symptoms of COVID-19 [27].

Asthma

Chronic inflammation of airways occur in asthma and research showed a relation between periodontal disease and asthma [27-29]. In adults it might be a threat element for periodontal illness however it can be due to genetics, inflammatory factors or dysbiosis [7]. It was stated that asthma might be a peril for severe COVID-19 disease. In COVID-19 patients, asthma had low prevalence [30]. In this patient with enhanced ACE2 and TMPRSS 2 (Transmembrane protease, serine 2) expression, increased SARS-CoV-2 infection vulnerability and Covid-19 morbidity is indicated. Along these findings could suggest that periodontal disease with asthma could refer as a strong risk for Covid-19 development [31].

Gender

It is stated in research studies that, women are less prone to the development of periodontal disease as compared to men [30, 32, 33]. Most likely immune function, environment and behavioral factor are involved to explain this difference [34]. Likewise in Covid-19 illness it was suggested that in men there are more chances than women. Immunity reaction to SARS-CoV-2 may explain this discrepancy therefore its alliance with immunologic factors and gender periodontal disease might show the risk of Covid-19 [35-37].

Rheumatoid arthritis

It is reported in studies that people with rheumatoid arthritis and periodontal disease have weakened systemic status, RA is a chronic inflammatory disease that has been allied with periodontal disease its prevalence is 0.3 to 1%. Its mechanism is unknown. However *Porphyromonas gingivalis* produces an enzyme that causes citrullination [38]. Synovial fluid has been found to contain periodontal bacteria [39]. Patients with rheumatoid arthritis are more prone to communicable diseases and death rates are increased due to bronchopulmonary infection [40]. Relationship among rheumatoid arthritis, periodontal disease, bacterial and inflammatory systems could influence the result in people having COVID-19 [41].

Liver Disease

Relationship has been found among periodontal and liver disease. Nonalcoholic Fatty Liver Disease (NAFLD), liver cirrhosis (LC), hepatocellular carcinoma (HCC), have 20-30% prevalence all throughout world. Significantly transplantation of liver is related with PD, as to stay away from sepsis by periodontal pathogens the person with disease must be inspected by an oral expert before LT [42-45]. Subgingival microbial niches promote periodontal tissues inflammation and cytokines "IL-1 β , IL-6, IL-10, IL-12, and TNF- α and INF- γ " that participate in the development of liver disease. It is likewise associated with Covid-19; patients who had history of liver disease are more liable to SARS-CoV-2 as by means of the ACE-2 receptor as virus binds to hepatocytes and cholangiocytes [46]. Therefore patients with periodontal disease and liver diseases aid to discover those individuals who are at risk for COVID-19.

HIV

Immune-compromised patients have more chances of systemic and oral indexes [47, 48]. According to researcher periodontal disease is linked with HIV because it is a chronic inflammation [49]. Some articles also stated that in prevalence of periodontal disease HIV is an important factor [50]. Whereas HIV is also associated with Covid-19 and the degree of immunosuppression is thought to show a part in the vulnerability to SARS-CoV-2 infection [51].

Complications

According to an international team of dental researchers, Covid-19 patients whose reports are positive if they suffered from periodontitis and are hospitalized are far more probable to die of respiratory failure. Patients who are hospitalized with COVID-19 have high interleukin (IL-6) levels, which is a harmful protein produced by periodontitis, are at considerably larger risk of suffering life-threatening respiratory problems and are probably in critical condition and unable to breathe without the ventilator. In recent study, it is shown that in COVID-19 patients who had gum disease inflammation in their body were clearly higher as compared to those who did not. The results of the study suggest that the oral cavity inflammation possibly will unlock the door to the corona virus being more aggressive [52].

Scientific Contribution: This paper contributes scientifically until now, evidence on oral health history counting periodontal status in patients with intense COVID-19 infection has not been reported.

Conclusion

PD could be allied with severe COVID-19. Many researchers have shown a potential connection between periodontal disease and coronavirus. The bacteria involved in covid-19 seems to be similar to the ones from the oral cavity. Gingival Tissue that is affected from periodontitis represent a board entry point for viral or bacterial pathogens such as "SARS-CoV-2". Individuals with severe medical conditions such as, respiratory disease, diabetes can be a major risk factor for the development of covid-19 as well as periodontitis since both of these share same risk factors which itself is an indicator for the urge of immediate attention. Diagnosis of SARS-CoV-2 in an individual along with the presence of periodontitis can worsen the condition and effects.

Future Recommendation

1. Further studies should be done to reveal the unknown mechanism between Covid-19 and periodontal disease.
2. Individual having co-morbidities like diabetes, respiratory disease, HIV, hypertension and other above mentioned, should take additional precautions.
3. Oral hygiene should be maintained especially in this pandemic to lower the risk of covid-19, since a possible link between Covid-19 and periodontitis is observed.
4. Studies should be conducted to assess the risk of Covid-19 transmission while going through aerosols procedures.
5. Public awareness sessions should be planned on how to maintain your oral health since it could play a key role in battling the virus it is stated that if good oral health is maintained, particularly

“healthy gums” risk of developing the most serious complications of corona virus are limited .

6. Further researches are necessary to identify the factors that are still unknown and can lead to the complications of Covid-19.

7. Periodontal education should be provided along with other forms of health education.

8. Further, clinical trials which can evaluate periodontal status in individuals suffering from covid-19 are required to conclude the correct mechanism as already mentioned that poor oral hygiene can elevate the Covid-19 infection.

9. Relationship between COVID-19 illness and smoking is not fully understandable; therefore, further research is important to identify the danger of smokers and succession of Disease.

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