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The outcome of olfactory impairment in patients with otherwise paucisymptomatic coronavirus disease 2019 during the pandemic

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Abstract

Objective. This study aimed to measure the duration and recovery rate of olfactory loss in patients complaining of recent smell loss as their prominent symptom during the coronavirus disease 2019 outbreak.

Method. This was a prospective telephone follow-up observational study of 243 participants who completed an online survey that started on 12 March 2020.

Results. After a mean of 5.5 months from the loss of smell onset, 98.3 per cent of participants reported improvement with a 71.2 per cent complete recovery rate after a median of 21 days. The chance of complete recovery significantly decreased after 131 days from the onset of loss of smell (100 per cent sensitive and 97.7 per cent specific). Younger age and isolated smell loss were associated with a rapid recovery, whereas accompanying rhinological and gastrointestinal symptoms were associated with longer loss of smell duration.

Conclusion. Smell loss, occurring as a prominent symptom during the coronavirus disease 2019 pandemic, showed a favourable outcome. However, after 5.5 months from the onset, around 10 per cent of participants still complained of moderate or severe hyposmia.

Main Article

Dr Z Azad takes responsibility for the integrity of the content of the paper

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Introduction

Coronavirus disease 2019 (Covid-19) is an ongoing viral pandemic that started in China in December 2019 and rapidly spread to the other countries of the world.[1] The World Health Organization (WHO) highlighted the triad of fever, cough and shortness of breath in the definition of a suspected and probable case of Covid-19 in the early guidelines.[2] At the same time as the Covid-19 pandemic, there was a rapid increase in self-reported olfactory dysfunction.[3] In February 2020, smell and taste dysfunction were identified as a symptom of Covid-19 in a survey of neurological manifestations of the disease.[4] Further studies confirmed the association between Covid-19 and chemosensory dysfunction with a wide range of reported prevalence from 3.2 per cent up to 98 per cent for loss of smell.[5]

By 9 May 2020, studies had provided sufficient evidence for the WHO to add loss of smell alongside other less common symptoms of Covid-19, and on 7 August, patients with sudden anosmia or ageusia without a known underlying cause were defined as a probable case of Covid-19.[6,7] Different factors were suggested to affect the prevalence of smell loss in various studies, including demographic factors (age, gender), the severity of the disease, and the methodology and design of the study. It seemed that smell loss was more prevalent among younger people, out-patient cases, females, Caucasians and whether the olfaction had been assessed objectively.[5,8–10] Smell loss was even shown to be related to the prognosis of Covid-19. Lower hospital and intensive care unit admission rates, lower rates of acute respiratory distress syndrome or a need for intubation are associated with the presence of olfactory loss.[11,12]

Loss of smell after a respiratory infection is not unique to Covid-19, and viruses such as adenovirus, rhinovirus, coronavirus and influenza are already known as aetiological factors.[13] Although olfactory dysfunction is often accompanied by other Covid-19 symptoms in many published reports, there is some evidence indicating that Covid-19 patients can present with chemosensory dysfunctions as their sole symptom of the disease.[14] Although the prognosis of post-viral olfactory loss is not exactly clear and reported recovery rates vary in related studies, early reports, which are mostly from Europe, suggest a more favourable prognosis for olfactory loss encountered in confirmed Covid-19 cases compared with previously described post-viral olfactory loss.[15,16] However, as was seen with prevalence rates, reported olfactory recovery rates vary between studies, and several factors have been reported to be associated with the prognosis of smell loss in Covid-19 cases.[17–20]

Healthy, young out-patients with subtle or no symptoms are not prioritised for real-time polymerase chain reaction in the diagnostic protocols in areas with limited resources.[21] Because of the high incidence of olfactory dysfunction in Covid-19 cases, this study aimed to investigate the duration and recovery rate of olfactory loss encountered in cases with mild or no additional Covid-19 symptoms (with no Covid-19 confirmed tests) that occurred during the pandemic in order to indicate the factors that may influence the duration or recovery rate of olfactory dysfunction in these patients.

Materials and methods

Study population

An online survey by Bagheri *et al.*[22] was run from 12 March to 8 April 2020. Out of 19 473 participants with smell loss, 6654 responders registered their phone numbers so their symptoms could be followed. Participants were selected for inclusion in this study if they had reported the absence of other accompanying Covid-19 symptoms (including cough, fever, shortness of breath, sore throat, myalgia, nausea or vomiting, and diarrhoea) or rhinological symptoms (including runny nose, sneeze, nasal congestion, nasal thick discharge and a need to blow the nose).

Participants aged under 18 years, or those who had mentioned a history of previous olfactory problems, chemotherapy, chronic respiratory infections, nasal polyps, head trauma, neurodegenerative diseases, receipt of specified treatment for their recent smell loss (including glucocorticoids, hydroxychloroquine or any antiviral medications) or those who could not be reached by three calls on three separate days through the provided telephone numbers were excluded.

Measurements and study design

In this prospective observational study, all eligible participants were interviewed on the telephone about the severity of recent smell loss at the onset and at the time of the interview (self-assessed by an ordinal scale from one to five corresponding to normal sense of smell, mild loss of smell, moderate loss of smell, severe loss of smell or anosmia) and the duration of the smell loss (the days since loss of smell onset to being fully recovered).[23]

Additional Covid-19 symptoms, presenting in one week prior until one week after the onset of loss of smell were self-graded as: no symptoms, mild symptoms, moderate symptoms and severe symptoms.[24] Rhinological symptoms in the same time limits were self-assessed based on the rhinological subscale of Sino-Nasal Outcome Test-22 (a Likert scale of 1 to 5).[25,26] Any diagnosis of Covid-19 by real-time polymerase chain reaction or chest imaging in the participants or their family members living in the same house or any recent smell loss in the family members was also recorded. The participants were followed up via telephone twice at least three months apart if they did not report a return of olfaction to the baseline. The patients who did not want to be followed up (despite their first consent), had not answered the questions completely (because of not remembering), had received medication during the follow ups, who reported moderate or severe rhinological or Covid-19 symptoms, or who were hospitalised were excluded from the analysis. Complete recovery was defined as self-reported restoration of smell ability, whereas partial recovery was defined as improvement in olfactory ability.

Statistical analysis

The data were described as mean and standard deviation or frequency (per cent). Chi-square or Fisher's exact test was utilised for assessing the relationship between categorical data with time to recovery categories (in correspondence with first and third quartile of time to complete recovery). Subsequently, rapid and moderately recovered patients were merged and odds ratios for measuring the effect size were calculated. The significant variables were included in multiple logistic models to assess the multiple relationships. The receiver operating characteristic curve was used to classify patients as with and without complete recovery, considering the time passed from the onset of smell loss. Kaplan–Meier estimates were reported to show the rate of complete recovery from the onset of the smell loss. All analysis was performed using SPSS® (version 24) statistical software. A p-value less than 0.05 was considered significant.

Results

Study population demographic data and symptoms

Data of 243 participants were included in the final analysis after application of inclusion and exclusion criteria. The mean age of participants was 32.96 ± 9.47 years. The participants were from 16 different provinces of Iran, mainly from Gilan ($n = 120$, 49.4 per cent), Tehran ($n = 63$, 25.9 per cent), Alborz ($n = 12$, 4.9 per cent), Esfahan ($n = 11$, 4.5 per cent) and Mazandaran ($n = 11$, 4.5 per cent). These provinces were among the first provinces of the country to be affected by Covid-19.[27] One-hundred and fifty-five (63.8 per cent) participants were female, and 54 (22.2 per cent) reported they were smokers. At the first follow up, 139 (57.2 per cent) participants had not recovered completely. Of this group, 130 (93.5 per cent) participants were reached in the second follow up.

Of 243 participants, 215 (88.5 per cent) reported total anosmia at the onset of the olfactory impairment. None of the responders reported any Covid-19 or sinonasal signs and symptoms in the original online survey. However, at the interview, 175 responders (72 per cent) reported mild symptoms: 153 responders (59.1 per cent) reported at least one of the Covid-19 symptoms and 66 responders (27.2 per cent) reported at least one of the rhinological symptoms. Loss of smell (with or without taste dysfunction) was reported as the first symptom by 119 participants (49 per cent) and as the sole symptom by 68 participants (28 per cent). None of the participants had undergone real-time polymerase chain reaction testing or had been evaluated by a computed tomography scan of the chest. Ten participants (4.1 per cent) reported Covid-19 diagnosis, and 77 participants (31.8 per cent) reported new onset loss of smell in at least one family member living at the same house. Accompanying symptoms are presented in Table 1.

Follow-up duration and final recovery rates

The mean total follow-up duration was 111.39 ± 59.34 days (median: 151, mode: 47, range: 26–203 days). The first interview was completed after a mean of 47.95 ± 12.44 days after the onset of smell loss (median: 46, mode: 40, range: 26–91 days).

At the first telephone interview, 104 patients (40.3 per cent) self-reported complete recovery. From the remaining 139 participants, 130 could be followed up with the second interview

Table 1. The distribution of existing symptoms of participants

Signs and symptoms	Total (*n* (%))
Coronavirus 19 symptoms	153 (59.1)
– Headache	63 (24.7)
– Myalgia	71 (27.4)
– Fever	55 (21.9)
– Cough	50 (19.3)
– Sore throat	44 (17)
– Dyspnoea	20 (7.7)
– Diarrhoea	20 (7.7)
– Nausea or vomiting	7 (2.7)
Rhinological symptoms	66 (27.2)
– Rhinorrhoea	47 (18.2)
– Sneeze	34 (13.2)
– Nasal congestion	16 (6.2)
– Nasal thick discharge	2 (0.8)
– Need to blow the nose	7 (2.9)

after a mean of 165.99 ± 9.34 days after the onset of their smell loss (median: 166, mode: 169, range: 142–203).

At the end of the study, those who had not completely recovered were followed for a mean of 149.38 ± 41.25 in 'partial recovery' (median: 164, mode: 166, range: 38–203) and 163.75 ± 10.81 in 'no recovery' groups (median: 161, mode: 154, range: 154–179). Finally, 239 participants (98.3 per cent) reported improvement: 173 (71.2 per cent) reported complete recovery and 66 (27.1 per cent) reported partial recovery. Mild, moderate and severe hyposmia was reported by 45 (18.5 per cent), 21 (8.6 per cent) and 4 (1.6 per cent) patients, respectively. No one reported anosmia at the last follow up.

Factors influencing complete recovery

The mean age of patients with and without complete recovery was 33.16 ± 10.24 and 32.48 ± 7.34 years, respectively ($p = 0.614$). Complete recovery was reported significantly more frequently in the patients with a family history of recent smell impairments (80.5 per cent ($n = 62$) *vs* 67.1 per cent ($n = 110$); $p = 0.031$) and less in those who reported fever as an accompanying symptom (58.3 per cent ($n = 28$) *vs* 74.6 per cent ($n = 144$); $p = 0.026$). Furthermore, the odds of complete recovery in patients without fever were 2.10 times higher in comparison with patients with fever (95 per cent confidence interval (CI): 1.08–4.07). There were no significant relationships between other symptoms and complete recovery. The rates of complete recovery were not significantly different between participants with rhinological symptoms, Covid-19 symptoms or those with isolated smell loss.

Duration of smell loss and predictive factors

The smell loss was self-reported to last for a mean of 32.54 ± 31.48 days (median: 21, mode: 30, range: 3–210) until complete recovery. Complete recovery of smell loss within the mean follow up of 111 days in 234 responders who could be reached at the last follow up showed the rate of improvement to be 56.2, 70.1, 71.5 and 74.7 per cent at 50, 100, 150 and 200 days following onset of smell loss, respectively (Figure 1).

In order to evaluate the factors influencing the duration of the smell loss, completely recovered participants were divided into three groups based on the first and third quartile of the time to recovery: rapid recovery (1–10 days), moderate recovery (11–45 days) and delayed recovery (more than 45 days). Rapidly recovered participants were significantly younger compared with the delayed recovery participants (31.3 ± 8.69 *vs* 35.55 ± 9.43; $p = 0.031$). Patients with smell loss as the sole symptom reported early recovery significantly more frequently compared with those who had any Covid-19 or sinonasal symptoms (88.7 per cent ($n = 47$) *vs* 73.1 per cent ($n = 87$); $p = 0.037$).

Although the prevalence of nasal congestion, headache, nausea or vomiting, and diarrhoea increased significantly in those who had a longer recovery period (Table 2), there was a statistically significant relationship only between diarrhoea and delayed recovery in the multiple logistic models (odds ratio = 4.65; $p = 0.031$; Table 3). However, the percentage of the patients with at least one rhinological symptom who had a delayed recovery was significantly higher (41.7 per cent ($n = 10$) *vs* 18.9 per cent ($n = 28$); $p = 0.020$, odds ratio = 3.06, 95 per cent CI = 1.13–5.19).

The receiver operating characteristic curve was used to classify the patients according to gaining complete recovery, considering the time passed from the onset of the smell loss. It showed that day 131 after the onset of olfactory dysfunction was the best cut-off for predicting that participants would not gain complete recovery (100 per cent sensitivity and 97.7 per cent specificity). The area under the receiver operating characteristic was 0.98 (95 per cent CI: 0.97–100; Figure 2).

Discussion

This study was carried out on patients with sudden smell loss that happened during the Covid-19 pandemic and who reported mild Covid-19 or rhinological symptoms or no accompanying symptoms at all. Although 98.3 per cent of participants ultimately reported some improvement, the rate of complete recovery reported after at least 4 months of follow up was 71.2 per cent. Although no one reported anosmia, 1.6 per cent of respondents still complained of severe hyposmia, and 8.6 per cent reported moderate hyposmia at the end of the study.

The reported chance of recovery in routinely encountered post-viral olfactory loss ranged from 32 to 67 per cent, and around 20 per cent of patients did not recover after 1 year of viral infection.[3,28] A review of articles published from 1 April to 31 October 2020 and focusing on the rate of recovery in confirmed cases of Covid-19 was carried out (Table 4).[29–67] In the confirmed Covid-19 patients, the reported rates of complete recovery varied greatly (4 to 96 per cent for a 1-month follow up and 63 to 91.4 per cent for a 2-month follow up).[29,52,57,64] The recovery rates for follow up of 3 and 6 months were reported to be 85.3 per cent and 86 per cent, respectively.[49,65] It should be emphasised that because Covid-19 had not been confirmed by polymerase chain reaction in our patients, they were considered to be probable cases of Covid-19 according to WHO criteria. Their rate of complete recovery of smell loss was more similar to the rate of recovery of Covid-19 cases compared with other post-viral olfactory impairment. Interestingly, even patients who reported isolated smell loss self-reported a complete recovery

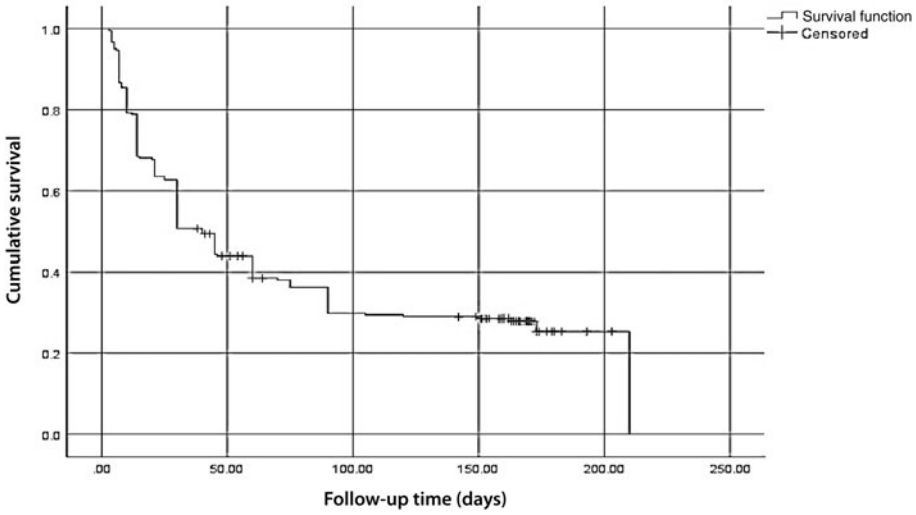

Fig. 1. Kaplan–Meier estimates showing the rate of regaining complete recovery (percentage) during the follow-up time.

Table 2. The association between symptoms and time to recovery

	Time to complete recovery				
Symptom	1–10 days (*n* (%))*	11–45 days (*n* (%))†	>45 days (*n* (%))‡	*P*-value	Odds ratio (95% CI)
Headache					
– With	8 (18.2)	21 (47.7)	15 (34.1)	0.043	2.36 (1.09–5.10)
– Without	42 (32.8)	63 (49.2)	23 (18)		
Diarrhoea					
– With	1 (10)	3 (30)	6 (60)	0.011	5.95 (1.61–22.73)
– Without	49 (30.4)	80 (49.7)	32 (19.9)		
Nausea or vomiting					
– With	0	2 (33.3)	4 (66.7)	0.016	7.69 (1.5–43.48)
– Without	50 (30.3)	81 (49.1)	34 (20.6)		
Nasal congestion					
– With	1 (10)	4 (40)	5 (50)	0.04	3.88 (1.06–14.29)
– Without	49 (30.4)	79 (49.1)	33 (20.5)		

Odds ratios show the odds of delayed complete recovery versus rapid or moderate complete recovery. *$n = 50$; †$n = 84$; ‡$n = 38$. CI = confidence interval

rate of 77.9 per cent (in a mean follow-up time of 3.3 months which lasted for a mean of 26 ± 25.12 days), which is well above the reported rate of recovery for post-viral olfactory impairment. These patients even showed a faster recovery period compared with the others.

Various factors have been reported to influence the rate of recovery of smell loss in Covid-19 patients. The mean duration of olfactory impairment was reported to be 8 to 9 days in a pooled analysis of 20 studies.[5] In our study, the duration of smell loss was significantly shorter in those with lower age and those who reported no additional symptoms besides the smell loss. There is a controversy in the reported effect of age on the duration of smell loss in Covid-19. Although Levinson *et al.*[68] reported a longer duration of smell loss in patients aged over 40 years, patients with severe loss of smell who recover later have been reported to be younger in 2 studies.[17,18] In a study by Fjaeldstad,[51] with a similar methodology and study population to this study (online survey for out-patients with a mean age of 39.4 years who were mainly without confirmation for Covid-19), there was no significant effect of age on the time of recovery or recovery rates. As transmembrane serine protease 2 expression is reported to increase with older age, this may explain the negative effect of older age on the recovery of the sense of smell in the patients.[69]

The duration of smell loss was significantly longer in the patients who reported nasal congestion or any rhinological symptoms. Nasal congestion has been shown to be associated with a slow resolution and lower recovery rate.[20,44] In the present study, nasal congestion did not affect the final complete recovery rates, but it slowed down the process of smell recovery. Only 10 per cent of the population with nasal congestion completely recovered within the first 10 days, and a report of rhinological symptoms increased the odds of the late recovery (complete recovery after 45 days) by 3 times. This may be a reflection of the conductive component effect (mucosal oedema) on the suggested mechanism of smell impairment.[47,70,71] However, an increased level of inflammation, induced by pre-existing rhinitis, may also be responsible.

Nasal goblet (secretory) cells and ciliated cells in the epithelium of respiratory and gastrointestinal systems have shown the highest angiotensin-converting enzyme 2 expression.[72]

Table 3. The multiple logistic models for assessing the association between mentioned symptoms with later recovery

Symptom	Odds ratio	Standard error (beta)	*P*-value	95% CI for odds ratio	
				Lower	Upper
Diarrhoea	4.65	0.71	0.031	1.15	18.87
Nausea or vomiting	3.85	0.97	0.163	0.58	25.64
Nasal congestion	2.46	0.75	0.229	0.57	10.75
Headache	1.70	0.44	0.229	0.72	4.03

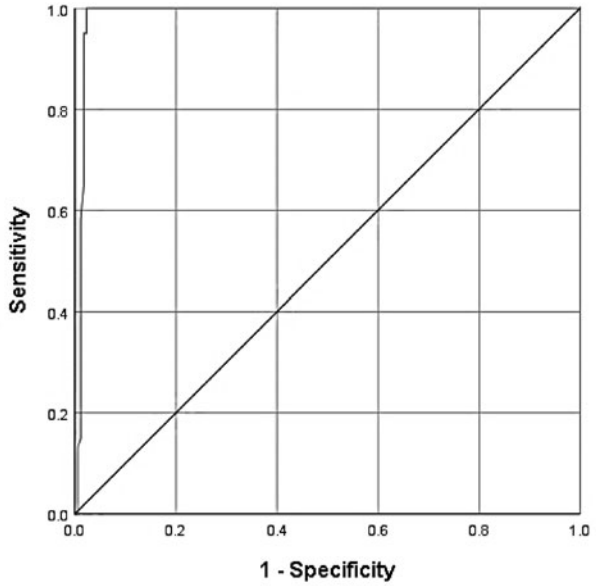

Fig. 2. The receiver operating characteristic curve to assess the efficacy of using the time passed from the onset of smell loss to predict the probability of not regaining complete recovery.

The exact mechanism of diarrhoea is still unclear, and any correlation between olfactory dysfunction and gastrointestinal symptoms has not been reported previously.[73] However, diarrhoea has been shown to be correlated with more severe systemic inflammation in Covid-19 patients.[74] It has also been considered as a risk factor for a more severe and poor prognosis course of the disease in several studies.[75–77] At the last follow up, only 50 per cent (10 out of 20) of our participants with diarrhoea reported complete recovery, and the patients with diarrhoea had a 4.65 fold increased risk for delayed recovery.

The present study demonstrated that although improvement of smell loss may happen with longer follow up, the chance of complete recovery after 131 days from the onset of smell loss dramatically decreases (100 per cent sensitive and 97.7 per cent specific). Total recovery was shown to be significantly related to a short time from the onset of smell loss to the onset of recovery.[44] Vaira *et al.*[32] also emphasised the role of time passed since the clinical onset in improvement or total recovery.

A lower complete recovery rate and a longer duration to complete recovery was shown in this study compared with some of the previous studies, perhaps because of the predominantly female population, cases with severe loss of smell at the beginning and the method of the patient selection. In the present study, the majority of the participants were anosmic (88.5 per cent), and the remaining 11.5 per cent were reported to be severely hyposmic. The severity of smell loss has been reported to play a role in the prognosis. Longer recovery duration has been reported for patients with severe loss of smell compared with patients with milder impairment.[17,18] Cases with severe smell loss in a study by Izquierdo-Domínguez *et al.* were younger, predominantly female and with a lower rate of pneumonia.[17] Similarly, anosmia was found as a risk factor for later recovery.[19,20] On the contrary, in a study by Paolo there was no significant difference in the time of resolution between hyposmic or anosmic patients.[78]

- Various recovery rates have been reported for sudden unexplained anosmia encountered during the coronavirus disease 2019 (Covid-19) pandemic
- Smell loss can be the prominent or sole symptom of Covid-19, although other viruses can induce olfactory dysfunction
- After a mean of 5.5 months, the rate of improvement, complete recovery, and moderate or severe hyposmia were 98.3, 71.2 and 10 per cent, respectively
- Complete recovery was associated positively with recent smell loss in at least one family member living with the patient and negatively with fever
- Younger age and isolated smell loss were associated with a rapid recovery, and rhinological and gastrointestinal symptoms were associated with a slow recovery
- After 131 days from the smell loss onset, the chance of regaining complete recovery dramatically decreased

A study by Paderno *et al.* discussed that women self-report recovery after a longer duration than men.[20] Around 64 per cent of the population in our study was female, which may explain why less than 30 per cent of completely recovered patients had a duration of fewer than 9 days. However, this study did not show any significant differences in the rate of recovery between the sexes.

Limitations

In this study, the included participants had subtle or no Covid-19 symptoms and had not been tested by real-time polymerase chain reaction test. Therefore, definite allocation of the smell loss to Covid-19 or routine post-viral olfactory impairment was impossible, which may be considered as a significant limitation. The smell loss was self-assessed by an ordinal scale that may have limited correlation with more objective measures.[79,80] In addition, we were unable to confirm self-reported recovery rates with psychophysical testing because of low compliance of paucisymptomatic participants for in-person attendance in the hospital for the tests during the pandemic.

Although the online surveys facilitate collecting information with minimal burden on healthcare personnel, they are prone to some biases. The results of this study show that subtle symptoms may not be reported properly in an online survey. This limitation was overcome by reconfirmation through

Table 4. A review of the studies on olfactory dysfunction in Covid-19 which focused on smell loss recovery rate and duration

Authors	Country	Followed cases with OD (*n*)	Covid-19 status	Follow-up duration	Method of assessment of OD	Recovery rate (%)	Time to recovery
Lechien *et al.*[29]	Europe	357	Positive	Mean ± SD of 9.2 ± 6.2 days	Subjective	44 early recovery	96.6% in <15 days
Yan *et al.*[12]	USA	40	Positive	<2 weeks	Subjective	72.5 resolution	76.52% in <15 days
Klopfenstein *et al.*[30]	France	54	Positive	28 days	Subjective	98 recovery	81% <2 weeks
Beltrán-Corbellini *et al.*[31]	Spain	31 smell/taste disorders	Positive	Not reported	Subjective	40 complete recovery & 16.7 partial recovery	Mean ± SD of 7.4 ± 2.3 days for complete recovery & 9.1 ± 3.6 days for partial recovery
Vaira *et al.*[32]	Italy	53 smell/taste disorders	Positive	Mean of 19.3 days	Subjective & objective	Subjective evaluation: 66 complete recovery. Objective evaluation: 13.2 complete recovery	54.28% in <5 days
Lee *et al.*[33]	Korea	232	Positive	Maximum of 40 days	Subjective	94% recovery in the first 35 days	Median of 7 days & most of them within 3 weeks
Hopkins *et al.*[34]	UK	382	80% positive of 15 tested cases	>4 weeks	Subjective	71	75% took more than 4 weeks from the onset
Vaira *et al.*[35]	Italy	225	Positive	Mean ± SD of 14.8 ± 7.4 days	Subjective & objective	Subjective evaluation: 31.3 regression. Objective evaluation: 9.3 complete recovery	Most took 10 days, then reached a plateau
Lechien *et al.*[36]	Belgium	86	Positive with RT-PCR or IgM, IgG	Mean ± SD of 18 ± 11 days	Subjective & objective	Subjective evaluation: 0 complete recovery. Objective evaluation: 38.3 normosmia.	Mean ± SD of 17 ± 11 days for normosmics
Kosugi *et al.*[37]	Brazil	145	Positive	Median of 31 days (range, 12–39)	Subjective	52.6 complete recovery & 33.6 partial recovery	15 days
Dell'Era *et al.*[38]	Italy	237	Positive	Median of 23 days	Subjective	62.9 complete recovery	Median of 10 days (range, 1–25 days)
Chung *et al.*[39]	China	6 patients subjectively evaluated	Positive	14 days	Subjective	50	Not reported
Chung *et al.*[39]	China	6 patients objectively evaluated	Positive	7–9 days	Objective	66.6	Not reported
Paderno *et al.*[40]	Italy	283	Positive	In-patients: mean ± SD of 15.9 ± 6.7 (range, 1–45) days; out-patients: mean ± SD of 20.9 ± 7.4 (range, 6–45) days	Subjective	52 complete recovery	Mean ± SD of 9 ± 5 days
Freni *et al.*[41]	Italy	46	Positive	Mean ± SD of 49.7 ± 18.9 days	Subjective	82 resolution	5–8 days in 56% of patients
Sakalli *et al.*[42]	Turkey	88	Positive	Mean ± SD of 4.3 ± 3.2 days (range, 1–11)	Subjective	22.7 complete recovery & 55.7 partial recovery	Mean ± SD of 8.02 ± 6.41 days
Cervilla *et al.*[43]	Spain	44	Positive	1 month	Objective	78 resolution	77% in >15 days
Paderno *et al.*[20]	Italy	126	Positive	Mean ± SD of 37 ± 9 days	Subjective	87 resolution	75.5% in <20 days

Gorzkowski *et al.*[44]	France	136	Positive	Mean of 26 days	Subjective	51.43 complete recovery	Recovery started between days 14 and 15 days in 78.4%
Boscolo-Rizzo *et al.*[45]	Italy	113	Positive	4 weeks	Subjective	48.7 complete recovery & 40.7 partial recovery	Mean of 11.2 days
Salmon Ceron *et al.*[46]	France	48	Positive	Mean ± SD of 15 ± 3 days	Subjective	27.1 complete recovery & 72.9 partial recovery	Not reported
Jalessi *et al.*[47]	Iran	22	Positive	Maximum 21 days	Subjective	95.45 complete recovery	Mean ± SD of 10.73 ± 8.26 days
D'Ascanio *et al.*[48]	Italy	7 in-patients and 19 out-patients	Positive	By 30 days	Subjective	85.7 resolution for in-patients & 84.3 resolution for out-patients	More than 5 days
Parente-Arias *et al.*[49]	Spain	75	Positive	Mean ± SD of 100.5 ± 3.3 days (range, 91–108)	Subjective	100 improvement & 85.3 complete recovery	Mean ± SD of 17.7 ± 8.9 days. 55.2% of them in the first 12 days
Barillari *et al.*[50]	Italy	207	Positive and perhaps untested.	Mean ± SD of 11.6 ± 7.4 days	Subjective	61.9 recovery	1–15 days, 60% in <9 days
Fjaeldstad[51]	Denmark	100	42% positive and 58% untested	Mean of 33.5 days	Subjective	44 complete recovery for smell loss	Mean of 15.1 and 14.9 days for positive and untested, respectively
Le Bon *et al.*[52]	Belgium	72	Positive with RT-PCR or IgM, IgG	Mean of 37 days	Subjective & objective	4 complete recovery 63 normosmic	A mean of 12 (range, 3–47) days
Spadera *et al.*[53]	Italy	180	89.6% of tested cases were positive	Not reported	Subjective	6.11 complete recovery	2–10 days
Moein *et al.*[54]	Iran	82	Positive	Maximum of 8 weeks	Objective	63 normosmia	Not reported
Klopfenstein *et al.*[55]	France	37	Positive	Maximum of 28 days	Subjective	99.97 recovery	Mean ± SD of 7.4 ± 5 days
Cocco *et al.*[56]	Italy	78	Positive	Mean ± SD of 46.1 ± 19 days	Subjective	51.3 smell recovery	Within 20 days
Vaira *et al*[57]	Italy	117 smell/taste disorders	Positive	Maximum of 60 days	Objective	91.4 recovery	Mainly regressed within 30 days
Cho *et al.*[58]	China	39	Positive	4–6 weeks	Subjective	71.8 complete recovery	Mean ± SD of 10.3 ± 8.1 days
Rojas-Lechuga *et al.*[18]	Spain	138	Positive	Not reported	Subjective	37.67 recovery	Median of 4, 6 and 7 days for mild, moderate and severe smell loss, respectively
Brandão Neto *et al.*[59]	Brazil	143	Positive	Median 76 days	Subjective	53.8 complete recovery & 44.7 partial recovery	Not reported
Chiesa-Estomba *et al.*[60]	France	751	Positive with PCR or serology	Mean ± SD of 47 ± 7 days	Subjective	49 complete recovery & 14 partial recovery	Mean ± SD of 10 ± 6 days for complete recovery & 12 ± 8 days for partial recovery
Amer *et al.*[19]	Egypt	96	Positive	1 month	Subjective	33.3 complete recovery & 41.7 partial recovery	Mean of 17 days for complete recovery & mean of 11 days for partial recovery
Hao Lv *et al.*[16]	China	39	Positive	Not reported	Subjective	89.7 complete recovery & 10.2 partial recovery	>4 weeks in 51.4%

(*Continued*)

Table 4. (*Continued.*)

Authors	Country	Followed cases with OD (*n*)	Covid-19 status	Follow-up duration	Method of assessment of OD	Recovery rate (%)	Time to recovery
Karimi-Galougah *et al.*[61]	Iran	76	Positive	2 weeks	Subjective	30.3 complete recovery & 44.7 partial recovery	Not reported
Iannuzzi *et al.*[62]	Italy	30	Positive	60 days	Subjective & objective	73.3 normosmics	Not reported
Konstantinidis *et al.*[63]	Greece	30	Positive	4 weeks post-diagnosis	Subjective	63.3 complete recovery & 36.6 partial recovery	Not reported
Panda *et al.*[64]	India	68	Positive	4 weeks	Subjective	96 complete recovery	More than half by 2 weeks
Klein *et al.*[65]	Israel	84	Positive	Maximum of 6 months	Subjective	86 recovery	Mean ± SD of 18.9 ± 19.7 days, durations censored at 60 days
Schönegger *et al.*[66]	Austria	3	Positive	11–30 days from the first examination followed by 3 weeks' follow up	Objective	0 complete recovery & 33 partial recovery	Even after 30 to 50 days, patients still suffered from objective smell and taste disorders
Al-Zaidi *et al.*[67]	Iraq	58	20% positive, others untested	1 month at least	Subjective	39.66 recovery	1–3 weeks, mainly in <1 week

Covid-19 = coronavirus disease 2019; OD = olfactory dysfunction; SD = standard deviation; RT-PCR = real-time polymerase chain reaction; Ig = immunoglobulin

telephone interview; however, it was still prone to recall bias or over-reporting because of prompting by the interviewer. On the other hand, in this study, in 50 per cent of the cases, a range of 14–28 days had passed from the initial loss of smell to their participation. This data shows a significant number of our participants were still suffering from smell loss after at least two weeks, and that was the possible reason they found the online survey in their searches and were more willing to participate. In other words, some patients who had rapidly recovered may not have participated.

Conclusion

Because of the high number of patients with Covid-19, the considerable prevalence of anosmia among the affected population and the huge negative impact of anosmia on quality of life, it is important to inform patients about favourable prognosis. However, a dramatic decrease in the rate of complete recovery happens after four months from the onset of smell loss, which may necessitate considering any optional treatments to start before this deadline. Although our patients were not definite cases of Covid-19 by WHO criteria, patients with smell loss as the sole symptom recovered significantly faster, whereas patients with rhinological or gastrointestinal symptoms may have a longer recovery period.

Competing interests. None declared

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