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Smell and Taste Corner

ORL
DOI: 10.1159/000525861

Received: March 28, 2022
Accepted: June 26, 2022
Published online: September 5, 2022

# COVID-19-Related Quantitative and Qualitative Olfactory and Gustatory Dysfunction: Long-Term Prevalence and Recovery Rate

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**Keywords**
COVID-19 · Gustatory dysfunction · Olfactory dysfunction · Parosmia · Prognosis · SARS-CoV-2

**Abstract**
***Introduction:*** No studies have reported data on 2-year prevalence and recovery rates of self-reported COVID-19-related quantitative and qualitative olfactory and gustatory dysfunction. The aim of the present study was to estimate the 2-year prevalence and recovery rate of self-reported COVID-19-related olfactory and gustatory dysfunction in a cohort of patients with antecedent mild-to-moderate disease. ***Methods:*** This is a prospective observational study, measuring the prevalence of altered sense of smell or taste at follow-up and their variation from baseline, on adult patients consecutively assessed at Trieste University Hospital, who tested positive for SARS-CoV-2 RNA by polymerase chain reaction during March 2020. ***Results:*** Overall, 174 (68.8%), 53 (20.9%), and 36 (14.2%) of 253 responders reported an altered sense of smell or taste (SNOT-22 >0) at baseline, 12 months, and 24 months, respectively. Among the 174 patients who have complained a COVID-19-associated olfactory or gustatory dysfunction at baseline, 138 (79.3%) reported complete resolution of smell or taste impairment with 17 subjects (9.8%) recovering after more than 1 year after the initial infection, 33 (19.0%) reported a decrease in the severity, and only 3 (1.7%) reported that the symptom was unchanged at the 24-month interview. Twenty subjects (7.9%) complained of at least one qualitative long-term symptom. ***Conclusion:*** Two years after the infection, most patients experience a favourable evolution of COVID-19-related olfactory or gustatory dysfunction. A late recovery was observed in 10% of subjects.


## Introduction

Two years after the outbreak of the COVID-19 pandemic in Europe, olfactory and gustatory dysfunction has appeared as a highly prevalent and persistent symptom of the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection at least until the advent of the Omicron variant [1–3]. Since in other forms of post-viral anosmia a recovery has been described even years after the onset [4], it is essential to reassess the persistence and recovery rate of these COVID-19-related disorders with long-term interviews.

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Olfactory and gustatory dysfunctions are categorized not only into quantitative but also into qualitative disorders: parosmia (perception of qualitatively altered smells in the presence of an odour source), phantosmia (perceived odour when no odorant is present), parageusia (perception of qualitatively altered taste in the presence of a gustatory stimulus), and phantogeusia (spontaneous abnormal taste with no gustatory stimulus) can accompany or follow a reduction in the perception of smell and taste [5]. While several papers have reported on the persistence and recovery rates of quantitative disturbances, few have focused on qualitative alterations [6, 7]. Nevertheless, qualitative olfactory and gustatory dysfunctions may significantly impact the quality of life more than quantitative alterations [8, 9].

We previously reported the prevalence of quantitative olfactory and gustatory dysfunction 12 months after COVID-19 [10]. The aim of the present study was to both estimate the 24-month prevalence and recovery rate of self-reported quantitative olfactory and gustatory dysfunction and the rate of long-term qualitative impairment in the same series of subjects with previous mild-to-moderate symptomatic COVID-19.

## Materials and Methods

We conducted a prospective observational study on adult patients consecutively assessed at Trieste University Hospital, who tested positive for SARS-CoV-2 RNA by polymerase chain reaction on nasopharyngeal and throat swabs performed according to World Health Organization recommendation [11] during the first wave of the pandemic in Italy (March 1–22, 2020). All patients were initially home-isolated with mild-to-moderate symptoms. Patients were considered mildly symptomatic if they had less severe clinical symptoms with no evidence of pneumonia, not requiring hospitalization, and therefore considered suitable for being treated at home. Patients with a history of previous craniofacial trauma, surgery, or radiotherapy in the oral and sinonasal area and those reporting a pre-existing olfactory dysfunction were excluded from the study. Demographic and clinical data were collected through ad hoc questions administered during the baseline interview and included gender, age, self-reported height and weight, smoking and alcohol habits, and the following comorbidities: immunosuppression, diabetes, cardiovascular diseases, active cancer, chronic respiratory disease, kidney disease, liver disease. Obesity was defined as having a body mass index of 30 or more. The sense of smell and taste was assessed by the Sino-Nasal Outcome Test 22 (SNOT-22) [12], item "sense of smell or taste," both at baseline and during the follow-up interviews at 12 and 24 months to evaluate their persistence and the recovery rate. The SNOT-22 grades symptom severity as none (0), very mild (1), mild or slight (2), moderate (3), severe (4), or as bad as it can be (5) and refers to the presence of self-reported alterations in the sense of smell alone, in the sense of taste alone, or both. Patients with SNOT-22 >0 were asked whether the alteration involved the sense of smell, taste, or both. During the last interview, patients were questioned about the presence at 24 months of qualitative olfactory or gustatory symptoms including parosmia ("Do you smell odours differently compared to previous experiences?"), phantosmia ("Do you smell odours in absence of an apparent source?"), parageusia ("Do you perceive tastes differently compared to previous experiences?"), and phantogeusia ("Do you have taste sensations in the absence of an apparent gustatory source?"), based on a binary outcome of yes and no. Symptoms prevalence was expressed as a percentage of total patients, and the 95% confidence interval (CI) was calculated using the Clopper-Pearson method; differences in prevalence were evaluated through Fisher's exact test. Analyses were performed using R 3.6., and statistical significance was claimed for $p < 0.05$ (two-tailed).

**Table 1.** Characteristics of 253 COVID-19 patients included in the study

| Characteristics | *n* | % (95% CI[a]) |
|---|---|---|
| Sex | | |
| Man | 95 | 37.6 (31.6–43.8) |
| Woman | 158 | 62.5 (56.2–68.4) |
| Tobacco smoking | | |
| Never | 149 | 58.9 (52.6–65.0) |
| Ever | 104 | 41.1 (35.0–47.4) |
| Comorbidity[b] | | |
| No | 169 | 66.8 (60.6–72.6) |
| Yes | 84 | 33.2 (27.4–39.4) |
| Smell or taste impairment SNOT-22 at baseline | | |
| 0 = none | 79 | 31.2 (25.6–37.3) |
| 1 = very mild | 2 | 0.8 (0.1–2.8) |
| 2 = mild or slight | 17 | 6.7 (4.0–10.6) |
| 3 = moderate | 25 | 9.9 (6.5–14.2) |
| 4 = severe | 37 | 14.6 (10.5–19.6) |
| 5 = as bad as it can be | 93 | 36.8 (30.8–43.0) |
| Type of chemosensory impairment | | |
| Smell | 159 | 62.8 (56.6–68.8) |
| Taste | 157 | 62.1 (55.8–68.1) |
| Smell or taste | 174 | 68.8 (62.7–74.4) |

COVID-19, coronavirus disease 2019; SNOT-22, Sino-Nasal Outcome Test 22. [a] 95% CIs were calculated using the Clopper-Pearson method. [b] Comorbidity includes obesity (body mass index ≥30), diabetes, hypertension, cardiovascular disease, chronic respiratory disease, active cancer, renal disease, and liver disease.

## Results

Of 315 patients completing the survey at baseline, 47 and other 15 did not respond or decline to take part at the 12 months and at 24 months follow-up interviews, respectively, leaving 253 responders with complete follow-

**Table 2.** Evolution of alteration of sense of smell or taste in 174 patients positive for SARS-CoV-2 infection

| Alteration of sense of smell or taste at baseline[a] | *N* (%) total | Alteration of sense of smell or taste after 24 months[a] | | | | | |
|---|---|---|---|---|---|---|---|
| | | 0: no | 1: very mild | 2: mild or slight | 3: moderate | 4: severe | 5: as bad as it can be |
| 1: very mild | 2 (1.1) | 2 | 0 | 0 | 0 | 0 | 0 |
| 2: mild or slight | 17 (9.8) | 17 | 0 | 0 | 0 | 0 | 0 |
| 3: moderate | 25 (14.4) | 20 | 3 | 0 | 2 | 0 | 0 |
| 4: severe | 37 (21.3) | 30 | 1 | 0 | 5 | 1 | 0 |
| 5: as bad as it can be | 93 (53.4) | 69 | 5 | 2 | 12 | 5 | 0 |
| Total | 174 | 138 (79.3) | 9 (5.2) | 2 (1.1) | 19 (10.9) | 6 (3.4) | 0 (0.0) |

SARS-CoV-2, severe acute respiratory syndrome coronavirus. [a] According to SNOT-22 item "sense of smell or taste."

up (80.3%; median [IQR] age, 48 [38–56] years; 158 [62.5%] women). Patients' characteristics are reported in Table 1. Associated comorbidities were reported by 84 participants (33.2%) with the most common being obesity reported by 30 patients (11.9%) followed by cardiovascular diseases ($n = 23$, 9.1%). Overall, 174 (68.8%, 95% CI: 62.7–74.4), 53 (20.9%, 95% CI: 16.1–26.5), and 36 (14.2%, 95% CI: 10.2–19.2) of 253 responders reported an altered sense of smell or taste (SNOT-22 >0) at baseline, 12 months, and 24 months, respectively. Thus, 121 subjects (69.5%, 95% CI: 62.1–76.3) completely recovered within 1 year, and 17 (9.8%, 95% CI: 5.8–15.2) fully recovered between one and 2 years. After 24 months, 12 participants (4.7%, 95% CI: 2.5–8.1) reported both taste and smell complaints, 21 (8.3%, 95% CI: 5.2–12.4) had only smell complaints, and 3 (1.2%, 95% CI: 0.25–3.4) had only taste complaints. At 24 months, 20 subjects (7.9%, 95% CI: 4.9–11.9%), also reporting a quantitative smell or taste impairment, complained at least one qualitative symptom with parosmia being the most frequent ($n = 13$; 5.1%, 95% CI: 2.8–8.6%) following by phantosmia ($n = 12$; 4.7%, 95% CI: 2.5–8.1%), phantogeusia ($n = 8$; 3.2%, 95% CI: 1.4–6.1%), and parageusia ($n = 2$; 0.8%, 95% CI: 0.1–2.8%). Among the 174 patients who have complained a COVID-19-associated olfactory or gustatory dysfunction at baseline, 138 (79.3%, 95% CI: 72.5–85.1%) reported complete resolution of smell or taste impairment, 33 (19.0%, 95% CI: 13.4–25.6%) reported a decrease in the severity, only 3 (1.7%, 95% CI: 0.4–5.0%) reported the symptom was unchanged, while none reported a worsening of the olfactory or gustatory alteration at the 24-month interview (Table 2).

## Discussion

Two years after COVID-19, 14% of patients with previous mild-to-moderate symptomatic disease still self-reported a quantitative olfactory or gustatory dysfunction. The complete and partial recovery rates were 79% and 19%, respectively. Consequently, most of the patients reported a complete resolution of the olfactory and gustatory symptoms or, in any case, an improvement with only a marginal proportion reporting the symptoms had remained unchanged. No subject reported a persistent and total loss of the sense of smell or taste 2 years after the infection.

Thus, although this may take a long time, patients should be reassured that most of them experience a favourable evolution of the loss of smell and taste following COVID-19 and that late recovery is possible. Despite this, given the enormous spread of the disease, it should be considered that, one in 7 patients still complaining of persistence of olfactory or gustatory dysfunction 2 years after COVID-19, may represent an unprecedented burden on health systems and a challenge for the specialists who have to treat these patients. Unfortunately, with the exception of olfactory training [13, 14] which should be recommended in all cases of persistent olfactory disorders after the acute event that caused it, other therapeutic strategies are mainly based on weak evidence [15]. Further efforts are therefore needed to design clinical trials aimed at testing the efficacy of new therapeutic opportunities as well as intense research activity, especially in areas likely to lead to therapies as recently pointed out by a panel of international experts [16].

During the COVID-19 pandemic, the attention of researchers has mainly focused on persistent quantitative olfactory disorders, while only few studies have investi-

gated the impact of qualitative dysfunction [6, 7, 17, 18]. In the present investigation, 8% of subjects complained of at least one symptom of qualitative impairment 2 years after SARS-CoV-2 infection with parosmia/phantosmia being the most prevalent. Previous studies observed that many patients report the onset of parosmia on average 3 months after the initial infection with the distortion being typically unpleasant and triggered by specific foods [19]. Consequently, these symptoms can be very distressing causing depression, anxiety, loss of appetite, significant weight loss, and malnourishment [20]. Nonetheless, many patients claim that their symptoms are underestimated by healthcare professionals. It is therefore of paramount importance to capture qualitative olfactory dysfunction and to be aware of its possible psychological and physical implications to offer support to the patients. While there are no evidence-based treatments for parosmia, some precautions such as avoiding trigger foods or consuming room temperature or cold foods may be helpful [20].

The data from the present study should be taken cautiously. Particularly, symptoms were self-reported, based on cross-sectional surveys, and may therefore contain suboptimal sensitivity, leading to underestimation of the prevalence of olfactory dysfunction compared to psychophysical tests [21].

In conclusion, only a marginal proportion of patients with previous mild-to-moderate symptomatic COVID-19 characterized by new onset of olfactory or gustatory dysfunction still complained of unchanged altered sense of smell or taste 2 years after the onset. Further assessments will be needed to establish whether in these cases smell and taste dysfunction will be permanent. Importantly, a late recovery was observed in 10% of subjects.

## Statement of Ethics

The study was conducted in accordance with the World Medical Association Declaration of Helsinki and was approved Ethics Committee of the Friuli Venezia Giulia Region (Application No. CEUR-2020-Os-156). All participants gave their verbal informed consent for a telephone interview. As the researchers did not engage in any medical treatment or direct patient-researcher interaction, verbal informed consent was approved by the Ethics Committee of the Friuli Venezia Giulia Region.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.


## Funding Sources

This manuscript did not receive any funding.


## Author Contributions

Paolo Boscolo-Rizzo contributed to the study conception, data analysis, and interpretation, as well as drafting and revising the article. Margherita Tofanelli, Enrico Zanelli, and Nicoletta Gardenal contributed to data collection and interpretation, as well as critical revision of the article. Giancarlo Tirelli contributed to the study conception, data interpretation, and critical revision of the article.

## Data Availability Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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