

## Correlation of Clinical Factors and Loss of Taste and Smell in Patients with Coronavirus Disease 2019

### Abstract

**Objective:** The Covid-19 pandemic continues to threaten the whole world. Early diagnosis of patients is very important to prevent the spread of the virus. Sudden loss of taste and smell is a common early symptom in patients. Therefore, it is thought that revealing the pathogenesis of the symptom will help both in early diagnosis and in predicting the prognosis.

**Materials and Methods:** The age, gender, predominant symptoms during Covid, length of stay at home/hospital, and smoking status of patients who had Covid and had loss of taste and smell between July 2020 and December 2020 were evaluated retrospectively.

**Results:** Patients with loss of taste and smell were significantly younger than those who did not. The majority were female patients, non-smokers, and patients needing significantly less hospitalization and receiving treatment at home. Among the accompanying symptoms, GIS symptoms were also significantly more common in this group.

**Conclusion:** Loss of taste and smell is an important symptom in Covid-19 infection. Revealing the demographic and clinical characteristics associated with this symptom is valuable in terms of early diagnosis of the disease, predicting the prognosis and reducing the contagiousness.

**Key words:** Covid-19, smell disorder, taste disorder



### Introduction

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which first appeared in East Asia and spread rapidly worldwide, still threatens the whole world. The clinical manifestations of the disease can emerge over a broad spectrum ranging from asymptomatic to acute respiratory failure and severe organ failure. Most of the symptoms, such as fever, cough, fatigue, and myalgia, are nonspecific and are also seen in upper respiratory tract infections (URTI), especially influenza. In particular, for patients without fever, dyspnea, and specific radiological pulmonary findings, diagnosis and admission to a healthcare facility may be delayed.<sup>1</sup> In addition, since contact history cannot always be followed up precisely, diagnostic tests cannot be routinely performed on all individuals in a risk group.

Furthermore, there may not be sufficient number of diagnostic equipment if the number of cases is high. Recognizing the characteristic symptoms while diagnosing the disease and predicting its prognosis is vital for reducing contamination and early diagnosis. It is known that the target receptor of the virus in human tissues and, therefore, the entrance gate to the organism, is the angiotensin-converting enzyme-2 (ACE-2) protein.<sup>2</sup> Many different types of tissues that produce this protein have been identified. Lung type II alveolar cells, myocardial cells, renal tubule cells, gastrointestinal (GI) system absorption mucosa, and oral and nasal epithelial cells are among the most important tissue types.<sup>3</sup> Consequently, disorders of the related tissues are an expected result.

As stated in many studies, the development of loss of taste and smell without nasal discharge or obstruction is considered an early sign of the disease.<sup>4,5</sup> It is reported that this is most likely caused by direct damage to the taste and smell receptors by the virus.<sup>6</sup> Ear, Nose, and Throat specialists agree that loss of taste and/or smell when seen with one or

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**Cite this article as:** Resul AS, Öktem F. Correlation of Clinical Factors and Loss of Taste and Smell in Patients with Coronavirus Disease 2019. *ENT Updates*. 2021; 11(1): 41-45.

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Received: February 10, 2021  
Accepted: February 13, 2021

**Table 1. Demographic Information About the Patients**

**Descriptive Statistics**

	<b>n</b>	<b>Minimum</b>	<b>Maximum</b>	<b>Average</b>	<b>Std. Error</b>
Age	96	15,00	59,00	29,8750	11,36685
Rest period at home (days)	96	.00	8,00	4,3958	1,67633
Duration of hospital stay (days)	96	.00	7,00	.9375	2,10169

more of the other possible symptoms is strong evidence for the diagnosis of COVID-19, and many scientific communities have also published recommendations in this direction.<sup>7</sup> When the research on this subject is examined, an extensive prevalence of 5%-48% is related to symptoms.<sup>8</sup> Previous studies have reported that loss of taste and smell is more common in women, certain age groups<sup>8,9</sup>, nonhospitalized patients, and patients with lower C-reactive protein levels.<sup>9</sup> Further research is required to determine which demographic and/or clinical factors are generally related to this symptom and whether its presence can predict the prognosis of the disease.

In this study, in patients with COVID-19, loss of taste and smell was interpreted by examining the relationship between the patient's age and sex, smoking status, fever, fatigue, symptoms of URTI, and the duration of home rest and hospitalization. Therefore, this study could provide evidence about specific groups likely to have these symptoms and their possible effects on the duration of treatment/prognosis.

## Methods

This research was carried out by retrospectively examining patients with COVID-19 at Istanbul Yeni Yüzyıl University Medical Faculty and Bahat Hospital Otorhinolaryngology Polyclinic between July 2020 and December 2020. The control group was selected from patients who have had COVID-19 without loss of taste and smell. The study aimed to reveal the profile of the patient group with loss of taste and smell according to age, sex, predominant symptoms during COVID-19, length of stay at home and hospital, and smoking status.

Ethics committee approval was obtained from the Istanbul Yeni Yüzyıl University Science, Social and Non-Interventional Health Sciences Research Ethics Committee (2021/01-554).

## Results

Table 1 shows the clinical and demographic information of the participants. The participants were aged 15-59 years, with an average age of 29.87 years. The average rest period of the participants at home was 4.39 days, and the average hospitalization period was 0.93 day.

Table 2 shows the clinical and demographic findings of the participants. Loss of taste and smell was observed in 67.7% of the participants but not in the remaining 32.3%. In this study, the group of patients who reported a loss of taste and smell is referred to as the study group, and the group of patients who did not report the symptoms is referred to as the control group. 53.1% of the participants were women, and 46.9% were men. Regarding symptoms, 71.9% of the patients reported fever, 92.7% reported fatigue, 78.1% reported URTI, and 51% reported GI symptoms; 41.7% of the participants were smokers.

**Table 2. Demographic and Clinical Information About Patients**

	<b>n</b>	<b>%</b>
Groups	Taste-Smell loss (+) (Study group)	65 67.7
	Taste-Smell loss (-) (Control group)	31 32.3
Gender	Male	45 46.9
	Female	51 53.1
Symptoms: Fever	(-)	27 28.1
	(+)	69 71.9
Symptoms: Fatigue	(-)	7 7.3
	(+)	89 92.7
Symptoms: URTI	(-)	21 21.9
	(+)	75 78.1
Symptoms: GIS	(-)	47 49.0
	(+)	49 51.0
Smoking	(-)	56 58.3
	(+)	40 41.7

**Table 3. Relationship Between Control and Study Groups and Some Study Data**

	<b>Control Group</b>	<b>Study Group</b>	<b>Mann Whitney U</b>	<b>P</b>
Age	41.09 ± 8.82	24.52 ± 8.07	185.500	.002
Rest period at home (days)	3.95 ± 1.60	5.32 ± 1.44	533.500	.001
Duration of hospital stay (days)	2.44 ± .43	1.96 ± 2.82	702.00	.001
Test: Mann-Whitney U, P <0,05				

Table 3 shows the differences between the control and working groups. Accordingly, it is seen that the age, home rest, and hospitalization periods of the groups showed a statistically significant difference ( $P < 0.05$ ). The average age of the control group (41.09 years) was higher than that of the study group (24.52 years), and the home rest period of the control group (3.95 days) was less than that of the study group (5.32 days). It was also observed that the hospitalization of the control group (2.44 days) was more prolonged than that of the study group (1.96 days).

Table 4 shows the differences in the participants' demographic and clinical variables between the control and study groups. There was a significant difference between the groups in terms of fatigue, fever, URTI and GI symptoms, sex, and smoking status ( $P < 0.05$ ). The number of women (43) in the study group was

Table 4. Relationship between clinical variables of study and control groups

			Control Group	Study Group	
Gender	Male	N	23	22	.001*
		%	51.1%	48.9%	
	Female	N	8	43	
		%	15.7%	84.3%	
Symptoms: Fever	(-)	N	0	27	.00*
		%	0.0%	100.0%	
	(+)	N	31	38	
		%	44.9%	55.1%	
Symptoms: Fatigue	(-)	N	0	7	.05
		%	0.0%	100.0%	
	(+)	N	31	58	
		%	34.8%	65.2%	
Symptoms: URTI	(-)	N	0	21	.00*
		%	0.0%	100.0%	
	(+)	N	31	44	
		%	41.3%	58.7%	
Symptoms: GIS	(-)	N	25	22	.00*
		%	53.2%	46.8%	
	(+)	N	6	43	
		%	12.2%	87.8%	
Smoking	(-)	N	10	46	.00*
		%	17.9%	82.1%	
	(+)	N	21	19	
		%	52.5%	47.5%	

\*Statistically the difference is significant; N: number

higher than the number of men (22), while the number of women (8) in the control group was less than the number of men (23). The number of patients who had fever in the study group (38) was higher than those who did not (27). Similarly, the number of patients who had fever in the control group (31) was higher than those who did not (0). In the study group, the number of patients who experienced URTI symptoms (44) was higher than that of those who did not (21). Similarly, the number of patients who experienced URTI symptoms in the control group (31) was higher than those who did not (0). The number of patients who experienced GI symptoms (43) was higher than that of those who did not (22), while the number of patients who experienced GI symptoms in the control group (6) was less than those who did not (25). In the study group, the number of smokers (19) was less than non-smokers (46), while in the control group, the number of smokers (21) was higher than non-smokers (10).

## Discussion

In the COVID-19 pandemic, which has become a severe public health problem, obtaining accurate information about specific symptoms will lead to early diagnosis and limit the progress of these symptoms in a short time; therefore, it is valuable in terms of both early patient isolation and early intervention for the right patient. The clinical features of respiratory tract infections are important in the diagnosis and follow-up of the disease. Loss of

smell is reported in almost all COVID-19 and severe respiratory failure syndromes (SARS) cases; however, its prevalence in other infections, including viral infections, is much lower. In addition, this symptom is usually accompanied by nasal obstruction and discharge in other infections<sup>10,11</sup> but not in COVID-19 infections. In this study, the rate of loss of taste and smell in patients diagnosed with COVID-19 and who received treatment at home or in the hospital was 67.7%. This rate and the results of this study support the finding that the loss of taste and smell indicates early COVID-19 infection. In a case study of 19 COVID-19 cases, the rates of loss of taste and smell in patients without nasal obstruction and in patients with other symptoms of rhinitis were 81.6% and 74.8%, respectively.<sup>12</sup> Another study that included four different European countries reported a high rate of loss of smell (86%) and/or taste (89%) in patients with mild-to-moderate COVID-19 infection.<sup>5</sup> In a meta-analysis of the data of 3563 patients with COVID-19, Borsetto et al.<sup>13</sup> reported that the rate of loss of taste and smell in mild-to-moderate cases was 67%. It has been reported that this symptom is the only and/or the first symptom to appear in 20% of cases. This finding suggests that although this symptom can occur in many medical conditions, because of nutritional deficiencies, or because of certain drugs<sup>14</sup>, the most likely pathophysiological explanation is the abundance of ACE2 receptors, which are considered to be the receptors of COVID-19 in the nasal mucosa and tongue epithelium, especially in cases where it is seen isolated, and the transmembrane protease called TMPRSS2, which allows the virus to enter the cell. For these reasons, the viral load that clings to and damages the neuroepithelium in this area is high.<sup>15</sup>

As shown by the results of many studies and clinical experiments, the prognosis of COVID-19 infection can vary. While some patients are completely asymptomatic, the clinical situation of symptomatic patients ranges from home treatment to intensive care support.<sup>16</sup> Many studies have been conducted on patient and nonpatient factors that may affect morbidity and mortality. In particular, the effects of demographic and clinical factors such as age, sex, ethnicity, smoking status, and drug use, and the presence of comorbidities are examined separately. Recognizing the relationship between loss of taste and smell and factors such as the patients' demographic characteristics, the severity of the disease, length of stay at home and in hospital, and other accompanying COVID-19 symptoms, may help both early diagnosis and prediction of prognosis.

In this study, it was noted that the average age of the patients with loss of taste and smell (24.52 years) was significantly lower than that of the group without the symptom (41.09 years). Similarly, Izquierdo-Domínguez et al.<sup>9</sup> and Kerm et al.<sup>17</sup> have reported that patients with COVID-19 who reported a loss of taste and smell were younger than those who did not. In contrast, Somekh et al.<sup>18</sup> and Mercante et al.<sup>19</sup> have reported that the incidence of loss of taste and smell in patients with COVID-19 increased until a certain age and decreased in the advanced age group; this finding was mostly observed in the middle age group but to a lesser extent in the pediatric and advanced age groups. In this study, when distributing the symptoms according to sex examined, 84.3% of the patients and 48.9% of men experienced loss of taste and smell. The difference is significantly higher. This finding is consistent with those of other studies in the literature.<sup>5,6,20</sup> The common feature of the previous studies and this study is

that loss of taste and smell is not based on objective tests but is evaluated according to the patients' report.

For this reason, the difference in rates between the sexes may have occurred because women are more sensitive than men to decreased taste and smell. Regarding other accompanying symptoms, although fatigue, fever, and URTI symptoms were significantly present in both groups, patients without these symptoms were also present in the group with the loss of taste and smell. GI symptoms were significantly more prominent in the group with the loss of taste and smell than in the group without it. Therefore, GI symptoms occur simultaneously with loss of taste and smell. Based on the data of our study, it has been detected in a significantly higher number of patients who do not smoke compared to those who use loss of taste and smell due to COVID-19. Although it has been reported in many studies that COVID-19 infection is more common in smokers and has a more severe course<sup>21</sup>, the rate of loss of taste and smell is observed to be lower.<sup>22</sup> One of the possible reasons for this may be that in smokers, the taste and smell perception is less than in nonsmokers.

Furthermore, all groups (i.e., young age, female sex, GI symptoms, non-smokers) that showed frequent loss of taste and smell were associated with relatively lower mortality and intensive care admission due to COVID-19.<sup>1, 16, 21, 23</sup> Generally, loss of taste and smell in patients with COVID-19 may indicate a better prognosis compared to those without this symptom. In support of this theory, in this study, the duration of hospitalization and home rest was significantly longer in patients without loss of taste and smell. Therefore, we can conclude that patients with loss of taste and smell are less likely to be hospitalized. Similarly, in a review of 48 separate studies, it was shown that loss of taste and smell was more common in outpatients with COVID-19.<sup>24</sup> The most reliable explanation for the pathophysiological mechanism of the greater incidence of loss of smell and taste in non-hospitalized patients and the relatively mild disease associated with this symptom is that in the first days of infection, a greater local inflammatory response mediated by increased expression of the ACE2 enzyme occurs, which increases the risk of SARS-CoV-2 adherence and leads to taste and smell disorders. This mechanism protects against pulmonary damage while causing.<sup>25</sup>

## Conclusion

Complete or partial loss of taste and smell is a common symptom in COVID-19 infection. In some cases, it may be the earliest and/or the only symptom. Therefore, its presence is critical in early diagnosis of the disease. According to our study, loss of taste and smell was found to be associated with young age, female sex, low hospitalization rate, non-smokers, and accompanying GI symptoms in COVID-19 infection. Recognizing the demographic and clinical features associated with this symptom is valuable for early diagnosis of the disease and predicting prognosis to reduce its spread.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee for Non-Invasive Health Sciences Research of Istanbul Yeni Yüzyıl University (Date: 11.01.2021, Decision No:2021/01-554).

**Informed Consent:** Informed consent was obtained from all participants who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - A.R.S.; Design - A.R.S.; Supervision - F.Ö.; Resource - A.R.S.; Materials A.R.S.; Data Collection and/or Processing - A.R.S; Analysis and/or Interpretation - F.Ö.; Literature Search - A.R.S.; Writing - A.R.S.; Critical Reviews - F.Ö.

**Acknowledgements:** The authors would like to thank the chief physician of Bahat Hospital Dr. Hamza Bahat, as well as Yeni Yüzyıl University and the Istanbul University Cerrahpaşa Medical faculty Department of ENT.

**Conflict of Interest:** The authors have no conflict of interest.

**Financial Disclosure:** The authors declared that this study has received no financial support.

## References

1. Guan WJ, Ni ZY, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020; 382(18): 1708-1720. [\[Crossref\]](#)
2. Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019- nCoV infection. *Front Med*. 2020; 14 (2): 185-192. [\[Crossref\]](#)
3. Cazzolla AP, Lovero R, Muzio LR, et al. Taste and smell disorders in COVID-19 patients: Role of interleukin 6. *ACS Chem. Neurosci*. 2020; 11: 2774-2781. [\[Crossref\]](#)
4. Santacroce L, Charitos IA, and Del Prete R. COVID19 in Italy: An overview from the first case to date. *Electron J. Gen Med*. 2020; 17 (6): No. em235. [\[Crossref\]](#)
5. Lechien JR, Chiesa-Estomba CM, De Sati 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. [\[Crossref\]](#)
6. Yamagishi M, Fujiwara M, Nakamura H. Olfactory mucosal findings and clinical course in patients with olfactory disorders following upper respiratory viral infection. *Rhinology*. 1994; 32(3): 113-118.
7. American Academy of Otolaryngology-Head and Neck Surgery Foundation. ENT Health. Hyposmia and anosmia. Alexandria, VA: American Academy of Otolaryngology-Head and Neck Surgery Foundation; 2020. [\[INTERNET\]](https://www.enthealth.org/conditions/hyposmia-and-anosmia/) <https://www.enthealth.org/conditions/hyposmia-and-anosmia/>. Accessed May 14, 2020.
8. Beltran-Corbellini A, Chico-Garcia JL, Martinez-Poles J, et al. Acute-onset smell and taste disorders in the context of COVID-19: A pilot multicentre polymerase chain reaction based case-control study. *Eur J Neurol*. 2020; 27(9): 1738-1741. [\[Crossref\]](#)
9. Izquierdo-Dominguez A, Rojas-Lechuga MJ, Chiesa-Estomba C, et al. Smell and taste dysfunctions in COVID-19 are associated with younger age in ambulatory settings - A multicenter cross-sectional study. *J Investig Allergol Clin Immunol*. 2020; 30(5): 346-357. [\[Crossref\]](#)
10. Suzuki M, Saito K, Min WP, Vladau C, Toida K, Itoh H, Murakami S. Identification of viruses in patients with postviral olfactory dysfunction. *Laryngoscope*. 2007; 117(2): 272-277. [\[Crossref\]](#)
11. De Haro-Licer J, Roura-Moreno J, Vizciti A, González-Fernández A, González-Ares JA. Long term serious olfactory loss in cold and/or flu. *Acta Otorrinolaringol Esp*. 2013; 64(5): 331-338. [\[Crossref\]](#)
12. Passarelli PC, Lopez MA, Bonaviri GNM, Garcia-Godoy F, D'adonna A. Taste and smell as chemosensory dysfunctions in COVID-19 infection. *Am J of Dentistry*. 2020; 33 (3): 135-137.
13. Borsetto D, Hopkins C, Philips V, Obholzer R, Tirelli G, Polesel J, Boscato-Rizzo P. Self-reported alteration of sense of smell or taste in patients with COVID-19: A systematic review and meta-analysis on 3563 patients. *Rhinology*. 2020; 58 (5): 430-436. [\[Crossref\]](#)
14. Boesveldt S, Postma EM, Boak D, et al. Anosmia-A Clinical Review. *Chemical Senses*. 2017; 42(7): 513-523. [\[Crossref\]](#)

15. Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci.* 2020; 12(1): 8. [\[Crossref\]](#)
16. AU Noor, F Maqbool, ZA. Bhatti, AU Khan. Epidemiology of CoViD-19 pandemic: Recovery and mortality ratio around the globe. *Pak J Med Sci.* 2020; 36: 79-84. [\[Crossref\]](#)
17. Kerr C, Hughes G, McKenna L, Bergin C. Prevalence of smell and taste dysfunction in a cohort of COVID19 outpatients managed through remote consultation from a large urban teaching hospital in Dublin, Ireland. *Infection Prevention in Practice.* 2020; 2(3): 100027. [\[Crossref\]](#)
18. Somekh I, Hanna HYH, Heller E, Bibi H, Somekh E. Age-dependent sensory impairment in COVID-19 infection and its correlation with ace2 expression. *The Pediatric Infectious Disease Journal.* 2020; 39(9): 270-272. [\[Crossref\]](#)
19. Mercante G, Ferreli F, De Virgilio A, et al. Prevalence of taste and smell dysfunction in coronavirus disease 2019. *JAMA Otolaryngol Head Neck Surg.* 2020; 146(8): 723-728. [\[Crossref\]](#)
20. Giacomelli A, Pezzati L, Conti F. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: A cross-sectional study. *Clin Infect Dis.* 2020. [\[Crossref\]](#)
21. Reddy RK, Charles WN, Sklavounos A, Dutt A, Seed PT, Khajuria A. The effect of smoking on COVID-19 severity: A systematic review and meta-analysis. *J Med Virol.* 2021; 93(2): 1045-1056. [\[Crossref\]](#)
22. Al-Ani RM, Acharya D. Prevalence of anosmia and ageusia in patients with COVID-19 at a primary health center, Doha, Qatar. *Indian J Otolaryngol Head Neck Surg.* 2020. [\[Crossref\]](#)
23. Nobel YR, Phipps M, Zucker J, Lebwohl B, Wang TC, Sobieszczyk MA, Freedberg DE. Gastrointestinal symptoms and coronavirus disease 2019: A case-control study from the United States. *Gastroenterology.* 2020 Jul; 159(1): 373-375.e2. [\[Crossref\]](#)
24. Liou JM, Chen MJ, Hong TC, Wu MS. Alteration of taste or smell as a predictor of COVID-19. *Gut.* 2020; 70(4):806-807. [\[Crossref\]](#)
25. Leung JM, Yang CX, Tam A. ACE-2 expression in the small airway epithelia of smokers and COPD patients: Implications for COVID-19. *Eur Respir J.* 2020; 14; 55(5): 2000688. [\[Crossref\]](#)