

The importance of identifying risk factors for the persistence of COVID-19 related olfactory disorders

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Dear Editor,

We have read with pleasure the article by Wu et al. [1], which analyzes the rate of olfactory dysfunction (OD) and recovery in a large series of 608 patients with confirmed diagnosis of SARS-CoV-2 infection. The authors have reported a frequency of OD during infection at 36.2 %, with complete resolution observed in 63.2 % of cases at a median follow-up of 36 days. Individuals presenting with other sinonasal and influenza-like symptoms, as well as those not requiring hospitalization, showed a higher rate of OD during infection. Meanwhile, a higher rate of persistent olfactory dysfunction (POD) was observed among women.

COVID-19 related POD have emerged as a real health emergency, with a frequency that hovers around 5–10 % of all infected individuals two years post-infection [2,3]. The short median follow-up in Wu et al. study does not permit definitive conclusions to be drawn, given that recovery is significant up to 3 months post-infection [4]. However, their search for risk factors for the development of POD is praiseworthy and of critical importance in identifying patients for early specific treatment, which is much more effective the sooner it is initiated [5,6].

Several authors have investigated potential risk factors in patient series with at least six months of follow-up, identifying possible correlations with the female [7] or male gender [8], OD as an initial symptom [9], baseline SNOT-22 ≥ 4 [10], duration of positivity [10], low levels of nasal IgA [11], advanced age [8,12–16], dyspnea during infection [13], absence of nasal congestion [13], complete anosmia during infection [15], presence of parosmia [17], cigarette smoking [18], abdominal pain or headache during infection [19], Mild COVID-19 [20], and infection during the first [21] or second [22] epidemic wave.

However, none of these factors have been definitively established probably due to the diversity in methodologies and patient populations across studies that can lead to varied findings. Additionally, many potential risk factors are likely interrelated, making it difficult to isolate

their individual impacts. These challenges highlight the need for more comprehensive, long-term studies that can better clarify the relationships between these factors and COVID-19-related POD. The identification of solid risk factors could significantly enhance early detection, intervention strategies, and potentially the prognosis of these patients.

Finally, it must be emphasized that the data we have obtained on these patient series dating back to the early pandemic waves are likely not comparable to the current waves driven by the Omicron variant. The latter has completely changed the epidemiology of COVID-19 related chemosensory disorders which, fortunately, appear to be less frequent and only rarely persistent [23–25].

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Declaration of competing interest

The authors declare that they have no conflict of interest.

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References

- [1] Wu SS, Cabrera CI, Quereshy HA, Kocharyan A, D'anza B, Otteson T. Olfactory dysfunction incidence and resolution amongst 608 patients with COVID-19 infection. *Am J Otolaryngol* 2023;44:103962.
- [2] Boscolo-Rizzo P, Hummel T, Invitto S, Spinato G, Tomasoni M, Emanuelli E et al. Psychophysical assessment of olfactory and gustatory function in post-mild COVID-19 patients: a matched case-control study with 2-year follow-up.
- [3] McWilliams MP, Coelho DH, Reiter ER, Costanzo RM. Recovery from Covid-19 smell loss: two-years of follow up. *Am J Otolaryngol* 2022;43:103607.
- [4] Boscolo-Rizzo P, Menegaldo A, Fabbri C, Spinato G, Borsetto D, Vaira LA, et al. Six-month psychophysical evaluation of olfactory dysfunction in patients with COVID-19. *Chem Senses* 2021;46:bjab006.
- [5] Hwang SH, Kim SW, Basurrah MA, Kim DH. The efficacy of olfactory training as a treatment for olfactory disorders caused by coronavirus disease-2019: a systematic review and meta-analysis. *Am J Rhinol Allergy* 2023;37:495–501.
- [6] Lechien JR, Vaira LA, Saussez S. Effectiveness of olfactory training in COVID-19 patients with olfactory dysfunction: a prospective study. *Eur Arch Otorhinolaryngol* 2023;280:1255–63.
- [7] Kim Y, Kim SW, Chang HH, Kwon KT, Bae S, Hwang S. Significance and associated factors of long-term sequelae in patients after acute COVID-19 infection in Korea. *Infect Chemother* 2021;53:463–76.
- [8] Capelli M, Gatti P. Anosmia in the first coronavirus disease 2019 outbreak in Europe: functional recovery after eight months. *J Laryngol Otol* 2021;135:224–8.
- [9] Biadsee A, Dagan O, Ormanian Z, Kassem F, Masarwa S, Biadsee A. Eight-month follow-up of olfactory and gustatory dysfunctions in recovered COVID-19 patients. *Am J Otolaryngol* 2021;42:103065.
- [10] Boscolo-Rizzo P, Guida F, Polesel J, Marcuzzo AV, Antonucci P, Capriotti V, et al. Self-reported smell and taste recovery in coronavirus disease 2019 patients: a one-year prospective study. *Eur Arch Otorhinolaryngol* 2022;279:515–20.
- [11] Saussez S, Sharma S, Thiriard A, Olislagers V, Vu Duc I, Le Bon SD, et al. Predictive factors of smell recovery in a clinical series of 288 coronavirus disease 2019 patients with olfactory dysfunction. *Eur J Neurol* 2021;28:3702–11.
- [12] Callejón-Leblic MA, Martín-Jiménez DI, Moreno-Luna R, Palacios-García JM, Alvarez-Cendrero M, Vizcarra-Melgar JA, et al. Analysis of prevalence and predictive factors of long-lasting olfactory and gustatory dysfunction in COVID-19 patients. *Life (Basel)* 2022;12:1256.
- [13] Coelho DH, Reiter ER, Budd SG, Shin Y, Kons ZA, Costanzo RM. Predictors of smell recovery in a nationwide prospective cohort of patients with COVID-19. *Am J Otolaryngol* 2022;43:103239.
- [14] Cristillo V, Pilotto A, Cotti Piccinelli S, Zoppi N, Bonzi G, Gipponi S, et al. Age and subtle cognitive impairment are associated with long-term olfactory dysfunction after COVID-19 infection. *J Am Geriatr Soc* 2021;69:2778–80.
- [15] Khan AM, Lee J, Rammaha T, Gupta S, Smith H, Kannampallil T, et al. Natural trajectory of recovery of COVID-19 associated olfactory loss. *Am J Otolaryngol* 2022;43:103572.
- [16] Petrocelli M, Cutrupi S, Salzano G, Maglito F, Salzano FA, Lechien JR, et al. Six-month smell and taste recovery rates in coronavirus disease 2019 patients: a prospective psychophysical study. *J Laryngol Otol* 2021;135:436–41.
- [17] Teaima AA, Salem OM, Teamia MAEM, Mansour Ol, Taha MS, Badr FM, et al. Patterns and clinical outcomes of olfactory and gustatory disorders in six months: prospective study of 1031 COVID-19 patients. *Am J Otolaryngol* 2022;43:103259.
- [18] Lucidi D, Molinari G, Silvestri M, De Corso E, Guaraldi G, Mussini C, et al. Patient-reported olfactory recovery after SARS-CoV-2 infection: a 6-month follow-up study. *Int Forum Allergy Rhinol* 2021;11:1249–52.
- [19] Messin L, Puyraveau M, Benabdallah Y, Lepiller Q, Gendrin V, Zayet S, et al. COVEVOL: natural evolution at 6 months of COVID-19. *Viruses* 2021;13:2151.
- [20] Peghin M, Palese A, Venturini M, De Martino M, Gerussi V, Graziano E, et al. Post-COVID-19 symptoms 6 months after acute infection among hospitalized and non-hospitalized patients. *Clin Microbiol Infect* 2021;27:1507–13.
- [21] Taziki Balajelini MH, Vakili MA, Rajabi A, Mohammadi M, Tabarrai A, Hosseini SM. Recovery of olfactory and gustatory dysfunctions in coronavirus disease 2019 patients: a prospective cohort study. *J Laryngol Otol* 2022. <https://doi.org/10.1017/S0022215121003935>.
- [22] Lechien JR, Wajsblat S, Horoi M, Boscolo-Rizzo P, Le Bon SD, Vaira LA, et al. Comparison of prevalence and evolution of COVID-19 olfactory disorders in patients infected by D614 (wild) and B.1.1.7. Alpha variant: a brief report. *Eur Arch Otorhinolaryngol* 2023;280:3461–7.
- [23] Boscolo-Rizzo P, Tirelli G, Meloni P, Hopkins C, Lechien JR, Madeddu G, et al. Recovery from olfactory and gustatory dysfunction following COVID-19 acquired during Omicron BA.1 wave in Italy. *Am J Otolaryngol* 2023;44:103944.
- [24] Vaira LA, Boscolo-Rizzo P, Lechien JR, Mayo-Yáñez M, Petrocelli M, Pistidda L, et al. Olfactory recovery following Omicron variant infection: a psychophysical prospective case-control study with 6 month follow-up. *J Laryngol Otol* 2023. <https://doi.org/10.1017/S0022215123000877>.
- [25] Vaira LA, Lechien JR, Deiana G, Salzano G, Maglito F, Piombino P, et al. Prevalence of olfactory dysfunction in D614G, alpha, delta and omicron waves: a psychophysical case-control study. *Rhinology* 2023;61:32–8.

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