



IS COVID INTENSITY INCREASED BY PERIODONTITIS ?

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ABSTRACT

There is sufficient evidence of a link between periodontitis and non-oral systemic diseases. Periodontal disease (PD) is a category of diseases that include inflammatory features of the host and dysbiotic activities that impact periodontal tissue and can have systemic consequences. In addition to mortality owing to pneumonia, the virus COVID-19 has been shown to cause a hyperinflammatory disease with the release of immune modulators and mediators.¹ This has been identified as a "cytokine storm" that has been shown to trigger cardiomyopathy, disseminated blood clots, stroke through broad vascular occlusion, neurological complications, thrombosis, and multi-organ failure, including heart, kidney, and brain.² The oral cavity is also a source for respiratory infections, and patients of periodontal infection are more prone to experience hospital-acquired pneumonia than healthy individuals. We also conclude that enhancing oral health may reduce the frequency of COVID-19 symptoms and reduce the related morbidity.

KEYWORDS :**INTRODUCTION**

COVID-19 is a disease caused by a novel coronavirus called SARS-CoV-2 that causes lung and other organ damage^[3]. Most COVID-19 patients have mild symptoms, but some may develop severe pneumonia, pulmonary edema, acute respiratory distress syndrome (ARDS), multiple organ dysfunction syndrome, or even die^[4]. The mortality rate from COVID-19 ARDS can approach 40%–50%.^[5]

The mortality rate of COVID-19 ARDS may be between 40% and 50%^[5].

The World Health Organization (WHO) declared COVID-19 a global emergency on 30 January 2020 and declared it a pandemic on 11 March 2020 when the highly contagious virus infects populations around the world.

As of today, 19,926,731 individuals have been diagnosed and 731,821 deaths have been linked to the virus worldwide owing to this outbreak.

Bacteria found in patients with extreme COVID-19 are synonymous with Oral cavity and better oral hygiene will reduce the likelihood of complications. Although COVID-19 has a viral cause, It is believed that bacteria play a part in severe cases of infection, raising the risk of infections such as pneumonia, acute respiratory distress syndrome, sepsis, septic shock and death⁹.

Oral hygiene should be enhanced during infection with COVID-19 in order to reduce the bacterial load in the mouth and the possibility of bacterial superinfection.

Poor oral hygiene is considered a risk to complications of COVID-19, especially in patients predisposed to altered biofilms related to diabetes, hypertension or cardiovascular disease. Periodontal disorder is a category of chronic inflammatory disorders, including gingivitis and periodontitis^[6-8]. Such diseases are caused by a variety of microbial

agents that induce inflammation and destruction of tooth supporting tissues^[9]. According to the World Health Organization (WHO), 10% of the world's population were impaired by PD^[10]. Poor oral hygiene, smoking, diabetes medications, age, genetic and obesity have been linked with an rise in the incidence of periodontal disease^[11-13]. Bacteria found in the mouth that may cause these infections are "Porphyromonas gingivalis." Such bacteria contribute to the production of cytokines such as Interleukin 1 (IL1) and Tumor Necrosis Factor (TNF) which can be found in the saliva and can enter the lungs. As a consequence, poor oral hygiene will raise the likelihood of respiratory infections and possibly postviral bacterial complications.

DISCUSSION

It has become evident that oral wellbeing has had a huge effect on general well being. Some research shows that cytokines or microbial products produced systemically in reaction to oral infection induce inflammation in distant tissues, which promotes the progression of systemic diseases such as Alzheimer's disease, asthma, atherosclerotic heart disease and cerebrovascular disease. ^[14-17].

The occurrence and extent of complications following infection with COVID-19 depends on a variety of host and viral factors that will influence the immune response of the patient. 80 per cent of patients with COVID-19 infection have moderate symptoms, 20 per cent have encountered serious infection along with elevated inflammatory marker levels (Interleukin 2, 6, 10) and bacteria^[18,19] They often have a surprisingly higher neutrophil count and a lower lymphocyte count than in mild patients.^[20] Increased neutrophil count is rare for viral infection, but typical for bacterial infection, indicating that in extreme cases of COVID-19, Bacterial super-infection is normal. Many mechanisms can explain the capacity of oral pathogens to intensify lung infections including the aspiration of oral pathogens into the lower respiratory tract, especially in high-risk individuals; the alteration of mucosal surfaces in the respiratory tract by salivary enzymes, which encourage

pathogen colonization; and the secretion of pro-inflammatory cytokines during periodontitis, which can promote adherence to the epithelium of the lungs and the colonization of the lungs by respiratory pathogens. [21,22].

Improving oral hygiene can therefore reduce oropharyngeal colonization and the risk of respiratory complications.

Periodontal disease is an inflammatory disorder in which microbial etiological factors cause a sequence of host reactions that mediate inflammatory events, with cytokine development contributing to tissue damage in susceptible individuals[23]. There are important inflammatory mediators between periodontal disease and COVID-19, and they further indicate that periodontal disease could be a contributing factor and/or worsen the incidence of COVID-19. Cytokine storm was consistent with the development of COVID-19 illness. Cytokine storm is a hyperactive immune reaction marked by interferon release, interleukin release(IL), tumour-necrosis factors (TNF), chemokines, and many other mediators that contribute to dysregulation of the immune system and the shutdown of the organ. Cytokine storm indicates that the amounts of cytokines produced are injurious to host cells.

Laboratory results from clinical studies and autopsies in patients with COVID-19 show elevated inflammatory markers, particularly with cytokines IL-6, IL-8 and TNF .Those same cytokines and chemokines are also implicated in both the biology and pathology of bone metabolism.[24] They are important triggers for the movement of osteoblast and osteoclast precursors and, thus, possible modulators of bone homeostasis. Compared to the exacerbation of COVID-19 by the deregulation of the immune system during the cytokine storm, the disruption of the equilibrium between osteoblast and osteoclast function by periodontal bacterial products and host inflammatory cytokines is the major underlying cause of inflammation-induced periodontal bone loss.[25]

Such same elevated inflammatory by-products observed during periodontal disease (i.e., IL-6, MAC-1, IL-8, and TNF) worsen or contribute to the intensity of symptoms associated with COVID-19.

Bacteria, Cytokine, Inflammatory mediator Protective mucin, Hydrolytic enzymes, Neutrophills

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Periodontal Inflammation & Tissue damage

Neutrophill, Bacterial and hydrolytic salivary enzymes destroy protective secretions



Aspiration of oral secretions

Elevated inflammatory by-products (IL -6, MAC-1, IL-8, and TNFα) exacerbates or contribute to covid 19 symptoms

CONCLUSION

Oral pathogens such as SARS-CoV-2 enter systemic circulation and may induce enhanced development of inflammatory mediators contributing to a lethal cytokine storm. Patients of periodontitis are vulnerable to the development of certain proinflammatory cytokines. In addition , oral bacteria may predispose individuals to pneumonia, chronic obstructive pulmonary disease, and potentially COVID-19 pulmonary complications. Poor oral hygiene raises the likelihood of having the same complications. Thus, improving oral health in people of any age, by reducing their chances of acquiring non-oral systemic diseases, can reduce the morbidity of COVID-19.

REFERENCES

- [1] Tay MZ, Poh CM, Rénia L, MacAry PA, Ng LFP. The trinity of COVID-19: immunity, inflammation and intervention. *Nat Rev Immunol.* 2020;20(6):363-374. doi:10.1038/s41577-020-0311-8
- [2] Rapkiewicz AV, Mai X, Carsons SE, et al. Megakaryocytes and platelet-fibrin thrombi characterize multi-organ thrombosis at autopsy in COVID-19: a case series. *EClinicalMedicine* 2020. <https://doi.org/10.1016/j.eclinm.2020.100434>
- [3] Guan W-J, Liang W-H, Zhao Y, Liang H-R, Chen Z-S, Li Y-M, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. *Eur Respir J [Internet].* 2020 Mar 26; Available from: [http:// www. ncbi.nlm.nih.gov/pubmed/32217650](http://www.ncbi.nlm.nih.gov/pubmed/32217650).
- [4] Liu F, Zhang Q, Huang C, Shi C, Shi C, Wang L, Shi N, et al. CT quantification of pneumonia lesions in early days predicts progression to severe illness in a cohort of COVID-19 patients Available from Theranostics [Internet]. 2020;10(12):5613–22<http://www.thno.org/v10p5613.htm>. available from: *Periodontol* 2000 [Internet]. 2002;29:177–206.
- [5] Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *Clin Infect Dis.* Published online March 12, 2020. 2020:ciaa248. doi:10.1093/cid/ciaa248
- [6] M.S. Tonetti S, Jepsen L, Jin J. Otomo-Corgel Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action *J Clin Periodontol [Internet].* 44 S 2017 May 456 462 Available from <http://www.ncbi.nlm.nih.gov/pubmed/28419559>.
- [7] Armitage GC. Periodontal diagnoses and classification of periodontal diseases Available from: *Periodontol* 2000 [Internet]. 2004;34:9–21.
- [8] A. Bascones-Martínez E. Figuero-Ruiz Periodontal diseases as bacterial infection. *Med Oral Patol Oral Cir Bucal [Internet].* Available from: 9 Suppl 2004 pp. 101–7; V. Pitones-Rubio, et al. *Medical Hypotheses* 144 (2020) 1099694 92–100.
- [9] Jin LJ, Chiu GKC, Corbet EF Are periodontal diseases risk factors for certain systemic disorders—what matters to medical practitioners? *Hong Kong Med J = Xianggang yi xue za zhi* Available from: [Internet]. 2003 Feb;9(1):31–7.
- [10] No Title. Available from: www.who.int/news-room/fact-sheets/detail/oral-health.
- [11] Bergstrom J. Smoking rate and periodontal disease prevalence: 40-year trends in Sweden 1970–2010 Available from *J Clin Periodontol [Internet].* 2014 Oct;41(10):952–7<http://www.ncbi.nlm.nih.gov/pubmed/25039432>.
- [12] Chapple ILC, Bouchard P, Cagetti MG, Campus G, Carra M-C, Cocco F, et al. Interaction of lifestyle, behaviour or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases Available from *J Clin Periodontol [Internet].* 2017 Mar;44(Suppl 1):S39–51<http://www.ncbi.nlm.nih.gov/pubmed/28266114>.
- [13] Albandar JM. Global risk factors and risk indicators for periodontal diseases Available from: *Periodontol* 2000 [Internet]. 2002;29:177–206.
- [14] Bui FQ, Almeida-da-Silva CLC, Huynh B, Trinh A, Liu J, Woodward J, et al. Association between periodontal pathogens and systemic disease. *Biomed J* 2019;42:27e35.
- [15] Wu Z, Nakanishi H. Connection between periodontitis and Alzheimer's disease: possible roles of microglia and leptomenigeal cells. *J Pharmacol Sci* 2014;126:8e13.
- [16] Jepsen S, Stadlinger B, Terheyden H, Sanz M. Science transfer: oral health and general health - the links between periodontitis, atherosclerosis and diabetes. *J Clin Periodontol* 2015;42:1071e3.
- [17] Khumaedi AI, Purnamasari D, Wijaya IP, Soeroes Y. The relationship of diabetes, periodontitis and cardiovascular disease. *Diabetes Metab Syndr* 2019;13:1675e8.
- [18] Gong J. Correlation Analysis Between Disease Severity and Inflammation-related Parameters in Patients with COVID-19 Pneumonia. *Tongji Hospital,* 2020.
- [19] Liu J. Neutrophil-to-Lymphocyte Ratio Predicts Severe Illness Patients with 2019 Novel Coronavirus. *Beijing Ditan Hospital,* 2020.
- [20] Zheng M, Gao Y, Wang G et al. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. *Cell Moll Immunol* 2020; DOI: 10.1038/s41423-020-0402-2.
- [21] Gomes-Filho IS, Passos JS, Seixas da Cruz S. Respiratory disease and the role of oral bacteria. *J Oral Microbiol* 2010;2.
- [22] Varamat M, Haase EM, Kay JG, Scannapieco FA. Activation of the TREM-1 pathway in human monocytes by periodontal pathogens and oral commensal bacteria. *Molecular oral microbiology* 2017;32:275e87.
- [23] Taubman MA, Kawai T. Involvement of T-lymphocytes in periodontal disease and in direct and indirect induction of bone resorption. *Crit Rev Oral Biol Med.* 2001;12(2):125-135. doi:10.1177/1045441101020020301
- [24] Cekici A, Kantarci A, Hasturk H, Van Dyke TE. Inflammatory and immune pathways in the pathogenesis of periodontal disease. *Periodontol* 2000. 2014;64(1):57-80. doi:10.1111/prd.12002
- [25] Yumoto H, Nakae H, Fujinaka K, Ebisu S, Matsuo T. Interleukin-6 (IL-6) and IL-8 are induced in human oral epithelial cells in response to exposure to periodontopathic *Eikenella corrodens*. *Infect Immun.* 1999;67(1):384-394.