Received: 8 July 2022 | Revised: 6 August 2022 | Accepted: 25 July 2022

DOI: 10.1002/alr.23067

IFAR: International Forum of Allergy & Rhinology

LETTER AND REPLY

Letter to the editor regarding "Nasal inflammatory profile in patients with COVID-19 olfactory dysfunctions"

I read with a great interest the recent article by Chang et al,[1] who evaluated nasal cytokine levels in coronavirus disease-2019 (COVID-19) patients in the acute stages of the infection. They collected nasal mucosal samples from COVID-19 patients and performed a multiplex assay to assess levels of cytokines, including interferon (IFN)-γ, interleukin (IL)-1β, IL-4, IL-6, IL-10, and tumor necrosis factor-alpha (TNF-α). The authors also compared cytokine levels between patients with and without olfactory dysfunction (OD). Undertaking such an important and valuable trial was essential for understanding the pathogenesis of OD in COVID-19 patients. Although it has been identified that COVID-19 patients usually have some degree of OD,[2,3] few studies have evaluated the pathogenic mechanisms of OD in COVID-19. Furthermore, the study suggests the potential of using nasal mucosa as a specimen to detect the objective OD in COVID-19 patients.

In their work, Chang et al used a Nasosorption FX-I device to obtain nasal samples. Previous studies in various diseases evaluated local inflammatory cytokine levels in the nasal cavity; however, those results have been heterogeneously reported depending on the method and protocol of sample collection. Various clinical conditions may affect the results, including age, presence of allergic rhinitis, smoking history, and presence of rhinosinusitis. The raw measurements presented by the authors were too low in most cases, usually <30 pg/mL, and the level of IL-4 was <1 pg/mL. If these values were from plasma samples, a tiny difference between samples could suggest significance; however, differences in picograms per milliliter from nasal mucosal samples could be too low to infer statistical significance between samples. The small differences observed could also be outside the range of the multiple assays used in the study. Therefore, I believe if the authors concentrated the nasal samples and performed the multiplex assay again, it would result in statistically significant differences between patients with and without OD. Furthermore, if the levels of these cytokines could be obtained from patients without COVID-19 following the same protocol as a control, the data would show much greater statistical significance.

It has been reported that IL-10 is significantly associated with recovery of gustatory dysfunction in COVID-19 patients.[4] We are also very curious about recovery from OD in the patients in the study. If authors could evaluate the relationship between the levels of inflammatory cytokines and the outcome of OD recovery, then nasal mucosal samples would appear to be a prognostic tool for identifying recovery of OD in COVID-19 patients.

Finally, the authors' results may have had greater meaning if they performed a correlation analysis between the University of Pennsylvania Smell Identification Test score and level of cytokines. Although cytokine levels were not significantly different between patients with and without OD, the correlation between cytokine levels and olfactory function test scores would offer valuable information.

Similar to the Chang et al study, a recently published trial to evaluate the levels of inflammatory cytokines in saliva from COVID-19 patients has suggested a correlation between systemic levels of inflammatory cytokines.[5] The researchers performed real-time polymerase chain reaction and compared the cycle threshold values of the cytokines instead of measuring protein levels of the cytokines, and suggested that saliva could be an alternative specimen to blood for monitoring inflammation in COVID-19 patients.[5] Nasal mucosa samples could be obtained in a noninvasive procedure, and we speculate that nasal mucosa sampling would valuable for the diagnosis and monitoring of respiratory virus–mediated diseases. I believe trials such as this are useful and must be performed more frequently in the future. I thank Chang and colleagues for sharing their work and advancing our understanding of the pathogenic mechanisms of OD in COVID-19 patients.

Hyun Jin Min MD, PhD

Department of Otorhinolaryngology-Head and Neck Surgery, Chung-Ang University College of Medicine, Seoul, Korea

Correspondence
Hyun Jin Min, MD, PhD, Department of Otorhinolaryngology-Head and Neck Surgery, Chung-Ang University College of Medicine, 224-1 Heukseok-dong, Dongjak-gu, Seoul 156-755, Korea;
e-mail: jjinient@cau.ac.kr

ORCID

Hyun Jin Min MD, PhD https://orcid.org/0000-0003-3075-1350

REFERENCES

1. Chang K, Kallogjeri D, Piccirillo J, et al. Nasal inflammatory profile in patients with COVID-19 olfactory dysfunction. *Int Forum Allergy Rhinol*. 2022;12(7):952-954.
2. Narayanan SN, Shivappa P, Padiyath S, Bhaskar A, Li YW, Merghani TH. The prevalence and pathophysiology of chemical sense disorder caused by the novel coronavirus. *Front Public Health*. 2022;10:839182.
3. Said M, Luong T, Jang SS, Davis ME, DeConde AS, Yan CH. Clinical factors associated with lower health scores in COVID-19-related persistent olfactory dysfunction. *Int Forum Allergy Rhinol*. 2022. doi:10.1002/alr.22978
4. Locatello LG, Bruno C, Maggiore G, et al. The prognostic role of IL-10 in non-severe COVID-19 with chemosensory dysfunction. *Cytokine*. 2021;141:155456.
5. Shakeeb N, Varkey P, Hynse A, Ajit A. Saliva as a potential specimen to monitor IL-6, TNF-α and IL-10 in COVID-19 patients. *Inflammation*. 2022. doi:10.1007/s10753-022-01698-x.1–7