

# Evaluating Patients with Olfactory Dysfunction after COVID-19 Infection by Questionnaire of Olfactory Disorders-Negative Statements

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## Abstract

**Background:** The number of patients with COVID-19-induced olfactory dysfunction has consistently increased since the onset of the pandemic. Since a considerable proportion of these patients have olfactory dysfunction for a relatively long period of time, their quality of life (QOL) may considerably be impacted as a result.

**Aim:** The aim of the present study was to investigate the adverse effects of olfactory dysfunction on QOL in patients with COVID-19-induced hyposmia or anosmia.

**Methods:** The data were obtained via self-reported online questionnaire in individuals who met the inclusion criteria. The questionnaire included demographics, olfactory status and Questionnaire of Olfactory Disorders-Negative Statements (QOD-NS).

**Results:** Among 1531 participants, 1072 individuals met the inclusion criteria, with 588 (54.85%) having hyposmia and 484 (45.15%) anosmia. Average age was 35.7 in the hyposmic group and 34.5 in the anosmic group. Concurrent hypogeusia/ageusia was reported in 398 (67.7%) of cases with hyposmia and in 346 (71.5%) of participants with anosmia. Lack of enjoyment of eating food was the most negative effect in both hyposmic and anosmic groups, followed by annoyance when eating food and a continuous awareness of the olfactory problem. The mean QOD-NS score was  $20.5 \pm 10.2$  in the hyposmic group and  $23.3 \pm 10.4$  in the anosmic group, demonstrating significant adverse impact on QOL.

**Conclusion:** Persistent olfactory dysfunction in patients with COVID-19 has adverse effects on QOL. Early diagnosis and treatment of olfactory dysfunction may be crucial in limiting the adverse impact on QOL by psychological and nutritional support and olfactory rehabilitation.

**Conflicts of Interest:** The Authors declare no conflicts of interest.

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## Introduction

Population-based studies have reported a degree of olfactory dysfunction in about 12.4% of the adults aged 40 or older in the US, with 3.2 % having severe hyposmia or anosmia (1).

Earlier studies have reported higher prevalence (2, 3). Post viral anosmia is one of the leading causes of olfactory dysfunction, which accounts for more than 40% of the cases (4).

Since the start of the COVID-19 pandemic, the prevalence of olfactory dysfunction has been reported to be as high as 70% in patients with mild COVID-19, but overall, the prevalence may vary according to the clinical setting (5, 6, 7).

Most patients with COVID-19 induced olfactory dysfunction have partial or complete resolution of their symptoms within a short follow up time (7, 8, 9). However, some patients have persistent symptoms without any improvement after several weeks (10). With increasing number of patients with COVID-19-induced olfactory dysfunction during the current pandemic, a significant number of patients experience persistent olfactory dysfunction that can significantly impact their quality of life (11).

Adverse impacts on quality of life in patients with olfactory disorders include impairment in food enjoyment, potentially hazardous inability to detect odors, disruption in social life, and mental health problems (12, 13, 14). Social anxiety, eating disorders, and depression are well-known complications of olfactory disorders. Impact on quality of life in olfactory disorders can be measured by using the modified version of the Questionnaire of Olfactory Disorders-Negative Statements (QOD-NS) (15). The aim of the present study was to investigate the adverse effects of olfactory disorders on quality of life in patients with COVID-19-induced hyposmia or anosmia (15).

## Methods

In this study, we published an online questionnaire about smell dysfunction during the COVID-19 pandemic on a national platform (the link to the online questionnaire: <https://survey.porsline.ir/s/yhfYb7W#?ref=wh>) collecting data from November 1st, 2020 until December 26th, 2020. We publicized the study through social media (Facebook, Twitter, Instagram) and by advertisement in the local printed media, aiming to recruit individuals

who have experienced olfactory dysfunction during the COVID-19 pandemic. The questions were designed in a manner that the participants could answer without specific training. Participation was voluntary and participants did not receive any compensation. The inclusion criteria were age $\geq$ 15 years with COVID-19, which was confirmed by polymerase chain reaction (PCR) assay and any form of new-onset olfactory dysfunction during the COVID-19 pandemic (i.e., since February 2020). We first inquired about the types of olfactory dysfunction in a simple language to determine whether the participants had hyposmia, anosmia and/or parosmia. A series of questions were then asked from the participants who had hyposmia/anosmia. Participants were asked about a positive polymerase chain reaction (PCR) assay result, and patients with COVID-19 confirmed by PCR assay were included in the present analysis. We included questions about the demographics (age, sex) and past medical history. Questions specific to hyposmia/anosmia included the onset and duration of olfactory disorder, presence of clinical symptoms related to COVID-19 prior to or in association with hyposmia/anosmia, sinonasal symptoms, and presence of taste disorders. Participants with a history of olfactory disorder due to trauma or infection before the pandemic began, or a history of neurodegenerative disease were excluded. Since we sought to determine the impact of quantitative olfactory dysfunction (hyposmia and anosmia), we excluded participants with a history of qualitative disorders (parosmia or phantosmia).

Participants who incompletely filled in the questionnaire (i.e., answering < 90% of all questions) were also excluded. To assess the impact of anosmia and hyposmia on quality of life, we used a modified version of the Olfactory Disorders-Negative Statements (QOD-NS) questionnaire (Online Supplement). This validated questionnaire is a tool for evaluating several negative impacts of olfactory

deficits on the daily life and contains 17 items (20). Participants could agree (3 points), somewhat agree (2 points), somewhat disagree (1 point) or disagree (0 point) with each item, thus each item had a score from 0 to 3, for a total score on the questionnaire that ranged from 0 to 51(20).

High scores represent poor quality of life while low scores indicate good quality of life. We selected a cut-off score of 12.5 for distinction between normal vs. abnormal quality of life according to the scoring method by Mattos et al (15).

The study was approved by the Institutional Review Board at our hospital.

## Results

### Demographic and Clinical Characteristics of Participants

A total of 1531 individuals participated in the study, of which 1072 were included in the present analysis. Of the included participants, 588 (54.85%) had hyposmia and 484 (45.15%) anosmia. The demographic and clinical characteristics of the participants are summarized in Table 1.

**Table 1.** Demographic and Clinical Characteristics of Participants with Anosmia/hyposmia.

Demographic and Clinical Characteristics	Total(n=1072)	Anosmia(n=484)	Hyposmia(n=588)
Sex	Male	108(22.3%)	137(23.3%)
	Female	376(77.7%)	451(76.7%)
Age	15-30	173(35.7%)	166(28.2%)
	31-45	261(54%)	354(60.2%)
	46-60	47(9.7%)	59(10%)
	60<	3(0.6%)	9(1.5%)
Past medical history	Allergy	108(22.3%)	132(22.4%)
	Asthma	18(3.72%)	22(3.7%)
	Diabetes mellitus	5(1%)	18(3.1%)
	Hypertension	22(4.5%)	41(7%)
	Cardiac disease	6(1.2%)	9(1.5%)
	Thyroid disease	61(12.6%)	107(18.2%)
Previous symptoms related to COVID-19	No specific disease	290(59.9%)	324(55.1%)
	Fever	169(34.9%)	182(31%)
	Headache	250(51.6%)	263(44.7%)
	Myalgia	239(49.4%)	275(46.8%)
	Bone pain	101(20.9%)	143(24.3%)
	Cough	144(29.7%)	176(29.9%)
	Dyspnea	65(13.4%)	90(15.3%)
	Vertigo/dizziness	95(19.6%)	95(16.1%)
	GI Symptoms	108(22.3%)	121(20.5%)
	No symptom	60(12.4%)	115(19.5%)
	Current Sinonasal Symptoms	Nasal obstruction	271(56%)
Nasal congestion		123(25.4%)	175(29.7%)
Nasal discharge		102(21.1%)	128(21.7%)
Nasal burning		132(27.3%)	132(22.4%)
Post-nasal discharge		160(33%)	186(31.6%)
Itchy nose		25(5.1%)	35(5.9%)
Facial pain		56(11.6%)	68(11.5%)
Headache		196(40.5%)	221(37.6%)

The average age was 35.7 in the hyposmic group and 34.5 in the anosmic group (range 10-72 years). Most patients in either group were female; 451 (76.7%) in the hyposmic and 376 (77.7%) in the anosmic group.

The most common concurrent symptom with hyposmia was myalgia (275 [46.8%]), while headache was the most-commonly associated symptom with anosmia (250 [51.6%]). In both groups, shortness of breath and vertigo/dizziness were the least commonly

associated symptoms (15.3% vs. 13.4% and 16.1% vs. 19.6%, respectively). Most common sinonasal symptom in participants with hyposmia and anosmia was nasal obstruction, in 278 (47.2%) and 271(56%) respectively.

### Clinical Characteristics of Hyposmia and Anosmia

Clinical characteristics related to the emergence and evolution of hyposmia/anosmia as well as gustatory dysfunction are summarized in Table 2.

**Table 2.** Characteristics of Anosmia/hyposmia and Gustatory Dysfunction in Patients with COVID-19

Characteristics of olfactory disorder		Anosmia (n=484)	Hyposmia (n=588)
Duration of olfactory disorder	≤ 3 months	464(95.9%)	481(82%)
	>3 months	20(4.1%)	107 (18%)
Onset	Sudden	374(77.3%)	397(67.5%)
	Gradual	110(22.7%)	191(32.5%)
Order of Symptoms	Olfactory First	35(7.2%)	61(10.4%)
	Concomitant /general first	395(81.6%)	445(75.7%)
	Isolated	54(11.2%)	82(13.9%)
Recovery from the Olfactory Symptoms	Partial recovery	152(31.4%)	451(76.7%)
	Full recovery	92(19%)	96(16.3%)
	No recovery	240(49.6%)	41(7%)
Weight change	Weight gain	42(8.7%)	48(8.2%)
	Weight loss	119(24.6%)	136(23.1%)
	NO change	323(66.7%)	404(68.7%)
Concurrent gustatory disorder	Ageusia/hypogeusia	346(71.5%)	398(67.7%)
	Parageusia	8(1.7%)	6(1%)
	Normal taste	130(26.8%)	184(31.3%)
Disturbance in the main tastes	Sweet	182(37.6%)	244(41.5%)
	Sour	183(37.8%)	259(44%)
	Salt	196(40.5%)	263(44.7%)
	Bitter	172(35.5%)	212(36%)

Olfactory dysfunction was sudden onset in 397 (67.5%) of participants with hyposmia and in 374 (77.3%) of participants with anosmia. In most participants with hyposmia (481 [82%]) and anosmia (464 [95.9%]), the olfactory dysfunction lasted for < 3 months. Concurrent hypogeusia/ageusia was reported in 398 (67.7%) of participants with hyposmia and in 346 (71.5%) of participants with anosmia. Disturbances in perception of primary tastes included in tasting saltiness (263 [44.7%] vs.

196 [40.5%]) and sourness (259 [44%] vs. 183 [37.8%]) in the hyposmic and anosmic participants, respectively.

### Olfactory-Specific Quality of Life Assessment in Participants with Hyposmia and Anosmia

The specific questions in the QOD-NS and scores per each item are summarized in Tables 3 and 4. The mean QOD-NS score was 20.5±10.2 in the group with hyposmia and 23.3±10.4 in the anosmic group.

**Table 3.** Scores on the Modified Olfactory Disorders-Negative Questionnaire Dysfunction in Patients with Hyposmia (n=588)

Questions	I agree	I agree partly	I disagree partly	I disagree
1 Because of the change in my sense of smell, I go to restaurants less often than I used to.	93(15.9%)	80(13.6%)	169(28.7%)	246(41.8%)
2 I am always aware of the change in my sense of smell.	243(41.3%)	191(32.5%)	50(8.5%)	104(17.7%)
3 Because of the Change in my sense of smell I don't enjoys drinks or food as much as I used to.	296(50.3%)	174(29.6%)	26(4.4%)	92(15.6%)
4 I am worried that I will never get used to the changes in my sense of smell.	212(36%)	133(22.6%)	51(8.7%)	192(32.7%)
5 Because of the change in my sense of smell I feel more anxious than I used to feel.	121(20.6%)	196(33.3%)	45(7.7%)	226(38.4%)
6 Because of the change in my sense of smell cause most of my problems.	60(10.2%)	104(17.7%)	70(11.9%)	354(60.2%)
7 Because of the change in my sense of smell, I am annoyed when I am eating.	219(37.2%)	193(32.8%)	48 (8.2%)	128(21.8%)
8 Because of the change in my sense of smell I visit friends, relatives, or neighbors less often.	71(12.1%)	76(12.9%)	160(27.2%)	281(47.8%)
9 Because of the Change in my sense of smell I try harder to relax.	135(22.9%)	155(26.4%)	48(8.2%)	250(42.5%)
10 Because of the Change in my sense of smell I have weight problems.	87(14.8%)	104(17.7%)	39(6.6%)	358(60.9%)
11 the Change in my sense of smell make me feel isolated.	45(7.7%)	105(17.8%)	48(8.2%)	390(66.3%)
12 Because of the change in my sense of smell I avoid groups of people.	72(12.2%)	88(15%)	96(16.3%)	332(56.5%)
13 Because of the Change in my sense of smell I eat less than I used to or more than I used to.	145(24.7%)	142(24.1%)	43(7.3%)	258(43.9%)
14 Because of the Change in my sense of smell I am scared of getting exposed to certain dangers (e.g., gas, rotten food).	173(29.4%)	156(26.5%)	32(5.4%)	227(38.6%)
15 Because of the Change in my sense of smell I have problems with taking part in activities of daily life.	52(8.8%)	114(19.4%)	51(8.7%)	371(63.1%)
16 Change in sense of smell has make me feel angry.	111(18.9%)	169(28.7%)	57(9.7%)	251(42.7%)
17 Because of the Change in my sense of smell, my relationship with my wife/husband/partner is affected.	43(7.3%)	68(11.6%)	44(7.5%)	433(73.6%)

The most negative effect on quality of life was the lack of enjoyment in eating food (Question 3) in both hyposmic and anosmic groups, followed by annoyance when eating food because of the inability to smell food (Questions 7) and a continuous awareness of the olfactory problem (Questions 2). In 54% of

cases, changes in the sense of smell during eating annoyed patients with anosmia compared with 37.2% in patients with hyposmia. 14.8% of patients with olfactory dysfunction (anosmia/hyposmia) had weight problems (Question 10), 27.7% of anosmic patients and 24.7% of hyposmic patients had a

change in eating (undereating or overeating) compared to the past.

Moreover, 51.9% of patients with anosmia were aware of their olfactory changes throughout the day, whereas a relatively lower proportion of

hyposmic patients (41.3%) reported this issue. 41.5% of anosmic patients and 29.4% of patients with hyposmia were afraid of being exposed to certain risks such as gas and rotten food.

**Table 4.** Scores on the Modified Olfactory Disorders-Negative Questionnaire Dysfunction in Patients with Anosmia (n=484)

Questions	I agree	I agree partly	I disagree partly	I disagree
1 Because of the change in my sense of smell, I go to restaurants less often than I used to	78(16.1%)	65(13.4%)	136(28.1%)	205(42.4%)
2 I am always aware of the change in my sense of smell.	251(51.9%)	132(27.3%)	26(5.3%)	75(15.5%)
3 Because of the Change in my sense of smell I don't enjoys drinks or food as much as I used to.	341(70.4%)	87(18%)	10(2.1%)	46(9.5%)
4 I am worried that I will never get used to the changes in my sense of smell.	231(47.7%)	99(20.5%)	36(7.4 %)	118(24.4%)
5 Because of the Change in my sense of smell I feel more anxious than I used to feel.	131(27.1%)	126(26%)	40(8.3%)	187(38.6%)
6 Because of the Change in my sense of smell cause most of my problems.	62(12.8%)	118(24.4%)	63(13%)	241(49.8%)
7 Because of the Change in my sense of smell annoy me when I am eating.	261(54%)	137(28.3%)	18(3.7%)	68(14%)
8 Because of the change in my sense of smell I visit friends, relatives, or neighbors less often.	63(13%)	58(12%)	134(27.7%)	229(47.3%)
9 Because of the Change in my sense of smell I try harder to relax.	121(25%)	142(29.3%)	57(11.8 %)	164(33.9%)
10 Because of the Change in my sense of smell I have weight problems.	71(14.7%)	97(20%)	39(8.1%)	277(57.2%)
11 the Change in my sense of smell make me feel isolated.	52(10.7%)	95(19.6%)	42(8.7%)	295(61%)
12 Because of the change in my sense of smell I avoid groups of people.	53(11%)	78(16.1%)	90(18.6 %)	263(54.3%)
13 Because of the Change in my sense of smell I eat less than I used to or more than I used to.	134(27.7%)	104(21.5%)	39(8.1%)	207(42.8%)
14 Because of the Change in my sense of smell I am scared of getting exposed to certain dangers (e.g., gas, rotten food).	201(41.5%)	117(24.2%)	27(5.6%)	139(28.7%)
15 Because of the Change in my sense of smell I have problems with taking part in activities of daily life.	76(15.7%)	103(21.3%)	42(8.7%)	263(54.3%)
16 Change in sense of smell has make me feel angry.	118(24.4%)	165(34.1%)	46(9.5%)	155(32%)
17 Because of the Change in my sense of smell, my relationship with my wife/husband/partner is affected.	40(8.3%)	69(14.2%)	39(8.1%)	336(69.4%)

A significant proportion of patients had changes in mood and affect due to the olfactory dysfunction. 70.4% of anosmic patients and 50.3% of hyposmic patients did not feel as happy as before, 47.7% of anosmic and 36% of hyposmic patients were worried that they will never get used to their olfactory changes, 18.9% of hyposmic and 24.4% of anosmic participants felt angry about their olfactory problem, 20.6% with hyposmia and 27.1% with anosmia felt more anxious than before, and 22.9% and 25%, respectively, reported needing more effort than before to calm down. In a relatively small proportion of patients (8.3% in anosmia and 7.3% in hyposmia), the olfactory dysfunction had a negative impact on personal relationships with wife/husband/partner. Problems with social interactions were also reported: 10.7% of patients claimed to be socially isolated compared with 7.7% of patients with hyposmia, 15.7% of anosmic patients and 8.8% of patients with hyposmia had difficulty participating in daily activities.

### Discussion

Olfactory and gustatory dysfunction have been increasingly described in patients with COVID-19 since the onset of the pandemic. Approximately, 80% of patients have reported olfactory dysfunction or chemosensory disturbances in the course of the disease (16). According to two recent meta-analyses, it is estimated that 41% to 62% of patients with COVID-19 have experienced smell and taste dysfunction (17, 18), which usually occurred within three days after the onset of symptomatic COVID-19 (19,20). In the present study, these symptoms lasted less than three months in the vast majority of patients. There was a slight preponderance for females in the participants of the present study, which may reflect the higher rates of post-viral olfactory dysfunction in women (21, 22), and a higher propensity among females to display emotional problems related to olfactory dysfunction such as depression and anxiety (23). Concomitant gustatory

dysfunction has been reported in 88.8% (78.9% hypogeusia/agueusia and 21.1% parageusia) (24) or 86.8% of patients with COVID-19 (10). In the present study, approximately 71.5% of patients with anosmia had a concomitant taste disorder (hypogeusia/agueusia) whereas 67.7% of hyposmic patients had taste disturbances. Basic tastes are often preserved because of direct stimulation of brain by these tastes via gustatory impulses(25). This is in contrast to impairment of retronasal olfaction and the resultant alteration in perception of tastes. However, the main flavors affected in our study were saltiness and sourness. This can be a result of direct invasion to taste buds, receptors or sensory cells by SARS-CoV-2, independent of olfactory dysfunction. Olfaction is also an important medium for facilitating social communication (26). It also plays an important role in eating behavior as it is one of the major determinants of appetite and flavor perception during eating (26). Consequently, and as shown in this study, post-viral taste dysfunction has a considerable impact on quality of life of patients with olfactory dysfunction (26), and long-lasting COVID-19-induced chemical sensory alteration has significant effects on the activities of daily living (27). While the mean QOD-NS score in both groups was higher than the cut of point that indicates impairment of quality of life, hyposmic patients had lower scores, indicating fewer problems compared with anosmic patients. People with olfactory dysfunction report problems with cooking, disruption of appetite, enjoyment of food, maintaining personal hygiene, and emotional security, with a higher likelihood of psychological problems such as depression and anxiety (23).

We observed that the loss of pleasure of eating was the most common problem in both anosmic and hyposmic groups, an observation that is consistent with our previous report (28). The annoyance with eating and continuous awareness of the olfactory problem had considerable adverse impact on quality of life.

Hyposmic patients still have some sense of smell and therefore are repeatedly reminded of their olfactory defects, with continuous awareness of the olfactory problem being the second most important issue reported by the participants of the present study, but annoyance of eating in parosmic patients was greater than anosmic or hyposmic patients. Also, worry about “never getting used to changes” in sense of smell in parosmic patients was greater than anosmic or hyposmic patients (28).

Olfaction acts as a warning system for environmental hazards (26). Fear of being exposed to certain dangers provoked anxiety in approximately half the participants.

Despite the issues related to eating food, unintentional weight loss was only observed in less than a quarter of the participants in the current study. This observation may be because the symptoms lasted less than 3 months in majority of participants and the effects on weight may have not been borne out yet. The nutritional impact of olfactory disorders can, nevertheless, be complicated. For instance, in previous studies, while 29% to 43.2% of patients with olfactory disorders had decreased appetite and less food than before (29,30), 21% had weight gain and 11% had weight loss (29). Due to the lack of food enjoyment, the affected patients may avoid eating or may add flavor to their food in an attempt to improve the taste. They may change their food preferences and may try to use the non-olfactory senses to maintain the pleasure of eating food, which leads to weight gain, especially among women (29). On the other hand, patients may lose their interest toward foods, especially in men which can result in weight loss (29). In the present study, participants reported fewer issues with food related activities, such as going to restaurants, which could be due to the effect of the pandemic that mandated lock-downs and physical distancing.

The major limitations of the study were self-reported data collection via online

questionnaire and the lack of objective tests to confirm olfactory loss.

### Conclusion

In conclusion, persistent olfactory dysfunction in patients with COVID-19 has adverse effects on quality of life, nutritional status, and psychological well-being, leading to anxiety and depression. Early diagnosis and treatment of olfactory dysfunction, e.g., by olfactory training, as well as psychological and nutritional support may be warranted to counter the deleterious impacts of COVID-19-induced olfactory dysfunction on quality of life.

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### Conflicts of Interest

The authors declare no conflicts of interest.

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### Ethics

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