

CLINICAL LETTER

Long-term olfactory dysfunction in COVID-19 patients: 18-month follow-up study

Fabio Ferreli MD^{1,2} | **Francesca Gaino MD^{1,2}** | **Elena Russo MD^{1,2}** |
Matteo Di Bari MD^{1,2} | **Vanessa Rossi MD²** | **Armando De Virgilio MDPhD^{1,2}** |
Arianna Di Stadio MDPhD³ | **Giuseppe Spriano MD^{1,2}** | **Giuseppe Mercante MD^{1,2}**

¹Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy

²Otorhinolaryngology-Head and Neck Surgery Unit, Humanitas Research Hospital-IRCCS, Rozzano, Milan, Italy

³Dipartimento GF Ingrassia, Otorinolaringoiatria, Università di Catania, Sicilia, Catania, Italy

Correspondence

Francesca Gaino, MD, Department of Biomedical Sciences, Humanitas University, via Rita Levi Montalcini 4, 20072 Pieve Emanuele, Milan, Italy.
Email: gaino.francesca@gmail.com

Supporting information can be found in the online version of this article.

Potential conflict of interest: None provided.

View this article online at wileyonlinelibrary.com.

KEYWORDS

COVID-19, follow-up, olfactory dysfunction, smell

Few studies exist on the evolution and recovery of COVID-19-related olfactory dysfunction (OD) in the long term. Due to the impact of OD on the quality of life of patients,¹ it is mandatory to better define its characteristics, clinical course, and recovery times to properly counsel patients during medical visits as well as to conceive new therapeutic strategies to address the problem. The aim of this study was to describe the recovery pattern of OD in a cohort of COVID-19 patients with an 18-month follow-up and to analyze the possible variables associated with spontaneous early or late recovery.

Patients were consecutively recruited after admission to a single academic institution from March 5 to March 23, 2020.² Inclusion criteria were both the presence of SARS-CoV-2 infection on nasopharyngeal swab polymerase chain reaction, and OD related to COVID-19. Patients did not undergo any specific treatment for OD. Patients were recruited at the time of laboratory diagnosis (T0) and were interviewed regarding the evolution of OD over time. All interviews were carried out by telephone. Surveys were administered at T0 and at 1, 3, 6, 9, 12, and 18 months from the diagnosis. Dates on which patients reported their olfactory function to be returned to the

baseline were recorded, when applicable. SARS-CoV-2 positivity duration was described as the number of days from COVID-19 diagnosis with nasopharyngeal swab to the date of the first of 2 consecutive negative swabs, performed after a minimum of 14 days from the first positive test, as per Italian Ministry of Health Guidelines. The study was approved by our local ethics committee (Protocol No. 1363). Patients rated the quality of their sense of smell as “good,” “average,” “mildly impaired,” “moderately impaired,” “severely impaired,” or “totally absent” (corresponding to a score of 5, 4, 3, 2, 1, or 0 points, respectively) at each follow-up. Patients also rated their olfactory function at the baseline (ie, before the COVID-19 outbreak) and gustatory function during COVID-19 with the same method. Scores of 5 to 4 were considered normal. OD was defined as “mild to moderate” (scores 3 to 2) or “severe to complete” (scores 1 to 0). Subjective perception of nasal obstruction during COVID-19 was assessed by a scale extending from 0 (unimpaired nasal breathing) to 4 or 5 (severe nasal obstruction). Furthermore, patients were asked whether they experienced an improvement in olfactory function within the first 7 days from the first presentation of OD. Data on the presence of self-reported

TABLE 1 Recovery rate of olfactory and gustatory functions and smell/taste scores at different time-points

	Number of patients (total = 99)	%		Average	SD
			Pre-COVID-19 smell score	4.9	0.3
			Smell score during COVID-19	0.4	0.8
Smell improvement in the first 7 days from the onset	52	52.5%			
Smell recovery at 1-month follow-up	53	53.5%	Smell score at 1-month follow-up	3.6	1.8
Smell recovery at 3-month follow-up	27	80.8%	Smell score at 3-month follow-up	4.4	1.3
Smell recovery at 6-month follow-up	0	80.8%	Smell score at 6-month follow-up	4.3	1.3
Smell recovery at 9-month follow-up	0	80.8%	Smell score at 9-month follow-up	4.5	1.0
Smell recovery at 12-month follow-up	4	84.9%	Smell score at 12-month follow-up	4.5	1.1
Smell recovery at 18-month follow-up	2	86.9%	Smell score at 18-month follow-up	4.6	0.9
Smell dysfunction present at 18-month follow-up	13	13.1%			

Average smell scores calculated for all patients included in the study (n = 99).

parosmia were also collected to identify any possible associations with qualitative dysfunction.

Of the 101 eligible patients, 99 were included in the study, whereas 2 were excluded due to loss to follow-up. The study population included 59 female (59.6%) and 40 male (40.4%) patients. Mean age was 47.0 (standard deviation [SD], 14.2) years. The average smell score was 0.4 at T0 (SD, 0.8); in particular, 84 patients (84.9%) reported severe-to-complete loss of smell (scores 0 or 1). No patient reported parosmia at OD presentation. Patients scored their pre-COVID-19 baseline olfactory function with an average smell score of 4.9 (SD, 0.3). Fifty-two (52.5%) patients reported an improvement in olfactory function within the first 7 days from the first self-reported OD presentation. At 1-month follow-up, 53 of 99 patients (53.5%) reported normal olfactory function. At 3-month follow-up, a further 27 (27.3%) reported normal olfactory function. At 18-month follow-up, a further 6 patients (6.1%) reported normal olfactory function, whereas 13 patients (13.1%) still reported OD. The average smell score at 18-month follow-up was 4.6 (SD, 0.9). Regarding parosmia, 38 patients reported parosmia (38.4%) at 9-month follow-up, and 3 patients reported parosmia (23.1%) among the 13 patients who reported OD at 18-month follow-up. Table 1 shows recovery rates of olfactory function and smell scores at different time-

points. Kaplan-Meier curves reporting the recovery pattern of olfactory function are shown in Figure 1. Kaplan-Meier curves showed a rapid recovery during the first weeks, with a flattening of the curve between the second and third month from COVID-19 diagnosis. By the third month of follow-up, >80% of patients recovered their sense of smell, whereas, at 18-month follow-up, 87% of patients reported normal olfactory function. On univariate analysis, late complete recovery in olfactory function was associated with severe OD at T0 ($p = 0.034$). An improvement in olfactory function over the first 7 days from the first self-reported OD presentation was significantly associated with faster recovery ($p < 0.001$) (Table S1). These aspects should be considered during counseling with patients, so they may be made aware of the possible evolution of the symptom and the relative recovery pattern. Parosmia seems to be a late-onset symptom and was still present in some patients at 18-month follow-up. Few studies exist on parosmia's etiology and clinical course in COVID-19³; therefore, further investigation is essential. In addition, further studies using multivariate analyses are needed based on an objective evaluation of smell in COVID-19 patients. One study demonstrated that patients with postviral OD may achieve recovery beyond 2 years from the acute phase,⁴ so it is imperative to extend the follow-up for these patients.

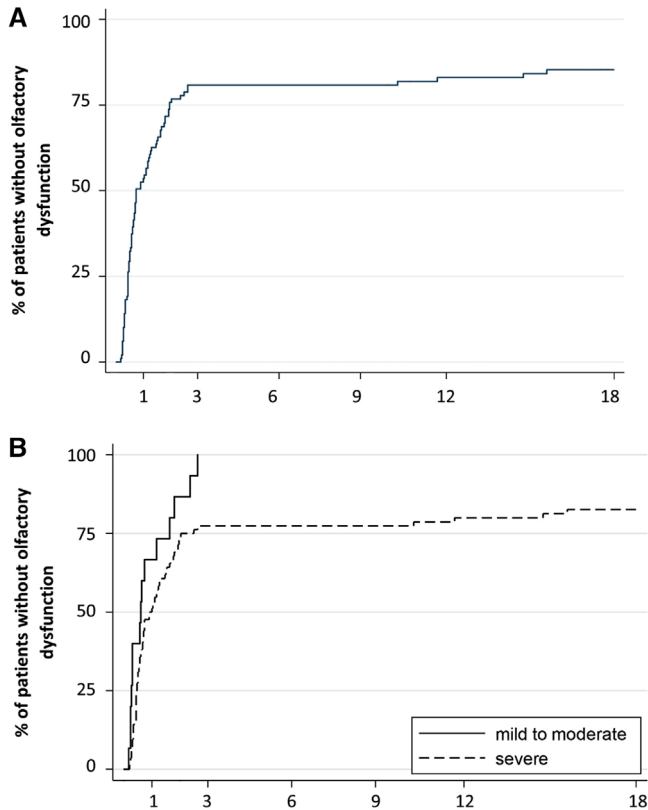




FIGURE 1 Kaplan-Meier curve showing the recovery pattern of olfactory dysfunction in the entire series (A) and according to the severity of olfactory dysfunction at presentation (B).

ORCID

Fabio Ferrelli MD  <https://orcid.org/0000-0003-2066-9572>

Francesca Gaino MD  <https://orcid.org/0000-0001-5670-0848>

Matteo Di Bari MD  <https://orcid.org/0000-0002-4028-7187>

REFERENCES

1. Saniasiaya J, Prepageran N. Impact of olfactory dysfunction on quality of life in coronavirus disease 2019 patients: a systematic review. *J Laryngol Otol.* 2021;135:947–952.
2. Mercante G, Ferrelli F, De Virgilio A, et al. Prevalence of taste and smell dysfunction in coronavirus disease 2019. *JAMA Otolaryngol Head Neck Surg.* 2020;146:723–728.
3. Liu DT, Sabha M, Damm M, et al. Parosmia is associated with relevant olfactory recovery after olfactory training. *Laryngoscope.* 2021;131:618–623.
4. Lee DY, Lee WH, Wee JH, Kim JW. Prognosis of postviral olfactory loss: follow-up study for longer than one year. *Am J Rhinol Allergy.* 2014;28:419–422.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Ferrelli F, Gaino F, Russo E, et al. Long-term olfactory dysfunction in COVID-19 patients: 18-month follow-up study. *Int Forum Allergy Rhinol.* 2022;12:1078–1080. <https://doi.org/10.1002/alr.22990>