

Olfactory Dysfunction in Mild-Moderate-Severe COVID-19 Patients

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ABSTRACT

Objective: The aim of this study is to investigate the factors that affect the occurrence of coronavirus disease 19-related olfactory dysfunction and the duration of this resulting symptom.

Methods: Patients over 18 years old with coronavirus disease 19 polymerase chain reaction (+) were included in the study. Patients were examined in 3 groups based on the severity of the infection they had and were asked to subjectively evaluate their sense of smell before and after coronavirus disease 19. Their olfactory dysfunction durations were compared statistically.

Results: We scanned 349 patients diagnosed with coronavirus disease 19 and 97 (27.79%) of these patients had olfactory dysfunction. Olfactory dysfunction was seen more often in mild coronavirus disease 19 patients. Coronavirus disease 19 infection was more severe in elderly patients and it was milder in women. Dyspnea and cough, suggesting involvement in the lower respiratory tract, were significantly higher in the group with a severe course. The olfactory dysfunction lasted significantly shorter in patients with nasal symptoms. In 34.02% of the patients, olfactory dysfunction was the first symptom, and coronavirus disease 19 infection was significantly milder in patients whose first symptom was olfactory dysfunction. There were 39 patients (group A; 40.2%) whose olfactory dysfunction lasted 0-7 days, 36 patients (group B; 37.1%) whose olfactory dysfunction lasted 8-30 days, and 22 patients (group C; 22.7%) whose olfactory dysfunction lasted longer than 30 days.

Conclusion: Olfactory dysfunction is a common and important symptom of coronavirus disease 19 infection, and its clinic and incidence frequency in societies has not been fully determined. It was observed that the majority of patients recovered within a month.

Key words: Anosmia, COVID-19, hyposmia, olfactory dysfunction, SARS-CoV-2

Introduction

Coronavirus disease 19 (COVID-19), whose first cases were reported in Wuhan, China, in late 2019, is an infectious respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).^{1,2} This infection, which has very high contagiousness, has spread to more than 220 countries and regions worldwide as of March 12, 2021, and infected more than 118 million people despite all the measures taken worldwide.³ Common symptoms of COVID-19 are asthenia, fever, cough, and dyspnea. Although they are not as often as these symptoms, muscle and joint pain, sore throat, headache, nausea or vomiting, diarrhea, and some nasal symptoms, especially smell and taste dysfunction, may also be seen.⁴⁻⁶

Olfactory dysfunction (OD) following a viral infection was first brought to the agenda in 1975.⁷ This condition, called postviral olfactory dysfunction (PVOD), constitutes 40% of ODs in adults. More than 200 viruses are blamed as its factor.⁸ Postviral olfactory dysfunction is more common in women, and the rate of spontaneous recovery is quite high.⁹ In some studies, loss of smell has been reported as an independent positive prognostic factor of a less severe COVID-19 infection.¹⁰ Olfactory dysfunction was observed in COVID-19 infection between the rates of 33.9% and 68%.¹¹ In fact, OD may also occur as the first symptom of COVID-19.¹² In 79% of COVID-19 patients, OD was present at the pre-diagnosis stage, and in more than a quarter of patients, the first symptom was anosmia. While the sense of smell decreases in some patients, complete anosmia can be observed in others.¹³

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It is not exactly clear when the OD that is associated with COVID-19 recovers. Some recovery cases in anosmia were reported on average 7-10 days after the infection was over.¹³ However, OD in patients is observed with different severity levels as well as the recovery period of this dysfunction also differs. Considering all the information, the aim of this study is to investigate the factors that affect the occurrence of COVID-19-related OD and the duration of this resulting symptom and to obtain information about the incidence of OD observed in COVID-19 patients in our region.

Methods

This study was carried out in a multicenter manner by taking the decision of approval dated March 1, 2021, numbered 2021/05-99 from the Clinical Research Ethics Committee of Erzurum Regional Training and Research Hospital. We started this study in March 2021 and ended in June 2021. The study included volunteer patients over 18 years old with a COVID-19 diagnosis confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR) of the nasopharynx and oropharynx swab or by serology. Patients were told in detail about the study and their written consents were received. Patients were called every 5 days and questioned their complaints about loss of smell and other symptoms. For odor evaluation, we wanted patients to compare their olfactory status post-disease with pre-disease. Data were collected in a standardized questionnaire (the questionnaire contained detailed information about COVID-19 and symptoms). Laboratory findings and imaging results were obtained from patients' hospital files. We followed the patients for 2 months.

Patients above 18 years old with COVID-19 PCR(+) were included in the study. Patientstthose with OD before the COVID-19 infection, (2) who were diagnosed with nasal polypsis or allergic rhinitis, (3) who had nasal surgery, (4) who had radiation therapy at the oral or nasal cavity, (5) those with a history of head trauma, (6) those with psychiatric and neurological diseases that affect their communication, (7) those who

received treatment in intensive care and those with a tracheostomy, (8) those who do not want to participate in the study were excluded from the study

Age, gender, and comorbid diseases of the patients, whether they are medical personnel, and their symptoms during infection were investigated. Their PCR results, thorax computed tomography (CT) imaging, and laboratory findings leukocyte counts (WBC), C-reactive protein (CRP), D-dimer, and procalcitonin were obtained from the patient files.

Patients were examined in 3 groups based on the severity of the infection they had. The first group was the ones who had the disease as outpatients (group 1), the second group was those who had a moderate infection and were hospitalized but did not need intensive treatment (group 2), and the third group was those who received intensive treatment in the hospital due to severe infection and whose saturation fell below 90 and needed oxygen therapy (group 3). Their OD durations were compared statistically.

In order to understand what factors probably affected the duration of the OD, patients were examined in 3 groups according to the duration of the olfactory disorder. The patients with OD that lasted for 0-7 days were evaluated as group-a, the patients with OD that lasted for 8-30 days were evaluated as group-b, and the patients with OD that lasted longer than 30 days were evaluated as group-c.

Statistical Analysis

Normality control of continuous variables was performed using the Shapiro-Wilk test. Since the variables do not conform to the normal distribution, the Kruskal-Wallis test was used for the median comparison according to the 3 independent groups. Chi-square test was applied in the analysis of categorical variables. Statistical significance level was taken as .05. Analysis of the data was carried out in Statistical Package for the Social Sciences 21 software.

The Treatment Administered for COVID-19

Some of the outpatients did not receive any medical treatment, and some received hydroxychloroquine (HQ) and/or favipiravir therapy (oral therapy). Hospitalized patients received HQ and/or favipiravir therapy for COVID-19, as well as antithrombotic therapy (enoxaparin and intramuscular), antibiotics, and plasma therapy (IVIG) based on the severity of pneumonia. None of the patients used nasal corticosteroids.

Results

In total, 349 patients diagnosed with Covid-19 were examined and 149 patients were in group 1, 107 patients were group 2, and 93 patients were group 3. Among them, 97 (27.79%) of these patients had OD. In group 1, 46 of 149 patients (30,87%) had OD; in group 2, 28 of 107 patients (26,16%) had OD; and in group 3, 23 of 93 patients (24,73%) had OD (Table 1). The age of the patients with OD ranged between 18 and 80 (mean age: 40.40 ± 16.75). Among these patients, women (54.6%) were the majority. The first symptom of 34.02% of the patients was OD.

Main Points

- Olfactory dysfunction (OD) in coronavirus disease 19 (COVID-19) patients can reveal itself in different levels. This can range from complete anosmia to mild hyposmia. It is an important symptom of COVID-19 infection and its clinic and in what condition and for how long this symptom is observed are still controversial.
- Olfactory dysfunction, already known as a fundamental symptom in the diagnosis of a severe acute respiratory syndrome coronavirus 2 infection, was present in 1/3 of our cohort, and in 34% of the cases, it was the first symptom of the infection.
- We noticed that OD is seen more often in those with mild COVID-19 patients and also found that the OD improves slower in mild COVID-19 patients.
- Our study found that COVID-19 infection is more severe in elderly patients and also showed that the disease is milder in women. Dyspnea and cough, suggesting involvement in the lower respiratory tract, were significantly higher in the group with a severe course.

Table 1. Characteristic Features, Symptoms, and Improvements of Patients with Olfactory Dysfunction

		Mean \pm SD (Min-Max)		
Age (year)		40.40 \pm 16.75 (18-80)		
		n = 97	Percent	
Sex	Female	53	54.64	
	Male	44	45.36	
Living place	Country	24	24.74	
	Town	73	75.26	
Current smoking		16	16.49	
Health worker		12	12.37	
Comorbid disease	Arterial hypertension	19	19.59	
	Diabetes mellitus	17	17.53	
	Cardiovascular disease	5	5.15	
	Asthma	4	4.12	
First symptom-olfactory dysfunction		33	34.02	
Olfactory dysfunction duration (days)	1-7	39	40.21	
	8-30	36	37.11	
	>30	22	22.68	
Symptoms	Taste dysfunction	83	85.57	
	Cough	42	43.30	
	Dyspnea	24	24.74	
	Sore throat	13	13.40	
	Nasal symptoms	10	10.30	
	Fever	32	32.99	
	Asthenia	50	51.55	
	Headache	9	9.28	
	Skin manifestations	2	2.06	
	Muscle/joint pain	54	55.67	
	Abdominal pain	2	2.06	
	Nausea/vomiting	4	4.12	
	Diarrhea	2	2.06	
	Thorax CT	Minimal	14	14.43
		Middle	14	14.43
Intense		11	11.34	
Total		39	40.20	
Severity of the infection COVID-19	Mild	46	47.43	
	Moderate	28	28.86	
	Severe	23	23.71	
Olfactory dysfunction recovery	Complete	80	82.47	
	Partial	14	14.43	
	No improvement	3	3.09	

SD, standard deviation; CT, computed tomography.

Olfactory Dysfunction Status by Clinical Severity of COVID-19

When the patients were grouped according to the clinical severity of the disease, there were 46 patients in group 1, 28 patients in group 2, and 23 patients in group 3 (details are available in Table 2). The number of patients in group 1 was significantly higher than the other 2 groups ($P < .05$).

The age of the patients in group 2 was higher than that of group 1, and the age of the patients in group 3 was higher than that of the other 2 groups ($P < .001$). In group 1, the female ratio was significantly higher than the other groups ($P = .031$).

Hypertension (HT) and diabetes mellitus (DM) were significantly higher in group 3 than the other groups ($P = .011$ for HT and $P < .001$ for DM).

In group 1, the number of those who had OD as the first symptom was significantly higher than group 3 ($P = .026$). There was no significant difference between the groups in terms of the time from diagnosis to the development of olfactory disorder.

The Symptoms That Were Seen According to the Clinical Severity of COVID-19

There were significant differences between the groups in terms of cough and dyspnea. The cough was significantly less common in group 1 than group 3 ($P = .01$). Dyspnea was significantly more common in group 3 than in the other 2 groups ($P < .001$). There was no significant difference in terms of other symptoms.

Laboratory and Imaging Findings Based on the Clinical Severity of COVID-19

There was no significant difference between the 3 groups in terms of leukocyte and lymphocyte counts. C-reactive protein values were significantly higher in group 3 than in other groups ($P < .001$). The D-dimer value was significantly higher in group 3 than the other groups ($P < .001$).

According to thorax CT, those with severe and moderate pulmonary involvement were significantly higher in group 3 and those with mild and moderate pulmonary involvement were more in group 2 than group 1 ($P < .001$).

Olfactory Dysfunction Recovery Rates Based on the Clinical Severity of COVID-19

Olfactory dysfunction of 76.1% of the patients in group 1, 71.4% of the patients in group 2, and 87% of the patients in group 3 showed complete improvement within the first month. After 2 months of follow-up, partial improvement in 14 (14.43%) patients were observed, while 3 (3.09%) patients had no improvement. Each of these 3 patients was in a different group. There were no significant differences between the groups in terms of the duration of the OD.

Patients by the Duration of Olfactory Dysfunction

Patients were examined in 3 groups according to the duration of the OD (details are available in Table 3). There were 39 patients (group A; 40.2%) whose OD lasted 0-7 days, 36 patients (group B; 37.1%) whose OD lasted 8-30 days, and 22 patients (group C; 22.7%) whose OD lasted longer than 30

days. While in group A and group C, the ratio of women was higher and the ratio of men was higher in group B, but there was no statistically significant difference. The age of the patients in group B was significantly higher than group A ($P = .010$).

In group B and group C, the number of patients having OD as the first symptom was significantly higher compared to group A ($P = .019$). There was no significant difference between the groups in terms of the duration after the diagnosis until the development of OD.

Nasal symptoms were significantly higher in group A than group C ($P = .020$). Asthenia was significantly higher in group B than group A ($P = .027$). There were no statistically significant differences between the other symptoms.

There was no statistically significant difference between leukocyte and lymphocyte counts and CRP values when laboratory results of the patients were compared according to the duration of OD. The D-dimer value was significantly higher in group B than group A ($P = .005$). There was no significant difference in thorax CT involvement between the groups.

Discussion

Postviral olfactory dysfunction is the most important cause of smell dysfunction in adults and constitutes 40% of ODs. More than 200 viruses have been identified that can cause OD.¹⁴ The SARS-CoV-2 virus, which is the factor of COVID-19 disease, can also cause OD.¹⁵ Recently, the number of publications suggesting that COVID-19 could cause OD has increased.^{13,16,17}

In our study, we included 349 COVID-19 patients with mild, moderate, and severe clinical course and found OD in 27.79% of the patients. In a European-based multicenter study conducted by Lechien et al., this rate was found to be 85.6%.¹⁶ It was noted that the clinic course of the patients in that study was mild to moderate, and the OD was more common in these groups of patients. Yan et al. also found that the incidence rate of OD was low in hospitalized patients who were severely ill.¹⁷ Similar to these data, we also noticed that OD is seen more often in those with a mild level of the disease. In the systematic review of Meng et al., the incidence of OD was found to be between 33.9% and 68%. These differences in the incidence of OD may be due to the variability of the number of cases taken in the study, differences in the clinical course of COVID-19 patients, differences in ethnicity, or geographical differences.

Many studies have shown that COVID-19-related OD is more common in women.^{11,13,16,19} Similarly, in our study, 54.6% of the patients with ODs were women. It is not clear why OD is more common in women. In fact, if it can be found why the COVID-19 is milder in women, it can also be explained why women have more frequent OD as it is thought that the smell disorder is more common in milder patients.

It has not been fully explained how the SARS-CoV-2 virus causes OD yet. It has been suggested that it could be affiliated with nasal obstruction or involvement of the nervous system.^{20,21} In publications, it is often stated that younger and milder patients experience OD more frequently.^{16,22} There

Table 2. Evaluation of Patient Groups According to the Clinical Severity of Covid-19

	Group 1 (n=46)			Group 2 (n=28)			Group 3 (n=23)			P
	Mean ± SD (Min-Max)	Median [IQR]	n	Mean ± SD (Min-Max)	Median [IQR]	n	Mean ± SD (Min-Max)	Median [IQR]	n	
Age (year)	31.76 ± 13.34 (17-68)	28 [21-37.25]	46	42.5 ± 16.05 (18-80)	41 [31.25-54.75]^a	28	56 ± 11.37 (40-84)	54 [49-63]^{a,b}	23	<.001
Sex (female/male)	31/15	67.4/32.6	14/14	14/14	50/50	14/14	8/15	34.8/65.2 ^a	8/15	.031
Living place (country /town)	6/40	13.0/87.0	7/21	7/21	25.5/75.0	7/21	11/12	47.8 ^a /52.2	11/12	.007
Current smoking	6	13.0	6	6	21.4	6	4	17.4	4	.636
Health worker	6	13.0	6	6	21.4	6	0	0.0	0	.068
Comorbid disease	4	8.7 ^a	6	6	21.4	6	9	39.1	9	.011
Arterial hypertension	1	2.2 ^{ab}	7	7	25.0	7	9	39.1	9	<.001
Diabetes mellitus	2	4.3	0	0	0.0	0	3	13.0	3	.105
Cardiovascular disease	2	4.3	0	0	0.0	0	2	8.7	2	.297
Asthma	21	45.6	9	9	32.1	9	3	13.0 ^a	3	.026
First symptom-olfactory dysfunction	18	39.1	13	13	46.4	13	8	34.8	8	.359
Olfactory dysfunction duration (days)	17	37.0	7	7	25.0	7	12	52.2	12	
>30	11	23.9	8	8	28.6	8	3	13.0	3	
Symptoms	40	78.3	25	25	82.1	25	18	73.9	18	.777
Taste dysfunction	13	28.3%	14	14	50.0	14	15	65.2 ^a	15	.010
Cough	5	10.9	5	5	17.9	5	14	60.9 ^{ab}	14	<.001
Dyspnea	9	19.6	2	2	7.1	2	2	8.7	2	.236
Sore throat	7	15.2	2	2	7.1	2	1	4.3	1	.303
Nasal symptoms	15	32.6	11	11	39.3	11	6	26.1	6	.606
Fever	26	56.5	11	11	39.3	11	13	56.5	13	.306
Asthenia	5	10.9	2	2	7.1	2	2	8.7	2	.861
Headache	1	2.2	1	1	3.6	1	0	0.0	0	.669
Skin manifestations	23	50.0	14	14	50.0	14	17	73.9	17	.131
Muscle/joint pain	1	2.2	1	1	3.6	1	0	0.0	0	.669
Abdominal Pain	3	6.5	1	1	3.6	1	0	0.0	0	.432
Nausea/vomiting	1	2.2	1	1	3.6	1	0	0.0	0	.669
Diarrhea	3	6.5	9	9	32.1 ^a	9	2	8.7 ^b	2	<.001
Minimal	0	0.0	3	3	10.7 ^a	3	11	47.8 ^{ab}	11	<.001
Middle	0	0.0	2	2	7.1	2	9	39.1 ^{ab}	9	<.001
Intense	3	6.5	14	14	50.0	14	22	95.7	22	<.001
Total	2.96 ± 1.74 (1-7)	2 [2-4]	4.13 ± 3.54 (1-15)	4.13 ± 3.54 (1-15)	3 [2-6]	4.67 ± 5.98 (1-25)	3 [2-6]	3 [2-6]	3 [2-6]	.660
The time from diagnosis to the development of olfactory dysfunction (day)	6.58 ± 1.37 (4.2-9.2)	6.4 [5.55-8]	7.12 ± 1.61 (4.5-11.9)	7.12 ± 1.61 (4.5-11.9)	7.2 [6.13-8.11]	6.54 ± 2.61 (3.78-12.2)	5.3 [4.8-9.2]	5.3 [4.8-9.2]	5.3 [4.8-9.2]	.150
WBC	6.31 ± 8.21 (0.1-27)	2.5 [0.4-12]	16.49 ± 25.43 (0.1-100)	16.49 ± 25.43 (0.1-100)	5.4 [0.5-19]	87.13 ± 58.63 (1.3-185)	66 [38-154] ^{a,b}	66 [38-154] ^{a,b}	66 [38-154] ^{a,b}	<.001
CRP	45.47 ± 151.81 (0.1-800)	0.2 [0.1-1.2]	90.14 ± 190.58 (0.1-800)	90.14 ± 190.58 (0.1-800)	0.6 [0.2-114.5]	490.5 ± 556.86 (0.2-2150)	410 [0.8-840] ^{ab}	410 [0.8-840] ^{ab}	410 [0.8-840] ^{ab}	<.001
D-Dimer	Bold values indicate statistically significant differences. (Statistical significance level was taken as .05.)									
^a Difference with group 1. ^b Difference with group 2. SD, standard deviation; CT, computed tomography; WBC, white blood cell; CRP, C-reactive protein; IQR, interquartile range.										

Table 3. Evaluation of Patient Groups According to the Duration of Olfactory Dysfunction

	Group A (n=39)			Group B (n=36)			Group C (n=22)			P
	Mean ± SD (Min-Max)	Median [IQR]	n	Mean ± SD (Min-Max)	Median [IQR]	n	Mean ± SD (Min-Max)	Median [IQR]	n	
Age (year)	36.59 ± 14.24 (18-65)	34 [23-50]	34	47.53 ± 18 (18-84)	50 [32-59.25]^a	50	36.41 ± 15.67 (17-68)	35 [22-49.25]	35	.010
Sex (female/male)	23/16	59.0/41.0	16/20	16/20	44.4/55.6	14/8	63.6/36.4	63.6/36.4	14/8	.283
Living place (country/town)	8/31	20.5/79.5	10/26	10/26	27.8/72.2	6/16	27.3/72.7	27.3/72.7	6/16	.730
Current smoking	7	17.9	6	6	16.7	3	13.6	13.6	3	.909
Health worker	2	5.1	4	4	11.1	6	27.3 ^a	27.3 ^a	6	.040
Comorbid disease	5	12.8	10	10	27.8	5	22.7	22.7	5	.268
Arterial hypertension	4	10.3	10	10	27.8	3	13.6	13.6	3	.118
Diabetes mellitus	0	0.0	3	3	8.3	2	9.1	9.1	2	.169
Cardiovascular disease	1	2.6	2	2	5.6	2	9.1	9.1	2	.537
Asthma	7	17.9	15	15	41.6 ^a	11	50.0 ^a	50.0 ^a	11	.019
First symptom-olfactory dysfunction	29	74.4	29	29	80.6	17	77.3	77.3	17	.815
Symptoms	17	43.6	17	17	47.2	7	31.8	31.8	7	.503
Taste dysfunction	8	20.5	13	13	36.1	3	13.6	13.6	3	.115
Cough	4	10.3	7	7	19.4	2	9.1	9.1	2	.403
Dyspnea	8	20.5	2	2	5.5	0	0.0 ^a	0.0 ^a	0	.020
Sore throat	10	25.6	13	13	36.1	9	40.9	40.9	9	.420
Nasal symptoms	14	35.9	24	24	66.7 ^a	12	54.5	54.5	12	.027
Fever	6	15.4	3	3	8.3	0	0.0	0.0	0	.134
Astenia	1	2.6	0	0	0.0	1	4.5	4.5	1	.477
Headache	25	64.1	20	20	55.6	9	40.9	40.9	9	.216
Skin manifestations	1	2.6	1	1	2.8	0	0.0	0.0	0	.743
Muscle/joint pain	2	5.1	0	0	0.0	2	9.1	9.1	2	.221
Abdominal pain	1	2.6	0	0	0.0	1	4.5	4.5	1	.477
Nausea/vomiting	6	15.4	6	6	16.7	2	9.1	9.1	2	.626
Diarrhea	7	17.9	6	6	16.7	1	4.5	4.5	1	
Minimal	4	10.3	5	5	13.9	2	9.1	9.1	2	
Middle	17	43.5	17	17	47.2	5	22.7	22.7	5	
Intense										
Total										
Thorax CT										
The time from diagnosis to the development of olfactory dysfunction (day)	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Mean±SD (min-max)	Median [IQR]	Mean±SD (min-max)	Mean±SD (min-max)	Median [IQR]	P	
	3.78 ± 4.5 (1-25)	3 [2-4]	4.11 ± 3.41 (1-15)	4.11 ± 3.41 (1-15)	3 [2-6.25]	3 ± 2.31 (1-7)	3 ± 2.31 (1-7)	2 [1-5.25]	.541	
WBC	6.25 ± 1.58 (3.78-9.2)	6.2 [4.8-7.4]	6.97 ± 1.77 (4.22-11.41)	6.97 ± 1.77 (4.22-11.41)	6.62 [6-8.11]	7.18 ± 2.09 (4.5-12.2)	7.18 ± 2.09 (4.5-12.2)	7.18 [5.47-8.35]	.164	
CRP	24.35 ± 35.8 (0.1-163)	5.4 [0.45-41.5]	45.38 ± 62.94 (0.2-185)	45.38 ± 62.94 (0.2-185)	12 [1.6-88]	14.68 ± 23.36 (0.1-100)	14.68 ± 23.36 (0.1-100)	12 [0.4-19]	.190	
D-Dimer	107.11 ± 255.75 (0.1-964)	0.32 [0.1-2.97]	275.59 ± 461.64 (0.1-2150)	275.59 ± 461.64 (0.1-2150)	11.75 [0.43-495.5] ^a	137.87 ± 360.5 (0.1-1360)	137.87 ± 360.5 (0.1-1360)	0.65 [0.2-21.5]	.005	

Bold values indicate statistically significant differences. (Statistical significance level was taken as .05)

^aDifference with group A; ^bDifference with group B.

SD, standard deviation; CT, computed tomography; WBC, white blood cell; CRP, C-reactive protein.

are studies showing that OD is the first symptom and it has been reported as the first symptom in more than a quarter of patients in the study by Kaye et al., and Lechien et al. reported this ratio as 11.8% in their study.^{13,16} In our study, OD was the first symptom in 34.02% of the patients, and we found that COVID-19 infection was significantly milder in patients having OD as the first symptom, but in those who did not have OD as the first symptom, the time until getting OD does not make a significant difference in terms of the course of the disease.

In the study by Dell'Era et al., it was noted that OD and taste dysfunction were observed together in 70% of patients, and OD alone was observed in 3.9% of patients.²³ In our study, the most common accompanying symptom with OD was taste dysfunction with the rate of 85.5%.

We found that the OD improves slower in the patients with the mild course. There were no statistically significant differences between the groups, but the recovery rates of OD were higher in the first month in patients with the severe course.

In the study conducted by Klopfenstein et al., 80% of the patients recovered from OD within 14 days.¹⁹ The study by Koul et al. showed that 78% of the patients had complete recovery from OD within a month.²⁴ In our study, 77.3% of the patients had full recovery during the first month, while 14.4% of the patients had partial improvement after 2 months of follow-up and 3 patients showed no improvement.

when we compared the patients according to the clinical severity, we found that the COVID-19 is milder in young patients and the disease is more severe in elderly patients. Similarly, in their study, Zhang et al. showed that the disease is more severe in elderly patients.²⁵ In addition, there are studies that indicate women are more resistant to viral infections due to released hormones and the immune system.²⁶ We also found out in our study that COVID-19 infection is milder in women. There was a statistically significant number of female patients in the group who survived the disease mildly ($P=.031$). The presence of comorbid diseases is a risk factor for complications in COVID-19 infection.^{27,28} In our study, we found that comorbid disease (HT and DM) rates were significantly higher in patients with severe clinic conditions. C-reactive protein and D-dimer values indicating the severity of inflammation were found to be higher in patients whose clinical course was severe.²⁵ In our study, CRP and D-dimer were significantly higher in severe patients in line with the literature.

According to the study of Guan et al., 59% of patients had thorax CT involvement.⁵ Another study found that involvement in thorax CT was more severe in severe disease.²⁹ In our study, we found that the disease was more severe as the thorax CT involvement increased. According to the study carried out by Mao et al., dyspnea was more common in patients with a severe course.¹⁷ In our study, dyspnea and cough, suggesting involvement in the lower respiratory tract, were significantly higher in the group with a severe course.

Our study has some limitations. First, the study did not include patients who were intubated in intensive care units and who could not communicate and could not evaluate the OD. This

prevented our study from involving all patients having COVID-19. Second, the assessment of the sense of smell was subjective. No objective test was used. Care was taken for the infectiousness of the current infection, and the health of the medical staff was kept at the forefront. Third, follow-up time was limited for the patients who still had OD.

Conclusion

Although OD is not a life-threatening symptom, it significantly reduces the quality of life. It is an important symptom of COVID-19 infection and its clinic and in what condition and for how long this symptom is observed are still controversial. The incidence frequency in societies has also been reported differently. The treatment process is uncertain too. Olfactory dysfunction is a common symptom, and it was observed that the majority of patients recovered within a month. More detailed information can be obtained when more comprehensive studies related to OD involving longer-term follow-up with larger groups of patients are conducted.

Ethics Committee Approval: This study was approved by Ethics committee of Erzurum Regional Training and Research Hospital, (Approval No: 2021/05-99).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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