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Evaluation of the presence of reinfection in patients presenting to the emergency department with COVID-19 symptoms after recovery

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Abstract
This study aimed to evaluate COVID-19 reinfection in patients that presented to the emergency department with similar or different COVID-19 symptoms after recovery from the disease. This retrospective study included patients aged over 18 years presenting to the emergency department between January 1, 2021 and July 1, 2021, who had been previously diagnosed with COVID-19 and received treatment for the disease. Statistical analysis was performed using SPSS version 22.0.A total of 199 patients, 54.3% female, were included in the study. PCR positivity was present in 2.5% of the patients, and it was statistically significantly low($p<0.001$). The most common symptom was fatigue (46.2%), and the least common symptom was loss of taste (3.0%). However, there was a statistically significant correlation between the loss of taste and smell and PCR positivity ($p=0.024$ and $p=0.043$, respectively). The logistic regression analysis revealed that the loss of taste and loss of smell alone did not have an effect on PCR positivity ($p=0.848$, 95% confidence interval: 0.005-71.83 and $p=0.287$, 95% confidence interval: 0.001-9.369). In the Covid-19 management and treatment guide, it is necessary to make changes in terms of symptoms for people who have had Covid-19 disease.

Keywords: Covid-19 reinfection, Covid-19 symptoms, PCR

1. Introduction

A previously unidentified viral pneumonia was detected in Wuhan at the end of December 2019, and by January 7, 2020, researchers identified the novel virus as SARS-CoV-2 and the disease caused by this virus was named COVID-19. The disease quickly spread to other countries within a few months and turned into a pandemic. In Turkey, the first case was seen on March 11, 2020, the first peak occurred toward the end of April, and the number of cases began to decrease by the end of May. From August 30 to December 10, 2020, there was a daily increase of 100-500 cases. After December 10, the number of cases entered a downward trend. End of February 2021, cases started to increase again, reaching 40,000 by the beginning of April 2021. With the measures taken, the number of cases decreased to 6,000 by the end of May. Since then, the gradual increase in the number of cases has continued, with more than 20,000 people testing positive everyday throughout August and September 2021 (1). Determining COVID-19 symptoms is very important for effective triage and early intervention. With growing information about COVID-19, different symptoms and signs have started to facilitate the diagnosis of the disease. As in many countries around the world, in Turkey, the approach to patients has been revised in line with the pandemic conditions. Accordingly, in addition to contact history, patients have begun to be questioned in terms of complaints such as fever, history of fever, cough, shortness of breath, flu symptoms, and loss of taste and/or smell (2). However, although these findings are of guiding nature at the time of first presentation, there are no guidelines concerning whether similar approaches can be effective in patients that have already recovered from COVID-19.

In this study, we aimed to evaluate COVID-19 reinfection in patients that presented to the emergency department with similar or different COVID-19 symptoms after recovery from the disease.

2. Materials and Methods

2.1. Study design

This clinical retrospective study was carried out in the Emergency Department of Ümraniye Education and Research Hospital, which has a COVID-19 outpatient clinic. This department is a comprehensive clinic serving an average of 500,000 patients every year with green, yellow and red zones and a resuscitation unit.

2.2. Patient population

Patients aged over 18 years presenting to the emergency

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department between January 1, 2021 and July 1, 2021, who had been previously diagnosed with COVID-19 and recovered from the disease, were included in the study. Patients with a saturation value of 98% and above, respiratory rate below 30/min, and no 30-day mortality were included in the sample. Patients who previously had symptoms of COVID-19 but had a negative PCR test at that time, those who presented within less than 30 days after recovering from COVID-19, patients under 18 years of age, those without a history of COVID-19, and those with missing data were excluded.

2.3. Data collection

The patients' presentation symptoms, whether the symptoms were the same or different from the first time they had tested positive for COVID-19, severity of symptoms, medical history, hospitalization history, and whether they had been vaccinated were recorded. The polymerase chain reaction test results and three-month mortality status were also noted.

2.4. Statistical analyses

Statistical analysis was performed using SPSS version 22.0. The conformance of variables to the normal distribution was examined with visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov test). The chi-square test was conducted to evaluate the relationship between categorical data. The Mann-Whiney U test was used to compare non-parametric numerical data between two groups. If there were more than two groups, the Kruskal-Wallis test was used to compare non-parametric numerical data. A correlation analysis was performed with the Spearman correlation test, and data were evaluated separately with the binary logistic regression analysis. A p value of <0.05 was accepted as statistically significant.

2.5. Ethical considerations

Ethical approval for the study was obtained from the local clinical research ethics committee of our hospital (date: June 17, 2021, number: B.10.1.TKH.4.34.H.GP.0.01/190).

3. Results

The study included a total of 199 patients, of whom 54.3% were female. The mean age of the whole sample was 37.35±13.87 years, and the mean time from the first COVID-19 diagnosis to referral to our Covid-19 clinic by triage due to COVID-19 symptoms was 140.32±80.49 days. When evaluated according to PCR positivity, the difference was not statistically significant (p =0.681).

The most common symptom of the patients was fatigue (46.2%) and the least common symptom was loss of taste (3.0%). There was a statistically significant correlation between taste loss and PCR positivity (p=0.024). When the patients with more than one symptom were examined, no statistically significant correlation was found between the increase in the number of symptoms and PCR positivity (p=0.331). No statistical significance was found between the patients having more than one comorbidity and PCR positivity (p=0.232) (Table 1).

Of our patients, 2.5% had a positive PCR test, and this was statistically significantly lower than in our entire patient population(p<0.001). While 52.3% of our patients presented with complaints similar to the initial COVID-19infection, 12.1% had more severe symptoms (p<0.001) (Table 2). There was no statistically significant correlation between the severity of symptoms and PCR positivity (p=0.802).

Table 1. Evaluation of the relationship of demographic data, symptoms and comorbidities with second-time PCR positivity

	n (%)	P value
Age (mean ± SD)	37.35 ± 13.87	0.177
Time(day) (mean ± SD)	140.32 ± 80.49	0.681
Gender, n (%)		
Female	108 (54.3%)	0.181
Male	91 (45.7%)	
Symptom severity, n (%)		
Similar	104 (52.3%)	0.802
Milder	71 (35.7%)	
More severe	24 (12.1%)	
Symptoms, n (%)		
Fever	35 (17.6%)	0.295
Enteritis	18 (9.0%)	0.619
Cough	20 (10.1%)	0.415
Myalgia	62 (31.2%)	0.497
Loss of taste	6 (3.0%)	**0.024**
Loss of smell	7 (3.5%)	**0.043**
Difficulty breathing	9 (4.5%)	0.792
Runny nose	21 (10.6%)	0.431
Headache	22 (11.1%)	0.553
Chest pain	9 (4.5%)	0.792
Hospitalization at first infection	16 (8.0%)	0.655
Hospitalization at second infection	1 (0.5%)	0.975
Comorbidities, n (%)		
Asthma	15 (7.5%)	0.673
CAD	5 (2.5%)	0.879
COPD	2 (1.0%)	0.950
CVD	1 (0.5%)	0.975
CRF	2 (1.0%)	0.950
Hypertension	20 (10.1%)	0.585
Depression	5 (2.5%)	0.879
Malignancy	5 (2.5%)	0.879
Single-dose vaccine	36 (18.1%)	0.635
Number of symptoms	1.79 ± 0.824	0.331
Number of comorbidities	0.33 ± 0.718	0.232

Time, the time between the day with covid-19 (+) for the first time and applying to the covid-19 polyclinic for the second time; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; CRF, chronic renal failure, p < 0.05

Table 2. Evaluation of PCR positivity and symptom severity in the whole sample at the time of second presentation

		n	%	p value
PCR result	Positive	5	2.5	**0.000**
	Negative	194	97.5	
Symptom	Similar	104	52.3	**0.000**
	Milder	71	35.7	
	More severe	24	12.0	

p < 0.05

The correlation analysis revealed that PCR positivity was not correlated with the time elapsed since the initial COVID-19 infection, symptom, or the increase in the number of symptoms (Table 3). In the logistic regression analysis, it was observed that the variables of loss of taste, loss of smell, and symptom severity did not have an effect on PCR positivity when evaluated independently (Table 4).

Table 3. Correlation analysis of the variables (Spearman's correlation test)

		Gender	Age	Time elapsed	Symptom severity	PCR	Number of symptoms	Number of comorbidities
Gender	Correlation coefficient	1	0.082	-0.005	0.025	0.11	-0.087	0.051
	p	.	0.249	0.948	0.722	0.12	0.222	0.477
	r	199	199	199	199	199	199	199
Age	Correlation coefficient	0.082	1	-0.028	-0.004	0.096	0.034	0.398**
	p	0.249	.	0.697	0.956	0.178	0.639	0
	r	199	199	199	199	199	199	199
Time elapsed	Correlation coefficient	-0.005	-0.028	1	0.042	-0.029	0.051	-0.071
	p	0.948	0.697	.	0.559	0.682	0.473	0.318
	r	199	199	199	199	199	199	199
Symptom severity	Correlation coefficient	0.025	-0.004	0.042	1	0.045	-0.039	0.029
	p	0.722	0.956	0.559	.	0.528	0.585	0.689
	r	199	199	199	199	199	199	199
PCR	Correlation coefficient	0.11	0.096	-0.029	0.045	1	0.069	-0.085
	p	0.12	0.178	0.682	0.528	.	0.332	0.233
	r	199	199	199	199	199	199	199
Number of symptoms	Correlation coefficient	-0.087	0.034	0.051	-0.039	0.069	1	0.118
	p	0.222	0.639	0.473	0.585	0.332	.	0.097
	r	199	199	199	199	199	199	199
Number of comorbidities	Correlation coefficient	0.051	0.398**	-0.071	0.029	0.085	0.118	1
	p	0.477	0	0.318	0.689	0.233	0.097	.
	r	199	199	199	199	199	199	199

$p < 0.05$

Table 4. Effect of investigated variables on PCR positivity at the time of second presentation (binary logistic regression analysis)

	p	*OR*	% confidence interval for OR Lower	95% confidence interval for OR Upper
Gender	0.168	0.187	0.017	2.026
Age	0.239	1.043	0.972	1.118
Time elapsed	0.923	1.001	0.989	1.013
Symptom severity (similar)	0.538	-	-	-
Symptom severity (milder)	0.285	0.231	0.016	3.387
Symptom severity (more severe)	0.337	0.256	0.016	4.135
Loss of taste	0.848	0.628	0.005	71.843
Loss of smell	0.287	0.070	0.001	9.369
Constant	0.705	0.454	-	-

$p < 0.05$, OR: odds ratio

4. Discussion

In this study, PCR positivity was found to be statistically significantly low at the second visit of patients with COVID-19-like symptoms. When we evaluated the time from the initial COVID-19 diagnosis to referral to our department by triage due to COVID-19-like symptoms according to PCR positivity, there was no statistical significance (p =0.681). Variability in symptom severity also did not affect PCR positivity when evaluated alone.

In some sources, reinfection is defined as a positive PCR test after 90 days without symptoms (3), while other sources indicate that the interval between two infection episodes should be at least one month in order to evaluate symptoms and compare PCR results in patients who have had two COVID-19 infections. In a multicenter case study, of the total 45 patients confirmed to have had two COVID-19 infections, all 12 that recovered from their first COVID-19 infection through home follow-up and experienced only mild dyspnea only presented with the mild form of the disease for the second time and only four of these patients had dyspnea at the time of the second infection. In contrast, the frequency of headache increased at the second presentation (4). In our study, the time from the first COVID-19 infection to the presentation with COVID-19-like symptoms was at least one month, and 52.3 % of our patients presented with symptoms of similar severity. Similarly, in a case series by Lechien et al. (4), reinfection was not observed in any of the patients who

had been hospitalized and had a relatively more severe form of the disease at the time of the first diagnosis.

In a study conducted in Denmark in which PCR positivity was evaluated for the second time, there was no statistically significant relationship between reinfection and gender, while the rate of reinfection was higher in the elderly population (5). In our study, there was no statistically significant relationship between gender and age and a second positive PCR test. In addition, we observed no statistically significant relationship between the presence and number of comorbidities and PCR positivity.

In Turkey, when patients refer to a hospital with different symptoms, they are referred to COVID-19 outpatient clinics by triage based on the symptoms of the disease in accordance with the guidelines of the Turkish Ministry of Health (2). In our study, loss of taste and loss of smell, which are symptoms specific to COVID-19, had a statistically significant relationship with PCR positivity for the second time, but we found that neither symptom had a significant effect on PCR positivity in the regression analysis. We also detected no statistically significant correlation between other complaints, such as flu symptoms and myalgia and PCR positivity. In a case report published by Jain et al. (6), a 21-year-old female patient with PCR positivity had the recurrence of loss of smell complaint at the end of the first-second week after her complaints had resolved. The authors performed a swab test 30 days after the first test and detected PCR positivity again.

To date, most COVID-19 reinfections have been known to be milder than the first encounter with the virus (7). In our study, the rate of patients with milder symptoms was 35.7 %, and the rate of those presenting with similar symptoms was statistically significantly higher. However, it should not be forgotten that our patients were those did not require intensive care.

In vaccine studies, it has been stated that immune response through vaccination may be stronger than immune response that occurs with COVID-19 transmission (7,8). At the time of our study, a single dose of a vaccine was being administered in the relevant patient group, and the rate of our patients that received a single dose of a vaccine was 18.1%. There was no statistically significant correlation between the second-time PCR positivity and presence/absence of vaccination. Our vaccinated patients did not receive the mRNA vaccine, but they were vaccinated with a subunit vaccine that inhibited T cell activation. It remains unclear whether vaccines that neutralize active T cells provide sustained and sterilizing immunity in the long term (3). In addition to knowing that reinfections can happen, it is also important to note that having a COVID-19 infection significantly increases antibody levels. Despite studies indicating that the antibody level decreased during the follow-up, Alter et al. showed that antibody titers were stable for four months (9).

In our study, the number of PCR positivity for the second time was quite low. In addition, at the time of the study, a single dose of vaccine was administered in our country and the number of patients who had covid was very low compared to the first applications. We aimed to reduce the PCR request in terms of cost and to reduce the density of patients with similar symptoms.

Symptoms specified in the guidelines should be re-evaluated when ordering a PCR test, and changes should be made to the PCR requests and patient referrals to COVID-19 outpatient clinics. Currently, when there are great efforts to achieve immunization against COVID-19, the rise in the number of hospital presentations will cause an increase in the risk of transmission and hospital costs. Current guidelines should be updated in light of the results of vaccination studies.

Conflict of interest

The authors declared no conflict of interest.

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Authors' contributions

Concept: A.H.S., K.T.K.., Design: A.H.S., Ö.S., Data Collection or Processing: A.H.S., K.T.K., Ö.S., Analysis or Interpretation: K.T.K., Ö.S., Literature Search: A.H.S., Ö.S., Writing: A.H.S., K.T.K., Ö.S.

References

1. Republic of Turkey Ministry of Health. Covid-19 Information page. [ınternet]. 2021(up-dated 2020 Dec 20; cited 2021 Oct 21) Available from: https://covid19.saglik.gov.tr/TR-66935/genel-koronavirus-tablosu.html.

2. Republic of Turkey Ministry of Health. Covid-19 Information page. [ınternet]. 2021(up-dated 2020 Jan 20; cited 2021 Oct 21) Available from:https://covid19.saglik.gov.tr/Eklenti/40719/0/covid-19rehberieriskinhastayonetimivetedavipdf.pdf.

3. Yahav D, Yelin D, Eckerle I, Eberhardt CS, Wang J, Cao B et al. Definitions for coronavirus disease 2019 reinfection, relapse and PCR re-positivity. Clin Microbiol Infect. 2021;27(3):315-8. Doi: 10.1016/j.cmi.2020.11.028.

4. Lechien JR, Chiesa-Estomba CM, Radulesco T, Michel J, Vaira LA, Le Bon SD et al. Clinical features of patients who had two COVID-19 episodes: a European multicentre case series. J Intern Med. 2021;290(2):421-9. Doi:10.1111/joim.13259.

5. Hansen CH, Michlmayr D, Gubbels SM, Mølbak K, Ethelberg S. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. Lancet. 2021;397(10280):1204-12. Doi:10.1016/S0140-6736(21)00575-4.

6. Jain A, Kaur J, Rai AK, Pandey AK. Anosmia: A Clinical Indicator of COVID-19 Reinfection. Ear, Nose & Throat Journal. 2021;100(2_suppl):180S-181S. Doi:10.1177/0145561320978169.

7. Stokel-Walker C. What we know about covid-19 reinfection so far. BMJ.2021;372:n99. Doi:10.1136/bmj.n99.

8. mRNA-1273 Study Group, Widge AT,Rouphael NG,Jackson LA, Anderson EJ, Roberts PC, Chappell JD et al. mRNA-1273 Study Group. Durability of responses after SARS-CoV-2 mRNA-1273 vaccination. N Engl J Med. 2021;384:80-2.Doi:10.1056/NEJMc2032195.

9. Alter G., Seder R. The power of antibody-based surveillance.N Engl J Med.2020 ;383(18):1782-4.Doi:10.1056/NEJMe2028079.