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ORAL DISEASES Leading in Oral, Maxillofacial, Head & Neck Medicine WILEY

LETTER TO THE EDITOR

Important evidence of the oral-lung axis, especially during the coronavirus pandemic

Dear Authors:

We appreciate the recognition of the importance of our systematic review that examined the association between periodontitis and lung diseases, with emphasis on the relationship with pneumonia (Gomes-Filho et al., 2020). Recently, attention has been given to the oral-lung axis (Gaeckle et al., 2020), due to the fact that, worldwide, the oral health of individuals with lung disease is severely underestimated. In your letter to the Editor, one of the possible biological mechanisms connecting periodontitis and pneumonia is emphasized: Poor oral hygiene allows heavy loads of bacterial biofilm, a fundamental factor for both the development of pneumonia and periodontitis. Dental biofilms are a known reservoir for opportunistic respiratory pathogens. The presence of these microorganisms depends on the subversion of the microbial community, induced by periodontal dysbiosis (Hajishengallis, 2014, 2015). The stability of the oral microbiome also depends on salivary flow and the stability of salivary pH (Rosier et al., 2018). It is not known, however, why the aspiration of bacteria leads to pulmonary infection in some individuals and not in others. It is probably a combination of factors, including the inherent virulence of the microbial pathogens, frequency and volume of the aspirated material, the effectiveness of the airway defense and pulmonary release mechanisms, comorbidities, and the individual's immune system. The use of 16S bacterial ribosomal RNA gene sequencing to characterize the microbiome reveals even more about the interrelation between the oral microbiota and the lung, emphasizing that the oral cavity is a reservoir for numerous bacteria, viruses, and inflammatory molecules (Charlson et al., 2011).

Inflammatory mechanisms allow for biological plausibility connecting periodontitis and pneumonia (Gaeckle et al., 2020). Numerous cytokines and hydrolytic enzymes are elevated in the saliva of individuals with periodontitis in comparison with those without the disease. Increased levels of IL-1, IL-6, TNF, and prostaglandin

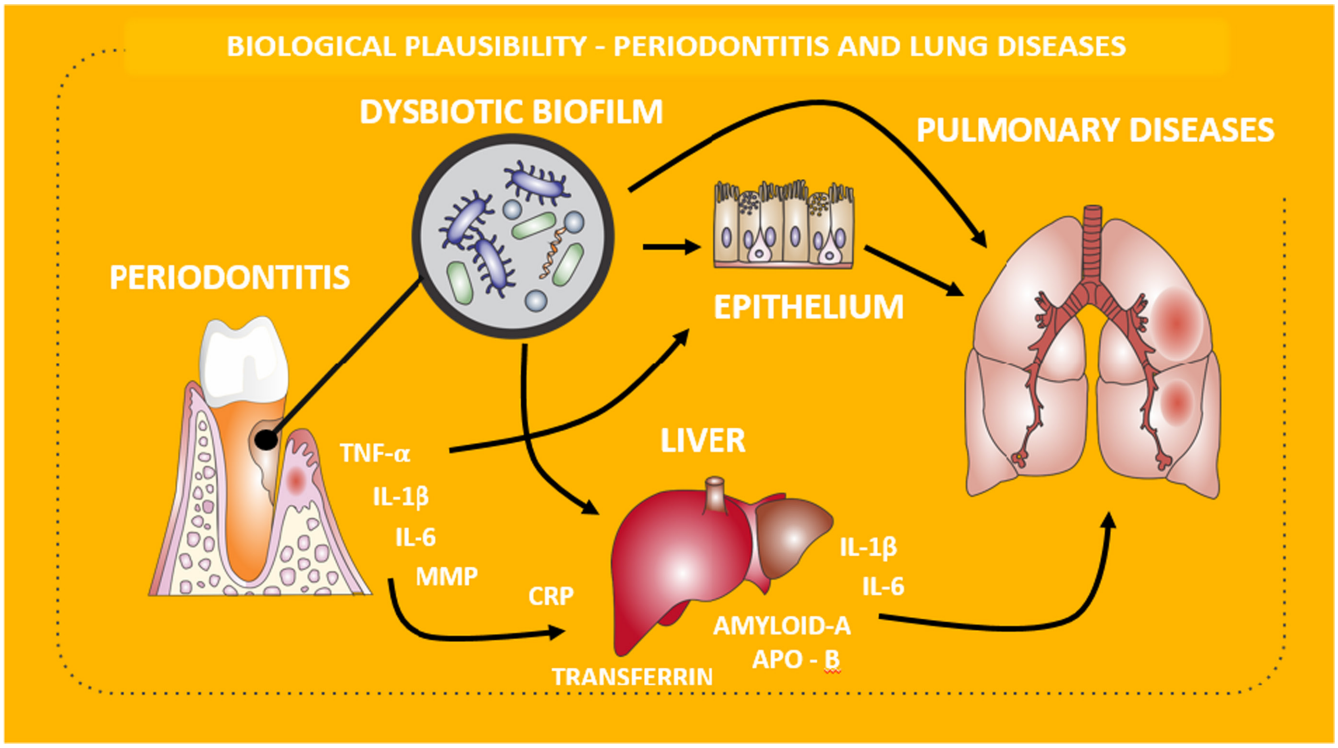

FIGURE 1 Biological plausibility mechanism between periodontitis and pulmonary diseases. (Adapted from Gomes Filho, I. S., Passos-Soares, j. S., Carvalho Filho, P. C., Cruz, s. S., Trindade, S. C., Are Periodontitis and Lung Diseases Associated? (In Portuguese). In: Kahn, s., Fischer, r. G., Dias, a. T., (Org.). Contemporary Periodontics and Implantodontics. (In Portuguese). 1st.edition. São Paulo: Quintessence Publisher, 2019, v. 15.4, p. 501–514)

E2 have been noted in gingival crevicular fluid and saliva, and some cytokines, such as IL-1β, IL-8, IL-17, IL-18, and MIP-1α, correlate with the severity of periodontitis. The persistent spread of these molecules from the inflamed oral cavity to the lung can impact respiratory symptoms, exacerbating lung disease or destroying the lung parenchyma, in addition to inducing hepatic synthesis of acute phase proteins (Figure 1). Individuals with periodontitis have high levels of systemic inflammatory markers, such as C-reactive protein (CRP), in the same way, that systemic inflammation is also present in lung diseases with CRP levels correlating inversely with forced expiratory volume. Thus, at a time when the world is looking for a way to control COVID-19 or better understand what factors contribute to the exacerbation of the hyperinflammatory characteristics of lung disease related to this disease (Lei Tang et al., 2020), the oral-lung axis can play an important role, since the mouth and lung are interconnected. Poor oral health may provide additional relevant comorbidity that contributes to the progression of COVID-19 severity, reinforcing the need for further investigations on the oral-lung axis, including studies with metagenomics, since the current scientific evidence on this topic remains unexplored.

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PEER REVIEW

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REFERENCES

Charlson, E. S., Bittinger, K., Haas, A. R., Fitzgerald, A. S., Frank, I., Yadav, A., Bushman, F. D., & Collman, R. G. (2011). Topographical continuity of bacterial populations in the healthy human respiratory tract. *American Journal of Respiratory and Critical Care Medicine*, *184*(8), 957–963. https://doi.org/10.1164/rccm.201104-0655OC

Gaeckle, N. T., Pragman, A. A., Pendleton, K. M., Baldomero, A. K., & Criner, G. J. (2020). The oral-lung axis: The impact of oral health on lung health. *Respiratory Care*, (*10*)pii:1211–1220. https://doi.org/10.4187/respcare.07332

Gomes-Filho, I. S., Cruz, S. S., Trindade, S. C., Passos-Soares, J. S., Carvalho-Filho, P. C., Figueiredo, A. C. M. G., Lyrio, A. O., Hintz, A. M., Pereira, M. G., & Scannapieco, F. (2020). Periodontitis and

respiratory diseases: A systematic review with meta-analysis. *Oral Diseases*, *26*(2), 439–446. https://doi.org/10.1111/odi.13228

Hajishengallis, G. (2014). Immunomicrobial pathogenesis of periodontitis: Keystones, pathobionts, and host response. *Trends in Immunology*, *35*(1), 3–11. https://doi.org/10.1016/j.it.2013.09.001

Hajishengallis, G. (2015). Periodontitis: from microbial immune subversion to systemic inflammation. *Nature Reviews Immunology*, *15*(1), 30–44. https://doi.org/10.1038/nri3785

Lei Tang, M. S., Xiaoyong Zhang, B. S., Yvquan Wang, B. S., & Xianchun Zeng, M. D. (2020). Severe COVID-19 pneumonia: Assessing inflammation burden with volume-rendered chest CT. *Radiology: Cardiothoracic imaging*, *2*(2), e200044. https://doi.org/10.1148/ryct.2020200044

Rosier, B. T., Marsh, P. D., & Mira, A. (2018). Resilience of the oral microbiota in health: mechanisms that prevent dysbiosis. *Journal of Dental Research*, *97*, 371–380. https://doi.org/10.1177/0022034517742139