Anosmia in COVID-19 Patients: Can We Predict the Severity of Chest Manifestations?

Ehsan Hendawy[1] Mohammad Waheed El-Anwar[1] Reda M. Elghamry[2] Amany M. Abdallah[3] Amin M. Ibrahim[4]

[1] Department of Otorhinolaryngology, Head and Neck Surgery, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[2] Department of Chest Disease, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[3] Department of Family Medicine, Faculty of Medicine, Zagazig University, Zagazig, Egypt
[4] Department of Diagnostic Radiology, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Address for correspondence Ehsan Hendawy, MD, Department of Otorhinolaryngology, Head-Neck Surgery, University of Zagazig, Zagazig, Egypt, Postal Code: 44511 (e-mail: ehsanhendawy@gmail.com).

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Abstract

Introduction Anosmia is one of the common symptoms of COVID-19, the link between severity of chest infection and anosmia was investigated by few studies.

Objectives To find an association between anosmia and severity of chest infection.

Methods An analysis of patients admitted to isolation hospital of our university with confirmed polymerase chain reaction positive testing for COVID-19, between March 2021 until September 2021. We called all patients who reported anosmia during their time of illness and asked them about anosmia. We examined their chest CT. A statistical analysis was done.

Results A total of 140 patients completed the study; 65% were female and 56.4% had complete anosmia. Anosmia was significantly associated with loss of taste. Smell returned in 92.5% of anosmic patients. Duration of smell loss was ~ 2 weeks in 40.5%. The most common symptoms associated with anosmia were running nose, sore throat, fever, and cough. Loss of smell was significantly associated with mild chest disease. 73.4% of anosmic patients had mild chest infection, 21.5% of them had moderate infection, and 5.1% had severe chest infection.

Conclusion The pattern of anosmia in COVID-19 patients has some common similarities in general; the way it starts, the associated symptoms, the time until smell returns and, the most important, the severity of chest infection. As anosmia is significantly associated with mild chest infection. the presence of anosmia could be an independent predictor of good COVID-19 outcome as reflected by a lower disease severity and less frequent ICU admissions.

Keywords
- anosmia
- COVID-19
- chest disease

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Introduction

Literature on ear, nose, and throat (ENT) manifestations for COVID-19 patients keeps growing. Thus, it is worth studying the smell dysfunctions and different ENT manifestations of such a novel virus and there is a demand to know and define, with more precision, the smell dysfunction epidemiology and characteristics in COVID-19.[1]

Many studies[2–6] appeared in the last year, in a trial to discover and define the solid criteria for COVID-19 related anosmia. However, behavior among anosmic patients showed a large diversity.[4,5]

It is clear now that olfactory dysfunction linked to COVID-19 infection has particular characters, it occurs mostly without nasal obstruction.[7] We noticed in our clinical practice, as other ENT doctors, the form of COVID-19 patients who came with minimal general manifestations but had anosmia. Another type of COVID-19 patients complained of symptoms like common cold for few days then they suddenly felt anosmia and agusia. At that time, they suspected COVID-19 infection and asked for medical advice.

From our practice, the course of the disease in some COVID-19 patients who had anosmia remains the same, while in other anosmic patients the course may progress, and some lower respiratory manifestations start to appear. Some patients progress to more severe forms of the disease. Still, there is no clear data about this.

The aim of the present study was to find the criteria of anosmia in a group of patients who were admitted to our university isolation hospital, and to examine their chest CT and investigate retrospectively the course of their disease to find if there is any correlation between anosmia and severity of chest infection. Can anosmia be an assuring symptom?

Patients and Methods

An analysis of patients who were admitted to our isolation hospital with confirmed polymerase chain reaction (PCR) positive testing for COVID-19 was performed between March 2021 and September 2021. Personal and clinical data (medical history, signs and symptoms, treatments, ICU admission, discharge, death, clinical course of the disease) were obtained from review of electronic medical records. We excluded patients < 18 years old, patients with a history of nasal polyps or allergic rhinitis, and patients who received head and neck radiotherapy. We aimed to assess the symptom of anosmia if reported with or without loss of taste during the time of illness, and the findings in the patient chest CT when available.

The present study was conducted according to the declaration of Helsinki on Biomedical Research Involving Human Subjects. The institutional review board (IRB) approved the research methodology, IRB number/6338. A prior informed consent was obtained from all included patients. Included subjects were not exposed to any harm.

We contacted all patients who reported anosmia during their hospitalization, either by phone or email. Patients were asked about the details of anosmia and taste loss; we guided them by another questionnaire used in a previous study.[8] we asked the following questions:

- At what day from the 1st symptom you lost your smell and/or taste sensation?
- Was the smell and /or taste loss complete or partial?
- Did you feel any bad smell and /or bad taste at the beginning of symptoms?
- Did you have any symptoms at time of loss of smell?
- What are other symptoms associated with loss of smell?
- In relation to other symptoms, the timing of the onset of an altered sense of smell or taste occurred before or after other symptoms?
- When did the sense of smell and/or taste return?
- Did the sense of smell and/or taste return completely or partial (0 did not return, 10 return completely normal)?
- Did you feel any bad smell and /or bad taste after the senses returned?

For all patients, chest CT findings were categorized into mild, moderate or severe;

1. Mild: mild respiratory symptoms without imaging features of pneumonia.
2. Moderate: fever, respiratory symptoms with imaging findings of pneumonia.
3. Severe: shortness of breath, systemic oxygen (O2) saturation $< 93\%$ at rest on room air, respiratory rate > 30 breathing/min, ratio of the systemic arterial partial O2 pressure to the fraction of inspired air O2 ≤ 300 mmHg, or $> 50\%$ progress of radiologic pulmonary lesions over 24 to 48 hours.[9]

Statistical analysis was done for all these findings aiming to know the characters of anosmia and if there were any correlations between loss of smell and severity of chest affection in COVID -19 patients.

The data were collected; tabulated, and analyzed using IBM SPSS Statistics for Windows version 20 (IBM Corp., Armonk, NY, USA). Numerical data were presented with mean and standard deviation (SD). Ordinal data were presented as number and percentage. Paired *t*-test was used to compare 2 variables. P-value was considered statistically significant if < 0.05.

Results

One-hundred and forty patients were included in the present study. About 62% of them aged from 20 to 40 years old, while 25.2% aged from 41 to 60 years old. Females represented 66.7% of the sample. A total of 79 patients (56.4%) had complete loss of smell, 77 of them reported sudden loss (55% of total patients). Regarding taste sensation, 65 of the anosmic patients had complete loss of taste also, with 61 patients reporting sudden loss. The most common symptoms in all patients (140 patients) were fever in 57.1%, cough in 47.9%, sore throat in 43.6%, running nose in 37.9%. The baseline data of the patients are shown in ►**Table 1**. A total of 22 patients with anosmia were male (27.8%), while 57 patients were female (72.2%), with female predominance. A

Table 1 Baseline data of the studied patients

	$n = 140$	%
Age (years old):		
20–40	87	62.1%
41–60	36	25.7%
61–70	17	12.1%
Gender:		
Male	49	35.0%
Female	91	65.0%
Complete loss of smell: Yes	79	56.4%
Sudden loss of smell Yes	77	55.0%
Change in smell: Yes	7	5.0%
Sudden loss of taste: Yes	61	43.6%
Complete loss of taste: Yes	66	47.1%
Change in taste: Yes	18	12.9%
Symptoms & signs		
Fever	80	57.1%
Shivering	19	13.6%
Cough	67	47.9%
Sore throat	61	43.6%
Running nose	53	37.9%
Difficult breathing	41	29.3%
Fatigue	61	43.6%
Headache	51	36.4%
Diarrhea	28	20.0%
Others	5	3.6%

total of 57 patients were aged between 20 and 40 years old (72.2%), 15 (19.0%) between 41 and 60 years old, and 7 between 61 and 70 (8.9%). A total no. of COVID patients 140 (79 had anosmia, 61 without anosmia) (22 out of 79 had chronic disease) (27 out of 61 had chronic disease) (►**Table 2**). Anosmia appeared after the onset of symptoms in 86.1% of the patients before or at the 5th day, and appeared in 13.9% after the 5th day. ►**Fig. (1)**.

The most common associated symptoms with anosmia were running nose and sore throat (55.7% for both), fever and headache (44.3%), cough (43%) and diarrhea (27.8%) (►**Fig. 2**).

Loss of taste was significantly associated with loss of smell ($p < 0.001$). On correlating loss of smell and presenting symptoms, fever, sore throat, running nose, headache, and diarrhea were significantly associated with loss of smell, while difficult breathing prevailed more in patients with preserved smell ($p < 0.05$) (►**Table 2**).

The relation between anosmia and severity of chest infection is shown in ►**Fig. 3**. On correlating severity of chest infection and anosmia, loss of smell was significantly associated with mild disease (Crude Odds Ratio (COR) for anosmia in producing severe disease = 0.28, 95% confidence interval [CI]: 0.05–1.02; while COR for anosmia in producing moderate disease = 0.48, 95%CI; 0.22–1.05) (►**Table 2**). Regarding ICU admission, only 10% of anosmic patients were admitted versus 54.1% of those who had preserved smell ($p < 0.001$); 5 patients with severe cases died and all of them had preserved smell and had different comorbidities (►**Table 2**).

On performing the multivariate regression backward analysis, the factors significantly associated with anosmia were; absence of comorbid chronic diseases (adjusted odds ratio (AOR) = 3.499; $p < 0.001$), fever (AOR = 5.68; $p < 0.001$), running nose (AOR = 11.706; $p < 0.001$), headache (AOR = 6.145; $p = 0.001$) and diarrhea (AOR = 4.602; $p = 0.013$) were significantly independently associated with it (►**Table 3**).

Smell returned in 92.5% of the patients; in 13 patients, the smell returned in form of perceiving bad smell for few days then smell returned to normal. In 40.5% (32 patients), smell returned within 2 weeks, while in 39.2% (31 patients) smell returned within 1 week and in 12.7% (6 patients) smell returned after 1 month (►**Fig. 4**). Strength of the smell return was ranged from 6 to 10 in 82.2% (10 means return completely to normal) (►**Fig. 5**).

On assessing the relation between return of smell and baseline data, there was a statistically nonsignificant relation between it and both age or gender. However, 66.7% anosmic patients with chronic disease denied return of smell versus 24.7% of those without comorbidities, with statistically significant difference. On correlating the return of smell to severity of chest infection, there was a statistically nonsignificant association between them (►**Table 4**).

Discussion

In the present study, we investigated 140 COVID-19 patients from our medical records trying mainly to find any correlation between anosmia and severity of chest manifestations. It is well-known now that sudden anosmia and/or loss of taste are COVID-19 symptoms; so we analyze these symptoms also.

From 140 patients, 79 patients (56.4%) had anosmia with female predominance. On assessing the relation between loss of smell and baseline data, there is a statistically nonsignificant relation between loss of smell and gender. However, in the studied group, females were affected with anosmia more than males. However, there is a significant relation between the loss of smell and age where loss of smell prevailed higher in patients from 20 to 40 years old, 72.2% of anosmic patients were < 40 years old.

Anosmia is less likely to affect patients with comorbidities such as hypertension, diabetes and cardiac. This agrees with other studies done in our Middle East region and in other countries in Europe and in the USA.[4,7,10,11] Some of these studies suggested that the middle age group is more vulnerable to infection as they go out for work and studying, beside females having more concern about sense of smell than

Table 2 Relation between loss of smell and the studied parameters

Parameter	Loss of smell		Test	
	Present	Absent	χ^2	*p-value*
	n = 79 (%)	*n* = 61 (%)		
Gender:				
Male	22 (27.8%)	23 (41.1%)	2.579	0.108
Female	57 (72.2%)	33 (58.9%)		
Age group (years old):				
20–40	57 (72.2%)	29 (51.8%)	4.058¥	0.032*
41–60	15 (19.0%)	19 (33.9%)		
61–70	7 (8.9%)	8 (14.3%)		
Chronic diseases	22 (27.9%)	27 (44.3%)	4.08	0.043*
Fever	35 (44.3%)	45 (73.8%)	12.201	< 0.001**
Shivering	18 (22.8%)	1 (1.6%)	11.949	0.678
Cough	34 (43.0%)	33 (54.1%)	1.687	0.14
Sore throat	44 (55.7%)	17 (27.9%)	10.841	< 0.001**
Running nose	44 (55.7%)	9 (16.1%)	24.526	< 0.001**
Difficult breathing	16 (20.3%)	25 (35.7%)	24	0.045*
Fatigue	39 (49.4%)	22 (36.1%)	2.477	0.116
Headache	35 (44.3%)	16 (41.0%)	7.143	0.008*
Diarrhea	22 (27.8%)	6 (9.8%)	6.97	0.008*
Other symptoms	5 (6.3%)	0 (0%)	Fisher	0.068
Chest affection:				
Mild	58 (73.4%)	33 (54.1%)	6.135¥	0.013*
Moderate	17 (21.5%)	20 (32.8%)		
Severe	4 (5.1%)	8 (13.1%)		
COR (95%CI) moderate	0.48	(0.22–1.05)		
COR (95%CI) severe	0.28	(0.08–1.02)		
ICU admission:				
Yes	8 (10.1%)	33 (54.1%)	32.138	< 0.001**
Loss of taste				
Yes	65 (82.3%)	1 (1.6%)	Fisher	< 0.001**
Mortality	0 (0%)	5 (8.2%)	Fisher	0.014*

Abbreviations: CI confidence interval, COR crude odds ratio.
¥Chi-squared for trend test χ^2 chi-squared test *$p < 0.05$ is statistically significant ** $p \leq 0.001$ is statistically highly significant

males. We found these explanations are reasonable for the wide agreement in different studies about the age and gender affected with anosmia.

We reported in a previous study[12] that most of ENT manifestations (sore throat, nasal congestion, obstruction, headache and olfactory dysfunction) are common in COVID-19 patients, and advised ENT doctors to suspect COVID-19 particularly if the nasal examination was non-significant. In the present study, sudden anosmia appeared in 97.4% with absence of nasal manifestations, 55.7% complained of running nose and sore throat for a few days before anosmia appeared. So, anosmia may appear before, during, or after the general symptoms. This was found in our patients as well as in other studies,[7,13,14] This means that COVID-19 patients could go to otolaryngologists as the first-line physicians either before or after anosmia appears.

Fever and cough are still the most common general manifestations in COVID-19 patients either with anosmia or not, but they were significantly associated with loss of smell in the present study besides other symptoms such as sore throat, running nose, headache, and diarrhea. Bianco et al. demonstrated that 52% SARS-CoV-2-positive patients reported smell/taste disorders. The symptoms reported by hospitalized patients were fever (71.4%), cough (64.2%), fatigue (82.1%), and dyspnea (100%), while in nonhospitalized patients, the most reported symptoms were sore throat

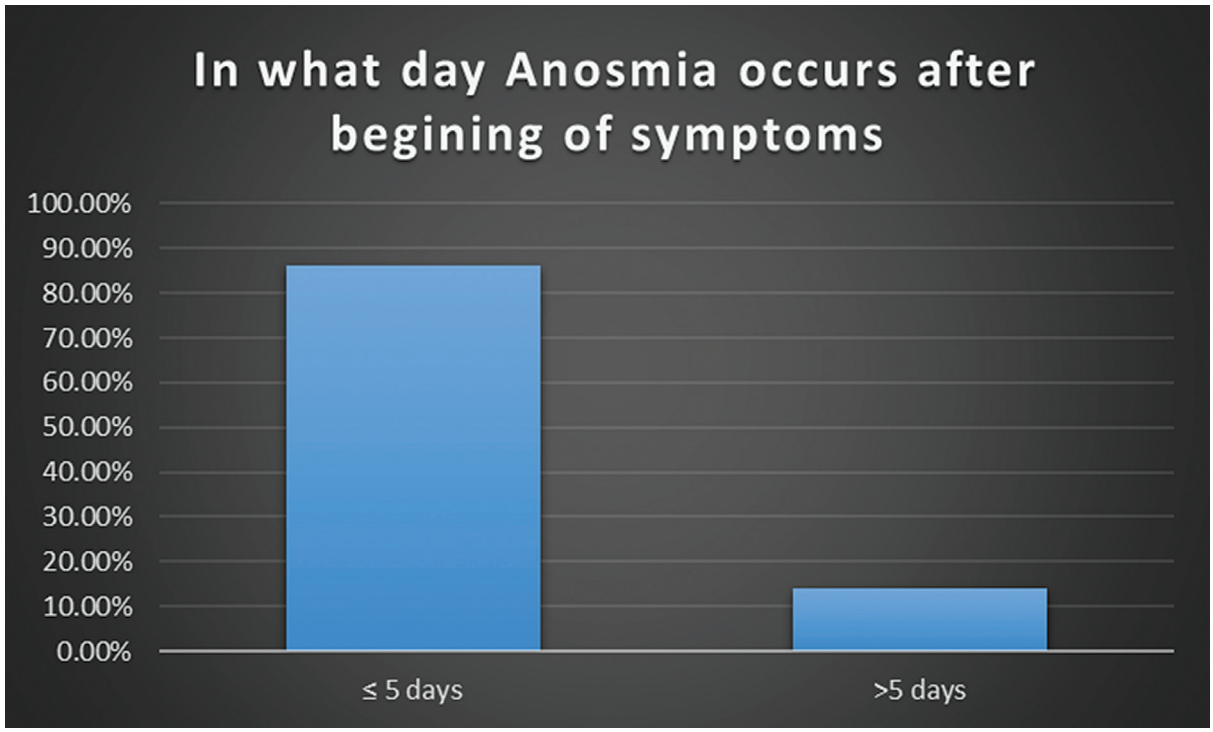

Fig. 1 Timing of loss of smell after beginning of symptoms.

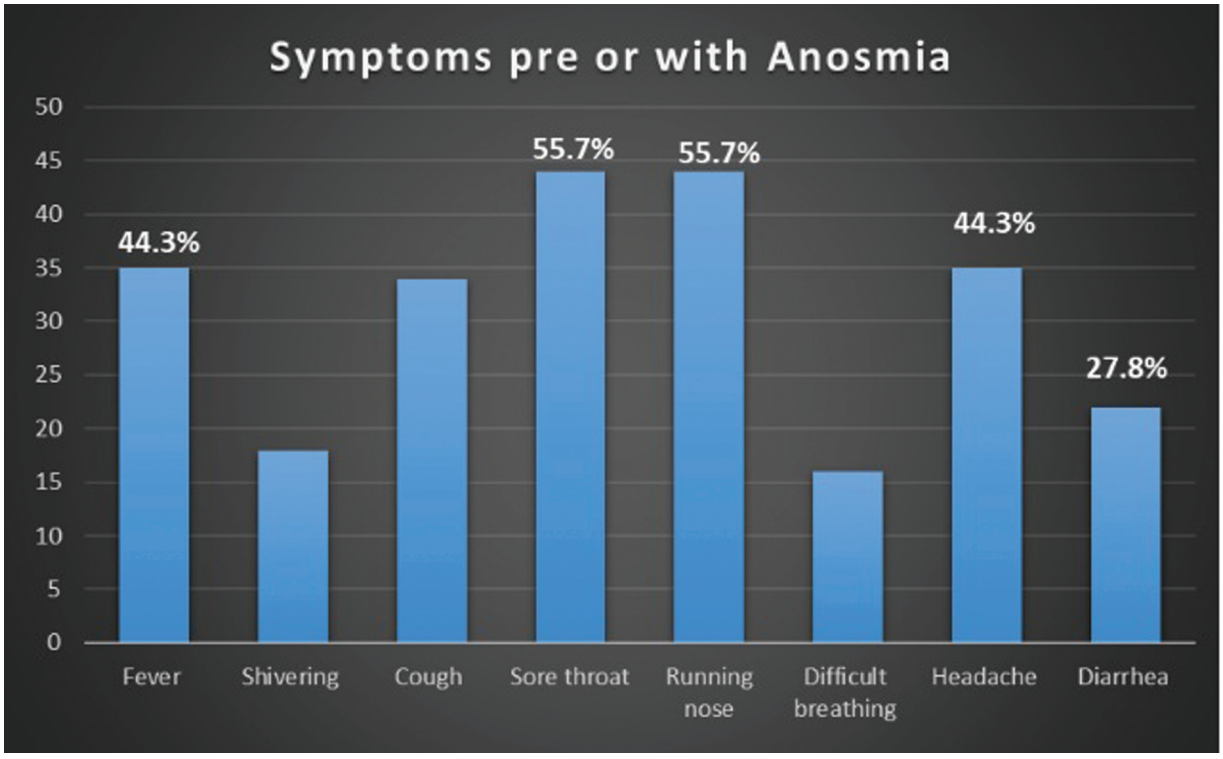

Fig. 2 Symptoms appeared before or after loss of smell had occurred.

(72.7%), rhinorrhea (77.2%), and altered smell (81.8%). Anosmia/hyposmia reported in the hospitalized and non-hospitalized were 28.5 and 81.8%, respectively ($p = 0.001$).[15] Some studies[7,16] reported diarrhea in $> 50\%$ of the patients. Another study reported that occurrence of diarrhea is $< 20\%$ in the medical literature.[17] In our study, the frequency of diarrhea was high in patients with anosmia (27.8%) versus (9.8%) in patients without anosmia. Regarding taste affection, loss of taste was significantly associated with loss of smell in $\sim 82\%$, which is quite near percentages reported by

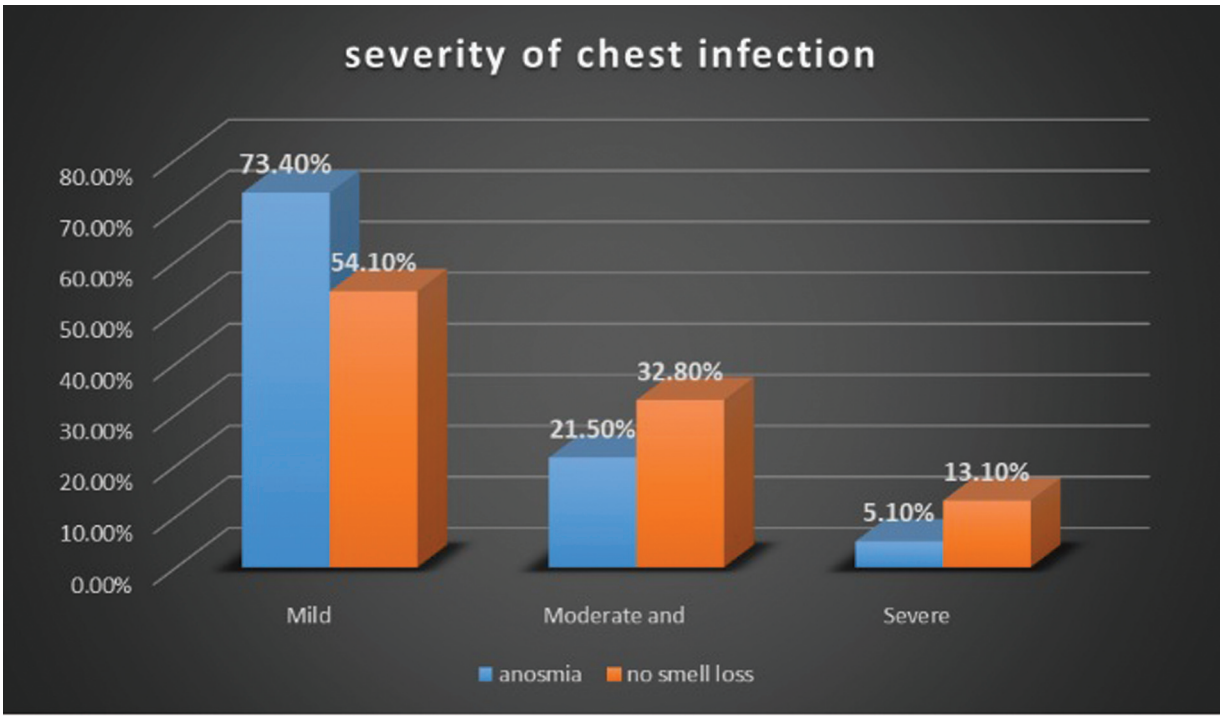

Fig. 3 The relation between anosmia and severity of chest infection.

Table 3 Multivariate analysis of factors associated with anosmia among the studied patients

	β	Wald	*p-value*	AOR	95%CI	
					Lower	Upper
Absence of chronic disease	1.252	6.971	0.008*	3.44	1.381	8.866
Fever	1.737	12.149	< 0.001**	5.68	2.139	15.086
Running nose	2.460	21.455	< 0.001**	11.706	4.133	33.150
Headache	1.816	10.692	0.001**	6.145	2.070	18.246
Diarrhea	1.252	6.109	0.013*	4.602	1.372	15.438

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval.
*$p < 0.05$ is statistically significant **$p \leq 0.001$ is statistically highly significant.

other studies.[7,10,16] Also, presence of chronic disease was significantly associated with preserved smell sensation in our study. Similar findings were reported in another study.[11] We did a multivariate analysis of factors associated with anosmia among the studied patients (►**Table 3**); anosmia was independently associated with higher odds of having running nose, fever and cough. Talavera et al.[11] reported that anosmia was independently associated with a higher odd of having cough, myalgia, and headache.

Spinato et al.[18] reported that alterations in smell or taste were common in mildly symptomatic patients with COVID-19 infection and often were the first apparent symptom, but these results must be interpreted with caution due to subjective reporting of anosmia in many studies. So, in our study, to overcome this limitation, we correlated anosmia to chest condition by examining the chest CT of all patients. Our data shows 73.4% of anosmic patients had mild chest infection according to their CT imaging, 21.5% of them had moderate chest infection, and 5.1% had severe chest infection ►**Fig. 3**. Also, anosmia was significantly associated with decreased ICU admission, 10% of anosmic patients were admitted versus 54.1% of those who had preserved smell ($p < 0.001$); 5 patients with severe cases died and all of them had preserved smell and had different comorbidities (►**Table 2**). This was reported by other studies.[10,11,16,19] This could be explained by what was reported by Sanli et al.,[20] that patients with COVID-19-related anosmia tend to have significantly lower serum levels of interleukin- 6 (IL-6) compared with patients without anosmia, and the lower IL-6 levels are related to a milder course of the disease.

Smell and taste returned to normal in ~ 80% of the patients with anosmia within 2 weeks after the beginning of general manifestations, as these 2 weeks were characterized by significant viral load reduction.[21] Lechien et al.[7]

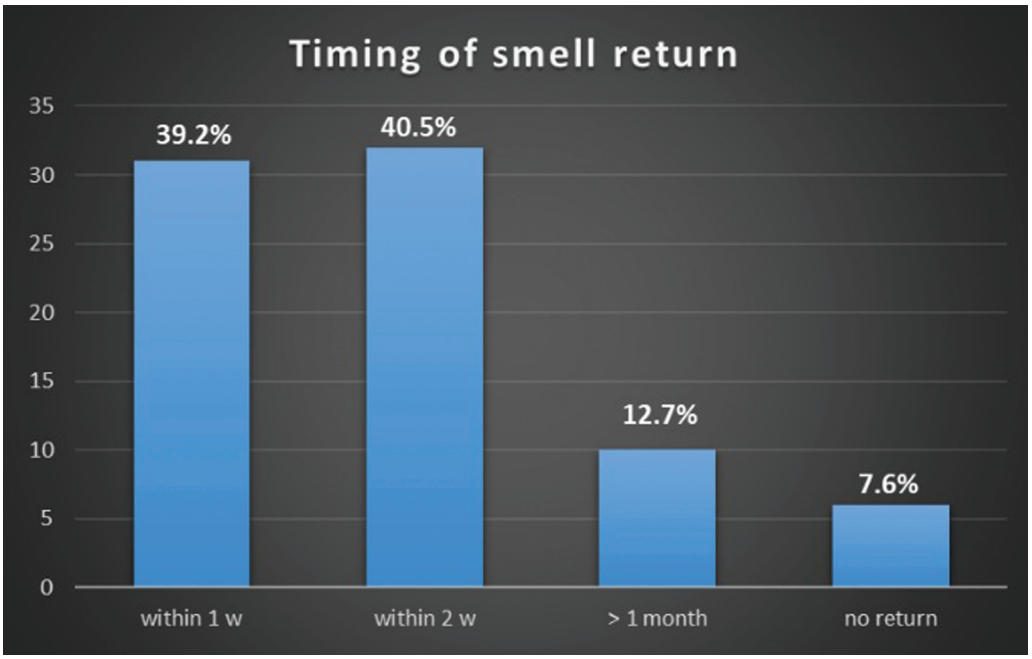

Fig. 4 Timing of smell return.

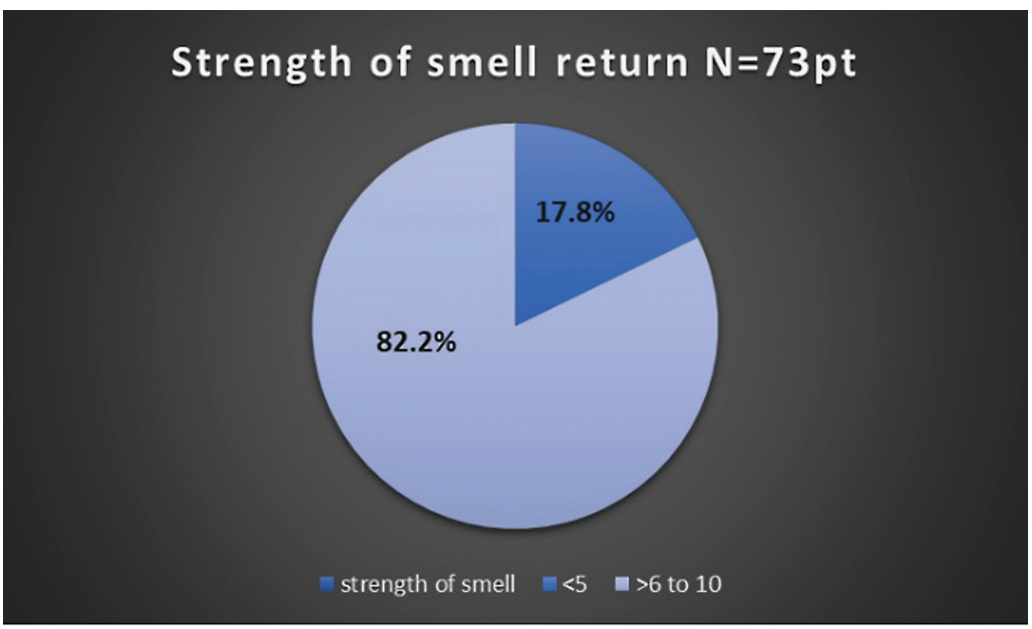

Fig. 5 The strength of smell return on a scale from 0 (no smell) to 10 (complete return).

reported a lower percentage (~25%) of smell return after 2 weeks and ~ 70% of smell return by day 8. Our data is in line with these findings. The strength of the smell return ranged from 6 to 10 in 82.2% (10 means return completely to normal). Smell returned in ~ 12.7% after 1 moth. Six patients suffered from permanent anosmia up until now, 4 of them had chronic disease while the remaining 2 had no comorbidities, with statistically significant difference (►**Table 4**). Although there is still no explanation why anosmia could be permanent in some patients, and if it will return after a long period, Paolo et al.[22] denied that the olfactory nerve damage

Table 4 Relation between baseline data and return of smell among anosmic patients

Parameter	Return smell		Test	
	Returned	Did not return	χ^2	*p-value*
	n = 73 (%)	*n* = 6 (%)		
Severity of chest infection:				
Mild	53 (72.6%)	5 (83.3%)	0.453¥	0.501
Moderate	16 (21.9%)	1 (16.7%)		
Severe	4 (5.5%)	0 (0.0%)		
Gender:				
Male	20 (27.4%)	2 (33.3%)	Fisher	0.669
Female	53 (72.6%)	4 (66.7%)		
Age group (years old):				
20–40	54 (74.0%)	3 (50.0%)	0.277¥	0.599
41–60	12 (16.4%)	3 (50.0%)		
61–70 years	7 (9.6%)	0 (0.0%)		
Chronic diseases	18 (24.7%)	4 (66.7%)	4.08	0.048*

¥Chi-squared for trend test χ^2 chi-squares test *$p < 0.05$ is statistically significant.

could be permanent. Actually, we face in some patients anosmia presenting post-COVID for very long periods.

On correlating the return of smell to severity of chest infection, there was a statistically nonsignificant association between them.

Our results support that olfactory and gustatory dysfunctions are both more common in patients with mild-to-moderate COVID-19 infection. So, studying if smell affection in the newly discovered stains and mutations of COVID-19 is also associated with less severe form of the disease is recommended. The main limitations of our study were its retrospective nature and the subjective nature of smell loss.

Limitation of the Study

The sample was relatively small; subjective reporting of anosmia.

Conclusion

The pattern of anosmia in COVID-19 patients has some common similarities in general; the way it starts, the associated symptoms, the duration until return of smell and, the most important, the severity of chest infection as anosmia is significantly associated with mild chest infection. The presence of anosmia could be an independent predictor of good COVID-19 outcome as reflected by lower disease severity and less frequent ICU admission. This could be related to a different clinical presentation that may be associated with a more benign immune and inflammatory response to COVID-19.

Conflict of Interests

The authors have no conflict of interests to declare.

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