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Review Article

Novel Corona Virus (SARS-COV-2) and Periodontal Disease Corelation: A Review

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Abstract

COVID-19 has been declared as the pandemic throughout the world-by-World Health Organization. Research scholars all over the world are scrambling to gain knowledge of this novel corona virus that has been associated with the disease. Periodontal disease is a group of infectious, inflammatory disorders with the main pathogenic mechanism rooted in cytokine release. COVID-19 and periodontal disease both show the same cytokine expression to a great extent. In this era of COVID-19 understanding of this association between the two seems very important.

Keywords: COVID-19; Periodontitis; Severe Acute Respiratory Syndrome Coronavirus 2((SARS-CoV-2); Cytokine Storm; Inflammation

Introduction

Periodontal disease is a group of infectious, inflammatory disorders involving various risk factors leading to the destruction of tooth supporting structures of the periodontium. Several studies over the years have established a bidirectional link between periodontal disease and various systemic conditions [1].

Inflammation of the periodontal tissues increases the systemic inflammatory burden that leads to the hyperresponsiveness of the host immune system and increased release of proinflammatory cytokines and other mediators into the circulatory system [2]. Tumor necrosis factor-α, interferon-γ, prostaglandin E2, interleukin (IL)-1β, IL-4, IL-6, IL-10 and C-reactive protein levels are markedly increased during periodontitis [3].

(COVID-19) Coronavirus disease initially named as 2019 novel coronavirus (2019-nCoV) is a severe acute respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [4]. The disease outbreak was first reported in Wuhan, Hubei, China with subsequent global spread [5]. There is an expression of Spike protein (S-protein) by this single stranded RNA virus SARS- CoV-2 that promotes invasion of host cells [6]. The S-protein binds specifically to angiotensin converting enzyme 2 (ACE-2). The bidirectional link between respiratory disease and periodontitis has been shown in various studies [7]. Alteration of cytokine profile could be part of the potential mechanism responsible for the association between periodontal disease and COVID-19.

The cytokine connection

Apart from the few patients that develop mild to moderate symptoms, mostly SARS-CoV-2-infected individuals remain asymptomatic. Less than 5% of individuals develop serious symptoms like acute respiratory distress syndrome (ARDS) and multiple organ failure requiring ICU support. The cytokine expression profile shows a lot of similarity in Periodontitis and COVID-19 patients suggesting a possible link [8,9]. There is a release of proinflammatory cytokines as a result of activation of NLRP3 inflammasome due to viral replication in the host cells. Exaggerated cytokine release is further enhanced by release of damage associated molecular patterns (DAMPs). This increased cytokine release is referred to as cytokine release syndrome [10,11].

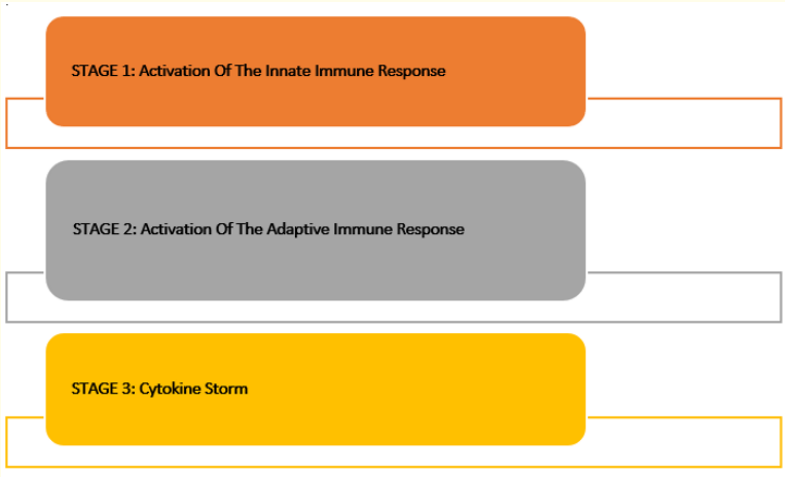

Figure 1

Host-virus interaction

- **Stage 1**: Can also be referred to as asymptomatic stage. PAMPs (Pathogen Associated Molecular Patterns) facilitate virus recognition that activates the innate immune response.
- **Stage 2**: Is associated with mild symptoms. It is characterized by the adaptive immune response. DAMP (Damage Associated Molecular Pattern) release further exaggerate the inflammatory response.
- **Stage 3**: Represents shock, multiorgan failure and cytokine storm [12].

Related studies

Huang., *et al.* 2020 compared cytokine release in COVID-19 patients treated in ICUs with those who did not require ICU support. The results showed enhanced release of IL- 1β, IFN-γ, chemokines (CCL2 and CXCL10), IL-6, IL-10, and TNF-α in patients admitted to the ICU compared with those who were not [13].

Herold., *et al.* 2020 assessed IL-6 levels in COVID-19 patients. The study showed a strong association between IL-6 levels and requirement for mechanical ventilation. The cut off value of IL-6 was 80 pg/mL. The risk of respiratory failure was 22 times higher compared with patients with low IL- 6 levels [14].

Coomes., *et al*. 2020 concluded that increased levels of IL-6 were significantly associated with adverse outcomes.2.9-fold higher levels of IL-6 in critically ill COVID-19 patients were found when compared to patients with mild or moderate disease. IL-6 could be considered a potential target to regulate host responses and minimize COVID-19-associated adverse events [15].

COVID -19 and periodontal disease

Poor periodontal health means increased bacterial load in the oral cavity. This leads to oral dysbiosis. There is relative increase in the number of pathogens and decrease in the number of beneficial species resulting in microbial shift. This also increases the risk for respiratory infections [16]. Recent Studies suggest that 50% of the critically ill COVID-19 patients died from secondary bacterial infections rather than the viral infection itself [17].

As stated above poor periodontal health increases the bacterial load in the oral cavity so we should acknowledge the potential link between COVID-19 and periodontal disease. Also there is established bidirectional link between Periodontitis and Diabetes Mellitus, hypertension, cardiovascular disease etc [18,19]. Patients with various systemic conditions like diabetes, hypertension, COPD, cardiovascular disease were at increased risk of post-viral complications and death from COVID-19 [20].

The (S-protein) expressed by this single stranded RNA virus SARS- CoV-2 that promotes invasion of host cells is activated by Trypsin like proteases. These enzymes are expressed in abundance by putative periodontal pathogens in the oral cavity, thereby help-

ing in viral infection spread [21]. The study conducted by Gupta S., *et al.* 2020 also suggest that periodontal pocket may act as a reservoir for virus replication and the gingival crevicular fluid (GCF) may act as a mode of transmission [22].

It can be concluded that oral dysbiosis, cytokine storm, immune hyper stimulation caused by periodontal disease can increase the severity of COVID-19. However further studies are needed to establish a firm link between SARS-CoV-2 and periodontal disease.

Conclusion

Periodontal disease increases the oral microbial load and leads to the increased production of pro-inflammatory cytokines. These cytokines are linked to adverse events associated with COVID-19. Various pre-existing systemic conditions like Diabetes Mellitus, cardiovascular diseases, COPD further increases the risk of mortality in COVID-19 patients. These comorbid conditions further have established bidirectional link with periodontal disease. Further clinical trials evaluating periodontal status in patients with COVID-19 are required to determine the exact mechanisms. Because poor oral hygiene could exaggerate SARS CoV-2 infection, it is essential to maintain good oral hygiene and periodontal health to preserve overall health.

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