Incidence of Olfactory Dysfunction in Patients with COVID-19 in a Tertiary Hospital in Saudi Arabia

Rayan Alfallaj, MBBS, Ghada AlSkait, MBBS, Nouf Alamari, MBBS, Lama Alfawzan, MBBS, Mohammed Abualgasem, MBBS, Naif H. Alotaibi, MD, Ibrahim Sumailly, MBBS, SB, Ibrahim Alarifi, MBBS, SB, and Saad Alsaleh, MBBS, FRCSC

Abstract

Background: Coronavirus disease (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2, a novel virus that emerged in China in December 2019. In many cases of COVID-19, olfactory dysfunction (OD) is the only symptom.

Objectives: This study aimed to examine the incidence of OD in patients with COVID-19 and identify an association between OD and COVID-19-related morbidity and admission.

Design: This was a cross-sectional study.

Methods: Real-time reverse transcription polymerase chain reaction-confirmed cases of COVID-19 from the Security Forces Hospital electronic registry from June 2020 to September 2020 were included in our study. Data on medical background, severity of the disease, and other related factors were collected through phone calls and electronic healthcare systems and analyzed to investigate OD in the participants.

Results: Of the participants, 68% had OD, with a mean recovery time of 18 days and a mean follow-up time of 129 days (76-211 days). OD was negatively correlated with admission and morbidity.

Conclusion: OD is a common presentation of COVID-19 and is more prevalent in mild cases of infection.

Keywords
olfactory dysfunction, smell disturbance, anosmia, taste, gustatory dysfunction, COVID-19, coronavirus

Introduction

Coronavirus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2, which is a novel virus that emerged in China in December 2019. Considerable morbidity and mortality rates have been attributed to COVID-19. The virus is a new strain of the coronavirus family that has become a major concern worldwide, threatening the global healthcare system, with over 2 million attributed deaths to date. Many clinical characteristics have been associated with this novel virus, ranging from asymptomatic cases to mild flu-like illnesses and life-threatening manifestations. The common symptoms include fever, fatigue, dry cough, anorexia, myalgia, and sputum production, with respiratory symptoms being the most life-threatening.

Many cases have been reported in which anosmia was the only symptom of COVID-19. Rapid detection and diagnosis of infected cases are crucial for preventing transmission. Real-time reverse transcription polymerase chain reaction (RT-PCR) remains the most efficient diagnostic test for COVID-19. Different hypotheses have been proposed for the mechanism of anosmia in COVID-19 infection involving inflammation, obstruction of the olfactory cleft, or injury to sustentacular supporting cells in the olfactory epithelium.

In a study conducted in Korea, Lee et al have reported...
that 15% of people with asymptomatic to mild cases of COVID-19 infection had anosmia or ageusia, with a higher prevalence among women and younger individuals, and a median recovery time of 7 days. Another multicenter European study has reported a prevalence of olfactory dysfunction (OD) of approximately 85.6% among mild to moderate cases of infection in terms of anosmia or hyposmia, with 88% also exhibiting gustatory disturbance.8

In terms of recovery, a study has revealed that those infected with COVID-19 who developed sudden hyposmia and anosmia had longer recovery times and lower recovery rates than those with other causes of OD. Moreover, patients with COVID-19 who developed sudden anosmia had a longer recovery time than those with hyposmia, with a time to full recovery of 10-21 days among positive cases.9 Regarding the association between smell and taste disorders and intensive care unit (ICU) hospitalization, Sayn et al10 have reported that those who experienced ICU hospitalization had a lower incidence of olfactory and gustatory disorders. Olfactory training has been identified as the only effective treatment for persistent OD in patients with COVID-19, with no reported adverse effects. Meanwhile, the benefits of other treatments, such as intranasal steroid administration, remain controversial.11 In this study, we present cases of OD and gustatory disorders due to COVID-19 considering their medical status, demographics, recovery time, effect of treatment, and other associated factors.

Methodology

This analytical cross-sectional study was conducted in a tertiary care center at the Security Forces Hospital (SFH) in Riyadh, Saudi Arabia. We included only adult (aged 14-87 years) RT-PCR-confirmed COVID-19 cases who presented to the swabbing clinic between June 2020 and September 2020. We excluded pediatric patients (age <14 years), non-Arabic or non-English speakers, those who died, and those with any previous history of olfactory disorders or other neurologic disorders. This research was approved by the Institutional Review Board (IRB) of the research committee of the SFH program research number: 20-455-67 and IRB registration number: H-01-R-069, and verbal consent was obtained from research participants or their representatives during telephone calls with an explanation of their right to withdraw from the study. Participants were recruited from a COVID case registry after applying inclusion and exclusion criteria. The data collected in this study were analyzed for epidemiological profiles, comorbidities, and presence of hyposmia or anosmia after COVID-19 infection with subjective scoring, using a visual analog scale for each symptom, with the following associated symptoms: nasal obstruction; rhinorrhea; sneezing; sore throat; and taste dysfunction for all taste types, including sourness, bitterness, saltiness, and sweetness. Other causes of OD, such as chronic rhinosinusitis, treatment provided including nasal steroids and nasal irrigation, hospital stay including ICU stay, recovery time, and olfactory training trials, were investigated. Electronic patient records from the SFH digital health system were used for data collection. Demographic information and prevalence of symptoms are described as percentages. The Raosoft sample size calculator (Raosoft Inc., www.raosoft.com) was used to compute the appropriate sample size for this study, which revealed that 385 participants would be required to achieve a 95% confidence interval and a 5% margin of error. A simple random sampling technique was used in this study.

Statistical Analysis

The Statistical Package for Social Sciences software program version 22 was used for data analysis. Descriptive statistics, based on simple tabulations, frequencies, and percentages, were used. The distribution of continuous variables was assessed using the Shapiro-Wilk or Kolmogorov-Smirnov test. For normally distributed variables, means with standard deviations were calculated, and categorical variables are described as frequencies and percentages. To assess the differences in demographics, we compared the means and medians of continuous variables using the Student’s t-test and Mann-Whitney U-test. Differences in the percentages of categorical variables between the 2 groups were assessed using the chi-square test. Logistic regression models were used to assess associations. Statistical significance was set at p < .05.

Results

In total, 3103 participants were enrolled in the study. After applying the exclusion criteria, 1255 out of the 3103 participants with RT-PCR-confirmed COVID-19 infection were included in the study, with a mean age of 38.26 (SD = 13 years, ranging = 14-87 years). Additionally, 69 deceased cases were excluded from the study, with a 2.2% mortality rate. Of the included participants, 61% were men. The majority of participants (69%) had a medical history free of comorbidities, and 84% were nonsmokers (Table 1). Additionally, 68% of the participants presented with OD; of the patients with OD, 86% fully recovered from OD, with a mean time of recovery of 18 days and a mean follow-up time of 129 days (Figure 1). Regarding the presence of other associated symptoms, 78% with OD had taste dysfunction (p < .05), and 38% with OD had nasal obstruction and rhinorrhea (p < .05; Table 1). Of the patients, 84% of patients experienced anosmia (score 10) but fully recovered from OD (p < .05). A low percentage of patients with OD who received antibiotics (20%) and nasal steroids (6.7%) demonstrated no significant association between using such medications and recovery from OD (p > .05) (Table 2). Moreover, 84% of participants had no history of hospital admission because of COVID-19, and only 2% of all participants were admitted to an ICU. By contrast, half of the patients with COVID-19 who were admitted to the hospital had OD (p < .05) (Table 2 and Figure 2). Female participants experienced OD more than
the male participants \((p < .05)\), while the rate of OD was higher among patients with comorbidities \((p < .05)\). Table 2 demonstrates the absence of any significant association between the presence of OD in COVID-19 patients and smoking history \((p > .05)\). In terms of recovery, male participants with complete OD had a more complete recovery than female participants with a significant difference \((p = .000)\). The majority of our participants were medically free; hence, comorbidities did not indicate any significant difference in the course of recovery. Specifically, smoking, hospital admission, and steroid and antibiotic use did not demonstrate any significant differences. Meanwhile, age significantly affected olfaction and improvement. The mean age of those with complete olfactory loss was 36.5 years, whereas that of those with no olfactory loss was 40.7 years \((p = .000)\). However, the improvement was better in the younger group, in which the mean age of those with complete recovery was 37 years and that of those with no recovery was 47.4 years \((p = .000; \text{Table 2})\).

### Discussion

Here, 68% of the patients with COVID-19 had OD, with a great majority presenting with anosmia after COVID-19 infection, similar to a regional prevalence of 72% reported by Alrouqi et al.\(^{12}\) We also addressed the incidence of taste dysfunction among our participants, which was 57%. The international incidence of OD is 85.6%, with 88.8% for taste dysfunction in Europe and 15% in Korea.\(^{8}\) A population survey of over 10,000 Iranian participants within 4 weeks of the COVID-19 pandemic revealed that 76.24% of the participants suffered from sudden OD with persistent anosmia in 60% of the affected individuals.\(^{13}\) Another study was
| Degree of Olfactory dysfunction | Recovery of OD | Age | Gender | Presence of comorbid conditions | Smoking | Admission to hospital | Steroids | Antibiotics |
|--------------------------------|----------------|-----|--------|--------------------------------|---------|----------------------|----------|-------------|
| Complete: 629                    | Partial: 90 [14.3%] | Mean: 36.26 | Male: 30 [33.3%] | No: 62 [68.8%] | No: 81 [90%] | No: 81 [90%] | No: 80 [89%] | No: 71 [79%] |
|                                |                | SD: 13.482 | Female: 60 | Yes: 28 [31.2%] | Yes: 9 [10%] | Yes: 9 [10%] | Yes: 10 [11%] | Yes: 19 [21%] |
|                                | Complete: 532 [84.5%] | Mean: 36.38 | Male: 314 [59%] | No: 377 [71%] | No: 48 [10%] | No: 468 [88%] | No: 501 [10%] | No: 422 |
|                                |                | SD: 12.708 | Female: 218 [41%] | Yes: 155 [29%] | Yes: 84 [29%] | Yes: 64 [22%] | Yes: 31 [6%] | Yes: 110 |
|                                | No recovery: 7 [1.1%] | Mean: 49.86 | Male: 2 [28.6%] | No: 5 [71%] | No: 7 [100%] | No: 5 [71%] | No: 7 [100%] | No: 5 [71%] |
|                                |                | SD: 8.327 | Female: 5 | Yes: 2 [29%] | Yes: 0 [0%] | Yes: 2 [29%] | Yes: 0 [0%] | Yes: 2 [29%] |

| P-value | .000 | .000 | .348 | .107 | .338 | .134 | .938 |

| Degree of Olfactory dysfunction | Recovery of OD | Age | Gender | Presence of comorbid conditions | Smoking | Admission to hospital | Steroids | Antibiotics |
|--------------------------------|----------------|-----|--------|--------------------------------|---------|----------------------|----------|-------------|
| Partial: 220                    | Partial: 22 [10%] | Mean: 38.59 | Male: 11 [50%] | No: 14 [63.3%] | No: 20 [91%] | No: 17 [77%] | No: 20 [91%] | No: 17 [77%] |
|                                |                | SD: 11.1 | Female: 11 | Yes: 8 [36.7%] | Yes: 2 [9%] | Yes: 5 [22%] | Yes: 2 [9%] | Yes: 5 [22%] |
|                                | Complete: 194 [88%] | Mean: 38.53 | Male: 140 | No: 159 | No: 159 | No: 159 | No: 159 | No: 159 |
|                                |                | SD: 12.784 | Female: 54 | Yes: 54 [28%] | Yes: 35 [18%] | Yes: 32 [27%] | Yes: 14 [7%] | Yes: 35 [28%] |
|                                | No recovery: 3 [1.3%] | Mean: 41.67 | Male: 2 [66.7%] | No: 3 [100%] | Yes: 1 | No: 3 [100%] | No: 3 [100%] | No: 3 [100%] |
|                                |                | SD: 3.33 | Female: 1 | Yes: 0 [0%] | Yes: 33.4 | Yes: 0 [0%] | Yes: 0 [0%] | Yes: 0 [0%] |

| P-value | .000 | .167 | .037 | .602 | .712 | .936 | .754 |
which is consistent with the findings and ICU admission were higher in the non-OD group. Saussez et al believe that older patients, who represent the great majority of critical cases, report symptoms of anosmia less frequently because they tend to have preexisting anosmia. Regarding the reasons behind the presence of OD among patients with COVID-19, previous studies have assumed that olfactory cleft obstruction could be the only mechanism and that ACE2 could be the gateway for viral entry into the olfactory cleft. Our study supports these hypotheses, as two-thirds of our participants with OD had no nasal obstructions. The majority of patients with OD recover within 2 weeks of infection; however, persistent loss of smell has remained a current issue with olfactory training as the only proven treatment thus far. Longer duration of infection, old age, and diabetes mellitus are reportedly risk factors for persistent loss of smell. The use of oral steroids or intranasal corticosteroids (INCs) for persistent anosmia is controversial, and evidence of their efficacy is limited. Nevertheless, authors have recommended using INCs with olfactory training, considering the safety of INCs. Some studies have reported a possible benefit of other medications such as caroverine, local injections of corticosteroids around the olfactory cleft, and alpha-lipoic acid in the management of post-COVID-19 persistent loss of smell. A recent randomized controlled trial in Italy has reported a possible improvement with the oral supplementation of palmitoylethanolamide and luteolin plus olfactory training. The main limitation of this study was its cross-sectional design; no long-term follow-up was performed for cases with persistent loss of smell. We recommend that future studies investigate the role of vaccination against COVID-19 in preventing OD or taste dysfunction, as none of our participants had been vaccinated during the study period.

**Conclusion**

The incidence of OD in patients with COVID-19 was 68%, with a full recovery rate of 86% during a mean period of 18 days. Among the patients, the prevalence of taste dysfunction was 57%. To the best of our knowledge, this is the only study to document the incidence of COVID-19-related taste dysfunction in the region.

**Declarations**

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**Author contribution(s)**

Rayan Alfallaj: Conceptualization; Data curation; Formal analysis; Methodology; Validation; Visualization; Writing – original draft; Writing – review & editing.

Ghada AlSkait: Methodology; Writing – original draft.

Naif Alamari: Methodology; Writing – original draft.

Lama AlFawzan: Methodology; Writing – original draft.

Mohammed Abualgasem: Methodology; Writing – original draft.

Naif H. Alotaibi: Conceptualization; Methodology; Visualization; Writing – original draft.

Ibrahim Sumaily: Conceptualization; Data curation; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Ibrahim Alarifi: Conceptualization; Data curation; Methodology; Writing – original draft; Writing – review & editing.

Saad Alsaleh: Conceptualization; Data curation; Formal analysis; Methodology; Project administration; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

**Ethics Approval and Consent to Participate**

This research was approved by the IRB of the research committee of the SFH program research number: 20-455-67 and IRB registration number: H-01-R-069, and verbal consent was obtained from...
research participants or their representatives during telephone calls with an explanation of their right to withdraw from the study.

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**ORCID iDs**

Rayan Alfallaj https://orcid.org/0000-0003-3230-1636
Nouf Alamari https://orcid.org/0000-0001-9685-9909
Ibrahim Sumaily https://orcid.org/0000-0003-2740-8682
Saad Alsaleh https://orcid.org/0000-0002-1236-2098

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