Original Article

# Are olfactory and gustatory symptoms useful at predicting disease severity markers in COVID-19 infection?


## ABSTRACT

**Context:** The relationship between olfactory and gustatory dysfunction (OGD) and COVID-19 infection severity is still unclear.

**Aim:** To investigate the correlation between OGD in COVID-19-infected individuals and RT-PCR results, chest CT scan abnormality, lymphocyte counts, hospital admission units, age, body temperature, and blood oxygen saturation.

**Setting and Design:** Case–control study.

**Materials and Methods:** The sample was composed of laboratory and chest X-ray confirmed COVID-19-infected patients from four hospitals. The patients were divided into case and control groups based on the presence of OGD symptoms. The predictor variable was OGD. The outcome variable was gender, hospital admission unit, chest CT scan abnormality, PCR, lymphocyte counts, age, body temperature, and blood oxygen saturation.

**Statistical Analysis Used:** Bivariate statistics were computed and the *P* value was set at 0.05.

**Results:** The sample consisted of 189 patients. Smell and taste disorders were found in 31.7% and 24.3% of patients, respectively. OGD was significantly correlated with positive PCR results ($P < 0.001$) and general unit admission ($P < 0.05$) during hospitalization. Additionally, patients with OGD had significantly lower mean age ($P < 0.001$), higher body temperature ($P < 0.01$), and blood oxygen saturation ($P < 0.01$). However, OGD was not correlated with gender, chest CT scan abnormality, or lymphocyte counts ($P > 0.05$).

**Conclusions:** OGD symptoms can be used to detect COVID-19-infected patients. OGD can be used to predict less severe disease mainly by its correlation with the less amount of hospital care, more negative PCR results, higher body temperature, and higher blood oxygen saturation.


**Keywords:** Ageusia, anosmia, COVID-19, dysgeusia, dysosmia


**Mojgan Falaki, Saeed Abdi[1,2], Shervin Shafiei[3], Mohammadreza Moslemi[4], Behrad Rahbani Nobar[5], Reza Tabrizi[3], Meysam Mohammadikhah[3], Hamidreza Moslemi[3]**

Department of Internal Medicine, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, [1]Department of Adult Gastroenterology and Hepatology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, [2]Member of Gastroenterology and Liver Diseases Research Center Research Institute, Ayatollah Taleghani Hospital, Tehran, [3]Department of Oral and Maxillofacial Surgery, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, [4]Department of Internal Medicine, School of Medicine, Tabriz University of Medical Sciences, Tabriz, [5]Dentist, Private Practice, Tehran, Iran

**Address for correspondence:** Dr. Meysam Mohammadikhah, Department of Oral and Maxillofacial Surgery, School of Dentistry, Shahid Beheshti University of Medical Sciences, Daneshjou Blvd, Velenjak, Shahid Chamran Highway, Tehran 1983963113, Iran.
E-mail: shahreyar333@gmail.com


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## INTRODUCTION

The coronavirus disease (COVID-19) is the global pandemic caused by the severe acute respiratory syndrome coronavirus type 2. The total confirmed cases for this disease as of March 21, 2021 are 121,969,223 resulting in 2,694,094 deaths globally up to date.[1] Although vaccination has been commenced in numerous countries, approximately only 1.3% of the world population has been fully vaccinated.[2] Therefore, this pandemic is still ongoing, necessitating


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further investigation about the prevention, diagnosis, and treatment of this disease.

The COVID-19 infection is mainly characterized by general symptoms, including fever, fatigue, dyspnea, headache, nausea, vomiting, and diarrhea. However, the first symptoms that present with COVID-19 infection are ear, neck, and throat (ENT) symptoms, including cough, anosmia, gustatory dysfunction, nasal obstruction, sore throat, vertigo, rhinorrhea, and hearing loss.[3] The role of ENT manifestations, especially olfactory and gustatory dysfunctions (OGD), should not be overlooked as the patients can detect these symptoms to initiate self-isolation, as has been demonstrated in previous studies.[4-7] The prevalence of OGD in COVID-19-infected patients has been shown to be 22–68% and 20–44% for olfactory and gustatory taste disturbances, respectively.[3,8-11]

OGD may result from damage to the central nervous system, degeneration of epithelial cells of the nasal mucosa, inflammation of the affected areas, direct toxicity to taste buds, or the considerable inter-dependency of the olfactory and gustatory senses meaning that whenever one sense is affected, the other one is also probably affected.[6,12,13] Considering the proposed mechanisms, OGD may not result in complete loss of the senses but rather a spectrum extending from mild sensory distortion to complete loss of the senses.

Although the role of OGD as diagnostic symptoms for COVID-19 infection has been confirmed, the relationship between these symptoms and disease severity has not been thoroughly investigated. Mair *et al*.,[3] which had conducted a meta-analysis on this matter, concluded that ENT symptoms, including cough and anosmia, might predict severe disease in the affected individuals who may require subsequent hospitalization. However, the amount of care necessary for the patients is not yet clear. Disease severity can be evaluated by the use of clinical, laboratory, radiographic, and demographic characteristics. However, the relationship between ENT symptoms, especially OGD, and other disease severity markers is not known.[14] Investigation of such relationships can provide valuable insights into patient management in addition to prevention. Thus, this case–control study aimed to answer the following questions:

1. What is the prevalence of different types of OGD in COVID-19-infected patients?
2. Are there any gender differences regarding OGD in COVID-19-infected individuals?
3. Is there a correlation between OGD in COVID-19-infected individuals and RT-PCR results, chest CT scan abnormality, lymphocyte counts, hospital admission units, age, body temperature, and blood oxygen saturation?

## SUBJECTS AND METHODS

The case and the control groups were defined as patients with or without OGD, respectively. These patients are selected form these major covid centers in Tehran those admitted for hospitalization in Loghman Hakim, ShahidModarres, Ayatollah Taleghani, and ShahidLabbafinejad hospitals from January 20, 2021 to March 20, 2021. The inclusion criteria were patients with chest X-ray confirmed COVID-19 infection and more than 15 years of age. The exclusion criteria were a history of hard tissue graft reception, steroid use, extended-spectrum antibiotic use, recent trauma, recent intramuscular injection, systemic or chronic diseases, or use of drugs that could have caused myositis, e.g., statins in the past 3 months. Patients with appropriate criteria had to willingly sign an informed consent form to be enrolled in the study. The patients bore no additional cost on enrollment in the study. Ethical Clearance was obtained from Shahid Beheshti University of Medical Sciences Institutional Ethical Committee with Ref no IR.SBMU.MSP.REC.1399.586 dated January 12th 2021 and this study was performed according to the principles outlined in the World's Medical Association's Declaration of Helsinki on experimentation involving human subjects, as revised in 2000.

On enrollment, the patients were clinically examined, and the following data were recorded: Demographic information, age, gender, medication use, signs including fever, respiratory distress, purulent or bloody sputum, dyspnea, and history of other illnesses such as cancer, gastrointestinal, renal, and hepatic diseases. Furthermore, the hospital admission unit, lymphocyte count, severity of chest CT-scan abnormality, and blood oxygen saturation were recorded for each patient. Additionally, OGD, respiratory symptoms, and the time of initial onset of symptoms were also recorded.

### Statistical analysis

The statistical analyses were performed using SPSS version 23 (SPSS Inc., IL, USA). The frequency and proportion of OGD presentations were calculated among the patients. Chi-square test was used to compare the distribution of qualitative variables among different groups. Regarding quantitative variables, Shapiro–Wilk test was used to determine the normal distribution of the data. Based on the normality of data distribution, appropriate statistical measures were used to compare quantitative variables' data distribution. A *P* value of less than 0.05 was considered statistically significant.

## RESULTS

In this case–control study, 189 patients, including 70 cases and 119 controls, were enrolled to determine the relationship between OGD and other COVID-19 variables. The type and intensity of OGD and the time of onset of OGD are presented in Table 1. Table 2 shows the correlations between OGD and gender, hospital admission unit, chest CT scan abnormality, PCR results, and lymphocyte counts. Other than PCR ($P < 0.001$) and hospital admission unit ($P < 0.05$), OGD was not correlated with any of the examined variables. Furthermore, the characteristics of patients with or without OGD regarding quantitative variables, namely, age, body temperature, and blood oxygen saturation, are presented in Table 3. Shapiro–Wilk test results revealed that the aforementioned variables did not have normally distributed data ($P < 0.05$). Thus, independent samples Mann–Whitney U test was used to examine the correlation between OGD and the mentioned variables. OGD was found to be significantly associated with lower patient age ($P < 0.001$), higher body temperature ($P < 0.01$), and blood oxygen saturation ($P < 0.01$).

**Table 1: Type, intensity, and time of onset of OGD**

| Variables | Result | Frequency | Percentage |
|---|---|---|---|
| Sensory involvement | Negative | 119 | 63.0 |
| | Positive | 70 | 37.0 |
| Olfactory involvement | Negative | 129 | 68.3 |
| | Positive | 60 | 31.7 |
| Anosmia | Negative | 133 | 70.4 |
| | Positive | 56 | 29.6 |
| Dysosmia | Negative | 185 | 97.9 |
| | Positive | 4 | 2.1 |
| Taste involvement | Negative | 143 | 75.7 |
| | Positive | 46 | 24.3 |
| Ageusia | Negative | 153 | 81.0 |
| | Positive | 36 | 19.0 |
| Dysgeusia | Negative | 179 | 94.7 |
| | Positive | 10 | 5.3 |
| Simultaneous olfactory and gustatory dysfunction | Negative | 153 | 81.0 |
| | Positive | 36 | 19.0 |
| Onset of OGD compared to admission time | Before admission | 24 | 34.3 |
| | Simultaneous with admission | 24 | 34.3 |
| | After admission | 22 | 31.4 |

OGD=olfactory or gustatory dysfunction

## DISCUSSION

In this case–control study, we aimed to investigate the correlation between OGD in COVID-19-infected patients and disease severity. Olfactory and gustatory involvement was found in 31.7% and 24.3% of patients, respectively. OGD was significantly correlated with positive PCR results and general unit admission during hospitalization. Additionally, patients with OGD had significantly lower mean age and higher body temperature and blood oxygen saturation. However, it was not correlated with gender, chest CT scan abnormality, or lymphocyte counts.

The significant correlation of OGD and positive PCR results is in line with previous studies concluding that anosmia and dysgeusia can be used to detect COVID-19 infection.[4-7] Additionally, patients with OGD were significantly less admitted to the intensive care unit, which may indicate less severe disease.[15] These findings are also consistent with other results of our study, mainly lower age and higher blood oxygen saturation of COVID-19 patients with OGD, which are important markers of disease severity.[16] The less severe disease may be because of different strains of viruses that the patients had contracted.[7] These dissimilar strains might have different pathogenicities concerning different organs. Thus, those strains that cause ENT symptoms such as OGD might have a lesser affinity for other vital organs, reducing the need for intensive care. The lesser need for intensive

**Table 2: Correlations between OGD and qualitative variables**

| Variables | Type | Sensory involvement | | Total | Value | df | *P* |
|---|---|---|---|---|---|---|---|
| | | No | Yes | | | | |
| Gender | Female | 46 | 36 | 82 | 2.928 | 1 | 0.87 |
| | Male | 73 | 34 | 107 | | | |
| Hospital admission unit | General unit | 62 | 48 | 110 | 4.915 | 1 | 0.027 |
| | Intensive care unit | 57 | 22 | 79 | | | |
| Chest CT scan abnormality | Moderate | 21 | 14 | 35 | 0.162 | 1 | 0.688 |
| | Severe | 98 | 56 | 154 | | | |
| PCR | Negative | 40 | 6 | 46 | 8.569 | 1 | 0.000 |
| | Positive | 78 | 64 | 143 | | | |
| Lymphocyte count | Normal | 71 | 40 | 111 | 0.625 | 2 | 0.732 |
| | Lymphocytopenia | 44 | 26 | 70 | | | |
| | Lymphocytosis | 4 | 4 | 8 | | | |

OGD=olfactory or gustatory dysfunction

**Table 3: Correlations between OGD and quantitative variables**

| OGD (*n*) | Variables | Minimum | Maximum | Mean | Standard deviation |
|---|---|---|---|---|---|
| Negative (119) | Age | 21 | 96 | 63.65 | 18.229 |
| | Body temperature | 35.50 | 39.70 | 37.0487 | 0.71103 |
| | Blood oxygen Saturation (%) | 60.00 | 98.00 | 88.0504 | 7.56536 |
| Positive (70) | Age | 26 | 94 | 52.57 | 16.107 |
| | Body temperature | 36.00 | 38.80 | 37.4000 | 0.71181 |
| | Blood oxygen Saturation (%) | 70.00 | 98.00 | 91.0857 | 6.28489 |

OGD=olfactory or gustatory dysfunction

care is further affirmed by the relatively higher blood oxygen saturation and lower age of patients with OGD.

Regarding gender differences, no significant difference was observed concerning the patients' gender, which contradicts previous studies' results.[7,12,17] Although we had used questionnaires to inquire about OGD, all patients were requested to complete the whole form. Thus, reasons related to gender differences in adherence to and completing the survey were not relatable to this study.[18] Furthermore, our results agree with Moein *et al*.[19] that had concluded that there is essentially no difference between genders regarding COVID-19 infection. Like Moein *et al*.,[19] our samples consisted more of men, which are in line with the population demographics of COVID-19.[20] Therefore, further studies with larger sample sizes are needed to clarify gender differences regarding OGD in COVID-19 infection.

Although lymphocyte counts,[16] especially lymphopenia,[21,22] have been used to predict disease severity, we found no significant correlation between OGD and either of the lymphocyte count results. However, lymphopenia was more common than lymphocytosis, which is in line with previous research.[3] Similarly, no correlation was either present between OGD and chest CT scan abnormalities. However, the disease severity prediction by the chest CT scan results is still debated.[3] Further studies are needed to determine the relationship between OGD and laboratory and radiographic diagnostic workups.

Thus, OGD can be used as a cost-effective tool to suspect COVID-19 infection and can refer patients for further diagnostic workup and predict disease severity. Inevitably, this study was not without limitations. The different strains of severe acute respiratory syndrome coronavirus type 2 were not detected in this study. Furthermore, treatment outcomes concerning olfactory and gustatory outcomes and the overall well-being of patients after treatment were not investigated.

Within this study's limitations, it can be concluded that OGD is correlated with disease severity clinical and laboratory markers, including hospital admission unit, PCR results, body temperature, and blood oxygen saturation. In patients with OGD symptoms, more hospital admission, more negative PCR results, higher body temperature, and higher blood oxygen saturation can be observed. However, further studies are needed to determine the relationship between OGD and other ENT symptoms with disease and treatment parameters.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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