Laryngology & Otology

cambridge.org/jlo

Main Article

Dr A Rajabi takes responsibility for the integrity of the content of the paper

*These authors (A Rajabi and S M Hosseini) are contributed equally to this work.

Cite this article: Taziki Balajelini MH, Vakili MA, Rajabi A, Mohammadi M, Tabarraei A, Hosseini SM. Recovery of olfactory and gustatory dysfunctions in coronavirus disease 2019 patients: a prospective cohort study. *J Laryngol Otol* 2022;1–8. https://doi.org/ 10.1017/S0022215121003935

Accepted: 23 November 2021

Key words:

COVID-19; Smell; Taste Disorders; Recovery of Function; Cohort Studies

Authors for correspondence:

Dr Abdolhalim Rajabi, Health Management and Social Development Research Center, Faculty of Health, Golestan University of Medical Sciences, Gorgan, Iran E-mail: drrajabi.a@goums.ac.ir Fax: +98 017 3245 6105

Seyed Mehran Hosseini, MD. PhD., Associate Professor of Medical Physiology, Department of Physiology, School of Medicine, Neuroscience Research Center Golestan University of Medical Sciences, Gorgan, Golestan, Iran E-mail: hosseini@goums.ac.ir Tel: 00989113736634

© The Author(s), 2022. Published by Cambridge University Press on behalf of J.L.O. (1984) LIMITED.

Recovery of olfactory and gustatory dysfunctions in coronavirus disease 2019 patients: a prospective cohort study

M H Taziki Balajelini¹, M A Vakili², A Rajabi^{3*} ¹, M Mohammadi⁴, A Tabarraei⁵ and S M Hosseini^{6*} ¹

¹Department of Otorhinolaryngology, School of Medicine, Golestan University of Medical Sciences, Gorgan, ²Department of Family and Community Medicine, School of Medicine, Golestan, University of Medical Sciences, Gorgan, ³Health Management and Social Development Research Center, Faculty of Health, Golestan University of Medical Sciences, Gorgan, ⁴Golestan Research Centre of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, ⁵Department of Microbiology, School of Medicine, Infectious Diseases Research Center, Golestan University of Medical Sciences, Gorgan and ⁶Department of Physiology, School of Medicine, Neuroscience Research Center, Golestan University of Medical Sciences, Gorgan, Iran

Abstract

Objective. This study aimed to determine the association of some demographic and clinical factors with recovery from olfactory and gustatory dysfunction in coronavirus disease 2019 patients in Iran.

Methods. This prospective cohort study was performed on 242 coronavirus disease 2019 patients with olfactory and gustatory dysfunction. The time from onset to recovery for olfactory and gustatory dysfunction was estimated by the Kaplan–Meier estimator.

Results. After six months, 239 patients (98.8 per cent) had completely recovered from olfactory dysfunction. Olfactory and gustatory dysfunction symptoms resolved in 80.99 per cent and 83.56 per cent of the patients, respectively, within the first 30 days of symptom onset. Mean recovery time for olfactory dysfunction (35.07 ± 4.25 days) was significantly longer in those infected during the first epidemic wave compared with those infected during the second wave (21.65 ± 2.05 days) (p = 0.004). A similar pattern in recovery time was observed for cases of gustatory dysfunction (p = 0.005).

Conclusion. The recovery rate for coronavirus disease 2019 related olfactory and gustatory dysfunction is high within the first month of symptom onset.

Introduction

Coronaviruses are a large family of viruses that can cause a variety of diseases, ranging from mild acute upper respiratory tract infections to life-threatening diseases such as severe acute respiratory syndrome, Middle East respiratory syndrome and coronavirus disease 2019 (Covid-19).^{1,2} The latter is caused by infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Clinical manifestations of Covid-19 are diverse and may include olfactory and gustatory dysfunction.^{3–5} However, the olfactory and gustatory symptoms are unique, and typically occur without nasal congestion or rhinitis.⁶

The reported incidence rates of olfactory dysfunction in Covid-19 patients range from 5 to 88 per cent.^{7,8} The virus has a strong tendency to colonise in the olfactory epithelium⁹ and can enter the brain through the olfactory bulb.^{10,11} People who develop olfactory dysfunction during the Covid-19 pandemic are strongly advised to self-isolate.¹² Developing olfactory dysfunction can disrupt daily activities, reduce appetite, decrease quality of life and lead to mood disorders.¹³ Patients with hyposmia or anosmia may also have difficulty in tasting food, which may ultimately alter appetite and food enjoyment.¹⁴ The prognosis of olfactory and gustatory dysfunction is still the subject of debate among otolaryngologists and neurologists.¹⁵ There are several short-term studies on olfactory and gustatory dysfunction in Covid-19, most of which have reported a good recovery rate.

Both olfactory dysfunction and gustatory dysfunction have been proposed as recurrent and early symptoms of Covid-19.¹⁶ The symptoms are more frequently observed in patients with mild Covid-19 and resolve rapidly and completely in most cases.¹⁷ One study suggested that hyposmia, with or without dysgeusia, could be a reliable indicator of potential Covid-19.¹⁸ A cross-sectional study also demonstrated the high prevalence of olfactory or taste disorders in Covid-19 patients, with half of the cases recovering on their own after about two weeks.¹⁹ A cohort study also reported that the Covid-19-related olfactory dysfunction and gustatory dysfunction symptoms often resolve within one month of onset, but may only improve partially in 10–15 per cent of patients.²⁰ Only a limited number of long-term studies have investigated olfactory dysfunction recovery and prognosis in Covid-19 patients. In some patients, the duration of olfactory dysfunction is longer.^{15,21} Most assessments of smell and taste rely on measuring the olfactory threshold and the ability to detect aromatic substances, respectively. Despite their accuracy, these tests are not objective and are mainly recommended for disease confirmation in Covid-19 cases. The olfactory test is completely objective but is only used in specialised neurophysiology laboratories.²²

Considering the high prevalence of olfactory and gustatory dysfunction in Covid-19 patients and the importance of the sense of smell and taste for quality of life, our study aimed to determine the association of some demographic and clinical factors with olfactory and gustatory dysfunction recovery time in Covid-19 patients in Iran.

Materials and methods

This clinically based, prospective cohort study was conducted in Golestan Province, northeastern Iran, from 25 March to 24 October 2020. The study was approved by the Ethics Committee of Golestan University of Medical Sciences (ethics code: IR.GOUMS.REC.1399.031). Subjects were selected from a local electronic health registry system. All patients had been diagnosed with Covid-19 based on the results of a reverse transcription polymerase chain reaction test for SARS-CoV-2 using nasopharyngeal swabs. Out-patients with Covid-19 who had olfactory dysfunction and gustatory dysfunction were included in the study after obtaining oral consent.

Recovery from olfactory dysfunction and gustatory dysfunction symptoms was followed up every two weeks for six months (from 25 March to 24 October) using a telephone survey. For this purpose, a valid Iranian questionnaire was used.

Patients were categorised into (complete and partial dysfunction) groups on the basis of severity of olfactory dysfunction and gustatory dysfunction. Patients with complete olfactory or gustatory dysfunction did not recognise any odour and/or taste. Patients with partial olfactory or gustatory dysfunction recognised some odours and/or tastes but only partially.

Progress from complete dysfunction to partial dysfunction or complete recovery, or from partial dysfunction to complete recovery, was recorded in the patient's information checklist. People who made a full recovery were excluded from the follow-up process, and those who had a partial recovery were questioned and followed up the next time. At the end of the study, the number of patients who had partially or fully recovered was determined.

Data on age, gender, ethnicity, the epidemic wave (February to April, and May to July) in which they were infected, olfactory dysfunction onset time (before, after or simultaneously with the onset of general Covid-19 symptoms), olfactory and gustatory dysfunction severity, presence of gastrointestinal dysfunction, and olfactory and gustatory dysfunction outcome (full, partial or non-recovery), were recorded.

Categorical data were described in terms of frequency rates and percentages, and continuous variables were described using means, medians and standard deviations. The recovery time from olfactory dysfunction and gustatory dysfunction was estimated by the Kaplan–Meier curve, considering complete recovery as the end point. Intragroup differences were evaluated using the log-rank test and Cox proportional hazards models when appropriate. Multivariable analysis was performed using the Cox proportional hazards models for all variables. All statistical analyses were carried out using SPSS for Windows (version 26; IBM, Armonk, New York,
 Table 1. Characteristics of Covid-19 patients presenting with olfactory or gustatory dysfunction

Variable	Values
Age (mean ± SD; years)	39.12 ± 11.89
Age group (n (%))	
– ≤40 years	137 (56.60)
– >40 years	105 (43.40)
Sex (n (%))	
– Female	127 (52.5)
– Male	115 (47.5)
Ethnicity (n (%))	
– Fars	120 (49.6)
– Turkmen	109 (45)
– Sistani Persian	13 (5.4)
Epidemic wave (n (%))	
– Infected in 1st wave	117 (48.3)
– Infected in 2nd wave	125 (51.7)
Olfactory dysfunction onset (n (%))	
- Simultaneous with general Covid-19 symptoms	200 (82.6)
– Before general Covid-19 symptoms	27 (11.2)
– After general Covid-19 symptoms	15 (6.2)
Olfactory dysfunction severity (n (%))	
- Complete dysfunction	188 (77.7)
- Partial dysfunction	54 (22.3)
Gustatory dysfunction severity (n (%))	
- Complete dysfunction	170 (70.2)
- Partial dysfunction	49 (20.2)
– No dysfunction	23 (9.5)
Gastrointestinal dysfunction? (n (%))	
– Yes	94 (38.8)
– No	148 (61.2)
Olfactory dysfunction outcome after 6 months (n (%))	
- Full recovery	239 (98.8)
– Partial recovery	1 (0.4)
– Non-recovery	2 (0.8)
Gustatory dysfunction outcome after 6 months $(n \ (\%))$	
– Full recovery	219 (100)

Covid-19 = coronavirus disease 2019; SD = standard deviation

USA). A *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 242 patients completed the study. The mean age of patients was 39.12 ± 11.89 years (range, 9–75 years). The majority of subjects were female (52.5 per cent), Fars (49.6 per cent) and affected during the second epidemic wave (51.7 per cent).

General symptoms of Covid-19 include fever, cough, dyspnoea, fatigue, diarrhoea, abdominal pain, anorexia, nausea and vomiting. As shown in Table 1, olfactory dysfunction



 ${\bf Fig.~1.}$ The pattern of recovery time for patients with olfactory dysfunction (OD) and gustatory dysfunction (GD).

occurred before, after and simultaneously with the onset of general Covid-19 symptoms in 27 (11.2 per cent), 15 (6.2 per cent) and 200 (82.6 per cent) cases, respectively. The mean time interval between the onset of general symptoms and onset of olfactory dysfunction was 10 ± 10.51 days, and the mean time interval between the onset of olfactory dysfunction and the onset of general symptoms was 5.03 ± 2.32 days.

The prevalence of complete and partial forms of olfactory dysfunction was 77.7 per cent and 22.3 per cent, respectively. Moreover, the prevalence of complete gustatory dysfunction, partial gustatory dysfunction and gastrointestinal dysfunction was 70.2 per cent, 20.2 per cent and 38.8 per cent, respectively.

During the six-month follow up of olfactory dysfunction symptoms, 239 patients (98.8 per cent) recovered completely, while one patient (0.4 per cent) partially recovered, and two patients (0.8 per cent) did not recover. However, all 219 cases with gustatory dysfunction fully recovered after six months (Table 1). As shown in Figure 1, 80.99 per cent and 83.56 per cent of Covid-19 patients recovered from olfactory dysfunction and gustatory dysfunction, respectively, within 30 days of the symptom onset.

The mean recovery time for both olfactory dysfunction and gustatory dysfunction was significantly longer for patients infected during the first epidemic wave than for those infected during the second epidemic wave. In addition, the mean recovery time for gustatory dysfunction was significantly longer for women than for men (p = 0.04) (Table 2).

Results of the final multivariate Cox regression analysis model indicated that the second epidemic wave and partial olfactory dysfunction were important predictors of olfactory dysfunction recovery. Compared with the first epidemic wave, the chance of olfactory dysfunction recovery increased by 54 per cent for those infected during the second epidemic wave (adjusted hazard ratio = 1.54; 95 per cent confidence interval (CI) = 1.09-2.18). Furthermore, the chance of complete olfactory dysfunction recovery in individuals with partial olfactory dysfunction was 2.97 times higher (adjusted hazard ratio = 2.97; 95 per cent CI = 1.21-7.29) than in those with complete olfactory dysfunction (Table 3 and Figures 2–4). In addition, infection during the second epidemic peak was significantly associated with an increased adjusted hazard ratio for taste (gustatory) dysfunction (Table 4, Figures 5 and 6).

Discussion

This study was carried out to investigate recovery from olfactory and gustatory dysfunction symptoms in patients with Covid-19 over a six-month follow-up period. The results indicated that olfactory and gustatory dysfunction symptoms resolved in approximately 81 per cent and 84 per cent of patients, respectively, within the first 30 days of symptom onset, with mean respective recovery times of 35.93 ± 27.71 days and 37.75 ± 29.52 days. In addition, being infected during the second epidemic wave and having partial olfactory dysfunction were determined as important factors that affect recovery from olfactory dysfunction. Similarly, being infected during the second epidemic wave was the most important factor affecting recovery from gustatory dysfunction.

In this study, 52.5 per cent of patients with olfactory and gustatory dysfunction were women. Most previous studies also demonstrated that the incidence rate of olfactory dysfunction is higher in female patients with Covid-19.^{23,24} However, a study by Meini *et al.* on 100 hospitalised Covid-19 patients reported a male-to-female ratio of 2:1 for olfactory and taste disorders.²⁵

In the present study, the mean age of patients with olfactory and gustatory dysfunction was 39.12 ± 11.89 years. Other studies on Covid-19 out-patients similarly reported a mean age of less than 40 years.^{23,24,26,27} However, in a study by Meini *et al.*, the mean age of Covid-19 in-patients was 65 ± 15 years.²⁵

Based on the results, olfactory dysfunction appeared simultaneously with, before and after the general Covid-19 symptoms in 82.6 per cent, 11.2 per cent and 6.2 per cent of cases, respectively. Likewise, Lv et al. showed that olfactory or gustatory dysfunction appeared simultaneously with the onset of general Covid-19 symptoms in more than 87 per cent of cases.²⁸ Ramasamy et al. also reported that olfactory or gustatory dysfunction and the general Covid-19 symptoms appeared concurrently in the majority of cases.²⁹ Moreover, in Covid-19 patients who did not develop olfactory dysfunction at the onset of general symptoms, the mean time window for olfactory dysfunction development was 5.03 ± 2.32 days before and 10 ± 10.51 days after the general symptoms. The authors also demonstrated that the median duration of olfactory dysfunction and the complete recovery time from olfactory dysfunction were 7 days in most Covid-19 patients.²⁹ Similarly, Chary et al. reported that olfactory dysfunction occurred from 3 days before to 7 days after the onset of general Covid-19 symptoms.¹⁷

In the present study, the rate of recovery from olfactory dysfunction was 80.99 per cent within the first 30 days of onset, which increased to 81.82 per cent after 90 days and 98 per cent after 6 months. A similar trend was observed for gustatory dysfunction; in fact, all cases with gustatory dysfunction recovered completely within the six-month follow up.

In the literature, Gorzkowski reported that symptoms of olfactory dysfunction resolved in 95.71 per cent of cases within 26 days of onset.²⁶ Meini et al. reported that 82 per cent of patients recovered from olfactory dysfunction during the fourweek follow up.²⁵ Lv et al. also reported that 89.7 per cent of Covid-19 patients recovered from gustatory and olfactory dysfunction after four weeks.²⁸ Paderno *et al.* reported 87 per cent and 82 per cent recovery rates for olfactory dysfunction and gustatory dysfunction, respectively, after one month.²⁰ Hopkins et al. reported a 79 per cent recovery rate from olfactory and gustatory dysfunction over the course of a month.³⁰ In a study by Amer et al., 33 per cent and 41 per cent of the patients achieved complete and partial recovery, respectively, from olfactory dysfunction within 11 days, while 25 per cent of the patients had not recovered after one month.²⁷ In a study by Vaira et al., 7.3 per cent of the patients still had severe

Table 2. Distribution of olfactory and gustatory dysfunction recovery time averages according to patients' characteristics

	Olfactory dysfunction rec	overy time	Gustatory dysfunction recovery time	
Variable	Mean ± SE	Median ± SE	Mean ± SE	Median ± SE
Total	28.05 ± 2.33	14 ± 0.56	29.52 ± 2.55	14 ± 0.60
Sex				
- Female	32.75 ± 3.82	14 ± 0.76	35.55 ± 4.33	14 ± 1.05
– Male	22.82 ± 2.39	14 ± 0.56	23.20 ± 2.46	14 ± 0.71
– <i>p</i> -value	0.06*		0.04 [†]	
Age group				
- ≤40 years	28.51 ± 3.21	12 ± 0.80	30.61 ± 3.62	12 ± 96
– >40 years	27.47 ± 3.37	14 ± 0.78	28.14 ± 3.53	14 ± 0.86
– <i>p</i> -value	0.85		0.93	
Ethnicity				
- Fars	34.05 ± 4.08	14 ± 0.95	36.03 ± 4.34	15 ± 0.98
– Turkmen	22.83 ± 2.46	12 ± 0.86	23.06 ± 2.61	12 ± 0.86
– Sistani Persian	17.92 ± 4.26	14 ± 3.59	19.20 ± 5.53	7 ± 4.34
– <i>p</i> -value	0.06		0.04 [†]	
Epidemic waves				
– Infected in 1st wave	35.07 ± 4.25	15 ± 1.56	36.36 ± 4.27	15 ± 1.68
– Infected in 2nd wave	21.65 ± 2.05	12 ± 0.64	21.66 ± 2.22	12 ± 0.65
– <i>p</i> -value	0.004 [†]		0.005 [†]	
Olfactory dysfunction onset				
- Simultaneous with general Covid-19 symptoms	27.27 ± 2.48	14 ± 0.59	29.12 ± 2.76	14 ± 0.63
- Before general Covid-19 symptoms	31.25 ± 7.59	12 ± 2.59	29.92 ± 7.88	12 ± 3.33
- After general Covid-19 symptoms	32.53 ± 11.93	14 ± 2.65	32.53 ± 11.93	14 ± 2.65
– <i>p</i> -value	0.91		0.98	
Olfactory dysfunction severity				
- Complete dysfunction	29.76 ± 2.69	14 ± 0.66	30.80 ± 2.92	15 ± 0.96
- Partial dysfunction	22.22 ± 4.51	11 ± 1.63	25.40 ± 5.22	12 ± 1.34
– <i>p</i> -value	0.07		0.16	
Gastrointestinal dysfunction?				
- No	29.93 ± 3.23	14 ± 0.69	30.91 ± 3.55	14 ± 0.75
– Yes	25.05 ± 3.14	12 ± 0.68	27.32 ± 3.44	12 ± 1.41
- <i>p</i> -value	0.15		0.28	

*Log-rank (Mantel-Cox) test. [†]Indicates significant difference. SE = standard error; Covid-19 = coronavirus disease 2019

olfactory or gustatory dysfunction at the two-month follow up.³¹ Cho *et al.* reported an olfactory dysfunction recovery rate of 71.8 per cent.³²

The results of our study and those of previous studies indicate that most patients recover from olfactory and gustatory dysfunction symptoms within a short time. The difference in recovery rates may be attributed to the olfactory dysfunction or gustatory dysfunction assessment method, the follow-up duration, and genetic susceptibility to the disease.

In the present study, the mean and median recovery times were 28.05 ± 2.33 and 14 ± 0.56 days for olfactory dysfunction and 29.52 ± 2.55 and 14 ± 0.60 days for gustatory dysfunction, respectively. Chary *et al.* reported a recovery time of 15 days for both olfactory and gustatory dysfunction.¹⁷ The olfactory dysfunction recovery time in the study of Meini *et al.* was 18 days.²⁵ In the study by Cho *et al.*, the mean recovery time for olfactory dysfunction was 10.3 ± 8.3 days.³² Gorzkowski *et al.*²⁶ and Romero-Gameros *et al.*²³ reported a mean recovery time of 11.6 and 10 days, respectively, for olfactory dysfunction. Cho *et al.* reported a mean recovery time of 9.5 ± 6.8 days and a complete recovery rate of 83.3 per cent for gustatory dysfunction.³²

In line with previous studies,^{17,28} we found no significant associations between the median olfactory dysfunction recovery time and patients' gender and ethnicity. However, the median time from onset to recovery was longer in people infected during the first epidemic wave compared with those infected during the second epidemic wave. This could be related to changes in the pathogenicity of the SARS-CoV-2 virus, improved adherence to preventive measures, and increased knowledge about the management of Covid-19related olfactory and gustatory dysfunction after the first wave. In a study by Gorzkowski *et al.*, on 229 patients with Covid-19, the frequency of olfactory dysfunction decreased

The Journal of Laryngology & Otology

Table 3. Crude and adjusted hazard ratios for recovery from olfactory dysfunction

Variable	Crude HR (95% CI)	<i>p</i> -value	Adjusted HR* (95% CI)	<i>p</i> -value
Sex				
– Female	Reference		Reference	
– Male	1.26 (0.97–1.63)	0.08	1.26 (0.96–1.64)	0.09
Age group				
- ≤40 years	1.03 (0.79–1.33)	0.81	1.06 (0.82–1.38)	0.62
– >40 years	Reference		Reference	
Ethnicity				
– Fars	Reference		Reference	
– Turkmen	1.31 (1.00–1.72)	0.04	1.09 (0.79–1.51)	0.56
– Sistani Persian	1.50 (0.84–2.69)	0.16	1.22 (0.63–2.34)	0.54
Epidemic waves				
– Infected in 1st wave	Reference		Reference	
- Infected in 2nd wave	1.43 (1.09–1.87)	0.008	1.54 (1.09–2.18)	0.01^{\dagger}
Olfactory dysfunction onset				
- Simultaneous with general Covid-19 symptoms	Reference		Reference	
- Before general Covid-19 symptoms	0.92 (0.61-1.38)	0.69	0.94 (0.60-1.48)	0.80
- After general Covid-19 symptoms	0.93 (0.97–1.65)	0.93	1.16 (0.66–2.04)	0.59
Olfactory dysfunction severity				
- Complete dysfunction	Reference		Reference	
- Partial dysfunction	1.30 (0.96–1.76)	0.09	2.97 (1.21-7.29)	0.01^{\dagger}
Gastrointestinal dysfunction?				
– No	Reference		Reference	
– Yes	1.19 (0.91–1.55)	0.18	1.08 (0.80–1.44)	0.60
Gustatory dysfunction severity				
- Complete dysfunction	0.71 (0.46-1.11)	0.13	0.86 (0.54–1.39)	0.55
- Partial dysfunction	0.89 (0.54-1.48)	0.67	0.42 (0.15–1.19)	0.10
- No dysfunction	Reference		Reference	

*Adjusted for all covariates. [†]Indicates significant difference for adjusted values. HR = hazard ratio; CI = confidence interval; Covid-19 = coronavirus disease 2019





Fig. 2. The cumulative hazard for olfactory dysfunction (OD) recovery based on age groups, from February to July 2020.

by almost 17 per cent after olfactory and gustatory loss were announced as symptoms of Covid-19 in the mainstream media. 26

Fig. 3. The cumulative hazard for olfactory dysfunction (OD) recovery based on the epidemic wave in which patients were infected, from February to July 2020.

We found no significant association between age and the likelihood of recovery from olfactory and gustatory dysfunction over time. In line with this finding, two other studies



Fig. 4. The cumulative hazard for olfactory dysfunction (OD) recovery based on the severity of dysfunction, from February to July 2020.



Fig. 5. The cumulative hazard for gustatory dysfunction (GD) recovery based on age group, from February to July 2020.

methods of assessing olfactory function are subjective. In these methods, the severity of the disorder is scaled based on the patient's self-report. In our study, because of the high number of patients and the inability to conduct in-person assessment during the Covid-19 crisis, we followed up patients'

In the present study, 98 per cent of the patients recovered from Covid-19-related olfactory and gustatory dysfunction symptoms within six months. Although an objectively based

approach to olfactory assessment would be ideal, most

also found no significant association between recovery time

from olfactory or gustatory dysfunction and age.^{20,28}

Table 4. Crude and adjusted hazard ra	atios for recovery fr	rom gustatory dysfunction
---------------------------------------	-----------------------	---------------------------

Variable	Crude HR (95% CI)	<i>p</i> -value	Adjusted HR* (95% CI)	<i>p</i> -value
Sex				
- Female	Reference		Reference	
– Male	1.31 (0.99–1.72)	0.05	1.27 (0.96–1.68)	0.09
Age group				
- ≤40 years	1.01 (0.77–1.32)	0.93	1.07 (0.81–1.42)	0.59
– >40 years	Reference		Reference	
Ethnicity				
- Fars	Reference		Reference	
– Turkmen	1.36 (1.03–1.81)	0.03	1.12 (0.80–1.58)	0.49
– Sistani Persian	1.56 (0.81-3.01)	0.17	1.21 (0.57–2.57)	0.60
Epidemic waves				
– Infected in 1st wave	Reference		Reference	
- Infected in 2nd wave	1.45 (1.10–1.92)	0.009	1.58 (1.11-2.26)	0.01^{\dagger}
Olfactory dysfunction onset				
- Simultaneous with general Covid-19 symptoms	Reference		Reference	
- Before general Covid-19 symptoms	1.00 (0.66–1.52)	0.98	1.00 (0.62–1.60)	0.99
– After general Covid-19 symptoms	1.03 (0.61–1.76)	0.88	1.23 (0.70-2.16)	0.46
Olfactory dysfunction severity				
– Complete dysfunction	Reference		Reference	
- Partial dysfunction	1.23 (0.90–1.68)	0.19	1.00 (0.33–2.97)	0.99
Gastrointestinal dysfunction?				
- No	Reference		Reference	
- Yes	1.15 (0.87–1.51)	0.31	1.02 (0.75–1.38)	0.88
Gustatory dysfunction severity				
- Complete dysfunction	Reference		Reference	

*Adjusted for all covariates. ¹Indicates significant difference for adjusted values. HR = hazard ratio; CI = confidence interval; Covid-19 = coronavirus disease 2019



Fig. 6. The cumulative hazard for gustatory dysfunction (GD) recovery based on the epidemic wave in which patients were infected, from February to July 2020.

condition by telephone. We recommend implementing a more appropriate assessment method for assessing Covid-19.^{33–35} We also suggest evaluating the potential effects of smoking, and co-morbidities or diseases, on olfactory and gustatory dysfunction recovery time.

- Coronavirus disease 2019 (Covid-19) is a public health emergency of international concern
- In addition to general respiratory disease symptoms, Covid-19 patients often have smell, taste and gastrointestinal disorders
- Incidence rates of olfactory and taste disorders vary, and recovery time and related factors are unknown
- Among Covid-19 patients, the incidence of smell and taste disorders is relatively high
- Significant recovery from olfactory and taste dysfunction is achieved in Covid-19 patients within the first 30 days
- Infection by Covid-19 in the second epidemic wave and partial olfactory and taste dysfunction are independently associated with earlier recovery of these dysfunctions

Conclusion

The results indicate a high rate of recovery from Covid-19-related olfactory and gustatory dysfunction within 30 days of symptom onset. The severity of olfactory or gustatory dysfunction, and infection during the second epidemic wave (as opposed to the first), may affect the likelihood of recovery from olfactory or gustatory dysfunction symptoms. We recommend reassuring Covid-19 patients about the good prognosis and likely recovery from olfactory and gustatory dysfunction.

Acknowledgements. We thank the staff of the 5-Azar Hospital of Golestan University of Medical Sciences for facilitating access to the relevant medical records. This study received financial support from the Golestan University of Medical Sciences, Gorgan, Iran.

Data availability statement. The datasets used and/or analysed in the study are available from the corresponding author on reasonable request.

Competing interests. None declared

References

1 Mao L, Jin H, Wang M, Hu Y, Chen S, He Q et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020;77:683–90

- 2 Bartenfeld M, Griese S, Uyeki T, Gerber SI, Peacock G. Middle East respiratory syndrome coronavirus and children: what pediatric health care professionals need to know. *Clin Pediatr (Phila)* 2017;**56**:187–9
- 3 Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. World J Pediatr 2020;16:223–31
- 4 Feng K, Yun Y, Wang X, Yang G, Zheng Y, Lin C *et al.* Analysis of CT features of 15 children with 2019 novel coronavirus infection [in Chinese]. *Zhonghua Er Ke Za Zhi* 2020;**58**:275–8
- 5 Pan X, Chen D, Xia Y, Wu X, Li T, Ou X et al. Asymptomatic cases in a family cluster with SARS-CoV-2 infection. *Lancet Infect Dis* 2020;20:410–11
- 6 Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: common findings in COVID-19 patients. *Laryngoscope* 2020;**130**:1787
- 7 Guo Y-R, Cao Q-D, Hong Z-S, Tan Y-Y, Chen S-D, Jin H-J *et al*. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak–an update on the status. *Mil Med Res* 2020;7:11
- 8 Guan W, Ni Z, Hu Y, Liang W, Ou C, He J *et al.* Clinical characteristics of coronavirus disease 2019 in China. J Emerg Med 2020;58:711-12
- 9 Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506
- 10 Vent J, Wang D-W, Damm M. Effects of traditional Chinese acupuncture in post-viral olfactory dysfunction. *Otolaryngol Head Neck Surg* 2010;142:505–9
- 11 Michael W. Anosmia treated with acupuncture. Acupunct Med 2003;21:153-4
- 12 Balajelini MHT, Vakili MA, Saeidi M, Tabarraei A, Hosseini SM. Using anti-SARS-CoV-2 IgG and IgM antibodies to detect outpatient cases with olfactory and taste disorders suspected as mild form of COVID-19: a retrospective survey. *SN Compr Clin Med* 2020;**2**:2554–60
- 13 Temmel AF, Quint C, Schickinger-Fischer B, Klimek L, Stoller E, Hummel T. Characteristics of olfactory disorders in relation to major causes of olfactory loss. Arch Otolaryngol Head Neck Surg 2002;128:635–41
- 14 Palheta Neto FX, Targino MN, Peixoto VS, Alcântara FB, de Jesus CC, de Araújo DC et al. Sensorial abnormalities: smell and taste. Int Arch Otolaryngol 2011;15:350–8
- 15 Dai Q, Pang Z, Yu H. Recovery of olfactory function in postviral olfactory dysfunction patients after acupuncture treatment. *Evid Based Complement Alternat Med* 2016;2016:4986034
- 16 Gupta V, Banavara Rajanna L, Upadhyay K, Bhatia R, Madhav Reddy N, Malik D et al. Olfactory and gustatory dysfunction in COVID-19 patients from northern India: a cross-sectional observational study. Indian J Otolaryngol Head Neck Surg 2021;73:218–25
- 17 Chary E, Carsuzaa F, Trijolet J-P, Capitaine A-L, Roncato-Saberan M, Fouet K et al. Prevalence and recovery from olfactory and gustatory dysfunctions in Covid-19 infection: a prospective multicenter study. Am J Rhinol Allergy 2020;34:686–93
- 18 Altin F, Cingi C, Uzun T, Bal C. Olfactory and gustatory abnormalities in COVID-19 cases. Eur Arch Otorhinolaryngol 2020;277:2775–81
- 19 Dell'Era V, Farri F, Garzaro G, Gatto M, Aluffi Valletti P, Garzaro M. Smell and taste disorders during COVID-19 outbreak: cross-sectional study on 355 patients. *Head Neck* 2020;42:1591–6
- 20 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;**163**:1144–9
- 21 Reden J, Mueller A, Mueller C, Konstantinidis I, Frasnelli J, Landis BN et al. Recovery of olfactory function following closed head injury or infections of the upper respiratory tract. Arch Otolaryngol Head Neck Surg 2006;132:265–9
- 22 Flint PW, Haughey BH, Robbins KT, Thomas JR, Niparko JK, Lund VJ et al. Cummings Otolaryngology – Head and Neck Surgery E-book: Edition 6. London: Elsevier Health Sciences, 2014
- 23 Romero-Gameros CA, Waizel-Haiat S, Mendoza-Zubieta V, Anaya-Dyck A, López-Moreno MA, Colin-Martinez T *et al.* Evaluation of predictive value of olfactory dysfunction, as a screening tool for COVID-19. *Laryngoscope Investig Otolaryngol* 2020;5:983–91
- 24 Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi 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
- 25 Meini S, Suardi LR, Busoni M, Roberts AT, Fortini A. Olfactory and gustatory dysfunctions in 100 patients hospitalized for COVID-19: sex

differences and recovery time in real-life. Eur Arch Otorhinolaryngol 2020;277:3519-23

- 26 Gorzkowski V, Bevilacqua S, Charmillon A, Jankowski R, Gallet P, Rumeau C *et al.* Evolution of olfactory disorders in COVID-19 patients. *Laryngoscope* 2020;**130**:2667–73
- 27 Amer MA, Elsherif HS, Abdel-Hamid AS, Elzayat S. Early recovery patterns of olfactory disorders in COVID-19 patients; a clinical cohort study. Am J Otolaryngol 2020;41:102725
- 28 Lv H, Zhang W, Zhu Z, Xiong Q, Xiang R, Wang Y et al. Prevalence and recovery time of olfactory and gustatory dysfunction in hospitalized patients with COVID-19 in Wuhan, China. Int J Infect Dis 2020;100:507–12
- 29 Ramasamy K, Saniasiaya J, Abdul Gani N. Olfactory and gustatory dysfunctions as a clinical manifestation of coronavirus disease 2019 in a Malaysian tertiary center. Ann Otol Rhinol Laryngol 2020;130:513–19
- 30 Hopkins C, Surda P, Whitehead E, Kumar BN. Early recovery following new onset anosmia during the COVID-19 pandemic–an observational cohort study. J Otolaryngol Head Neck Surg 2020;49:1–26

- 31 Vaira LA, Hopkins C, Petrocelli M, Lechien J, Chiesa-Estomba C, Salzano G et al. Smell and taste recovery in coronavirus disease 2019 patients: a 60-day objective and prospective study. J Laryngol Otol 2020;134:703-9
- 32 Cho RH, To ZW, Yeung ZW, Tso EY, Fung KS, Chau SK *et al.* COVID-19 viral load in the severity of and recovery from olfactory and gustatory dys-function. *Laryngoscope* 2020;**130**:2680–5
- 33 Hannum ME, Ramirez VA, Lipson SJ, Herriman RD, Toskala AK, Lin C et al. Objective sensory testing methods reveal a higher prevalence of olfactory loss in COVID-19-positive patients compared to subjective methods: a systematic review and meta-analysis. Chem Senses 2020;45:865–74
- 34 Gerkin RC, Ohla K, Veldhuizen MG, Joseph PV, Kelly CE, Bakke AJ et al. Recent smell loss is the best predictor of COVID-19 among individuals with recent respiratory symptoms. *Chem Senses* 2021;**46**:bjaa081
- 35 Yan CH, Faraji F, Prajapati DP, Ostrander BT, DeConde AS. Self-reported olfactory loss associates with outpatient clinical course in COVID-19. *Int Forum Allergy Rhinol* 2020;**10**:821–31