Prevalence, Patterns, Prognosis, and Psychosocial Impact of Olfactory and Gustative Dysfunctions Among Saudi COVID-19 Patients

Mohammad H. Shaheen 1, Abdullah Alghamdi 2, Abdullah Alrajhi 3, Meshal F. Khan 1, Alaa Babkour 1

1. Otolaryngology, Al-Noor Specialist Hospital, Makkah, SAU 2. Otolaryngology, Alhada Armed Forces Hospital, Altaif, SAU

Corresponding author: Mohammad H. Shaheen, mishaheen1@gmail.com

Abstract

Objective

The objective of this study is to estimate the prevalence of olfactory and gustative dysfunctions (OGD) and analyze their pattern and psychosocial impact among COVID-19 patients.

Method

A cross-sectional study was conducted among 194 confirmed COVID-19 cases at Al-Noor Specialist Hospital between 1 September 2020 and 30 September 2021. A questionnaire was translated and modified from another study to collect the baseline demographic data and medical history; characterization of smell and taste loss separately, including timing, level, practices or treatment used to restore, recovery, and symptom duration; and the psychological impact of OGD using six items to explore the multidimensional impact, such as daily activity, job performance, and social life. A four-point Likert-type agreement scale was used, and an impact score was calculated.

Result

As high as 97.4% and 94.8% of the participants declared having experienced a certain level of olfactory and gustative dysfunction, respectively. In the majority of these cases, the dysfunction occurred after the acute phase of the disease and persisted less than one month after onset. Social life (78.4%), job performance (64.4%), and daily life activities (42.8%) were the most frequently impacted dimensions, and 32% of the participants were deemed to have experienced a high psychosocial impact. Younger participants, females, and certain job categories were significantly more impacted than their counterparts.

Conclusion

OGDs are highly frequent in COVID-19 patients. They are described to be relatively severe and have frequent psychosocial impacts, notably in females and the younger age category. Further research is warranted to determine efficacious preventive and management strategies in order to prevent their long-term impact on wellbeing.

Categories: Otolaryngology, Public Health
Keywords: impact, social, psychological, covid-19, ageusia, anosmia

Introduction

The COVID-19 infection manifests with a wide range of clinical symptoms ranging from asymptomatic cases to severe multiorgan failure [1]. Although the virus has an evident pulmonary tropism, several atypical extrapulmonary symptoms have been identified and added to the list of clinical presentations of the disease [2]. Among these atypical signs, olfactory and gustative dysfunctions (OGDs) were identified as hallmarks of SARS-COV-2 infection since the start of the pandemic and had a high diagnostic value, notably for paucisymptomatic cases [3]. Although described as common since the early series of cases, the prevalence of OGDs varied greatly, ranging between 6% up to 70% [5-8]. These symptoms are characterized by partial (hyposmia and hypogeusia) or total (anosmia and ageusia) loss of the senses of smell and taste, respectively, and were mainly reported in the acute phase of the disease, either isolated, preceding, or associated with other symptoms such as fever, dry cough, or headache [6,9,10].

OGDs are considered among a multiple set of neurological manifestations of COVID-19, owing to the selective tropism of coronaviruses for neurons, using axons as transportation and propagation means. This neuro-invasiveness is explained by three main mechanisms including transneuronal spread, olfactory pathway, and hematogenous spread [11]. Further pathophysiological explanations suggest the role of angiotensin-converting enzyme 2 (ACE2) receptors, which are the entry receptors for the virus into the host.
cells given their strong binding affinity with the virus spike protein, and which are diffusely expressed in the oral cavity leading to gustative dysfunction [12,13]. Another mechanism involves systematic inflammation leading to deleterious effects on the central nervous system, which explains the multiple neurological symptoms [11]. Finally, olfactory dysfunction may also be explained by damage to the olfactory epithelium, which is commonly caused by the SARS-COV-2 virus as well as other viruses such as rhinovirus and parainfluenza virus [14].

The other characteristic of OGDs is their relatively long persistence after recovery from other symptoms, making them one of the most common long-term complications of COVID-19 [8]. This may result in significant inconvenience for the patients and may impact their quality of life.

In the present study, we estimated the prevalence of OGDs and analyzed their pattern and psychosocial impact. Such data would highlight the clinical significance of these symptoms and provide indications on specific measures to prevent their impact.

Materials And Methods

Design and setting
A cross-sectional study was conducted at Al-Noor Specialist Hospital between 1 September 2020 and 30 September 2021. The study protocol and questionnaire were reviewed and ethically approved by the institutional review board of the Ministry of Health, Makkah region.

The study involved adult individuals who were diagnosed with COVID-19 in any of the outpatient clinics, emergency wards, or hospitalization wards at Alnoor Specialist Hospital between 1 September 2020 through 30 September 2021. Eligibility applied for cases with diagnosis confirmation based on a positive polymerase chain reaction (PCR) test. Patients having no positive PCR test and those aged less than 18 years were excluded.

Sampling
To estimate the sample size, we used the WHO recommendations for the minimum sample size needed for a prevalence study. A previous meta-analysis showed that the prevalence of olfactory dysfunction in COVID-19 patients is 48%. In addition, according to the Ministry of Health (MOH) statistics, around 14,500 patients were confirmed with COVID-19 in Makkah from 1 September 2020 through 30 September 2021. Using a confidence interval of 95%, a standard deviation of 0.5, and a margin error of 5%, the required sample size is 194 participants to be representative of the study population.

Data collection
A semi-structured questionnaire was used to collect the study data, and was adapted from a previous study [15]. The questionnaire was divided into four parts to collect the following data: 1) baseline participant’s characteristics including demographic data (age, gender, and occupation) and medical history; 2) characterization of smell loss during COVID-19 infection (six items) including occurrence of anosmia, its level (partial or total), timing (before, concomitant with, or after the other symptoms), practices or treatment used to restore smell, recovery (partial, total, or no recovery), and symptom duration; 3) characterization of taste loss during COVID-19 infection including occurrence of ageusia, type of taste concerned (salty, sweet, etc.), timing (before, concomitant with, or after the other symptoms), practices or treatment used to restore smell, recovery (partial, total, or no recovery), and symptom duration; 4) psychological impact of olfactory and gustative dysfunctions (OGD) using a four-point Likert-type agreement scale (1=disagree, 2=somewhat disagree, 3=somewhat agree, and 4=agree) including six items exploring the multidimensional impact such as daily activity, job performance, and social life. The latter section enabled calculating an OGD impact score, which was computed as the sum of the item scores (range 6-24).

The questionnaire was redacted to the Arabic language and underwent face and content validity by a working group of four local, native Arabic-speaking healthcare professionals, including two consultant physicians and two medical residents. The consented version was pilot tested for clarity and suitability among a group of 10 participants who were not included in the parent study.

Procedure
The questionnaire was edited for an online survey using the SurveyMonkey platform (Momentive, San Mateo, California). The electronic link was sent to participants via WhatsApp.

Statistical methods
Statistical analysis was performed with the Statistical Package for Social Sciences version 21.0 for Windows (IBM Inc., Armonk, New York). Categorical variables are presented as frequency and percentage, while continuous variables are presented as mean ± standard deviation (SD). Factors associated with OGD impact were analyzed by comparing the mean (SD) OGD impact score between the demographic and baseline
medical history factors using an independent t-test or one-way analysis of variance (ANOVA) as applicable. A p-value of <0.05 was considered to reject the null hypothesis.

**Results**

**Baseline participant's characteristics**

One hundred and ninety-four confirmed COVID-19 patients were included. The majority were female (70.1%) and in the younger age categories, including <18 years (27.3%), 18-25 years (30.9%), and 25-34 years (15.5%). Students (29.9%), healthcare professions (17.5%), and education (13.9%) were the most frequent occupations. Only 20.6% of the participants declared having a chronic disease. Regarding attitudes toward the COVID-19 vaccine, 16.0% were not expecting to take the vaccine, and 32.5% were hesitating (Table 1).
| Parameter                        | Category      | Frequency | Percentage |
|---------------------------------|---------------|-----------|------------|
| **Age category (years)**        | <18           | 53        | 27.3       |
|                                 | 18-25         | 60        | 30.9       |
|                                 | 26-34         | 30        | 15.5       |
|                                 | 35-42         | 29        | 14.9       |
|                                 | 43-50         | 15        | 7.7        |
|                                 | >50           | 7         | 3.6        |
| **Gender**                      | Female        | 136       | 70.1       |
|                                 | Male          | 58        | 29.9       |
| **Occupation**                  | Student       | 58        | 29.9       |
|                                 | The medical section | 34    | 17.5       |
|                                 | Military sector | 10    | 5.2        |
|                                 | Education sector | 27    | 13.9       |
|                                 | Private sector | 26     | 13.4       |
|                                 | Retired       | 13        | 6.7        |
|                                 | Free business | 13        | 6.7        |
|                                 | Other         | 13        | 6.7        |
| **Chronic diseases**            | No            | 154       | 79.4       |
|                                 | Yes           | 40        | 20.6       |
|                                 | Nose and sinus allergies | 16   | 8.2        |
|                                 | Asthma and respiratory allergies | 16 | 8.2        |
|                                 | Diabetes      | 11        | 5.7        |
|                                 | High blood pressure | 12   | 6.2        |
|                                 | Heart disease | 1         | 0.5        |
|                                 | Chest allergy | 1         | 0.5        |
|                                 | Thyroid dysfunction | 2   | 1          |
| **COVID-19 vaccine expectation**| Yes, I expect to take the vaccine | 56   | 28.9       |
|                                 | No, I do not expect to take the vaccine | 31  | 16         |
|                                 | Already received the vaccine | 44 | 22.7       |
|                                 | I haven't decided yet | 63  | 32.5       |

**TABLE 1: Demographic characteristics and medical history (N=194)**

**Patterns of smell loss during COVID-19**

The prevalence of olfactory dysfunctions during COVID-19 infection was 97.4%, of which 25.8% occurred at the start of the infection, 71.6% after the acute phase, and 82.0% experienced a complete loss of smell. Eighty-six (44.3%) participants declared having attempted to restore their sense of smell using medications such as corticosteroids nasal spray (10.3%), salt water (23.7%), or vitamins (33.5%). On the day of the survey, 36.1% had fully and 54.6% had partially restored their smell, while 6.7% had no recovery. Restoration time was less than three weeks in 55.1%, less than one month in 70.6%, and took longer than one month in 14.4% of the cases (Table 2).
### Table 2: Patterns of smell loss during COVID-19 (N=19)

| Parameter                                                                 | Category                                       | N   | %    |
|---------------------------------------------------------------------------|-----------------------------------------------|-----|------|
| Any change in sense of smell during COVID-19 infection?                   | No loss or weakness of the sense of smell     | 5   | 2.6  |
|                                                                           | Yes, before infection                          | 50  | 25.8 |
|                                                                           | Yes, after infection                           | 139 | 71.6 |
|                                                                           | Before any other symptoms appear               | 56  | 28.9 |
| Was the change or loss of the sense of smell the first sign of the COVID-19 infection? | In conjunction with COVID-19 symptoms         | 81  | 41.8 |
|                                                                           | After other symptoms appeared                  | 57  | 29.4 |
| Level of smell loss                                                       | Full                                           | 159 | 82.0 |
|                                                                           | Partial                                        | 30  | 15.5 |
|                                                                           | Not applicable (no smell loss)                 | 5   | 2.6  |
| Treatments or practices used to restore the sense of smell                | None                                           | 108 | 55.7 |
|                                                                           | Yes                                            | 86  | 44.3 |
|                                                                           | Cortisone nasal spray                          | 20  | 10.3 |
|                                                                           | Saltwater                                      | 46  | 23.7 |
|                                                                           | Smell recovery exercises                       | 35  | 18.0 |
|                                                                           | Vitamins                                       | 65  | 33.5 |
|                                                                           | Decongestants                                  | 11  | 5.7  |
| Smell restoration                                                         | Full                                           | 70  | 36.1 |
|                                                                           | Partial                                        | 106 | 54.6 |
|                                                                           | No recovery                                    | 13  | 6.7  |
|                                                                           | Not applicable (no smell loss)                 | 5   | 2.6  |
| Duration of smell loss to recovery                                        | 1-11 days                                      | 46  | 23.7 |
|                                                                           | 12-21 days                                     | 61  | 31.4 |
|                                                                           | 22-30 days                                     | 30  | 15.5 |
|                                                                           | >1-3 months                                    | 24  | 12.4 |
|                                                                           | 4-5 months                                     | 2   | 1.0  |
|                                                                           | >6 months                                      | 2   | 1.0  |
|                                                                           | I did not recover                              | 13  | 6.7  |
|                                                                           | I do not know                                  | 11  | 5.7  |
|                                                                           | Not applicable (no taste loss)                 | 5   | 2.6  |

#### Patterns of taste loss during COVID-19

The prevalence of gustative dysfunctions during COVID-19 infection was 94.8%, of which 24.7% occurred at the start of the infection, 70.1% after the acute phase, and 58.8% experienced a complete loss of taste. Further characterization of taste loss showed salty (9.3%), sweet (9.3%), and bitter (8.2%) tastes to be the most commonly affected. The majority of participants experienced taste restoration, which was full (22.7%) or partial (63.4%); however, 8.8% had not recovered at the time of the survey. Recovery time was less than three weeks in 55.7% of the cases, less than one month in 70.0%, and longer than one month in 17.5% (Table 3).
| Parameter                                                      | Category                              | N  | %      |
|---------------------------------------------------------------|---------------------------------------|----|--------|
| Any change in the sense of taste during the COVID-19 infection? | No loss or weakness of the sense of smell | 10 | 5.2    |
|                                                               | Yes, before infection                  | 48 | 24.7   |
|                                                               | Yes, after infection                   | 136| 70.1   |
|                                                               | Before any other symptoms appear       | 54 | 27.8   |
| Was the change or loss of the sense of smell the first sign of the COVID-19 infection? | In conjunction with COVID-19 symptoms | 76 | 39.2   |
|                                                               | After other symptoms appeared          | 54 | 27.8   |
|                                                               | I haven’t lost my sense of taste       | 10 | 5.2    |
|                                                               | None                                   | 122| 62.9   |
|                                                               | Yes                                    | 72 | 37.1   |
| Treatments or practices used to restore the sense of smell    | Cortisone pills                        | 4  | 2.1    |
|                                                               | Taste recovery exercises               | 8  | 4.1    |
|                                                               | Vitamins                               | 62 | 32.0   |
| Taste restoration                                             | Full                                   | 44 | 22.7   |
|                                                               | Partial                                | 123| 63.4   |
|                                                               | No recovery                            | 17 | 8.8    |
|                                                               | Not applicable (no taste loss)         | 10 | 5.2    |
| Duration of taste loss to recovery                           | 1-11 days                              | 51 | 26.3   |
|                                                               | 12-21 days                             | 57 | 29.4   |
|                                                               | 22-30 days                             | 20 | 10.3   |
|                                                               | >1-6 months                            | 22 | 11.3   |
|                                                               | >6 months                              | 12 | 6.2    |
|                                                               | I do not know                          | 22 | 11.3   |
|                                                               | Not applicable (no taste loss)         | 10 | 5.2    |

**TABLE 3: Patterns of taste loss during COVID-19 (N=194)**

**Psychosocial impact of olfactory and gustative dysfunctions**

The majority of the participants declared that OGD impacted their social life (78.4%), while 42.8% declared it had significantly affected their daily life (Table 4). The impact score was calculated, and the mean±SD score was 15.54±4.40 (range 6-24). The score was divided into three levels: weak (40, 20.6%), moderate (92, 47.4%), and high impact (62, 32.0%) (Table 4).
| Impact dimension                          | Agree | Somewhat agree | Somewhat disagree | Disagree | Agreement rate |
|------------------------------------------|-------|----------------|-------------------|----------|----------------|
|                                          | N %   | N %            | N %               | N %      |                |
| OGD had an effect on my daily activity   | 43    | 22.16          | 40                | 20.62    | 58             | 29.9       | 53             | 27.32       | 42.8%       |
| My job performance is affected by OGD    | 86    | 44.33          | 39                | 20.1     | 44             | 22.68      | 25             | 12.89       | 64.4%       |
| I feel depressed or anxious due to OGD   | 23    | 11.86          | 33                | 17.01    | 70             | 36.08      | 68             | 35.05       | 28.9%       |
| My social life was affected due to OGD   | 104   | 53.61          | 48                | 24.74    | 25             | 12.89      | 17             | 8.76        | 78.4%       |
| OGD impacted my appetite                 | 26    | 13.4           | 28                | 14.43    | 76             | 39.18      | 64             | 32.99       | 27.8%       |
| I’ve been afraid of losing my smell or   | 21    | 10.82          | 19                | 9.79     | 45             | 23.2       | 109            | 56.19       | 20.6%       |

**TABLE 4: Psychosocial impact of olfactory and gustative dysfunctions**

OGD: olfactory and gustative dysfunction

**Factors associated with the impact of olfactory and gustative dysfunctions**

The OGD impact score was significantly higher among the younger age group (p<0.005), females (p<0.001), and certain occupations, including students, free business, and retired individuals (p<0.001). No significant association of OGD impact was observed with past medical history (p>0.05) (Table 5).
| Factor                | Level | N  | Mean | SD  | Statistics (test) | p-value |
|-----------------------|-------|----|------|-----|-------------------|---------|
| **Age (Years)**       |       |    |      |     |                   |         |
| <18                   | 53    | 17.21 | 4.72 |    |                   |         |
| 18-25                 | 60    | 15.35 | 4    |    |                   |         |
| 26-34                 | 30    | 13.73 | 3.32 |    |                   |         |
| 35-42                 | 29    | 15.86 | 4.84 |    |                   |         |
| 43-50                 | 15    | 13.47 | 4.34 |    |                   |         |
| >50                   | 7     | 15.43 | 3.65 | 3.467 (t) | 0.005* |
| **Gender**            |       |    |      |     |                   |         |
| Female                | 136   | 16.23 | 4.5  |    |                   |         |
| Male                  | 58    | 13.93 | 3.72 | 3.422 (f) | 0.001* |
| **Occupation**        |       |    |      |     |                   |         |
| Student               | 58    | 16.93 | 4.46 |    |                   |         |
| The medical section   | 34    | 13.88 | 3.98 |    |                   |         |
| Military sector       | 10    | 15.9  | 2.85 |    |                   |         |
| Education sector      | 27    | 14.93 | 4.39 |    |                   |         |
| Private sector        | 26    | 14.96 | 3.56 |    |                   |         |
| Retired               | 13    | 17.46 | 4.12 |    |                   |         |
| Free business         | 13    | 17.46 | 4.67 |    |                   |         |
| Other                 | 13    | 12    | 4.44 | 3.966 (f) | <0.001* |
| **Nose and sinus allergy** | No       | 178 | 15.71 | 4.42 |                   |         |
|                       | Yes    | 16   | 13.69 | 3.75 | 1.770 (t) | 0.078  |
| **Asthma and respiratory allergy** | No       | 178 | 15.65 | 4.47 |                   |         |
|                       | Yes    | 16   | 14.31 | 3.4  | 1.168 (t) | 0.244  |
| **Diabetes**          | No     | 183  | 15.44 | 4.36 |                   |         |
|                       | Yes    | 11   | 17.18 | 4.96 | 1.138 (t) | 0.28   |
| **Hypertension**      | No     | 182  | 15.54 | 4.35 |                   |         |
|                       | Yes    | 12   | 15.5  | 5.25 | 0.028 (t) | 0.978  |

**TABLE 5: Factors associated with the impact of olfactory and gustative dysfunctions**

**Discussion**

The present study addressed the clinical significance of OGD in COVID-19 by estimating its prevalence, levels, patterns, and by assessing its perceived psychosocial impact. As high as 97.4% and 94.8% of the participants declared having experienced a certain level of olfactory and gustative dysfunction, respectively. In a majority of these cases, the dysfunction occurred after the acute phase of the disease and persisted less than one month after onset. Social life, job performance, and daily life activities were the most frequently impacted dimensions, and 32% of the participants were deemed to have experienced a high psychosocial impact. Younger participants, females, and certain job categories were significantly more impacted than their counterparts.

There is great variability in the figures of OGD across the studies, reaching up to 74% [3-8,16]. Despite this discrepancy, both anosmia and ageusia were consistently defined as typical clinical features for COVID-19 infection and attracted much attention. Early data from Wuhan reported hypogeusia and hyposmia as the most frequent peripheral neurological symptoms of COVID-19; however, the reported prevalence was less than 6% [17]. An interesting study by Nocini et al. showed a substantial increase in the weekly Google trends scores for the search terms ‘ageusia’ and ‘anosmia’ between the pre-COVID to the COVID-19 period [18]. Nevertheless, findings from the present study are relatively high compared with the literature, concerning almost 100% of the participants. This high prevalence may be due to the recentness of our study influencing...
the awareness of people about OGD symptoms and consequently increasing their related subjective perception. Other explanations for the variability in the prevalence involve differences in the neurological tropism between the different SARS-COV-2 strains, notably differences in the structure of the spike protein, which result in variable cellular and molecular interplay in the olfactory and gustative epithelia [19].

On the other hand, anosmia and dysgeusia are often associated. A study that estimated the prevalence of anosmia among COVID-19 patients found that dysgeusia was present among 85% of patients with anosmia, and the prevalence of anosmia was 47% [20]. In another cohort, both hyposmia and dysgeusia developed in 33% of the COVID-19 patients, and the two symptoms were concomitantly reported in 27% of the cases (representing 82% of agreement) [21]. This suggests that anosmia and dysgeusia share common pathophysiological mechanisms and or the presence of individual susceptibility to both symptoms.

The duration of both anosmia and dysgeusia was less than three weeks in a majority of the cases in the present study. This is consistent with a study showing a mean anosmia duration of nine days, for a confidence interval 1–21 days. The same study showed that anosmia occurred more than four days, on average, after the disease onset and thus was never the first or second symptom [20]. In another multicenter European study, anosmia developed before the other symptoms in only 12% of the cases [22]. This is consistent with our data showing that approximately 72% of the patient developed anosmia after the acute phase of the disease. However, the timing of OGD onset, by reference to other symptoms, varies greatly in the literature [22,23]. This variability may be explained by the detectability of the symptom, which depends on its severity and the patient’s perception, besides eventual pathophysiological mechanisms. On the other hand, the proportion of patients who experience long-term persistence of OGD should not be disregarded. A study showed that as high as 28% and 35% of the cases continued to experience OGD after recovery from COVID-19 [16].

The majority of the participants in the present study declared having used various medications to treat OGDs. Among the most common methods used include vitamins, saltwater (for anosmia), and smell and taste recovery exercise, besides local or systemic corticosteroids. However, the study has not documented whether these methods were recommended or prescribed by a physician or were taken as self-treatment. This is consistent with observations by Lechien et al., who showed that saline irrigation was one of the most frequent methods used to treat OGD, followed by local and oral corticosteroids [22]. The efficacy of corticosteroids in anosmia and ageusia was not evidenced in clinical trials and is, therefore, not recommended [24]. Regarding smell exercise, it consists of a simple and safe form of sensory training that has shown efficacy in restoring smell after post-traumatic and post-infectious olfactory dysfunction [25,26].

The high prevalence, relative duration, and inconvenience of OGD have raised concerns about their impact on individuals’ quality of life and psychosocial wellbeing. The present study showed that OGD was frequently associated with a perceived impact on social life, job performance, and daily life activity. There is overwhelming evidence about the COVID-19 impact on psychological and social wellbeing, showing a range of disorders such as anxiety, depression, and post-traumatic stress syndrome, along with social and financial hardships. Such an impact was multifactorial and concerned all age and social and professional categories of the population [27–29]. Nevertheless, not many studies investigated the specific psychosocial impact of OGD during the pandemic. Interestingly, a study involving 15,821 COVID-19 patients demonstrated a significant association between sensory dysfunctions, including anosmia and ageusia, with an increased risk of developing depression and suicidal ideation, which may persist in the long term [30]. Although this may concord with our findings, establishing the causal relationship of OGD with psychological and social impact requires further evidence. It remains, however, necessary to consider these symptoms, particularly in the case of long-term persistence, as these may alter the quality of life.

**Limitations**

The present study is limited by the cross-sectional design and the self-reported methodology, which entails a high risk of information bias, notably in determining the chronology and appraising the authenticity and severity of the symptoms.

**Conclusions**

Olfactory and gustative dysfunctions are highly frequent in the present cohort of COVID-19 patients, appear more frequently after the other symptoms, and persist for less than one month in a majority of the cases. They are described to be relatively severe and have frequent psychosocial impacts, notably in females and the younger age category. Further research and clinical trials are warranted to explore their pathophysiology and best treatment options, along with preventing their long-term persistence and impact on individuals’ wellbeing.

**Additional Information**

**Disclosures**

**Human subjects:** Consent was obtained or waived by all participants in this study. The Institutional Review Board of the Ministry of Health, Makkah region issued approval H-02-K-076–1021–588. This is to inform you
References

1. Macera M, De Angelis G, Sagnelli C, Coppola N, Vanvitelli Covid-Group: Clinical presentation of COVID-19: case series and review of the literature. Int J Environ Res Public Health. 2020, 17:5062. 10.3390/ijerph17145062

2. Abobaker A, Raba AA, Alzwi A: Extrapulmonary and atypical clinical presentations of COVID-19. J Med Virol. 2020, 92:2458-64. 10.1002/jmv.26157

3. Vaira LA, Salzano G, Deiana G, De Riu G: Anosmia and ageusia: common findings in COVID-19 patients. Laryngoscope. 2020, 130:1787. 10.1002/lary.28692

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 Otalaryngol Head Neck Surg. 2020, 1-7. Accessed: August 2020. 10.1007/s12070-020-02064-9

5. Rocha-Filho PA, Magalhães JE: Headache associated with COVID-19: frequency, characteristics and association with anosmia and ageusia. Cephalalgia. 2020, 40:1445-51. 10.1111/ceph.14067

6. Lee Y, Min P, Lee S, Kim SW: Prevalence and duration of acute loss of smell or taste in COVID-19 patients. J Korean Med Sci. 2020, 35:e174. 10.3346/jkms.2020.35.e174

7. Subaraki AA, Albaiai GT, Sibyani AK, Alhulayfi RM, Almasi A, Almaski HS: Prevalence of anosmia among COVID-19 patients in Taif City, Kingdom of Saudi Arabia. Saudi Med J. 2021, 42:38-43. 10.15573/smj.2021.1.25588

8. Moraschini V, Reis D, Sacco R, Calasans-Maia MD: Prevalence of anosmia and ageusia symptoms among long-term effects of COVID-19. Oral Dis. 2022, 28:2533-7. 10.1111/odi.15919

9. Kandakure VT, Valvi HR, Khokle P, More MS, Chouhan R: Prevalence and recovery from newly onset anosmia and ageusia in Covid 19 patients at our tertiary care centre. Indian J Otalaryngol Head Neck Surg. 2021, 1-8. 10.1007/s12070-021-02546-w

10. Mak PQ, Chung KS, Wong JS, Shek CC, Kwan MY: Anosmia and ageusia: not an uncommon presentation of COVID-19 infection in children and adolescents. Pediatr Infect Dis J. 2020, 39:e199-200. 10.1097/INF.0000000000002718

11. Johansson A, Mohamed MS, Moulin TC, Schiöth HB: Neurological manifestations of COVID-19: a comprehensive literature review and discussion of mechanisms. J Neurolimmunol. 2021, 358:57668. 10.1016/j.neuroim.2021.57558

12. Vaira LA, Salzano G, Fois AG, Piombino P, De Riu G: Potential pathogenesis of ageusia and anosmia in COVID-19 patients. Int Forum Allergy Rhinol. 2020, 10:1103-4. 10.1002/air.22595

13. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS: Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med. 2020, 46:586-90. 10.1007/s00134-020-05895-9

14. Dicpinigaitis PV: Post-viral anosmia (loss of sensation of smell) did not begin with COVID-19!. Lung. 2021, 199:237-8. 10.1007/s00408-021-00448-4

15. Sayın İ, Yaşar KK, Yazıcı ZM: Taste and smell impairment in COVID-19: an AAO-HNS anosmia reporting tool-based comparative study. Otalaryngol Head Neck Surg. 2020, 163:473-9. 10.1001/jama.2020.5985

16. Horvath L, Lim JW, Taylor JW, Saief T, Stuart R, Rimmer J, Michael P: Smell and taste loss in COVID-19 patients: assessment outcomes in a Victorian population. Acta Otolaryngol. 2021, 141:299-302. 10.1080/00016489.2020.1855266

17. Mao L, Jin H, Wang M, et al.: Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020, 77:683-90. 10.1001/jamanetw.2020.1127

18. Nocini R, Mattiuzzi C, Lippi G: Estimating the worldwide burden of COVID-19-related anosmia and ageusia. Oral Dis. 2022, 28:2623-5. 10.1111/odi.14322

19. Butowt R, von Bartheld CS: Anosmia in COVID-19: underlying mechanisms and assessment of an olfactory route to brain infection. Neuroscientist. 2021, 27:582-603. 10.1177/1073858420955005

20. Klopfenstein T, Kadiane-Oussou NJ, Toko L, Royer PY, Lepiller Q, Gendrin V, Zayet S: Features of anosmia in COVID-19. Med Mal Infect. 2020, 50:436-9. 10.1016/j.medmal.2020.04.006

21. Nouchi A, Chastang J, Miyara M, et al.: Prevalence of hyposmia and hypogeusia in 390 COVID-19 hospitalized patients and outpatients: a cross-sectional study. Eur J Clin Microbiol Infect Dis. 2021, 40:691-7. 10.1007/s10096-020-04056-7

22. 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, 277:2251-61. 10.1007/s00408-020-05965-1

23. Spinato G, Fabbri C, Polesel J, Cazzador D, Borsetto D, Hopkins C, Boscolo-Rizzo P: Alterations in smell or taste in mildly symptomatic outpatients with SARS-CoV-2 infection. JAMA. 2020, 325:2089-90. 10.1001/jama.2020.6771

24. 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, 42:103035. 10.1016/j.amjoto.2021.103035

25. Damm M, Pikart LK, Reimann H, et al.: Olfactory training is helpful in postinfectious olfactory loss: a case series and review of the literature. Int J Environ Res Public Health. 2020, 17:5062. 10.3390/ijerph17145062

Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.
26. Hummel T, Stupka G, Haehner A, Poletti SC: Olfactory training changes electrophysiological responses at the level of the olfactory epithelium. Rhinology. 2018, 56:330-5. 10.4195/Rhin17.165

27. Saladino V, Algeri D, Auriemma V: The psychological and social impact of Covid-19: new perspectives of well-being. Front Psychol. 2020, 11:577684. 10.3389/fpsyg.2020.577684

28. Ghosh R, Dubey MJ, Chatterjee S, Dubey S: Impact of COVID-19 on children: special focus on the psychosocial aspect. Minerva Pediatr. 2020, 72:226–35. 10.23736/S0026-4946.20.05887-9

29. Shimazu A, Nakata A, Nagata T, Arakawa Y, Kuroda S, Inamizu N, Yamamoto I: Psychosocial impact of COVID-19 for general workers. J Occup Health. 2020, 62:e12152. 10.1002/1348-9585.12152

30. Yom-Tov E, Lekkas D, Jacobson NC: Association of COVID19-induced anosmia and ageusia with depression and suicidal ideation. J Affect Disord Rep. 2021, 5:100156. 10.1016/j.jadr.2021.100156