
ANALYSIS OF RECURRENT POSITIVE COVID-19 PATIENTS IN A HOSPITAL**Ensar Durmus^{1*}, Fatih Guneyisu¹**¹Sakarya University Training and Research Hospital, Turkey*Correspondence email: ensar.durmus@saglik.gov.tr

ABSTRACT

The studies about COVID-19 began to show that people who have already had COVID-19 were re-admitted to the hospital due to COVID-19 positivity. This study aims to identify recurrent positive patients and the demographic characteristics of these patients. The number of recurrent COVID-19 positive patients was 190. Of these patients, 97 (51.1%) were male, the average age was 44 years (± 16), 147 (77.4%) were never hospitalized, Of the hospitalized patients, 28 (65.1%) were male, and the average age of the inpatients was 54.67 years (± 16.15). Looking at the duration of hospital stay of the inpatients, it was observed that the average was 11.16 days (± 8.9). A positive correlation was found between the age of the patients and the duration of their hospital stay ($r=0.386$). The average time between the two positives was 53 days. Patients who have a recurrent positive result usually survive the disease with outpatient treatment for their mild illness. Hospitalization rates of male patients were higher than those of females, and the duration of hospital stay was found to increase as the age of the patients' increases.

Keywords: COVID-19; Pandemic; Recurrence

INTRODUCTION

The COVID-19 disease, which emerged in late 2019, spread all over the world and was declared as a pandemic, continued to have its impact throughout 2020. Numerous methods and constraints, such as international travel bans, closure of borders between countries, the need to wear a mask, social distancing, meeting bans, prohibition of collective activities, and curfew to reduce the spread of the virus.^{1,2} Despite all this, COVID-19 disease continued to rise, although it sometimes reduced its impact regionally. Some countries have begun to discuss the second wave of COVID-19 and its effects.³ In addition to all the measures taken, intensive vaccine development activities have been started in many countries to cope with the virus, restricting our social life.⁴ Although there is no definitive experience of the effectiveness of vaccines yet, vaccine studies for a permanent solution continue to be followed by people with hope.

Although the world was expecting relief, studies began to show that people who have already had COVID-19 were again admitted to the hospital due to COVID-19 positivity.⁵ When someone who has had COVID-19 tests positive again for COVID-19? Is reinfection possible? How long antibodies protect us? How long will the protection last through the vaccines that induce antibodies in the fight against COVID-19? These questions come to mind without an answer yet. There must be a sufficient number of studies in the current medical literature on recurrent COVID-19 cases to find answers to these questions.

This study aims to identify whether there were recurrent RT-PCR positive patients who have tested positive for COVID-19 before, the demographic characteristics of these patients, the duration between recurrent positive test results, re-hospitalization status, and mortality. In this way, the study aims to contribute to the current medical literature in

terms of supporting the studies of valuable researchers looking for answers to the above-mentioned questions.

MATERIAL AND METHODS

This study was conducted at the 1300-bed Sakarya University Training and Research Hospital (SEAH), the largest hospital in Sakarya province, which served as a pandemic hospital during the COVID-19 pandemic. In SEAH, admission for the first suspected or symptomatic cases is handled in reserved areas in the emergency department. All cases tested positive again at least 14 days after the first RT-PCR positive test result, who were admitted to the SEAH emergency department from 19/03/2020, which is the time of the first Real-Time Reverse transcription-polymerase Chain Reaction (RT-PCR) positive COVID-19 case until 05/01/2021 were included in the research. Undecided cases, those with typical chest tomography findings without a positive RT-PCR test, and patients under the age of 18 were excluded from the research. First nasopharyngeal and then oropharyngeal RT-PCR samples were collected in a combined and sequential manner.

According to the COVID-19 guidelines of the Ministry of Health in Turkey, 14 days of isolation were applied to patients who tested positive for COVID-19 RT-PCR in the first days of the pandemic, without requiring a negative RT-PCR test immediately after the treatment and isolation periods. Later, with the updates made in the guidelines, isolation was applied for ten days for outpatient patients, 14 days for patients hospitalized for more than one day in the service, and 20 days for patients hospitalized in intensive care. Therefore, since there was no routine to perform RT-PCR test again in the first 14 days for the patients who tested positive, patients whose time between two RT-PCR positives more than 14 days were included in the study.

The data were obtained from the hospital automation system and patient files with the

permission obtained from the SEAH Chief Physician Office on 14/01/2021 by paying attention to the confidentiality of personal data. The data obtained were evaluated using the IBM Statistical Package for the Social Sciences (SPSS) version 21 statistics program, and the Skewness and Kurtosis values in the range of $-2/+2$ were tested for compliance with the normal distribution of the data.⁶ The Pearson correlation test was used for the correlation of those within this interval. Values outside this range were considered to have non-normal distribution, and the Spearman correlation test was used for non-parametric correlation analysis. A Chi-square test was used to compare categorical data. For the results, $p < 0.05$ was considered statistically significant. A Scientific Research permit, dated 11/01/2021, was obtained from the Republic of Turkey Ministry of Health.

RESULTS AND DISCUSSION

The number of patients who tested positive for RT-PCR for the second time was 190, with at least 15 days intervals during the study period. Of these patients, 97 (51.1%) were male, and 93 (48.9%) were female. The average age was 44 years (± 16), the median age was 41.5 years, the minimum was 19 years, and the maximum was 86 years.

Of the patients, 147 (77.4%) were never hospitalized, and 43 (22.6%) were hospitalized at least once and treated. The hospitalization status of the patients is shown in Table 1.

Table 1. Hospitalization Status of Patients

Hospitalization Status	Number	Percent %
Never hospitalized	147	77.4
At the first admission	29	15.2
At the second admission	7	3.7
At both admissions	7	3.7
Total	190	100

A statistically notable distinction was found when the outpatient treatment was analyzed with the gender of the patients ($p=0.036$, See Table 2). Of the hospitalized patients, 28 (65.1%) were male, and 15 (34.9%) were female. As 16.1% of female patients and 28.9% of male patients were

hospitalized, it was observed that male patients were hospitalized at a higher rate. The average age of the inpatients was 55 years (± 16), the median age was 55 years, the minimum was 25 years, and the maximum was 86 years.

Table 2. Gender and Age Statistics of Patients

Variable		Gender Statistics			Age Statistics	
		Male Count	Female Count	p Value	Median Age	Statistical Value
Mortality Status	Ex	6	1	0.066 ¹	73	$t(8,509)=-9,873, p<0.005^2$
	Alive	91	92		41	
Hospitalization Status	Inpatient	28	15	0.036 ¹	55	$t(188)=-5,210, p<0.05^2$
	Outpatient	69	78		38	
Hospital Unit ³	Ward	18	13	0.176 ¹	48	$p=0.077^4$
	ICU	5	0		72	
	Ward+ICU	5	2		57	
Duration Between Two Positive Tests	15-30 days	60	57	0.870 ¹	46	$p=0.054^4$
	31-60 days	12	14		35	
	61-90 days	7	8		36	
	91 days <	18	14		36,5	

¹Pearson Chi-Square test; ²Independent t test; ³Unit of inpatients; ⁴Kruskal Wallis Test

Of the inpatients, 31 (72.1%) received treatment only in the service, and 12 (27.9%) received treatment in intensive care. Looking at the duration of hospital stay of the inpatients, it was observed that the average was 11.16 days (± 8.9), between a minimum of 2 days and a maximum of 34 days. A weak but significant positive correlation was found between the age of the patients and the duration of their hospital stay ($r=0.372$). Accordingly, the duration of hospital stays increases as the age of patients increases.

The average time between the two positives was 52.92 days, the median value was 21.5 days, the minimum was 15 days, and the maximum was 244 days. Of these patients, 9 (4.7%) maintained their positivity despite hospitalization for 14 days. The average duration between two positive tests of patients in this group was 18.9 days (± 5.01), between a minimum of 15 days and a maximum of 30 days. Looking at the time between the two positives on a monthly basis, it is seen that 117 patients (61.6%) tested positive for RT-PCR again within the first 30 days. Only 59

patients (31.1%) were found to have a negative RT-PCR result between the two RT-PCR positives. Of the patients, 131 patients (68.9%) had no negative RT-PCR results

between two positive RT-PCR results. See Table 3 for two RT-PCR test positives and elapsed time between the two positives.

Table 3. Time Intervals between the Two Positive RT-PCR Tests

Duration ^a	There is a Negative in between ¹		No Negatives between ²		Total Count	Percent % ³
	Count	Percent % ³	Count	Percent % ³		
15-30	26	13.68	91	47.89	117	61.57
31-60	8	4.21	18	9.47	26	13.68
61-90	7	3.68	8	4.21	15	7.89
91<	18	9.47	14	7.36	32	16.84
Total	59	31.05	131	68.94	190	100

^a Number of days between two positive RT-PCR test results; ¹ There were negative RT-PCR test result(s) in between two positive RT-PCR tests; ² No negative RT-PCR test results between the two positive RT-PCR tests; ³ It is the percentage value in the total number of patients.

Looking at the mortality rates of the patients, 7 out of 190 patients (3.68%) decreased. Of the deceased patients, six were male (3.15% in total), and 1 (0.53% in total) was female. However, no statistically significant difference was found between the mortality status and the gender of the patients ($p=0.119$). The average age of these patients was 71.43 years (± 6.99), and the median value was 73 years. Of the patients, five died in intensive care, 1 died in inpatient service, and 1 in outpatient treatment.

The issue that will need to be discussed most in this study is the time interval between positive RT-PCR results. Indeed, samples collected from 117 (61.57%) of 190 patients tested positive for RT-PCR within the first 30 days. In this group of 117 patients, although 26 patients tested negative for RT-PCR after the first positive RT-PCR result, they tested positive in the subsequent PCR tests. In the remaining 91 people of this group of 117 patients, RT-PCR positivity was observed again in their subsequent admissions, regardless of whether there was a negative after the first positive RT-PCR result during their outpatient or inpatient treatment. In this case, how will we interpret this fact? Is there a false negative associated with the difficulty

of taking the RT-PCR swab, or should we consider that patients who have tested negative are infected again within a month?

In their systemic review of 2568 patients, Mahalul Azam et al. found a recurrent positive incidence of 14.8% and reported that the time from the onset of the disease to the date of re-positivity was an average of 35.4 days, and the time between the last negative result and the re-positive result was 9.8 days.⁷ Bo Yuan et al. also found that 20 (10.99%) out of 182 COVID-19 patients under medical isolation had recurrent positivity, of which 13 tested positive on the 7th day and 7 of them on the 14th day.⁸ Tie-Jun Shui et al. examined 758 COVID-19 patients who had at least two negative test result before being discharged from the hospital and concluded that 59 patients (7.78%) tested positive again 33 days after their first admission on average.⁹ In a meta-analysis conducted by Tung Hoang, about 15% of 3644 discharged COVID-19 patients were tested positive again at a later time.¹⁰ It has been noted by Steven Woloshin et al. that swab samples taken for COVID-19 can give false-negative results at different rates.¹¹ In addition, it has been reported that although there were negative results in the upper respiratory tract samples, positive

results continued to be obtained in gastrointestinal tract samples.¹² Ai Tang Xiao et al. examined 70 COVID-19 patients who were tested positive again in their study and suggested that 15 (21.4%) may be false-negative and that these patients may show positive again due to prolonged nucleic acid conversion.¹³ Since there were reports on the detection of the virus in the upper respiratory tract of the COVID-19 patients for at most 83 days, Falahi and Kenarkoohi reported that positive results after 83 days could be considered reinfection if there was a symptom-free period between them; otherwise, it could be considered as a prolonged COVID-19 infection.¹⁴

In a meta-analysis study, Muge Cevik et al. examined 79 COVID-19 studies and found that the average time to detect the virus in the upper respiratory tract, lower respiratory tract, feces, and serum was 17 days 14.6 days, 17.2 days, and 16.6 days, respectively. In addition, they noted that the longest duration of time for virus positivity was 83 days, 59 days, 35 days, and 60 days, respectively, in the same areas.¹⁵

In our study, 117 patients were found to be tested positive for RT-PCR again within the first 30 days, but 32 patients (16.84%) were RT-PCR positive in their re-admissions after 91 days and above. It is impossible to make a final decision on this issue until there is a guideline to help us decide which case is a prolonged COVID-19 infection and which case is reinfection. However, despite the negative RT-PCR test results in upper respiratory tract samples, it may be correct to consider the positive RT-PCR results within the first three months as the manifestation of a prolonged infection due to the fact that the virus can continue to exist in the gastrointestinal tract, and the virus can remain positive for up to 83 days. Moreover, although it is not certain, it is understood that further research and information is needed to consider the new positive test results that will occur in hospital admission after the first three months as a recurrent COVID-19 infection.

Tie-Jun Shui et al. noted that patients who tested positive for the second time were

mostly mild and moderately severe, while Bo Yuan et al. reported that recurrent positivity was more common in young people and asymptomatic.^{8,9} In line with this, Anna Gidari found that the mortality rate of the patients who were positive again was only 2.1% in her research.¹⁶ As a result of the present study, 147 (77.4%) of the patients received outpatient treatment, only 12 patients (6.31%) needed intensive care, and the number of deaths was seven people (3.68%), which are in line with these results.

CONCLUSION

Recurrent positive RT-PCR can be observed in COVID-19 patients after their discharge. Although it is not yet possible to make a clear decision on whether this recurrent positivity is a symptom of a prolonged infection or reinfection, it is clear that further research is needed in this regard. Patients who have a recurrent positive result survive the disease with outpatient treatment for their mild illness. Hospitalization rates of male patients were higher than those of females, and the duration of hospital stay was found to increase as the age of the patients increases.

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