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LETTER TO THE EDITOR

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"Olfactory dysfunction in COVID-19, new insights from a cohort of 353 patients: The ANOSVID study": Author's reply

Dear Editor,

We thank Angelo Vaira et al.[1] for their interest on our ANOSVID study results[2] and their critical comments.

First, we agree that our analysis is based on self-reported olfactory loss alone, which is a source of important bias as it significantly underestimates the real prevalence and severity of olfactory dysfunction (OD) compared to psychophysical tests. However, our study was conceptualized in a practical way to determine in real life the impact of OD; we are not sure that there is an interest to detect OD which is not perceived by the patient himself in daily life. In any case, we strongly agree that the retrospective study design is at risk of recall bias, and a prospective study would have been more appropriate.

Vaira et al.[3] mentioned that prospective studies have failed to demonstrate an inverse association between severity of coronavirus disease 2019 (COVID-19) and associated OD by citing two studies.[4] The first study conducted by Vaira et al.[3] involved a small sample of a selected population of healthcare workers; only 28% of the 106 cases required hospitalization, with no deaths. The required number of patients to concluded for severity (hospitalization, intensive care unit admission, deaths) have not been estimated in the methodology section; therefore the results must be taken with caution due to the sample size and the selected population. The second study was clearly not performed to discuss the association between severity of COVID-19 and associated OD as the objective was to assess tolerability and viral kinetics after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) inoculation.[4]

Furthermore, meta-analysis suggested an inverse association between COVID-19 severity and OD,[5,6] for example, Goshtasbi et al.[6] observed that COVID-19 patients without OD (in comparison to COVID-19 patients with OD) experienced 5.3 times more hospitalization, 7 times more need for intubation, and 7 times more death. In contrary, limited studies found that patients with olfactory OD experience severe COVID-19.[7]

The aim of our study was to compare demographic characteristics, comorbidities, clinical, and paraclinical findings in COVID-19 patients with and without OD. We have not performed this study to demonstrate the hypothesis that anosmia and hyposmia have a different pathogenesis. However, as a secondary objective of our study, we performed a second analysis which compared severe OD patients versus non-severe and non-OD patients to explore this hypothesis and mainly to reduce the risk of bias based on self-reported olfactory loss.

Finally, we never mentioned or explained in the discussion and conclusion sections that anosmia and hyposmia have a different pathogenesis. We agree with authors that anosmia and hyposmia are essentially the results of a same pathogenetic mechanism and mainly the result of the olfactory epithelium lesions, and that neuroinvsasion pathogenetic mechanism is possible in some cases.[8,9]

AUTHOR CONTRIBUTIONS

Timothée Klopfenstein: conception, review of the literature, writing and reviewing the manuscript, and final approval. **Vincent Gendrin**: reviewing the manuscript and final approval. **Souheil Zayet**: conception, reviewing the manuscript, and final approval.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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