Self-reported olfactory and gustatory dysfunctions in COVID-19 patients: a 1-year follow-up study in Foggia district, Italy

Francesca Fortunato1, Domenico Martinelli1, Giuseppina Iannelli1, Marica Milazzo1, Umberto Farina1, Gabriella Di Matteo1, Rosella De Nittis2, Leonardo Ascatigno1, Michele Cassano3, Pier Luigi Lopalco4 and Rosa Prato1*

Abstract

Background: From the initial stages of the pandemic in early 2020, COVID-19-related olfactory and gustatory dysfunctions have been widely reported and are emerging as one of the most frequent long-term sequelae of SARS-CoV-2 infection. However, data regarding the long-term recovery of the sense of smell and taste are lacking. This study aimed to characterize the evolution up to one year after the diagnosis of self-reported olfactory and gustatory dysfunctions in COVID-19 cases.

Methods: Based on the data of the active surveillance platform of the Apulia region, Italy, we selected the residents of Foggia district who were confirmed positive for SARS-CoV-2 from March 1st to June 16th, 2020, and home-quarantined with paucisymptomatic-to-mild clinical presentation. Self-reported olfactory and gustatory dysfunctions were recorded at baseline through a survey of dichotomous questions. The evolution of these symptoms at approximately one year was prospectively assessed via telephone by the validated sino-nasal outcome test 22 (SNOT-22, Italian version).

Results: Among the 1,175 COVID-19 cases notified in the Foggia district during the first epidemic wave, 488 had paucisymptomatic-to-mild clinical presentation. Of these, 41.2% (n = 201, 95% confidence interval [CI] 36.8–45.7%) reported at least one sensory dysfunction. A total of 178 to 201 (88.5%) patients agreed to participate in the follow-up survey. According to the SNOT-22 results, the persistence of a sensory dysfunction was observed in the 29.8% (n = 53, 95% CI 23.2–37.1%) of them. Particularly, loss of smell persisted in 25.8% (n = 46, 95% CI 19.6–32.9%), loss of taste in 21.3% (n = 38, 95% CI 15.6–28.1%), loss of both in 17.4% (n = 31, 95% CI 12.2–23.8%) of participants in the follow-up. The rates of full recovery increased over time: from 59% at 30 days to 71.9% at 90 days for the sense of smell; from 61.3% at 30 days to 74.7% at 90 days for the sense of taste.

Conclusions: The persistence of COVID-19-related olfactory and gustatory dysfunctions up to 12 months after the disease onset in a noteworthy proportion (approximately 3 out of 10) of patients with paucisymptomatic-to-mild clinical presentation deserves further investigations due to its possible pathophysiological implications and impact on the quality of life.

*Correspondence: rosa.prato@unifg.it
1 Hygiene Unit, Policlinico Riuniti Foggia Hospital, Department of Medical and Surgical Sciences, University of Foggia, Ospedale Colonnello D’Avanzo, Viale degli Aviatori 2, 71122 Foggia, Italy
Full list of author information is available at the end of the article
**Background**

From the earliest stages of the coronavirus disease 19 (COVID-19) pandemic, in March 2020, the American Academy of Otolaryngology—Head and Neck Surgery proposed including anosmia and dysgeusia to the list of screening tools for possible COVID-19 infection [1]. In April 2020, the Centers for Disease Control and Prevention added “new loss of taste or smell” to the list of symptoms that may appear 2 to 14 days after exposure to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. As of December 3rd, 2020, the European Centre for Disease Prevention and Control included the “sudden onset of anosmia, ageusia or dysgeusia” among the clinical criteria of the new case definition for COVID-19 [3].

To date, several studies have documented a high prevalence of olfactory and gustatory dysfunctions in COVID-19. These sensory dysfunctions represent specific and sometimes early-onset symptoms, which differentiate SARS-CoV-2 infection from other acute respiratory diseases, mainly in paucisymptomatic patients [4–12].

The pathophysiological mechanism through which SARS-CoV-2 causes sensory dysfunctions of various severity has not been fully clarified yet. It is well known that SARS-CoV-2 infects alveolar epithelial cells by directly binding the Angiotensin-Converting Enzyme 2 (ACE2) cell receptors, thereby decreasing their expression and protective function. ACE2 receptors are expressed by cells of the gut, kidney, heart, and oral mucosa. In particular, they are highly expressed in the tongue compared with other areas of the oral cavity (vestibular and gingival), suggesting a peculiar vulnerability of the oral mucosa to COVID-19 infection [13]. Furthermore, anosmia could be ascribed to the involvement of the central nervous system and damage of the nasal epithelium. Indeed, a potential neuroinvasiveness of coronaviruses through the olfactory nerve pathway or the peripheral trigeminal endings has been described [6, 14]. Accordingly, SARS-CoV-2 RNA has been isolated in the cerebrospinal fluid [6, 15]. More recently, in patients who have recovered from COVID-19, neuroimaging has revealed localized inflammation in intracranial olfactory structures with alterations of primary olfactory neurons putatively leading to a persistent impairment [16]. Gupta et al. [17] suggested that loss of smell in SARS-CoV-2 infection is probably due to the susceptibility of a subgroup of cells (i.e., sustentacular cells, Bowman’s cells, and olfactory stem cells) to virus entry, rather than to the direct impairment of the olfactory sensory neurons. Sustentacular cells, Bowman’s cells and olfactory stem cells do not have a sensory function but play a crucial role in the maintenance of the olfactory organ and its homeostasis. Recent evidence from combined investigations of COVID-19-associated olfactory dysfunction in humans and experimentally-infected animals suggests that multiple cell types of the olfactory neuroepithelium are infected during the acute phase and that protracted viral infection and inflammation in the olfactory neuroepithelium may account for prolonged anosmia [18, 19].

In most cases, olfactory and gustatory dysfunctions resolve naturally and completely in the short term. However, several studies have demonstrated that moderate-to-severe olfactory or gustatory disturbances persist in a significant proportion of patients even months after the clinical onset of COVID-19 [20–29]. This observation is in agreement with the long-term sequelae referred to as “Long COVID”, which includes smell/taste disorders and chronic fatigue, among a variety of symptoms [30].

In this context, limited studies on the duration of olfactory and gustatory dysfunctions are available to date, and they predominantly document the mid-term evolution of these symptoms. Indeed, only a few studies have exceeded a 6-month follow-up and investigated the recovery of olfactory and gustatory dysfunctions beyond this period providing long-term information [21–23, 27, 28]. Nevertheless, considering the large number of people affected worldwide by COVID-19, the definition of duration and persistence of olfactory and gustatory disorders deserve to be addressed because of their potential impact on the quality of life [31].

This study aimed to characterize the long-term evolution of self-reported olfactory and gustatory dysfunctions in COVID-19 cases with previous paucisymptomatic-to-mild clinical presentation, estimating their persistence and recovery rate one year after the diagnosis.

**Methods**

**Design, setting and participants**

This was a prospective study conducted in the district of Foggia (Apulia region, Italy) between March 1st, 2020, when the first case of SARS-CoV-2 infection was confirmed by molecular testing, and June 16th, 2021.

During the first phase of the COVID-19 epidemic (March 1st—June 16th, 2020), all residents in the Foggia district testing positive for SARS-CoV-2 and home-quarantined with paucisymptomatic-to-mild clinical presentation were considered eligible for the initial survey. According to the definition of clinical status adopted by
the “Integrated Surveillance of COVID-19 cases” of the National Institute of Health (Istituto Superiore di Sanità), paucisymptomatic referred to a COVID-19 case with generally mild symptoms but no clear signs of disease whereas mild referred to a COVID-19 case with clear signs and symptoms of disease which, however, were not severe enough to require hospitalization.

Residents in long-stay residential care homes were excluded.

Data sources
Cases’ demographic and clinical characteristics were collected through the regional information system for health emergency management (Sistema informativo regionale per la gestione dell’emergenza sanitaria) named “GIAVACOVID©”. GIAVACOVID© was an active surveillance platform with twice-daily follow-up of cases until complete recovery with viral RNA clearance from the upper respiratory tract (two serial negative PCR tests at least 24 h apart) [32]. At the time of diagnosis, participants were contacted via telephone to answer four non-validated dichotomous questions. Subjects were asked to self-report subjective loss of smell and taste functions (Yes/No) and temporally relate its onset to that of other COVID-19 symptoms (fever, rhinorrhea, nasal congestion, cough, dyspnea; Yes/No). A quantitative assessment of the dysfunctions was not performed at this stage of the study [21, 25, 33].

Participants who had reported chemosensory dysfunctions at the time of the first questionnaire were contacted via telephone for a follow-up interview approximately 12 months after the study entry. In case of missed response, subjects were recontacted twice over fourteen days to minimize the possibility of a response bias. Loss of the sense of smell and/or taste was assessed retrospectively at the time of the follow-up interview in terms of duration (from the onset to the resolution dates, days) and severity according to sino-nasal outcome test 22 (SNOT-22), item “sense of smell or taste”. 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) (SNOT-22, Italian version) [9, 34, 35]. If SNOT-22 >0, participants were also asked whether the chemosensory dysfunction involved the sense of smell, taste, or both.

Variables and definitions
The prevalence of olfactory and gustatory dysfunctions at baseline was calculated as the ratio of COVID-19 cases with self-reported impairment or loss of smell and/or taste to the total number of COVID-19 cases. The persistence of these symptoms at follow-up was calculated as the ratio of COVID-19 cases with persistent olfactory and gustatory dysfunctions on the date of the follow-up interview to the total number of participants in the follow-up phase. Complete recovery was defined as self-reported full resolution of smell and/or taste dysfunctions, whereas partial recovery was defined as an improvement in olfactory and/or gustatory functions [25]. The duration of chemosensory dysfunctions was calculated from the onset to the resolution dates of each symptom. If patients reported unresolved symptoms (no resolution date), the symptoms duration was registered at 365 days, as this was the longest calculated duration [29].

The number of incident cases in the Apulia region between March 1st and June 16th, 2020, determined the sample size.

Statistical analysis
Descriptive statistics were performed. Categorical variables (sex, age group, comorbidities, clinical presentation) were expressed as counts and percentages in each category, continuous variables (age, incubation period, time to viral clearance, duration of chemosensory dysfunctions) as means (± standard deviation [SD]) and medians (interquartile ranges [IQR]). The prevalence, the persistence and the recovery rate of olfactory and gustatory dysfunctions were expressed as percentage with 95% confidence interval (CI) using Clopper-Pearson method [22].

The association between self-reported presence of sensory alterations at baseline and putatively related variables in the study group was assessed computing the chi-square test ($\chi^2$) and the odds ratio (ORs) with 95% CIs. Differences in continuous variables were tested with Student’s $t$ test for normally distributed ones, or the Mann–Whitney $U$ test when variables showed a non-normal distribution.

Multivariate logistic regression analysis was performed to evaluate whether demographics (sex: male vs. female; age group: above vs. below the median age), clinical characteristics (presence vs. absence of at least one underlying medical condition) and clinical presentation (paucisymptomatic vs. mild) were independently associated with baseline sensory dysfunctions and complete recovery.

Moreover, Kaplan–Meier estimates were reported to show the rates of complete recovery from the onset of the smell and/or taste loss [25].

The level of statistical significance was set at $p \leq 0.05$. Analysis was conducted with STATA/SE 15.0.

Results
From March 1st to June 16th, 2020, a total of 1175 COVID-19 confirmed cases were notified in the Foggia district, of which 653 (mean age: 42.9 ± 17.9 years,
median age: 45 years, IQR 44–47 years; 53.9% females) were home-quarantined. Clinical presentation of COVID-19 was classified as paucisymptomatic in 55.6\% (n = 363) of cases and mild in 19.1\% (n = 125) of cases; 165 (25.3\%) cases were classified as asymptomatic (Fig. 1, Table 1). The mean estimated incubation period was 9.6 ± 9.8 days (median: 7 days, IQR 3–13.5 days). As of June 16th, 2020, 94.5\% (n = 617) of cases were fully recovered with complete viral clearance (mean time to viral clearance: 28 ± 11.9 days; median: 25 days, IQR 18–38 days).

Baseline prevalence of self-reported olfactory and gustatory dysfunctions
Among the 488 cases with paucisymptomatic-to-mild clinical presentation, 41.2\% (n = 201, 95% CI 36.8–45.7\%) reported at least one sensory dysfunction. In particular, 36.1\% (n = 176, 95% CI 31.8–40.5\%)
reported anosmia, 37.7% (n = 184, 95% CI 33.4–42.2%) reported ageusia and 32.6% (n = 159, 95% CI 28.4–36.9%) reported both sensory dysfunctions (Fig. 1). Olfactory or gustatory loss was an isolated symptom in 26.8% (n = 131, 95% CI 22.9–30.8%) of cases; namely, only anosmia was reported in 5.5% (n = 27, 95% CI 3.7–7.9%) of cases whereas only ageusia in 3.9% (n = 19, 95% CI 2.4–6.01%) of cases. The co-occurrence of at least one sensory dysfunction and other COVID-19 symptoms was described by 34.8% (n = 70, 95% CI 28.3–41.9%) of cases, with chemosensory dysfunctions preceding the onset of the other COVID symptoms in 10% (n = 7) of cases.

Ageusia, but not anosmia, was significantly more prevalent in females than in males (42% vs. 32.6%, p < 0.05) and related to a slower viral clearance (30.3 ± 13.5 vs. 27.1 ± 11.3 days, p < 0.05; Additional file 1 and Additional file 2). No significant association was observed between self-reported presence of olfactory and gustatory dysfunctions and age, underlying comorbidities, and clinical presentation (Additional file 2).

Table 1 Demographic and clinical characteristics of home-quarantined COVID-19 cases. District of Foggia (Apulia region, Italy), March 1st—June 16th, 2020

| Cases (n = 653) | Sex       |
|----------------|-----------|
|                | n (%)     |
| Male           | 301 (46.1) |
| Female         | 352 (53.9) |
| Age (years)    |           |
| Mean (SD)      | 42.9 (17.9) |
| Median (IQR)   | 45 (44–47) |
| Age groups     |           |
| 0–9            | 28 (4.3)  |
| 10–19          | 44 (6.7)  |
| 20–29          | 86 (13.2) |
| 30–39          | 103 (15.8)|
| 40–49          | 136 (20.8)|
| 50–59          | 147 (22.5)|
| 60–69          | 73 (11.2) |
| 70–79          | 26 (3.9)  |
| 80–89          | 9 (1.4)   |
| ≥ 90           | 1 (0.2)   |
| Comorbidity    |           |
| None           | 536 (82.1)|
| At least one comorbidity | 117 (17.9)|
| Clinical presentation |       |
| Asymptomatic   | 165 (25.3)|
| Paucisymptomatic | 363 (55.6)|
| Mild           | 125 (19.1)|

SD Standard Deviation, IQR Interquartile Ranges

**Evolution of self-reported olfactory and gustatory dysfunctions**

Among the 201 cases that had reported at least one sensory dysfunction, 178 (88.5%) agreed to participate in the follow-up telephone survey (23 [11.4%] dropouts).

After 12 months, 53 cases still reported partial chemosensory dysfunctions (29.8%, 95% CI 23.2–37.1%). Particularly, loss of smell persisted in 25.8% (n = 46, 95% CI 19.6–32.9%) and loss of taste in 21.3% (n = 38, 95% CI 15.6–28.1%) of cases; dysfunctions of both olfactory and gustatory sense were reported in 17.4% (n = 31, 95% CI 12.2–23.8%) of cases (Fig. 1).

Complete resolution of olfactory and gustatory dysfunctions was reported in 70.2% (n = 125, 95% CI 63.5–76.9%) of the respondents in the follow-up interview. The mean duration was 116.6 ± 150.6 days (median 30 days, IQR 13–365 days) for olfactory dysfunction and 104.4 ± 142.3 days (median 30 days, IQR 10–120 days) for gustatory dysfunction. No correlation was observed between the mean duration of chemosensory symptoms and any baseline patients’ demographic and clinical characteristics or the clinical presentation (Table 2).

The rates of full recovery of the sense of smell increased over time, from 59% at 30 days to 67.4% at 60 days and 71.9% at 90 days (Fig. 2a). The rates of full recovery of the sense of taste increased from 61.3% at 30 days to 69.7% at 60 days and 74.7% at 90 days (Fig. 2b). No association was observed between the complete recovery of sensory dysfunctions and any baseline demographic and clinical characteristics or the clinical presentation (Additional file 3).

**Discussion**

Olfactory and gustatory dysfunctions are widely reported by COVID-19 patients [4–12] and are emerging as one of the most frequent long-term sequelae of SARS-CoV-2 infection [21–29]. Although chemosensory disorders recover spontaneously in the short-term period in most cases [25, 36, 37], a significant portion of SARS-CoV-2 infected patients continues to suffer from persisting symptoms long after having recovered from the acute illness [30, 38, 39]. The persistence of these symptoms after recovery commonly lasts for 2–3 weeks but may sometimes exceed 6 months. Therefore, the long-term persistence (i.e., six months after clinical onset) of such symptoms deserves to be assessed and investigated. Additionally, considering the large number of people affected by COVID-19 worldwide and the negative impact of anosmia and ageusia on the quality of life [31, 40–43], it is important to quantify the extent and duration of these symptoms to develop effective interventions able to manage the disorders in subjects with SARS-CoV-2 infection.
Our study was conducted on a cohort of confirmed SARS-CoV-2 positive patients with paucisymptomatic or mild disease who did not require hospitalization and were managed by the community healthcare system. At baseline, olfactory or gustatory dysfunctions were present in more than 40% of cases, in agreement with several studies [44–46] and meta-analyses [47, 48].

A higher prevalence of anosmia and dysgeusia symptoms have been reported in studies that included severe cases requiring hospitalization (74.9 and 81.3% of cases, respectively) [12, 49] or healthcare professionals [12].

We performed a prospective evaluation of patients with self-reported gustatory and olfactory dysfunctions. Of the 201 participants included in our study, 178 agreed to participate in the follow-up phase, and only 23 withdrew. Although the majority of the participants (approximately 7 out of 10) in the follow-up reported complete resolution of the olfactory and gustatory disorders after 12 months, a substantial proportion of cases (approximately 3 out of 10) was still complaining of these symptoms. This proportion is remarkable, mainly because our data refer to a population with mild COVID-19. Few other studies comparable to ours in terms of sample size, demographic or clinical characteristics, adherence rates to the follow-up phase, have exceeded a 6-month follow-up and have investigated the recovery of olfactory and gustatory functions beyond this period [21–23, 27, 28].

Of these, only two [22, 27] had a larger sample size at baseline and included a higher number of participants in the follow-up phase.

Most available studies used online questionnaires or telephone interviews for the follow-up phase to collect general and specific clinical information on chemosensory disorders. As opposed to other studies [27, 28], we did not conduct intermediate follow-up surveys. However, we collected data on the persistence and evolution of chemosensory dysfunctions through specific questions (persistence/recovery). These specific questions were administered together with the SNOT-22 test which, in turn, represents a validated subjective method to explore their severity [34, 35].

The rate of persistence of self-reported olfactory and gustatory dysfunctions observed in our study (29.8%) falls within the range reported by available studies (16 to 48%). In particular, Nguyen et al. [23] found that the persistence rate of chemosensory disorders was 24% at 7 months, Nehme et al. [27] reported 16.8% from 7 to 9 months, and Biadsee et al. [21] observed that smell and taste dysfunctions persist respectively in 48% and 38.5% of patients after a mean follow-up of 229 days. Boscolo-Rizzo et al. [22], whose study was similar to ours in design and length of follow-up, estimated that the prevalence of self-reported COVID-19 associated chemosensory dysfunctions was 21.3% at 12 months, roughly in line with our result. Only Renaud et al. [28], who used an objective measurement, described a higher rate of smell recovery (96.1%) at one year.

The reason for the differences between the studies are still unclear and might be of various nature. Primarily, the estimated prevalence may be affected by the methodology used for the data collection. Indeed, it has been proven that the proportion of sensory dysfunctions is affected by the detection instruments, being higher with the use of objective measurements [48, 50]. On the contrary, the assessment of chemosensory dysfunctions based on anamnestic data may fail to detect a considerable proportion of cases [7].

### Table 2
Duration (days) of self-reported olfactory and gustatory dysfunctions within 12 months follow-up of COVID-19 cases. District of Foggia (Apulia region, Italy), March 1st, 2020—June 16th, 2021

| Sex               | Olfactory dysfunction | Gustatory dysfunction |
|-------------------|-----------------------|-----------------------|
|                   | Mean time (SD)        | p value               | Mean time (SD)        | p value               |
| Male              | 100.9 (143.8)         | 0.1357                | 102.8 (144.0)         | 0.4500                |
| Female            | 126.3 (154.9)         |                       | 105.5 (141.7)         |                       |
| Age groups        |                       |                       |                       |                       |
| ≥ 45 years        | 128.5 (158.1)         | 0.1361                | 116.5 (151.7)         | 0.1289                |
| < 45 years        | 103.6 (142.5)         |                       | 92.3 (131.9)          |                       |
| Comorbidity       |                       |                       |                       |                       |
| None              | 117.2 (151.6)         | 0.4112                | 103.3 (141.6)         | 0.4117                |
| At least one comorbidity | 110.3 (147.5) |                       | 109.8 (148.3)         |                       |
| Clinical presentation |                   |                       |                       |                       |
| Paucisymptomatic  | 117.8 (151.6)         | 0.4056                | 104.3 (142.3)         | 0.4914                |
| Mild              | 111.9 (149.6)         |                       | 104.8 (143.5)         |                       |

SD Standard Deviation
Fig. 2 Kaplan–Meier estimates showing the rate of complete recovery of self-reported olfactory A and gustatory B dysfunctions in COVID-19 cases. District of Foggia (Apulia region, Italy), March 1st, 2020—June 16th, 2021
Two very recent case–control studies have evaluated the persistence of smell and taste disorders at least one year after the onset of COVID-19 using psychophysical tests [51, 52]. More specifically, Boscolo-Rizzo et al. estimated that, overall, 58% of cases vs. 18% of controls had an olfactory or gustatory dysfunction, while 33% of cases self-reported a persistently altered sense of smell or taste at the time of the psychophysical evaluation [51]. Vaira et al. found that 26.5% of cases vs. 3.5% of controls had olfactory dysfunction on psychophysical tests, while 25.9% of patients self-reported some form of persistent olfactory loss, suggesting that qualitative and quantitative disturbances of smell may have similar clinical implications on the quality of life [52].

We did not find any baseline demographic or clinical predictive factors for the persistence of symptoms. Interestingly, the occurrence of the syndrome defined “Long COVID” has been reported independently of the severity of the acute phase, being present also in patients with a mild disease [30, 38, 39].

The recovery time is putatively dependent on the underlying pathophysiological mechanisms of sensory dysfunctions. These mechanisms were not investigated in our study but can hopefully be clarified with further purposely designed researches. In our analysis, patients were also asked to estimate the approximate duration of their symptoms. It emerged that a complete recovery of smell and taste tended to occur mostly in the first month after the acute phase of COVID-19. This is in agreement with Nguyen et al. [23], who documented the recovery of the sense of smell and taste mainly during the first 6 weeks after onset using a retrospective questionnaire, and with Nehme et al. [27], who performed an interim interview at 30–45 days after COVID-19 diagnosis.

Olfactory and gustatory dysfunctions are generally considered less disabling and life-threatening than other sensory impairments. Thus, they may not receive adequate medical attention despite their impact on quality of life, especially if prolonged over months. However, olfactory and gustatory deprivations of various cause have been documented as disruptive on daily activities already before the spread of SARS-CoV-2 [31, 40], and their negative impact has been recently confirmed by properly designed studies [41–43]. It is apparent that COVID-19 patients with loss of smell and taste experience a reduced quality of life related to those situations or functions in which the chemical senses play a significant role. Furthermore, they also present with higher levels of psychological distress. In particular, the presence of chemosensory dysfunctions is positively correlated to anxiety and depression, which are attributable to a sense of frustration as the patient often struggles to be fully understood [43]. Our study has some limitations. The self-reported assessment of the severity of symptoms and the retrospective investigation of their persistence within the 12-months follow-up period could be inaccurate due to a recall bias. Moreover, we did not record any possible pharmacological or rehabilitative intervention that could potentially affect the evolution of the olfactory and gustatory dysfunctions during the study period. As previously discussed, another possible limitation lies in the fact that, in our study, chemosensory dysfunctions were not assessed using objective examinations, such as psychophysical and electrophysiological tests, but only on a subjective basis. Therefore, underreporting of chemosensory dysfunctions cannot be excluded. However, in the perspective of a clinical approach taking into account the quality of life, a subjective evaluation may be more significant than an objective assessment of the disorders. Moreover, due to the absence of a control group, our findings could have been biased by the underlying prevalence of chemosensory dysfunctions in the general population [53, 54]. Also the inclusion of only patients with paucisymptomatic-to-mild COVID-19 may have influenced both the prevalence of sensory disorders and the characteristics or the timing of their evolution. Finally, the possibility of spontaneous recoveries of a post-viral olfactory loss even beyond one year from the onset cannot be excluded [55].

Conclusions

Olfactory and gustatory dysfunctions persist in a substantial portion of patients with previous paucisymptomatic-to-mild clinical COVID-19 up to 12 months after disease onset. As SARS-CoV-2 infection may be associated with long-term smell and/or taste loss that may significantly impact the quality of life, there is a need for a better understanding of the extent and duration of these symptoms. In addition, a better understanding of the physiological mechanisms driving the recovery is required to facilitate the development of effective preventive and therapeutic strategies.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-022-07052-8.

Additional file 1: Univariate analysis of variables associated with self-reported chemosensory dysfunctions in COVID-19 cases. District of Foggia (Apulia region, Italy), March 1st - June 16th, 2020.

Additional file 2: Multivariate analysis of variables associated with self-reported chemosensory dysfunctions in COVID-19 cases. District of Foggia (Apulia region, Italy), March 1st - June 16th, 2020.

Additional file 3: Multivariate analysis of variables associated with complete recovery of self-reported olfactory and gustatory dysfunctions in COVID-19 cases. District of Foggia (Apulia region, Italy), March 1st, 2020–June 16th, 2021.
Acknowledgements

The Authors would like to thank all the frontline health workers at Foggia Local Health Unit, Foggia, Italy: Giovanni Iannucci, Vitro Piazzolla, Antonio Nigrì, Raffaele Angellis, Marianna Amnese, Viviana Balena, Lorelia Balestrucci, Costantina Borazio, Vittorio Bramante, Matteo Buono, Alessia D’Ambrosio, Chiara Gasparo, Antonio Giuliani, Michele Martino, Giuseppina Moffia, Maria Nestà, Stefano Notarangelo, Lucia Palumbo, Daniela Pesce, Vittoria Pistacchi, Rachele Maria Russo, Leonardo Salvemini, Lilletta Savino, Aurora Scimens, Giuseppina Totaro, and Policlinico Ruiniti Foggia University Hospital: Vitangelo Dattoli, Franco Mezzadri, Roberto Iannetti, Maria Pia Laviano, Martina Meola, for their dedication and valuable work into pandemic control. Special thanks to Maria Rosa Valetto, Silvia Emrendi, Lucia Massi, and Pietro Dri (Zadig Scientific Publisher, Milan, Italy) for editorial assistance, manuscript development and writing support.

Authors’ contributions

Conceptualization, FF and DM; methodology FF and DM; validation MC; formal analysis RDN; investigation MM, UF, GDM and LA; data curation GI; writing-original draft preparation FF, DM and RP; writing-review and editing, FF, DM, PL and RP; supervision, PL and RP. All authors read and approved the final manuscript.

Funding

This research received no external funding.

Availability of data and materials

The authors declare that the data supporting the findings of this study are available within the article and its Additional file 1, Additional file 2, and Additional file 3.

Declarations

Ethics approval and consent to participate

The study was conducted within the public health surveillance program established by the Apulia region; ethical approval was not required. All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Moreover, according to the Italian regulation (DETERMINAZIONE AIFA—20 marzo 2008, GL n. 76 del 31-3-2008), a retrospective epidemiological study only required notification to the Regional Public Health Authority (IRB) due to the nature of the study itself. For the baseline survey, consent was not obtained from participants because surveillance data were provided and analysed anonymously. For the follow-up phase, the informed consent was obtained from all participants at the beginning of the telephone survey at 12-month. Moreover, according to the Italian Data Protection Authority in the context of the COVID-19 health emergency, it is indicated that, in the event of the impossibility of obtaining the consent of the interested parties, observational studies take advantage of a derogation regime for the duration of the COVID-19 emergency (art. 110 of the Code regarding the protection of personal data).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

1Hygiene Unit, Policlinico Ruiniti Foggia Hospital, Department of Medical and Surgical Sciences, University of Foggia, Ospedale Colonnetto D’Avanzo, Viale degli Aviatori 2, 71122 Foggia, Italy. 2Microbiology and Virology Section, Policlinico Ruiniti Foggia Hospital, Foggia, Italy. 3Otolaryngology - Head and Neck Surgery Unit, Policlinico Ruiniti Foggia Hospital, Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy. 4Department of Biological and Environmental Sciences and Technology, University of Salento, Lecce, Italy.

Received: 23 March 2021 Accepted: 12 January 2022 Published online: 22 January 2022

References

1. American Academy of Otolaryngology-Head and Neck Surgery. Anosmia, hyposmia, and dysgeusia symptoms of Coronavirus Disease. 2020. https://www.entnet.org/content/aao-hns-anosmia-hyposmia-and-dysgeusia-symptoms-coronavirus-disease. Accessed 10 Jun 2021.
2. Centers for Disease Control and Prevention (CDC). Coronavirus disease 2019 (COVID-19) symptoms. 2020. https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html. Accessed 10 Jun 2021.
3. European Centre for Disease Prevention and Control (ECDC). Case definition for coronavirus disease 2019 (COVID-19), as of 3 December 2020. https://ecdc.europa.eu/en/covid-19/surveillance/case-definition. Accessed 10 Jun 2021.
4. Villarebel C, Makinson A, Jaussent A, Picot MC, Ngre Pagé L, Rouvère JA, et al. Diagnostic value of patient-reported and clinically tested olfactory dysfunction in a population screened for COVID-19. JAMA Otolaryngol Head Neck Surg. 2021;147:271–9. https://doi.org/10.1001/jamaoto.2020.5074.
5. Paderno A, Mattavelli D, Rampinelli V, Grammatica A, Raffetti E, Tomasoni M, et al. Olfactory and gustatory outcomes in COVID-19: a prospective evaluation in nonhospitalized subjects. Otolaryngol Head Neck Surg. 2020;63:1144–9. https://doi.org/10.1177/0194599820939538.
6. Mihraeen E, Behnezafad F, Salehi MA, Noori T, Harandi H, SeyedAliNagh S. Olfactory and gustatory dysfunctions due to the coronavirus disease (COVID-19): a review of current evidence. Eur Arch Otorhinolaryngol. 2021;278:307–12. https://doi.org/10.1007/s00410-020-01612-6.
7. Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: common findings in COVID-19 patients. Laryngoscope. 2020;130:1787. https://doi.org/10.1002/lary.28692.
8. Vaira LA, Salzano G, De Riu G. The importance of olfactory and gustatory disorders as early symptoms of coronavirus disease (COVID-19). Br J Oral Maxillofac Surg. 2020;58:615–9. https://doi.org/10.1016/j.bjoms.2020.08.024.
9. Spinato G, Fabbris C, Polese J, Cazzador D, Boschetto D, Hopkins C, Boscolo-Rizzo P. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. JAMA. 2020;323:2089–90. https://doi.org/10.1001/jama.2020.6771.
10. Russell B, Moss C, Rigg A, Hopkins C, Papa S, Van Hemelrijck M. Anosmia and ageusia are emerging as symptoms in patients with COVID-19: anosmia and ageusia are emerging as symptoms in patients with COVID-19: what does the current evidence say? Euracingermedicalscience. 2020. https://doi.org/10.3332/ercancer.2020.ed98.
11. Lechien JR, Chiesa-Estomba CM, Hans S, Barillari MR, Jouve L, Sausse S. Loss of smell and taste in 2013 European patients with mild to moderate COVID-19. Ann Intern Med. 2020;173:672–5. https://doi.org/10.7326/M20-2428.
12. Lechien JR, Chiesa-Estomba CM, De Siat D, Hori M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol. 2020;277:2251–61. https://doi.org/10.1007/s00405-020-05965-1.
13. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci. 2020;12:8. https://doi.org/10.1038/s41368-020-0074-x.
14. Keyhan SQ, Falahai HR, Cheshmi B. Dysosmia and dysgeusia due to the 2019 Novel Coronavirus: a hypothesis that needs further investigation. Maxillofac plast Reconstr Surg. 2020;42:9. https://doi.org/10.1186/s40902-020-00254-7.
15. Moriguchi T, Harri N, Goto J, Harada D, Sugawara H, Takamino J, et al. A first case of meningitis/encephalitis associated with SARS-CoV-2. Int J Infect Dis. 2020;94:55–8. https://doi.org/10.1016/j.ijid.2020.03.062.
16. Xydakis MS, Albers MV, Holbrook EH, Lyon DM, Shih RY, Frasnelli JA, et al. Post-viral effects of COVID-19 in the olfactory system and their implications. Lancet Neurol. 2021;20:753–61. https://doi.org/10.1016/S1474-4422(21)00182-4.
17. Gupta K, Mohanty SK, Mittal A, Kalra S, Kumar S, Mishra T, et al. The cellular basis of the loss of smell in 2019-nCoV-infected individuals. Brief Bioinform. 2020;22:873–81. https://doi.org/10.1093/bib/bbaa166.
18. Vaira LA, Hopkins C, Sandiosa A, Manca A, Machouchas N, Turilli L, et al. Olfactory epithelial histopathological findings in long-term coronavirus disease 2019 related anosmia. J Laryngol Otol. 2020;134:1123–7. https://doi.org/10.1017/S0022215120002455.
S4. Hummel T, Whitcroft KL, Andrews P, Altundag A, Cinghi C, Costanzo RM, et al. Position paper on olfactory dysfunction. Rhinol Suppl. 2017;54:1–30. https://doi.org/10.4193/Rhino16.248.

S5. 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;28:419–22. https://doi.org/10.2500/ajra.2014.28.4102.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.