

CLINICAL STUDY

The factors affecting the prolonged PCR positivity in COVID-19 patients

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OBJECTIVES: The aim of this study is to investigate the effects of factors such as age, gender, comorbid diseases and treatments applied on the positive duration of the PCR test in COVID-19 patients.

Background: The duration of PCR positivity in COVID-19 patients varies. Studies in the literature investigating factors that may affect this duration are limited.

METHODS: Between March and September 2020, individuals with two or more positive PCR results with a 14-day interval were included in the case group, and those whose PCR results turned negative within 14 days were included in the control group. The relationship between age, gender, contact environment, presence of additional disease, drugs used, smoking and alcohol consumption; type, duration and severity of COVID-19 symptoms, treatment applied for COVID-19 and duration of PCR positivity were examined.

RESULTS: Among 126 participants the mean duration of PCR positivity was 23.38 days (min 6, max 52). Symptoms lasted 15–30 days in 41 patients (32.5 %) and 5–10 days in 30 patients (23.8 %). The positivity duration varied according to age, smoking and alcohol consumption status, and body mass index. Patients with chronic disease, and who had loss of taste and smell during the disease had a longer positive stay. This period was shorter in favipiravir users.

CONCLUSION: In COVID-19 infection, there are several factors that affect the PCR test to remain positive.

Early-term favipiravir use may shorten this period as a modifiable factor (*Tab. 3, Ref. 14*). Text in PDF www.elis.sk

KEYWORDS: COVID-19, PCR, positivity duration.

Introduction

Since 2019, many studies have been published on the pathophysiology and epidemiology of SARS-CoV-2 (COVID-19) infection, which has rapidly turned into a pandemic. The relationship between the positivity of the polymerase chain reaction (PCR) test, which is widely used in the diagnosis of the disease, and the course of the disease is important in the planning of infection control strategies (1). From this point of view, besides mild or moderate case series that present viral positivity and symptomatology comparison; there are also studies examining viral dynamics in critically ill patients (2–4).

When the infection parameters of the patients are examined in general terms, it is seen that viral RNA can be detected first in the respiratory tract in a short time after infection.

Even 1–2 days before the patient becomes symptomatic, it is possible to detect viral RNA in the upper respiratory tract (5). However, virus can be isolated from the nasopharynx for an average of 14–21 days from the onset of symptoms (6).

The first COVID-19 case in our country was detected in March 2020 (7). Within the scope of the contact tracing studies carried out since this date, the isolation times of the patients have been updated many times in the light of new data. In this context, while the quarantines of the people in isolation are terminated, control PCR tests are not performed, but there are also cases where the test is done at the end of isolation for reasons such as employer demand. During these follow-ups, it was noticed that some patients were PCR negative in as short as 5 days period, but some had PCR positivity for more than 30 days.

When the literature data is examined, it is observed that PCR positivity is prolonged or fluctuating after discharge in COVID-19 patients (8). There are studies and case reports showing that the infectiousness does not continue in people with long-lasting PCR positivity (9). There are also publications reporting that prolonged PCR positivity is not associated with the strength of the antibody response or the severity of symptoms (10). On the other hand, studies investigating factors that may affect PCR positivity duration are limited.

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The aim of this study is to investigate the effects of factors on the positive duration of the PCR test in COVID-19 patients.

Methods

Study population and sample

Between March 1 and September 30, 2020, 1817 people registered on Tuzla District Health Directorate, Public Health Management Systems program were screened. Eighty-seven people with a positive stay of 14 days or more were identified. After eliminating the missing data in the system, the remaining 79 people were included in the study.

Data collection tools

The data were analyzed so that persons with two or more positive PCR results with an interval of 14 days were recorded as the case, and those whose PCR results turned negative within 14 days were recorded as the control group. Since the isolation duration is applied as 14 days in many countries, this period has been determined as the separation point for short and long positivity periods. Persons with full records of age, gender, contact environment, presence of additional disease, drugs used, smoking and alcohol consumption; type, duration and severity of COVID-19 symptoms, treatment applied for COVID-19 were included in the study. The relationship between the recorded parameters and the positivity duration of the PCR test was examined.

Statistical analysis

Statistical analyzes were performed with Python 3 Jupyter Notebook and Pandas, Scipy, Numpy, Seabornlibraries. While the proportional differences of the categorical variables in the 2x2 crosstables were analyzed with the Fischers' Exact test, the chi-square test was used for the proportional differences between the categorical variables in the nxn crosstables. Statistical significance was tested at the alpha=0.05 level.

Ethics Committee approval was obtained from Marmara University, School of Medicine (Decision No.09.2021.670).

Results

Among the 126 persons who participated in the study, 0–17 age group comprised 4% of the general population, while 18–50 years old 81 %, 51–65 years old 9.5 %, 69–79 years old 4.8 % and over 80 years old age constituted 0.8 %. Half of the patients were women and half were men (Tab. 1).

Subjects with chronic illness were 19.0 % (n=24), subjects without illness represented 81.0 % (n=102); 17.5 % of patients had regular drug use. 61.1 % of the patients did not consume alcohol or cigarettes at all (Tab. 1). The most frequently used treatments were favipiravir and hydroxychloroquine (37.2 % and 36.7 %), 1.5 % of the patients were followed without medication. While 29.9 % of the patients did not take any supplements other than drugs, the most commonly used supplement was vitamin C (24.6 %).

The mean duration of PCR test positivity of the cases was 23.38 days, with a minimum of 6 and a maximum of 52 days.

Tab. 1. General characteristics of participants.

	Frequency	%	
Age	0–17	5	4.0
	18–50	102	85.0
	51–65	12	9.5
	≥69	7	5.5
	Total	126	100.0
Gender	Male	63	50.0
	Female	63	50.0
	Total	126	100.0
BMI	<18.5	4	3.2
	18.5–24.9	47	37.3
	25–29.9	56	44.4
	≥30	18	15.07
	Total	126	100.0
Education	High school and below	42	33.3
	University and above	84	66.7
	Total	126	100.0
Occupation	Healthcare worker	63	50.0
	Non healthcare worker	63	50.0
	Total	126	100.0
Marital status	Single	59	46.8
	Married	67	53.2
	Total	126	100.0
Comorbid disease	No	102	81.0
	Yes	24	19.0
	Total	126	100.0
Drug use	No	104	82.5
	Yes	22	17.5
	Total	126	100.0
Smoking	Occasionally	6	4.8
	Regularly	26	20.6
	Quitter	17	13.5
	Never	77	61.1
	Total	126	100.0
Alcohol consumption	Never	77	61.1
	≥2 times a month	18	14.3
	Rarely	31	24.6
Total	126	100.0	

When the symptoms seen during the disease are examined, it is seen that the most common symptom is taste and smell disorders (48.4 % and 46 %, respectively). The least common symptom was diarrhea (8.7 %) (Tab. 2).

We examined the relationship between the age and time of the PCR test to turn negative. All of the patients in the 0–17 and 69–79 years of age groups stayed positive for more than 14 days; 55.9 % of the patients in the 18–50 age group and 83.3 % of the patients in the 51–65 age group were also positive for more than 14 days. This difference was statistically significant (p=0.023). No statistically significant difference was found in the comparison made according to gender (p=0.14).

In the analyzes made according to body mass index (BMI), it was observed that the rate of test positivity for more than 14 days increased as the BMI increased (p=0.039). While the rate of long positivity is 56.3 % in those who exercise regularly, it is 65.6 % in those who do not. The difference was not found statistically significant (p=0.398).

Tab. 2. Distribution of symptoms.

		Frequency	%
Loss of taste	No	65	51.6
	Yes	61	48.4
	Total	126	100.0
Loss of smell	No	68	54.0
	Yes	58	46.0
	Total	126	100.0
Joint pain	No	72	57.1
	Yes	54	42.9
	Total	126	100.0
Weakness	No	76	60.3
	Yes	50	39.7
	Total	126	100.0
Headache	No	77	61.1
	Yes	49	38.9
	Total	126	100.0
Dry cough	No	86	68.3
	Yes	40	31.7
	Total	126	100.0
Fever	No	91	72.2
	Yes	35	27.8
	Total	126	100.0
Myalgia	No	94	74.6
	Yes	32	25.4
	Total	126	100.0
Sore throat	No	96	76.2
	Yes	30	23.8
	Total	126	100.0
Chest pain	No	104	82.5
	Yes	22	17.5
	Total	126	100.0
Anorexia	No	108	85.7
	Yes	18	14.3
	Total	126	100.0
Shortness of breath	No	114	90.5
	Yes	12	9.5
	Total	126	100.0
Diarrhea	No	115	91.3
	Yes	11	8.7
	Total	126	100.0
Other	No	100	79.4
	Yes	26	20.6
	Total	126	100.0

Considering the smoking status, the group with the highest rate of staying positive for more than 14 days is “former user” (82.4 %), while the group with the lowest rate is “regular smokers” (26.9 %). The difference between the groups was statistically significant ($p < 0.001$).

Similarly, while this rate is highest in non-alcoholics (72.7 %), it is lowest in those who consume alcohol once a week (25 %) ($p = 0.005$).

The contact status of the patients with the index case and the time to turn negative were compared. The rate of lasting more than 14 days in those with unknown contact status was 80.0 %. This rate was 80.0 % in those in contact with low-risk, 81.0 % in those

Tab. 3. Multivariable analysis of results.

Variable	Odds Ratio	95% CI (profile likelihood)
Age 51–64	10.71	0.32–922.1
Sex	1.35	0.34–5.28
Married	1.29	0.29–5.79
Comorbid disease	19.82	2.24–521.6
Smoker	0.94	0.87–1.02
Hospitalization	8.89	1.23–110.6
Weakness	0.31	0.06–1.24
Loss of taste	14.69	3.12–107.6
Favipiravir	0.14	0.02–0.7
Vitamin C	0.67	0.07–5.38

in contact with medium-risk, and 51.6 % in those in contact with high-risk. The difference was statistically significant ($p = 0.013$).

The presence of symptoms at the time of testing did not significantly affect the duration of positivity ($p = 0.223$).

When the follow-up period was examined, the rate of staying positive for more than 14 days in those who were followed up at home was significantly lower in than those who were hospitalized ($p = 0.02$). When analyzed according to the type of symptoms developing during the disease, the rate of lasting longer than 14 days was significantly higher in those with taste-smell loss or joint pain and fatigue ($p = 0.04$ and $p = 0.002$, respectively). The difference was not significant in patients with fever, cough, chest pain, headache, sore throat, anorexia and diarrhea ($p > 0.05$).

As a result of the multivariable analysis made with statistically significant values, being between the ages of 51 and 65 was associated with 10.71 times, the presence of chronic disease 19.82 times, being hospitalized 8.89 times, and taste disorder 14.69 times associated with long positivity; using favipiravir reduces this by 0.146 times (Tab. 3).

Discussion

In the literature, there are studies with different results regarding the positive stay of PCR test. In a study of 7093 patients, 69.8 % of patients had the first negative result at 20 days, with approximately one-third remaining positive for 40 days (11).

Studies comparing the positive duration of PCR with clinical and demographic characteristics of patients are limited. In a study conducted with 47 patients in China, positive stays for less than 1 week and for longer than 1 week were examined. In this study, unlike our study, no significant relationship was found between age, contact history, smoking status and duration (12).

In a cohort, the mean detection time of SARS-CoV-2 RNA was found to be 17 days from the onset of the disease, and especially male gender and severe course requiring invasive mechanical ventilation were found to be risk factors for the prolongation of positivity (13). In the retrospective cohort conducted by Fu et al, the short positivity period was accepted as 20 days, and it was seen that demographic characteristics did not have a serious effect on persistent viral positivity (1). In another study, it was reported that persistent positivity could be observed in patients over 70 years of age, in the presence of chronic renal failure, hy-

pertension, hyperlipidemia, obesity and coronary artery disease, and this period was extended up to 4 weeks after diagnosis (4). In the cohort conducted by Carmo et al., the characteristics of 210 patients who had repeated PCR tests were investigated (11). It was determined that those with moderate disease remained positive for longer, and it was concluded that RNA persistence was not related to the severity of the disease, but was related to the clearance capacity of the immune system. In a study investigating the duration of viral shedding in critically ill patients and the factors affecting it, it was reported that viral shedding took longer in cases with severe disease (14).

Since free control PCR testing was not included in the guideline for a long time in our country, most of the cases in our study were healthcare professionals, while the others consisted of people who had been tested on their own request or a limited population followed during hospitalization. Therefore, developing the study within a larger and heterogeneous group will increase its power. On the other hand, since studies examining the factors affecting PCR positivity in cases in our country are very limited, we think that this study will make an important contribution to the literature.

Conclusion

The positive duration of the PCR test in COVID-19 infection may differ from person to person. According to the results of our study, while being between the ages of 51-65, presence of chronic disease, high body mass index, being hospitalized and taste disturbance were associated with long positivity; using favipiravir shortens the positivity period.

References

1. Fu Y, Li Y, Guo E, He L, Liu J, Yang B et al. Dynamics and Correlation Among Viral Positivity, Seroconversion and Disease Severity in COVID-19: A Retrospective Study. *Ann Intern Med* Nisan 2021; 174 (4): 453–461.
2. Li H, Liu L, Zhang D, Xu J, Dai H, Tang N et al. SARS-CoV-2 and viral sepsis: observations and hypotheses. *Lancet Lond Engl* 2020; 395 (10235): 1517–1520.
3. Liu Y, Yan LM, Wan L, Xiang TX, Le A, Liu JM et al. Viraldynamics in mildand severe cases of COVID-19. *Lancet Infect Dis* 2020; 20 (6): 656–657.
4. Aldhaefi M, Tahir Z, Cote DJ, Izzy S, El Khoury J. Comorbidities and Age Are Associated With Persistent COVID-19 PCR Positivity. *Front Cell Infect Microbiol* 2021; 11: 650753.
5. Erensoy S. COVID-19 Pandemisinde SARS-CoV-2 ve Mikrobiyolojik Tani Dinamikleri. *MİKROBİYOLOJİ Bül*: 13.
6. Rabaan AA, Tirupathi R, Sule AA, Aldali J, Mutair AA, Alhumaid S et al. Viral Dynamics and Real-Time RT-PCR CtValues Correlation with Disease Severity in COVID-19. *Diagn Basel Switz* 2021; 11 (6): 1091.
7. Bulut C, Kato Y. Epidemiology of COVID-19. *Turk J Med Sci* 2020; 50 (SI-1): 563–570.
8. Cento V, Colagrossi L, Nava A, Lamberti A, Senatore S, Travi G et al. Persistent positivity and fluctuations of SARS-CoV-2 RNA in clinically-recovered COVID-19 patients. *J Infect* 2020; 81 (3): e90–92.
9. Suri T, Mittal S, Tiwari P, Mohan A, Hadda V, Madan K et al. COVID-19 Real-Time RT-PCR: Does Positivity on Follow-up RT-PCR Always Imply Infectivity? *Am J Respir Crit Care Med* 2020; 202 (1): 147.
10. Ikegami S, Benirschke R, Flanagan T, Tanna N, Klein T, Elue R et al. Persistence of SARS-CoV-2 nasopharyngeal swab PCR positivity in COVID-19 convalescent plasma donors. *Transfusion (Paris)* 2020; trf.16015.
11. Carmo A, Pereira-Vaz J, Mota V, Mendes A, Morais C, Silva AC et al. Clearance and persistence of SARS-CoV-2 RNA in patients with COVID-19. *J Med Virol* 2020; 92 (10): 2227–2231.
12. Lu J, Yin Q, Li Q, Fu G, Hu X, Huang J et al. Clinical characteristics and factors affecting the duration of positive nucleic acid test for patients of COVID-19 in XinYu, China. *J Clin Lab Anal* 2020; 34 (10): e23534.
13. Xu K, Chen Y, Yuan J, Yi P, Ding C, Wu W et al. Factors Associated With Prolonged Viral RNA Shedding in Patients with Coronavirus Disease 2019 (COVID-19). *Clin Infect Dis Publ Infect Dis Soc Am* 2020; 71 (15): 799–806.
14. van Kampen JJA, van de Vijver DAMC, Fraaij PLA, Haagmans BL, Lamers MM, Okba N et al. Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19). *Nat Commun* 2021; 12 (1): 267.

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