Received: 26 July 2021 | Revised: 19 October 2021 | Accepted: 23 October 2021

DOI: 10.1002/lio2.690

ORIGINAL RESEARCH

Laryngoscope Investigative Otolaryngology

Factors associated with anosmia recovery rate in COVID-19 patients

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Abstract

Objectives: The present study aimed to assess the 4- and 8-week recovery rate of anosmia and determine the factors associated with recovery in COVID-19 patients.

Method: This retrospective study was conducted from December 2020 to March 2021. RT-PCR-proven COVID-19 adult patients (over 18 years of age) with a positive history of anosmia were included in this study. Anosmia was assessed based on the COVID-19 Anosmia Reporting Tool. The recovery rate of anosmia after 4 and 8 weeks were evaluated, and the relationship between the patients' recovery and their clinical and demographic data was assessed.

Results: A total of 235 patients were included. Their mean age (±SD) was 43.95 ± 15.27 years. Anosmia recovery was reported in 207(88.51%) and 219 (93.19%) participants till 4 and 8 weeks. The mean recovery time was 19.42 ± 8.81 days. The result of logistic regression showed that smoking ($P = .031$; OR = 10.813), ageusia ($P = .002$; OR = 5.340), headache ($P = .006$; OR = 0.243), and nasal discharge ($P < .001$; OR = 0.080) were significantly associated with 4 weeks anosmia recovery. The only risk factor which was associated with a lower rate of 8 weeks anosmia recovery was presence of nasal discharge (OR = 0.106, $P = .002$).

Conclusion: The only risk factor which was associated with a lower rate of 8 weeks anosmia recovery was presence of nasal discharge. Our result demonstrated that although smoking was associated with higher recovery rate till 4 weeks, it could not be considered as a protective factor after 8 weeks. More studies are recommended to investigate the relationship between anosmia and the associated factors by consideration of both short- and long-term recovery rates and assess the possible mechanisms that could justify this association.

Levels of Evidence: 3b

KEYWORDS
ageusia, anosmia, COVID-19, olfaction disorders, smoking

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The common symptoms of COVID-19 include dry cough, fever, dyspnea, fatigue, anorexia, diarrhea, chest pain, headache, and muscle ache.[1,2]

Anosmia and dysgeusia are two complaints that were reported among individuals with positive PCR tests of SARS-CoV-2 infection.[3] This has led to an increased diagnosis of olfactory and gustatory dysfunction, which has overlapped with the COVID-19 pandemic. The Center for Disease Control (CDC) accepted anosmia and dysgeusia as major signs of COVID-19 infection.[4]

A recent meta-analysis including 32 142 COVID-19 patients from 107 studies reported anosmia in 12 038 patients with a prevalence of 38.2% (95% CI: 36.5%, 47.2%).[5] Other studies have reported that anosmia is resolved in most patients within 2 to 3 weeks.[6,7] Currently, there is no definite treatment for post-COVID anosmia.

Olfaction is an important sense in human life, and for responses to the environment, determining the recovery time of olfactory damage and its related factors is important in patients with anosmia. Lucidi et al investigated olfactory recovery after COVID-19 infection using the patient-reported "American Academy of otolaryngology-head and neck surgery COVID-19 anosmia reporting tool for clinicians" to evaluate the status of anosmia. They reported that the only factor that was adversely related to anosmia recovery was cigarette smoking.[8]

In the present study, 4 and 8 weeks periods were considered to determine the factors associated with recovery from anosmia among COVID-19 patients.

2 | MATERIALS AND METHODS

This retrospective study was conducted from December 2020 to March 2021 in inpatient wards of teaching hospitals affiliated with Shiraz University of Medical Science, Iran. RT-PCR-proven COVID-19 adult patients (over 18 years of age) with a positive history of anosmia who were admitted to the hospital were included in this study. Patients with a previous history of gustatory or olfactory dysfunctions, anosmia, sinusitis, Sjogren syndrome, autoimmune disease, traumatic and traumatic brain injuries, recurrent upper respiratory tract infections, or nasal polyposis were excluded from the study. Patients who were intubated during the course of their hospitalization were also excluded.

No patient received intranasal steroid or olfactory training for resolving anosmia.

The current study was approved by the Ethics Committee of Shiraz University of Medical Science (ethic code: IR.SUMS.MED.REC.1399.135), and informed consent was obtained from each participant.

The data collected comprised patient age, gender, anosmia onset and recovery time, systolic and diastolic blood pressure, height, body weight, BMI, the presence of headache, ageusia, fever, comorbidities, nasal symptoms, previous history of alcohol usage, smoking status, and ICU admission.

Positive history of cigarette smoking was defined as "at least one cigarette per day" and positive alcohol use was defined as "at least one drink per week."

Positive history of allergy was obtained by asking patients about symptoms of allergic rhinitis (seasonal, occupational, etc.).

All data were gathered through interviews. Anosmia was assessed based on the COVID-19 Anosmia Reporting Tool, developed by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS).[9]

The demographic and clinical data of the two groups were compared. The recovery rate of anosmia after 4 and 8 weeks (30 and 60 days) was evaluated as the main outcome, and the relationship between the patients' recovery and their clinical and demographic data was assessed. Moreover, the status of anosmia was compared between these two periods.

Categorical variables were reported as frequency and percentage, and quantitative variables were expressed as mean (±SD). Chi-square or Fisher's exact tests were used to evaluate possible associations among the categorical variables, if appropriate. Parametric and non-parametric continuous variables were analyzed using paired sample *t*-test, independent t-test, Mann-Whitney *U* tests, and Wilcoxon, where applicable. Then, all associations with a $P < .2$ were included in the logistic regression. A $P < .05$ was considered statistically significant. Analyses were conducted using SPSS 25 software (SPSS Inc., Chicago, Illinois).

3 | RESULTS

In total, 235 patients with a mean age (±SD) of 43.95 ± 15.27 years were included in this study. Complete self-reported anosmia recovery was stated in 207 participants (88.51%) at 4 weeks. After 8 weeks, recovery was reported in 12 patients (5.10%) with a mean of 40.50 days and the overall recovery rate was 93.19% (219 patients) after 8 weeks. The mean recovery time was 19.42 ± 8.81 days. Quantitative demographic and clinical data of the patients are presented in Table 1.

In 23 patients (9.8%), anosmia was the first symptom of COVID-19 infection. Univariate analysis showed smoking, ageusia, headache, and nasal discharge were significantly correlated with recovery after 4 weeks ($P = .008$, $P = .006$, $P = .013$, and $P < .001$, respectively) (Figure 1). Detailed qualitative demographic and clinical data of the patients after 4 weeks are reported in Table 2.

Univariate analysis showed smoking, allergy, headache, and nasal discharge were significantly correlated with recovery after 8 weeks ($P = .026$, $P = .006$, $P = .020$, and $P = .001$, respectively) (Figure 2).

TABLE 1 The patients' quantitative demographic and clinical data

	Total		Anosmia recovery				
			Yes		No		
Variable	Mean	SD	Mean	SD	Mean	SD	*P*-value
Recovery till 4 weeks							
Age (year)	43.95	15.27	44.23	15.16	41.81	16.31	.448[a]
Anosmia recovery (day)	19.42	8.81	18.31	7.31	40.50	8.73	<.001[b]
Anosmia onset (day)	3.88	3.29	3.83	3.13	4.27	4.38	.551[a]
Diastolic blood pressure (mmHg)	79.80	10.75	80.41	11.14	75.63	6.29	.120[b]
Systolic blood pressure (mmHg)	118.64	12.69	119.36	12.68	113.75	12.04	.146[b]
Weight (kg)	75.49	16.76	76.14	16.66	70.58	17.00	.112[a]
Height (cm)	167.20	8.45	167.26	8.15	166.72	10.72	.764[a]
BMI (m^2/kg)	26.81	4.72	27.03	4.71	25.11	4.53	.055[a]
Recovery till 8 weeks							
Age (year)	43.95	15.27	44.36	15.19	38.13	15.83	.127[a]
Anosmia recovery (day)	19.42	8.81	19.42	8.81	NR	NR	ND
Anosmia onset (day)	3.88	3.29	3.83	3.14	4.44	4.79	.475[a]
Diastolic blood pressure (mmHg)	79.80	10.75	80.22	10.98	75.45	6.88	.208[b]
Systolic blood pressure (mmHg)	118.64	12.69	119.12	12.48	113.64	14.33	.394[b]
Weight (kg)	75.49	16.76	75.87	16.41	70.27	20.98	.212[a]
Height (cm)	167.20	8.45	167.32	8.15	165.60	12.15	.449[a]
BMI (m^2/kg)	26.81	4.72	26.92	4.68	25.25	5.24	.186[a]

Abbreviations: ND, nondeterminable; NR, no recovery.
[a]Independent sample.
[b]Mann-Whitney *U* test.

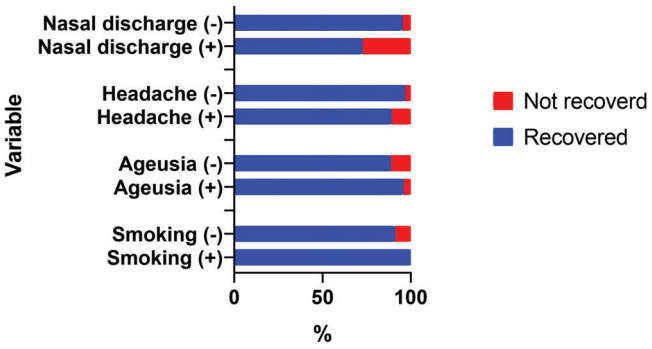

FIGURE 1 Four weeks recovery rate in patients with (+) and without (−) nasal discharge, headache, ageusia, and smoking

Detailed qualitative demographic and clinical data of the patients after 8 weeks are reported in Table 3.

The result of logistic regression showed that smoking, ageusia, headache, and nasal discharge were significantly associated with anosmia recovery ($P = .031$, $P = .002$, $P = .006$, and $P < .001$, respectively) after 4 weeks. Smoking and ageusia were associated with a higher rate of recovery (OR = 10.813 and OR = 5.340, respectively). The presence of headache and nasal discharge was associated with a lower rate of recovery (OR = 0.243 and OR = 0.080, respectively).

The result of logistic regression showed that nasal discharge was significantly associated with a lower rate of recovery (OR = 0.106, $P = .002$) after 8 weeks. Table 4 shows the results of the logistic regression test.

Based on the rate of cigarette smoking after 4 weeks and considering $\alpha = 0.05$ and $\beta = 0.2$, the study power was calculated at 91.2%.

4 | DISCUSSION

This study assessed the association between anosmia and the demographic and clinical characteristics of patients with COVID-19. The results showed that a history of smoking and the presence of ageusia in patients were associated with a higher rate and the presence of headache and nasal discharge was associated with a lower rate of 4-week recovery. The only risk factor which was associated with a lower rate of 8 weeks anosmia recovery was presence of nasal discharge.

Altered smell and taste sensations are important complaints during the pandemic of COVID-19. Anosmia can occur with or without ageusia, and it is a prevalent symptom among patients with COVID-19 with a range of 19.4% to 88%.[10,11] This wide

TABLE 2 The patients' qualitative demographic and clinical data and anosmia recovery till 4 weeks

				Anosmia recovery till 4 weeks				
		Total		Yes		No		
Variable		Count	%	Count	%	Count	%	*P*-value[a]
Anosmia as the first symptom of COVID-19	No	212	90.2	187	89.9	25	92.6	1.000
	Yes	23	9.8	21	10.1	2	7.4	
Gender	Male	131	56.0	120	58.0	11	40.7	.102
	Female	103	44.0	87	42.0	16	59.3	
Smoking	No	181	77.0	155	74.5	26	96.3	.008
	Yes	54	23.0	53	25.5	1	3.7	
Ageusia	No	89	37.9	72	34.6	17	63.0	.006
	Yes	146	62.1	136	65.4	10	37.0	
Alcohol usage	No	222	94.5	195	93.8	27	100.0	.372
	Yes	13	5.5	13	6.3	0	0.0	
Allergy	No	215	91.5	193	92.8	22	81.5	.062
	Yes	20	8.5	15	7.2	5	18.5	
Cough	No	57	24.3	48	23.1	9	33.3	.241
	Yes	178	75.7	160	76.9	18	66.7	
Dyspnea	No	88	37.4	76	36.5	12	44.4	.527
	Yes	147	62.6	132	63.5	15	55.6	
Ear pain	No	206	87.7	182	87.5	24	88.9	1.000
	Yes	29	12.3	26	12.5	3	11.1	
Facial pain	No	185	78.7	165	79.3	20	74.1	.617
	Yes	50	21.3	43	20.7	7	25.9	
Fatigue	No	46	19.6	40	19.2	6	22.2	.796
	Yes	189	80.4	168	80.8	21	77.8	
Fever	No	40	17.0	34	16.3	6	22.2	.422
	Yes	195	83.0	174	83.7	21	77.8	
Headache	No	126	53.6	118	56.7	8	29.6	.013
	Yes	109	46.4	90	43.3	19	70.4	
Hypertension	No	212	90.2	188	90.4	24	88.9	.735
	Yes	23	9.8	20	9.6	3	11.1	
ICU admission	No	181	77.0	157	75.5	24	88.9	.148
	Yes	54	23.0	51	24.5	3	11.1	
Nasal discharge	No	213	90.6	195	93.8	18	66.7	<.001
	Yes	22	9.4	13	6.3	9	33.3	
Nasal obstruction	No	194	82.6	173	83.2	21	77.8	.589
	Yes	41	17.4	35	16.8	6	22.2	

Abbreviation: ICU, intensive care units.
[a]Fisher's exact test.

range could be due to the variation in the race, sample size, patient age, hospitalization, presence of other symptoms and comorbidities, and disease severity.[12]

In the current study, the rate of recovery by 4 and 8 weeks was 88.51% and 93.19%, respectively, which was in line with previous studies. In previous studies, recovery rates varied based on the follow-up period. Printza et al reported 2- and 4-week recovery rates of 58% and 77%, respectively.[13] Karthikeyan et al reported 88% recovery in a 5-week follow-up period.[12] In another study, the 2-week recovery rate of anosmia was 63.69%.[11]

In the current study, 9.8% of patients experienced anosmia as the first symptom of COVID-19 infection. Several previous studies have reported this finding.[14,15] In a study by Spinato et al, olfactory and

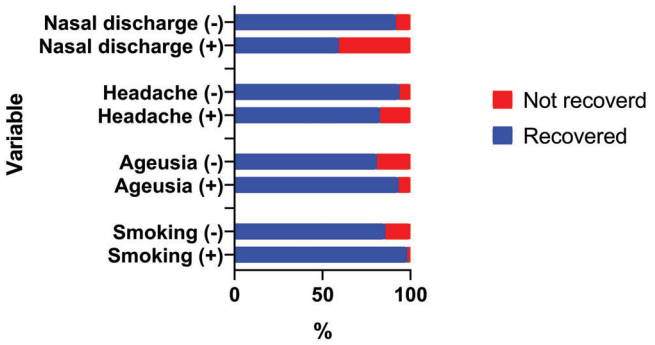

FIGURE 2 Eight weeks recovery rate in patients with (+) and without (−) nasal discharge, headache, ageusia, and smoking

gustatory dysfunction was the initial symptom in 14.9% of patients.[16] Another study reported anosmia as the first symptom in 24% of patients.[11]

In the present study, the mean age of participants was near 44 years. The mean age was lower in the group without recovery than in the groups with anosmia recovery, but the difference was not statistically significant. One research concluded that the risk of olfactory dysfunction was higher in younger patients than older ones.[17] Such a result was reported by Giacomelli et al, who stated that anosmia was more common in younger patients (median age, 56 vs 66 years).[18] The reason may be more comorbidities in older patients, and olfactory dysfunction may not be recognized; consequently, this issue has not been commonly described.[17] Numerous studies have shown that the median age for anosmia is about 50 years.[11,17]

Most of the patients in the current study were male, in line with some other studies. However, the majority of studies have reported that females are more susceptible to COVID-19-related anosmia.[19-21]

Interestingly, the current study revealed that cigarette smoking was associated with an increased rate of anosmia recovery rate by 4 weeks but not after 8 weeks. Several previous studies have mentioned that anosmia is more prevalent among smokers, and the recovery rate of anosmia is reduced in smoker patients.[4,17,22,23] An experimental study by Vent et al on rats concluded that the rate of anosmia was higher in smokers than nonsmokers because of increased death in olfactory sensory neurons by cigarette smoking.[24] On the other hand, other studies have shown that cigarette smoking was not linked with a higher rate of anosmia. In a study by Tarifi et al, the recovery rate of anosmia was higher in smoker patients (6/7; 85.71%) than nonsmokers (9/14; 64.28%) after 6 weeks. However, they stated that this could be due to the small sample size.[25] A study investigated the recovery rate of parosmia on 268 patients. Although the results showed higher recovery among smokers (4/46; 8.7%) than non-smokers (14/222; 6.3%) after 1 month, the difference was not statistically significant.[26] In a recent study by Lucidi et al, multivariate analysis showed that smoking was significantly associated with a higher rate of recovery of anosmia after 6 months ($P = .044$; odds ratio: 25.96).[8] Our result demonstrated that although smoking was associated with higher recovery rate till 4 weeks, but it could not be considered as a protective factor after 8 weeks.

Some researchers have mentioned a lower rate of COVID-19 infection among smoker individuals. They justify this observation with two hypotheses. The first hypothesis considers a global effect on the renin-angiotensin system, of which ACE2 is only a part, by up-regulating the ACE1 receptor and down-regulating the ACE2 receptor. The second theory emphasizes the interaction between ACE2 and the nicotinic receptors (especially α7 nicotine receptors). This receptor is near the ACE2 receptors on the cell membrane. The dysregulation of these receptors might trigger a Th1 immune response. Nicotine and SARS-Cov2 might as well compete for binding to nicotinic acetylcholine receptors (nAchRs).[27] These mechanisms could be considered to justify the higher 4 weeks recovery rate of olfactory dysfunction in the current study and other recent studies.

Smell and taste sensations are closely related to each other. Anosmia may cause dysgeusia or ageusia.[28] The recommended pathophysiology for dysgeusia in COVID-19 is cranial nerve dysfunction (particularly the seventh cranial nerve), zinc deficiency, interaction with sialic acid receptors, direct virus attack to the buccal and gingival tissues, taste buds in the tongue, and salivary glands.[5] In the current study, 62.1% of the patients reported ageusia. Similarly, in a study by Thakur et al, 77.7% of anosmic patients complained of gustatory dysfunction.[11] The current results showed that the presence of ageusia was associated with a higher rate of 4 weeks anosmia recovery but not 8 weeks anosmia recovery. This was in line with the results of Rashid, who reported that the co-presentation of anosmia and ageusia had a positive significant effect on the recovery time of anosmia in patients using nasal betamethasone drops.[23]

In the current study, the presence of headache was linked with a lower 4 weeks recovery rate. The association between headache and anosmia has been reported in previous investigations as well.[29] Headache is generally diffuse, very severe, and with a migraine phenotype.[30]

In the present study, nasal discharge was associated with a lower rate of anosmia recovery both till 4- and 8-week periods. Although it could be justified with conductive anosmia, some studies have mentioned that it was not correlated with olfactory dysfunction.[15,31]

One of the strengths of the present study was its use of a uniform and available anosmia reporting tool which permits comparison with the current and forthcoming investigations. Another strength of the study was the relatively long length of the follow-up period. Another strength was the comparison of 4- and 8-week recovery rates and their associated factors.

Although this study included a large sample size in comparison with other similar studies, which is an important strength, the association between smoking and the higher rate of anosmia recovery till 4 weeks is related to the small number of patients in the no-recovery

TABLE 3 The patients' qualitative demographic and clinical data and anosmia recovery till 8 weeks

				Recovery till 8 weeks				
		Total		Yes		No		
Variable		Count	%	Count	%	Count	%	*P* value[a]
Anosmia as the first symptom of COVID-19	No	212	90.2	196	89.5	16	100.0	.378
	Yes	23	9.8	23	10.5	0	0.0	
Gender	Male	131	56.0	126	57.8	5	31.3	.065
	Female	103	44.0	92	42.2	11	68.8	
Smoking	No	181	77.0	165	75.3	16	100.0	.026
	Yes	54	23.0	54	24.7	0	0.0	
Ageusia	No	89	37.9	79	36.1	10	62.5	.058
	Yes	146	62.1	140	63.9	6	37.5	
Alcohol usage	No	222	94.5	206	94.1	16	100.0	.608
	Yes	13	5.5	13	5.9	0	0.0	
Allergy	No	215	91.5	204	93.2	11	68.8	.006
	Yes	20	8.5	15	6.8	5	31.3	
Cough	No	57	24.3	52	23.7	5	31.3	.547
	Yes	178	75.7	167	76.3	11	68.8	
Dyspnea	No	88	37.4	80	36.5	8	50.0	.296
	Yes	147	62.6	139	63.5	8	50.0	
Ear pain	No	206	87.7	192	87.7	14	87.5	1.000
	Yes	29	12.3	27	12.3	2	12.5	
Facial pain	No	185	78.7	172	78.5	13	81.3	1.000
	Yes	50	21.3	47	21.5	3	18.8	
Fatigue	No	46	19.6	43	19.6	3	18.8	1.000
	Yes	189	80.4	176	80.4	13	81.3	
Fever	No	40	17.0	35	16.0	5	31.3	.159
	Yes	195	83.0	184	84.0	11	68.8	
Headache	No	126	53.6	122	55.7	4	25.0	.020
	Yes	109	46.4	97	44.3	12	75.0	
Hypertension	No	212	90.2	198	90.4	14	87.5	.661
	Yes	23	9.8	21	9.6	2	12.5	
ICU admission	No	181	77.0	166	75.8	15	93.8	.128
	Yes	54	23.0	53	24.2	1	6.3	
Nasal discharge	No	213	90.6	203	92.7	10	62.5	.001
	Yes	22	9.4	16	7.3	6	37.5	
Nasal obstruction	No	194	82.6	182	83.1	12	75.0	.491
	Yes	41	17.4	37	16.9	4	25.0	

Abbreviation: ICU, intensive care units.
[a]Fisher's exact test.

group and, by chance, the small number of smokers ($N = 1$) in that group. Therefore, it may be susceptible to spectrum bias related to the patient population and, hence, possibly not a real association. As mentioned above, our result demonstrated that although smoking was associated with higher recovery rate till 4 weeks, but it could not be considered as a protective factor after 8 weeks.

The current study has some limitations. The first one was the retrospective nature of the study. The second limitation was that pack-years of smoking and its relation to the recovery rate of anosmia were not evaluated. Due to the substantial risk of contamination in the acute phase of infection and initial stage of anosmia, no objective olfactory tests were conducted, and data were gathered using the

TABLE 4 Logistic regression test for factors associated with anosmia recovery

	Variables	Beta coefficient	SE	Wald test	Degree of freedom	*P*-value	Odds ratio	95% confidence interval for odds ratio	
								Lower	Upper
Recovery till 4 weeks	Gender	0.310	0.500	0.384	1	.536	1.363	0.511	3.634
	Smoking	2.381	1.106	4.638	1	.031	10.813	1.239	94.396
	Ageusia	1.675	0.550	9.276	1	.002	5.340	1.817	15.694
	Allergy	0.194	0.719	0.073	1	.788	1.214	0.296	4.973
	Headache	−1.416	0.514	7.591	1	.006	0.243	0.089	0.665
	ICU Admission	0.524	0.709	0.546	1	.460	1.689	0.420	6.786
	Nasal discharge	−2.526	0.627	16.232	1	<.001	0.080	0.023	0.273
Recovery till 8 weeks	Gender	−0.061	0.647	0.009	1	.925	0.941	0.265	3.346
	Smoking	18.563	5082.461	0.000	1	.997	115 332 285.205	0.000	
	Ageusia	1.149	0.703	2.669	1	.102	3.154	0.795	12.514
	Allergy	−0.627	0.730	0.737	1	.391	0.534	0.128	2.234
	Fever	0.596	0.692	0.741	1	.389	1.815	0.467	7.050
	Headache	−1.258	0.676	3.468	1	.063	0.284	0.076	1.068
	ICU Admission	1.018	1.112	0.839	1	.360	2.769	0.313	24.475
	Nasal discharge	−2.242	0.740	9.167	1	.002	0.106	0.025	0.454

COVID-19 Anosmia Reporting Tool. This limitation is common in most investigations on anosmia in COVID-19 patients.

5 | CONCLUSION

The only risk factor which was associated with a lower rate of 8 weeks anosmia recovery was presence of nasal discharge. Our result demonstrated that although smoking was associated with higher recovery rate till 4 weeks, but it could not be considered as a protective factor after 8 weeks. More studies are recommended to investigate the relationship between anosmia and the associated factors by consideration of both short- and long-term recovery rates and assess the possible mechanisms that could justify this association. Surely, smoking should not be suggested in patients with post-COVID anosmia.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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REFERENCES

1. Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. *J Med Virol*. 2020;92(6):568-576. doi:10.1002/jmv.25748
2. Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis*. 2020;34:101623. doi:10.1016/j.tmaid.2020.101623
3. Marinosci A, Landis BN, Calmy A. Possible link between anosmia and COVID-19: sniffing out the truth. *Eur Arch Otorhinolaryngol*. 2020;277(7):2149-2150. doi:10.1007/s00405-020-05966-0
4. Al-Ani RM, Acharya D. Prevalence of anosmia and ageusia in patients with COVID-19 at a primary health center, Doha, Qatar. *Indian J Otolaryngol Head Neck Surg*. 2020;19:1-7. doi:10.1007/s12070-020-02064-9
5. Mutiawati E, Fahriani M, Mamada SS, et al. Anosmia and dysgeusia in SARS-CoV-2 infection: incidence and effects on COVID-19 severity and mortality, and the possible pathobiology mechanisms—a systematic review and meta-analysis. *F1000Res*. 2021;10:40. doi:10.12688/f1000research.28393.1
6. 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. doi:10.1186/s40463-020-00423-8
7. Al-Zaidi HMH, Badr HM. Incidence and recovery of smell and taste dysfunction in COVID-19 positive patients. *Egypt J Otolaryngol*. 2020;36(1):47. doi:10.1186/s43163-020-00050-0
8. Lucidi D, Molinari G, Silvestri M, et al. Patient-reported olfactory recovery after SARS-CoV-2 infection: a 6-month follow-up study. *Int Forum Allergy Rhinol*. 2021;11:1249-1252. doi:10.1002/alr.22775
9. American Academy of Otolaryngology–Head and Neck Surgery. COVID-19 Anosmia Reporting Tool for Clinicians. Accessed April 6, 2020. https://www.entnet.org/content/reporting-tool-patients-anosmia-related-covid-19
10. Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and COVID-19 in patients presenting with influenza-like symptoms. *Int Forum Allergy Rhinol*. 2020;10(7):806-813. doi:10.1002/alr.22579
11. Thakur K, Sagayaraj A, Prasad KC, Gupta A. Olfactory dysfunction in COVID-19 patients: findings from a tertiary rural centre. *Indian J Otolaryngol Head Neck Surg*. 2021;18:1-7. doi:10.1007/s12070-021-02364-8

12. Karthikeyan P, Sivanand N, Vijayan N, Latheef MN. A clinical study of smell disorders in COVID-19 patients in a tertiary care hospital in Pondicherry: a cross sectional study. *Indian J Otolaryngol Head Neck Surg*. 2021;13:1-6. doi:10.1007/s12070-021-02499-8
13. Printza A, Katotomichelakis M, Valsamidis K, et al. Smell and taste loss recovery time in COVID-19 patients and disease severity. *J Clin Med*. 2021;10(5):966. doi:10.3390/jcm10050966
14. Lechien JR, Chiesa-Estomba CM, De Siati DR, 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(8):2251-2261. doi:10.1007/s00405-020-05965-1
15. Speth MM, Singer-Cornelius T, Oberle M, Gengler I, Brockmeier SJ, Sedaghat AR. Olfactory dysfunction and sinonasal symptomatology in COVID-19: prevalence, severity, timing, and associated characteristics. *Otolaryngol Head Neck Surg*. 2020;163(1):114-120. doi:10.1177/0194599820929185
16. Spinato G, Fabbris C, Polesel J, et al. Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. *JAMA*. 2020;323(20):2089-2090. doi:10.1001/jama.2020.6771
17. Hasan MM, Tamanna NA, Jamal MN, Uddin MJ. The prevalence of olfactory dysfunction and its associated factors in patients with COVID-19 infection. *medRxiv*. 2021.
18. Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. *Clin Infect Dis*. 2020;71(15):889-890. doi:10.1093/cid/ciaa330
19. Paniz-Mondolfi A, Bryce C, Grimes Z, et al. Central nervous system involvement by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). *J Med Virol*. 2020;92(7):699-702. doi:10.1002/jmv.25915
20. Parente-Arias P, Barreira-Fernandez P, Quintana-Sanjuas A, Patiño-Castiñeira B. Recovery rate and factors associated with smell and taste disruption in patients with coronavirus disease 2019. *Am J Otolaryngol*. 2020;42(5):102648-102648. doi:10.1016/j.amjoto.2020.102648
21. Gómez-Iglesias P, Porta-Etessam J, Montalvo T, et al. An online observational study of patients with olfactory and Gustory alterations secondary to SARS-CoV-2 infection. *Front Public Health*. 2020;8:243-243. doi:10.3389/fpubh.2020.00243
22. Glennon SG, Huedo-Medina T, Rawal S, Hoffman HJ, Litt MD, Duffy VB. Chronic cigarette smoking associates directly and indirectly with self-reported olfactory alterations: analysis of the 2011–2014 National Health and Nutrition Examination Survey. *Nicotine Tob Res*. 2019;21(6):818-827. doi:10.1093/ntr/ntx242
23. Rashid RA, Zgair A, Al-Ani RM. Effect of nasal corticosteroid in the treatment of anosmia due to COVID-19: a randomised double-blind placebo-controlled study. *Am J Otolaryngol*. 2021;42(5):103033. doi:10.1016/j.amjoto.2021.103033
24. Vent J, Robinson AM, Gentry-Nielsen MJ, et al. Pathology of the olfactory epithelium: smoking and ethanol exposure. *Laryngoscope*. 2004;114(8):1383-1388. doi:10.1097/00005537-200408000-00012
25. Tarifi A, Al Shdaifat AA, Al-Shudifat AM, et al. Clinical, sinonasal, and long-term smell and taste outcomes in mildly symptomatic COVID-19 patients. *Int J Clin Pract*. 2021;75(7):e14260. doi:10.1111/ijcp.14260
26. Rashid RA, Alaqeedy AA, Al-Ani RM. Parosmia due to COVID-19 disease: a 268 case series. *Ind J Otolaryngol Head Neck Surg*. 2021;1-8. doi:10.1007/s12070-021-02630-9
27. Paleiron N, Mayet A, Marbac V, et al. Impact of tobacco smoking on the risk of COVID-19. A large scale retrospective cohort study. *Nicotine Tobac Res*. 2021;23:1398-1404. doi:10.1093/ntr/ntab004
28. Gane SB, Kelly C, Hopkins C. Isolated sudden onset anosmia in COVID-19 infection. A novel syndrome? *Rhinology*. 2020;58(3):299-301. doi:10.4193/Rhin20.114
29. Sampaio Rocha-Filho PA, Voss L. Persistent headache and persistent anosmia associated with COVID-19. *Headache*. 2020;60(8):1797-1799. doi:10.1111/head.13941
30. Rocha-Filho PAS, Magalhães JE. Headache associated with COVID-19: frequency, characteristics and association with anosmia and ageusia. *Cephalalgia*. 2020;40(13):1443-1451. doi:10.1177/0333102420966770
31. Klopfenstein T, Zahra H, Kadiane-Oussou NDJ, et al. New loss of smell and taste: uncommon symptoms in COVID-19 patients on Nord Franche-Comte cluster, France. *Int J Infect Dis*. 2020;100:117-122. doi:10.1016/j.ijid.2020.08.012

How to cite this article: Babaei A, Iravani K, Malekpour B, Golkhar B, Soltaniesmaeili A, Hosseinialhashemi M. Factors associated with anosmia recovery rate in COVID-19 patients. *Laryngoscope Investigative Otolaryngology*. 2021;6(6):1248-1255. doi:10.1002/lio2.690