

# Could *Neisseria* in oral microbiota modulate the inflammatory response of COVID-19?

To the Editor,

The coronavirus 2019 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is ongoing. Despite the 2 years of addressing infections caused by this virus, the immunopathogenesis mechanism is still not clearly understood (Bortolotti et al., 2021). Interactions between the innate immune system and oral microbiota can alter the host's balance between disease and health (Yu et al., 2019). It is known that the dominant genera in the oral microbiota and the lung microbiota are quite similar, but more diversity in the oral microbiota is found. The oral microbiota migrates more to the lungs, and cytokines associated with oral microbiota may affect the respiratory tissues (Bao et al., 2020). After searching Pubmed on October 1, 2021 using the keywords "Oral microbiota" and "COVID-19", 62 articles were found, but only four of them investigated the effects of COVID-19 on the oral microbiota using next-generation sequencing (NGS). Two-hundred thirty-seven healthy controls and 181 COVID-19 patients included in these articles were analyzed at the genus level (Iebba et al., 2021; Ma et al., 2021; Ren

et al., 2021; Wu et al., 2021). Regardless of age differences, three studies, except for Ren et al. (2021), reported that *Neisseria* genus shows a decrease in the oral microbiota of COVID-19 patients compared with healthy controls (Iebba et al., 2021; Ma et al., 2021; Wu et al., 2021). Wu et al. (2021) reported that oral microbiota disruption after infection with SARS-CoV-2 was attributed to *Neisseria*, and this decrease also was shown to cause suppression of important metabolic pathways, such as the host tricarboxylic acid cycle (TCA) (Wu et al., 2021). Figure 1 shows a comparison of some important genera in the oral microbiota that were found in COVID-19 patients versus healthy controls. Although Ren et al. (2021) reported that the *Neisseria* genus was elevated in the oral microbiota of COVID-19, they also reported white blood cell and lymphocyte counts positively correlated with *Neisseria* genus (Ren et al., 2021). It is known that a decrease in oral microbiota in terms of *Neisseria* genus in studies on influenza virus occurs (Bao et al., 2020). Recently, de Castilhos et al. reported that low abundance of *Neisseria* (especially *N. subflava*) led to an increase in the risk of mortality from COVID-19, but they also

## Oral Microbiota change in COVID-19 Patients

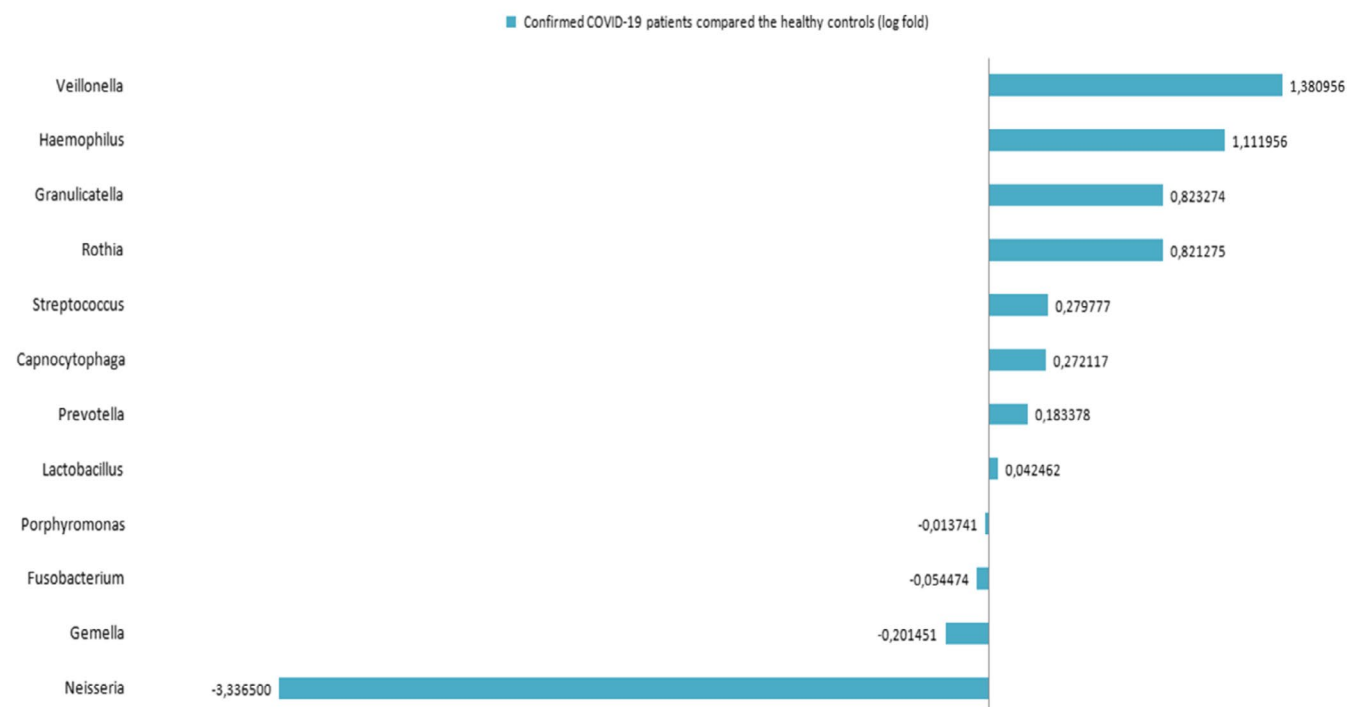


FIGURE 1 Oral Microbiota change in COVID-19 patients (log fold)

found that *N. subflava* did not change with the SARS-CoV-2 viral load, a finding that seems to be contrary to the hypothesis (Castilhos et al., 2021). *Neisseria* genera are reported as the fourth most abundant bacterial genus in the oral microbiota of adults and nonpathogenic *Neisseria* species is thought to have a physiological role in preventing colonization of potential pathogens in oral and nasal sites and is also important in developing the T-cell-independent polyclonal IgM response and maintaining the immune ignorance in the acquired immune response (Dorey et al., 2019). Powell et al. studied the stimulation of macrophages with nonpathogenic *Neisseria* species in the oral microbiota of mice and reported that macrophages stimulated interleukin 6 (IL-6) at low levels. On the contrary, they reported that IL-6 stimulation was higher when they used ultraviolet (UV)-inactivated *Neisseria* species (Powell et al., 2018).

In conclusion, the hypothesis stated that nonpathogenic *Neisseria* genera might be declining in the oral microbiota. Although this decrease has been reported in different studies, unfortunately, studies on the relationship between oral microbiota and COVID-19 in this challenging period seem to be limited. Only after new standardized and comprehensive studies are performed will the effect of oral microbiota on COVID-19 be understood.

#### KEYWORDS

COVID-19, IL-6, *Neisseria*, oral microbiota, SARS-CoV-2

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#### CONFLICT OF INTEREST

None to declare.

#### AUTHOR CONTRIBUTIONS

**Mehmet Demirci:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Writing – original draft; Writing – review & editing.

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