Title Page (with Author Details)

**News and Perspectives** 

Is There an Association Between Oral Health

and Severity of COVID-19 Complications?

Nathalie Botros <sup>a</sup>, Parvati Iyer <sup>b</sup>, David M. Ojcius <sup>c\*</sup>

<sup>a</sup> Doctor of Dental Surgery Program, University of the Pacific, Arthur Dugoni School of

Dentistry, San Francisco, CA 94103, USA

<sup>b</sup> Department of Diagnostic Sciences, University of the Pacific, Arthur Dugoni School of

Dentistry, San Francisco, CA 94103, USA

<sup>c</sup> Department of Biomedical Sciences, University of the Pacific, Arthur Dugoni School of

Dentistry, San Francisco, CA 94103, USA

\* Corresponding author

E-mail: dojcius@pacific.edu

1

### **News and Perspectives**

Is There an Association Between Oral Health and Severity of COVID-19 Complications?

### **Abstract**

Most patients with severe complications from COVID-19 have underlying conditions such as obesity, diabetes, and hypertension. In parallel, there is growing evidence for a link between periodontitis and non-oral systemic diseases. The oral cavity is also a reservoir for respiratory pathogens, and patients with periodontal disease are more likely to develop hospital-acquired pneumonia than healthy individuals. We therefore hypothesize that improving oral health could decrease the severity of COVID-19 symptoms and reduce the associated morbidity.

#### Introduction

The new coronavirus SARS-CoV-2 was first detected in late 2019 and has quickly developed into a global pandemic [1]. Age is one of the highest risk factors for developing severe symptoms of COVID-19, the disease caused by infection with SARS-CoV-2 [2]. Thus, individuals over the age of 65 and those living in long-term care facilities are especially vulnerable to morbidity and mortality due to infection with SARS-CoV-2. However, persons with chronic lung disease, moderate to severe asthma, severe obesity, diabetes, chronic kidney disease, and liver disease are also at high risk for severe COVID-19 symptoms. A recent study lists hypertension, obesity, and diabetes as the three major underlying conditions with the most unfavorable outcomes in COVID-19 patients requiring hospitalization [3].

While COVID-19 can affect multiple organs in the body, including the kidneys and liver [4, 5], the main cause of mortality is due to the ability of SARS-CoV-2 to infect the respiratory tract, leading to severe pneumonia. Patients with COVID-19 display symptoms of fever, cough, dyspnea, and other complications associated with acute respiratory distress syndrome [6-8].

A salient feature of COVID-19 is its ability to trigger an excessive immune reaction in the host, termed a 'cytokine storm', which causes extensive tissue damage, particularly in the connective tissue of the lungs [9]. The lung pathology of patients who die from COVID-19 pneumonia includes edema, focal reactive hyperplasia of pneumocytes with patchy inflammatory cellular infiltration, and multinucleated giant cells [10].

## **Oral Health and Non-Oral Systemic Diseases**

Over the past few years, it has been clear that oral health has a large impact on general health. Several studies suggest that cytokines or microbial products released systemically in

response to oral infection causes inflammation in distant organs, which enhances development of systemic diseases such as Alzheimer's disease, diabetes, atherosclerotic heart disease and cerebrovascular disease [11-14]. Research has also shown that poor oral health can increase complications of systemic diseases like diabetes, chronic kidney disease and liver disease [11, 15, 16]. Conversely, obesity predisposes individuals to oral diseases, especially gingivitis and periodontitis [17].

Furthermore, the oral cavity is a significant reservoir for respiratory pathogens, including *Chlamydia pneumoniae*; and patients with periodontal disease are more likely to develop hospital-acquired pneumonia as a complication [18-20]. Several mechanisms may explain the ability of oral pathogens to exacerbate lung infection, including aspiration of oral pathogens into the lower respiratory tract, especially in high-risk individuals; modification of mucosal surfaces along the respiratory tract by salivary enzymes, which thereby facilitate colonization by pathogens; and secretion of pro-inflammatory cytokines during periodontitis, which can promote adhesion to lung epithelium and lung colonization by respiratory pathogens [21, 22]. Improving oral hygiene may thus reduce oropharyngeal colonization and the risk of respiratory complications.

It has also been shown that improved oral hygiene and frequent professional oral health care reduces the progression or occurrence of respiratory diseases, particularly in the elderly population and those in intensive care units [23]. This population is also most at risk for developing serious complications related to COVID-19 [24, 25].

### **Concluding Statement**

Older adults and people of any age who have serious medical conditions such as chronic lung disease, diabetes, heart conditions or chronic kidney disease are at high risk for developing severe illness due to SARS-CoV-2 infection. At the same time, poor oral health increases the risk of developing the same medical conditions. Therefore, improving oral health in people of any age, by reducing their risk of developing non-oral systemic diseases, may reduce the morbidity of COVID-19 (Figure 1). Although the association between oral health and severity of COVID-19 symptoms appears logical, more research is needed to demonstrate the association empirically.

### **Conflicts of interest**

One of the authors (DMO) is an editor with Biomedical Journal. The other authors do not declare any competing interests.

# Figure Legend

Figure 1. Mechanisms that could cause poor oral health to exacerbate symptoms of COVID-19.

Poor oral health: Lu Lu Ghro Gingivitis

Increased risk for severe COVID-19 symptoms

#### References

- [1] Liu YC, Kuo RL, Shih SR. COVID-19: the first documented coronavirus pandemic in history. Biomedical journal, in press (2020), pp.
- [2] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet, 395 (2020), pp 1054-62.
- [3] Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA, (2020), pp.
- [4] Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty, 9 (2020), pp 45.
- [5] Kissling S, Pruijm M. [COVID-19 from the nephrologist's point of view]. Rev Med Suisse, 16 (2020), pp 842-4.
- [6] Ren LL, Wang YM, Wu ZQ, Xiang ZC, Guo L, Xu T, et al. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. Chin Med J (Engl), 133 (2020), pp 1015-24.
- [7] Chen J. Pathogenicity and transmissibility of 2019-nCoV-A quick overview and comparison with other emerging viruses. Microbes Infect, 22 (2020), pp 69-71.
- [8] Li JY, You Z, Wang Q, Zhou ZJ, Qiu Y, Luo R, et al. The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future. Microbes Infect, 22 (2020), pp 80-5.
- [9] Pedersen SF, Ho YC. SARS-CoV-2: a storm is raging. J Clin Invest, 130 (2020), pp 2202-5.
- [10] Tian S, Hu W, Niu L, Liu H, Xu H, Xiao SY. Pulmonary Pathology of Early-Phase 2019 Novel Coronavirus (COVID-19) Pneumonia in Two Patients With Lung Cancer. J Thorac Oncol, 15 (2020), pp 700-4.
- [11] Bui FQ, Almeida-da-Silva CLC, Huynh B, Trinh A, Liu J, Woodward J, et al. Association between periodontal pathogens and systemic disease. Biomedical journal, 42 (2019), pp 27-35.
- [12] Wu Z, Nakanishi H. Connection between periodontitis and Alzheimer's disease: possible roles of microglia and leptomeningeal cells. J Pharmacol Sci, 126 (2014), pp 8-13.
- [13] 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, 42 (2015), pp 1071-3.
- [14] Khumaedi Al, Purnamasari D, Wijaya IP, Soeroso Y. The relationship of diabetes, periodontitis and cardiovascular disease. Diabetes Metab Syndr, 13 (2019), pp 1675-8.
- [15] Ghezzi EM, Ship JA. Systemic diseases and their treatments in the elderly: impact on oral health. J Public Health Dent, 60 (2000), pp 289-96.
- [16] Han P, Sun D, Yang J. Interaction between periodontitis and liver diseases. Biomed Rep, 5 (2016), pp 267-76.
- [17] Goodson JM. Disease reciprocity between gingivitis and obesity. J Periodontol, (2020), pp.
- [18] Scannapieco FA. Role of oral bacteria in respiratory infection. J Periodontol, 70 (1999), pp 793-802.

- [19] Scannapieco FA. Pneumonia in nonambulatory patients. The role of oral bacteria and oral hygiene. J Am Dent Assoc, 137 Suppl (2006), pp 21S-5S.
- [20] Almeida-da-Silva CLC, Alpagot T, Zhu Y, Lee SS, Roberts BP, Hung SC, et al. Chlamydia pneumoniae is present in the dental plaque of periodontitis patients and stimulates an inflammatory response in gingival epithelial cells. Microb Cell, 6 (2019), pp 197-208.
- [21] Gomes-Filho IS, Passos JS, Seixas da Cruz S. Respiratory disease and the role of oral bacteria. J Oral Microbiol, 2 (2010), pp.
- [22] Varanat 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, 32 (2017), pp 275-87.
- [23] Azarpazhooh A, Leake JL. Systematic review of the association between respiratory diseases and oral health. J Periodontol, 77 (2006), pp 1465-82.
- [24] Boccardi V, Ruggiero C, Mecocci P. COVID-19: A Geriatric Emergency. Geriatrics (Basel), 5 (2020), pp.
- [25] Swiss Academy Of Medical S. COVID-19 pandemic: triage for intensive-care treatment under resource scarcity. Swiss Med Wkly, 150 (2020), pp w20229.