Objective Evaluation of Smell and Taste Senses in COVID-19 Patients

Original Investigation

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Abstract

Objective: The severe acute respiratory syndrome-coronavirus-2 pandemic is one of the largest of the recent times and can cause many symptoms including smell and taste disorders. In the literature, smell disorders caused by coronavirus disease-2019 (COVID-19) have been reported within a wide range from 3.2% to 98.3%. A small number of these studies demonstrated smell and taste disorders through objective tests. Our aim in this study was to determine the prevalence of smell and taste disorders in hospitalized patients due to COVID-19 infection.

Methods: The study was carried out with 100 patients who were positive for real-time polymerase chain reaction and treated at the Kayseri City Hospital, and 100 healthcare worker relatives. We used the Connecticut Chemosensory Clinical Research Center test to evaluate the sense of smell. Sense of taste was evaluated using four different standardized bottles of preparations, and the results were scored according to the patients' statements.

Results: Patient (Group 1) and control (Group 2) groups were compared for age, gender, smell and taste disorders. There were 39 women and 61 men in the patient group, and 40 women and 60 men in the control group. Mean age was 50.2±1.37 (range 21–70) years in Group 1 and 47.6±1.25 (range 18–70) years in Group 2, and there was no significant difference between the two groups. While the rate of smell disorder was 80% in Group 1, we found this rate as 35% in Group 2. Taste disturbance was identified in 38 patients, of whom 16 had mild hypogeusia, 17 had moderate hypogeusia, four had severe hypogeusia, and one patient had ageusia. We found that taste disorder was 38% in Group 1 and 3% in Group 2.

Conclusion: Smell and taste dysfunctions are very common symptoms in COVID-19 patients. The results obtained using objective test methods are higher than the rates obtained from patient statements.

Keywords: COVID-19, anosmia, olfactory dysfunction, taste disorders

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Introduction

The World Health Organization named the disease, which was first seen in Wuhan, China in the last months of 2019 and thought to be a type of viral pneumonia, as coronavirus disease-2019 (COVID-19). Since it appeared, the disease was shown

to cause many symptoms such as fever, fatigue, cough, sputum, muscle pain, anorexia and shortness of breath, and more information was obtained on these symptoms overtime (1).

Another symptom seen in COVID-19 patients is smell and taste disorders, and its frequency was thought to be relatively low at the onset of the pandemic (2). In many later studies, however, these rates were shown to be much higher. Since the beginning of the pandemic, many studies were conducted to assess the senses of smell and taste in COVID-19 patients; while a small portion of these studies involved objective tests, most were observational studies. Since there are many variables such as the method of the studies, the tests used, and the regions where the studies were conducted, the prevalence of smell disorder in these studies varies between 3.2% and 98.3% (3). In this study, we aimed to assess the senses of smell and taste in COVID-19 patients with the Connecticut Chemosensory Clinical Research Center (CCCRC) test and comparative to a control group.

Methods

The study protocol was approved by the Kayseri City Hospital Ethics Committee (decision no: 196, date: 27.10.2020). Informed consent was obtained from all participants. The study was carried out with 100 patients who were positive for real-time polymerase chain reaction (RT-PCR) and were treated at the Kayseri City Hospital's pandemic departments between 1-21 November 2021. The control group was chosen from among the relatives of the hospital's healthcare workers.

Inclusion criteria were determined as patients aged 18–70 years, with a positive nasopharyngeal swab sample for COVID-19, and without neurological or psychiatric diseases. Those who had a history of smell and taste loss, sinonasal and cranial surgery, head trauma, allergic rhinitis, and chronic sinusitis and those who had been previously infected with COVID-19 or could not cooperate with the test in structions were excluded.

Age, sex, smell test and taste test results were recorded for all participants. All participants were first told how to do the test. The mean duration of symptoms of patients who reported loss of smell was 8.8 days (3–27 days). The tests were carried out by the same two otolaryngologists, taking all personal protective measures. No physical examinations were performed on the individuals in the study groups.

The CCCRC test described by Cain in 1988 was used to assess sense of smell. The CCCRC test includes the butanol threshold test and the smell identification test.

In the butanol threshold test, participants were asked to smell the contents of 8 bottles. Seven of the bottles contained butanol concentrations at different ratios (the strongest butanol concentration contained 4% butanol in deionized water and the concentration was diluted at a ratio of 1:3 for each subsequent bottle), and marked from one to seven. One bottle (bottle 0) was filled with water. The outer appearance of all bottles was the same.

Participants were asked to close a nostril with their finger, the apparatus was placed at the tip of the bottle and placed under the open nostril. Apparatus changed for each patient. The participants were asked to identify which bottle had smell, starting with the lowest concentration (bottle 7), with one bottle of water in each trial. In cases where the participant could not discriminate between water and smell, a more concentrated bottle was used. When a participant correctly identified the concentration four times in a row, the score was recorded as the threshold value. The same procedure was repeated for the other nostril and the value was recorded. The threshold value of butanol was calculated by taking the mean of the threshold values for the right and left nostrils.

The smell identification test used common odorants familiar to the Turkish population (4). One of these was Vicks®, VapoRub™ (Eczacıbaşı, Turkey) which was thought to evaluate trigeminal nerve function and was not taken into account in scoring. Other odorants presented to the participants included peanut butter, soap, coffee, chocolate, cinnamon, mothballs, and baby powder. Participants were asked to identify the odorants placed in opaque jars by closing their eyes and using one nostril. After each procedure, the participants were given a form containing a total of 20 scents along with distracting odorants and asked to choose from these (Table 1). Each odorant was presented to the participants twice. Calculation was made over seven points in total. The same procedure was repeated for the other nostril, and the smell identification score was calculated by taking the mean of the two sides. The mean of the butanol threshold and odorant identification test scores was calculated. The value found was recorded as anosmia between 0 and 1.75, severe hyposmia between 2 and 3.75, moderate hyposmia between 4 and 4.75, mild hyposmia between 5 and 5.75 and normosmia between 6 and 7 (Table 2).

Table 1. Smell identification test

Ammonia	Coffee
Peanut butter	Tobacco
Baby powder	Garlic
Black pepper	Ketchup
Burnt paper	Pine (turpentine) oil
Rubber	Vicks
Chocolate	Naphthalene
Fish	Grape jam
Cinnamon	Onion
Soap	Wood shavings

To evaluate the sense of taste, four different standardized bottles were prepared. They were prepared by adding 30 g of refined sugar in 1 L of distilled water to obtain a sweet solution, 30 g of table salt in 1 L of distilled water to obtain a saline solution, and 90 mL of lemon juice in1 L of distilled water to obtain a sour solution. For the bitter solution, hydroxychloroquine dissolved in water was used. The solutions were prepared as spray formulations and sprayed on the dorsal part of the tongue. Participants were asked to identify one of these four flavors and the results were recorded as correct or incorrect. They were asked to rinse their mouth with distilled water and the test paused for 30 seconds between two applications. The flavors were presented to the participants in random order. However, the bitter taste was applied last in order not to suppress other tastes. The patient's taste scores ranging from 0 to 4 were classified as: normal (score 4), mild hypogeusia (score 3), moderate hypogeusia (score 2), severe hypogeusia (score 1), and ageusia (score 0).

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 22 (IBM Corp.; Armonk, NY, USA). The normality of the data distribution was analyzed using the Kolmogorov-Smirnov test. Data were expressed as mean ± standard deviation. The Independent sample t-test was used for parametrically distributed data, and the Mann–Whitney U test was used for nonparametrically distributed data. A p-value of <0.05 was considered statistically significant.

Table 2. CCCRC test mean scoring system

Score	Clinical diagnosis
0–1.75	Anosmia
2–3.75	Severe hyposmia
4–4.75	Moderate hyposmia
5–5.75	Mild hyposmia
6–7	Normosmia

CCCRC: Connecticut Chemosensory Clinical Research Center

Table 3. Characteristics and test results of the patient and control groups

	Group 1	Group 2	p-value
Age	50.2±1.37	47.6±1.25	0.157
Sex	39 F 61 M	40 F 60 M	0.885
BTT	4.93±0.13	5.88±0.09	0.001
SID	4.31±0.19	5.84±0.09	0.001
CCCRC	3.42±1.16	4.55±0.68	0.001
Gustatory test	3.34+0.96	3.97+0.17	0.001

BTT: Butanol threshold test, SID: Smell identification test, CCCRC: Connecticut Chemosensory Clinical Research Center, F: Female, M: Male

Results

The patient (Group 1) and the control (Group 2) groups were compared for age, gender, smell and taste scores (Table 3). There were 39 women and 61 men in Group 1, and 40 women and 60 men in Group 2. Mean age was 50.2±1.37 (range, 21–70) years in Group 1 and 47.6±1.25 (range, 18–70) years in Group 2. There was no statistically significant difference between the two groups in terms of age and gender. Additionally in Group 1, loss of smell was observed in 30 of the 39 female patients and in 50 of the 61 male patients, and no statistically significant association was found between loss of smell and gender (p=0.539).

The mean score of the butanol threshold test done to assess smell functions was 4.93±0.13 in Group 1, and 5.88±0.09 in Group 2. The mean score of the smell identification test was 4.31±0.19 in Group 1 and 5.84±0.09 in Group 2. As stated above, the mean CCCRC scoring system calculated based on butanol threshold test and smell identification tests were found 3.42±1.16 for Group 1 and 4.55±0.68 for Group 2. All these olfactory function evaluation test results were statistically significant between the two groups (p<0.001).

While 80 patients in the patient group (Group 1) had smell disorder, this number was 35 in the control group (Group 2). In Group 1, 6 patients had anosmia, 17 had severe hyposmia, 26 had moderate hyposmia, 31 had mild hyposmia, and 20 patients had normosmia (Table 4). The number of patients subjectively reporting smell disorder in Group 1 was 30. Objectively, smell disturbance was detected in 29 of these. Fifty-one of the 70 patients who did not report any loss of smell were found to have loss with the CCCRC test.

As a result of the test performed to evaluate the sense of taste, 38 participants in Group 1 and three participants in Group 2 were found to have taste disturbances. The mean scores of the taste tests were 3.34±0.96 in Group 1 and 3.97±0.17 in Group 2, and the difference was statistically significant (p<0.001). Of the 38 patients with taste disturbance, 16 had mild hypogeusia, 17 had moderate hypogeusia, for had severe hypogeusia, and one patient had ageusia (Table 5). Taste dysfunction was most common for salty (27 patients) and sour (six patients) tastes. While 35 of 80 patients with smell disorder had taste loss, 45 patients had no taste disorder.

Table 4. CCCRC test results

Clinical diagnosis	Group 1 (n)	Group 2 (n)
Anosmia	6	0
Severe hyposmia	17	1
Moderate hyposmia	26	8
Mild hyposmia	31	26
Normosmia	20	65

CCCRC: Connecticut Chemosensory Clinical Research Center

Table 5. Gustatory function results

Score	Clinical diagnosis	Group 1 (n)	Group 2 (n)
0	Ageusia	1	0
1	Severe hypogeusia	4	0
2	Moderate hypogeusia	17	0
3	Mild hypogeusia	16	3
4	Normal	62	97

Discussion

Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is one of the largest infectious diseases in history, affecting millions of people worldwide for more than two years. Many symptoms caused by the virus were reported over time. Although smell and taste disorders were thought to be less common in the early stages of the pandemic, they were shown to be more common in subsequent studies (1, 2).

Viral infections are the most common etiological cause of olfactory dysfunction with a rate of 30–40% (5). Although many clinicians attribute postviral olfactory dysfunction to inflammatory irritation in the nasal mucosa and rhinorrhea, its etiopathogenesis is not clearly understood. Some studies have shown that viral infections caused olfactory dysfunction through the olfactory neuroepithelium and the central nervous system (6-7). Previous studies showed coronavirus to be a member of the virus family that causes anosmia and reported that this effect could not be explained solely by rhinorrhea and inflammatory causes (8). In a previous animal study, it was argued that the brain was the main target organ for coronaviruses through the SARS-CoV receptor (human angiotensin-converting enzyme 2) and that it entered the brain mainly through the olfactory bulb (9).

Smell dysfunction is a very important symptom seen in patients infected with SARS-CoV-2. The fact that the smell disorder can be seen with other symptoms and its emergence as the first symptom has increased attention in this direction (10). In a multi-center European study based on a questionnaire, they reported the loss of smell as 85.6% and reported that the first symptom was smell disorder in 11.8% of the cases (11). Most of the studies examining the relationship between COVID-19 and the sense of smell are subjective studies in the form of questionnaires or retrospective anamnesis, and there are a few objective studies. Agyeman et al. (3) in a systematic review and meta-analysis where they examined 24 studies, of which five included objective methods, they determined the smell dysfunction rate as 41%, the taste dysfunction rate as 38%, and stated that the smell dysfunction rates were higher in studies using objective methods. Borsetto et al. (12) in their systematic examinations involving 3,563 patients, found the rate of smell and taste dysfunction as 47%, and they reported that smell disturbance emerged as the first symptom in 20% of the cases. In our study, we used the CCCRC test, which was previously performed and thought to be more suitable for the Turkish population (4). We found the smell dysfunction rate to be 80% and that six of these patients had anosmia, 17 of them had severe hyposmia, 26 of them had moderate hyposmia, and 31 of them had mild hyposmia. In our study, the rate of olfactory disorders in Group 2 (controls) was 30%. Veyseller et al. (4) investigated the rate of smell disorders in the healthy Turkish population using the CCCRC test and found this rate as 19.4%. In a study investigating the smell disorder in COVID-19 patients, the authors reported the rate of smell disorders as 18% in their control group (13). That olfactory disorders are seen in otherwise healthy individuals at certain rates has been revealed by a number of studies and relatively similar rates were found in our study.

It is thought that the cause of taste disorders in COVID-19 patients is the dysfunction of taste receptors or the spread of infection to the cranial nerves responsible for transmitting the sense of taste (14). In a study by Hintschich et al. (15) they investigated taste disorders in COVID-19 patients using the Taste Strip test and found the rate as 28%. In another study which used Burghart taste strips to evaluate the sense of taste, the authors found the rate of taste impairment as 25% and reported that this loss was mostly in sour and salty tastes (16). We found the rate of taste dysfunction as 38%. Of our 38 patients with taste disturbance, 16 had mild hypogeusia, 17 had moderate hypogeusia, four had severe hypogeusia, and one patient had ageusia. Consistent with other studies, we found the most significant loss of taste in salty (27%) and sour (6%) tastes.

In their respective studies with objective tests, Vaira et al. (17) found the rate of smell dysfunction as 73% with the CCCRC test, and Gözen et al. (18) found a rate of 83% by with the Sniffin' Sticks test. Moein et al. (13) found this rate as 98% with the University of Pennsylvania Smell Identification test method. In a study using quick smell identification test to investigate smell disorder, the prevalence of olfactory disorder was found as 16.3% (19).

In some studies conducted to evaluate the sense of smell, objective tests were compared with self-reports. Lechien et al. (20) assessed 86 patients who reported smell loss with the Sniffin' Sticks test and found smell dysfunction in only 62% of these patients. In another study, although 61% of the participants self-reported loss of smell, this rate was found to be 83% with the psychophysical test. Gözen et al. (18) found the rate of olfactory dysfunction as 52.5% with a questionnaire, while this rate was found as 83% with a psychophysical test. In our study, we did not use a special questionnaire for smell assessment in order not to prolong the contact time with the patient. Participants were asked whether or not they had loss of smell. Out of our 30 patients who self-reported to have loss of smell, dysfunction was

identified in 29, whereas 51 of the 70 patients who did not report any loss of smell were identified to have smell loss with the CCCRC test. The differences between the mentioned studies may be due to the use of questionnaires to assess the loss, the degree to which patients care about loss of smell, and viral or ethnic differences.

The relationship between the symptoms of smell loss and the prognosis of the disease have also been the subject of studies. Yan et al. (21) reported that patients with olfactory dysfunction needed hospitalization ten times less than the patients without loss of smell. Aziz et al. (22) reviewed 51 studies in a meta-analysis they conducted and reported that smell dysfunction was shown as a positive prognostic factor in all seven studies examining the relationship between smell and prognosis, but they reported that these results were limited. Since we conducted our study on hospitalized patients with mild-to-moderate COVID-19, we could not have the opportunity to examine the effect of smell dysfunction on prognosis. Another study reported that loss of smell were associated with better prognosis (23). Although, basing on the current knowledge, there is a general belief that olfactory dysfunction is a positive prognostic factor, new studies are needed on this subject.

There are some limitations in the presented study. First, we did not utilize any questionnaires to assess the loss of smell and taste. Also, any association between olfactory dysfunction and the severity of the disease could not be established since the presented study did not include the patients with more severe symptoms. In addition, since we did not perform RT-PCR testing on healthy volunteers, it is possible that there were COVID-19 positive individuals in the control group.

Conclusion

Smell and taste dysfunction is a very common symptom in COVID-19 patients. In the presented study, 80% of our COVID-19 patients had smell dysfunction, whereas 35% had taste dysfunction. In the control group, these rates were 35% and 3%, respectively. Of the 70 patients who did not report any loss of smell, 51 were found to have loss with the CCCRC test. The results obtained using objective test methods are higher than the rates obtained from patient statements. More detailed studies are needed to assess the senses of smell and taste in COVID-19 patients.

Ethics Committee Approval: The study protocol was approved by the Kayseri City Hospital Ethics Committee (decision no: 196, date: 27.10.2020).

Informed Consent: Informed consent was obtained from all participants.

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Authorship Contributions

Surgical and Medical Practices: A.K., S.A., Concept: A.K., S.A., M.Y., İ.Ö., Design: A.K., S.A., M.Y., İ.Ö., Data Collection and/or Processing: A.K., S.A., İ.Ç., Analysis and/or Interpretation: A.K., S.A., İ.Ç., Literature Search: A.K., S.A., İ.Ç., Writing: A.K., S.A., M.Y., İ.Ö., İ.Ç.

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Main Points

- Smell and taste dysfunction is a very common symptom in COVID-19 patients.
- The results obtained using objective test methods are higher than the rates obtained from patient statements.
- 80% of COVID-19 patients had smell dysfunction, whereas 35% had taste dysfunction.

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