

# Sociodemographic and Clinical Features of COVID-19 Reinfection Cases Among Healthcare Workers in Turkey

**Hatice İkişik**

Istanbul Medeniyet University Faculty of Medicine: Istanbul Medeniyet Universitesi Tıp Fakültesi

**Yasemin Çağ**

Istanbul Medeniyet University Faculty of Medicine: Istanbul Medeniyet Universitesi Tıp Fakültesi

**Mehmet Akif Sezerol**

Uskudar Health Directorate

**Aral Surmeli** (✉ [aralsurmeli@hotmail.com](mailto:aralsurmeli@hotmail.com))

Medical Rescue Association of Turkey <https://orcid.org/0000-0002-5173-3867>

**Yusuf Taşçı**

Uskudar Health Directorate

**Çağrı Emin Şahin**

Istanbul Health Directorate: Istanbul İl Sağlık Müdürlüğü

**Işıl Maral**

Istanbul Medeniyet University Faculty of Medicine: Istanbul Medeniyet Universitesi Tıp Fakültesi

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## Research article

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# Abstract

**Background:** Global pandemic of novel Coronavirus Disease (SARS- COV-2) has spread across all continents and infected almost 80 million people. Since it is a novel disease, unknowns about the disease characteristic, treatment and length of immunity still persist. This study aims to characterize reinfection, personal protective equipment use and disease progress in healthcare workers in İstanbul.

**Methods:** 23 healthcare workers who had confirmed negative PCR results after infection and another positivity later were questioned about both infection progress, their symptoms and treatment through an online questionnaire.

**Results:** While the symptoms during both courses did not change drastically, 73.9% were treated as outpatient during the first infection while all but one (95.7%) were treated as such during second time around. Median time between two infections were 106 days. All participants were cleared of disease and none had to be treated in intensive care unit.

**Conclusion:** Use of personal protective equipment was found subpar compared to World Health Organization recommendations. This is the first study from Turkey characterizing reinfected cases in healthcare workers.

## Introduction

COVID-19 pandemic has become a global concern with almost 80 million cases around the World and more than 1.6 million fatalities almost a year after the announcement of the first case [1]. As it is a novel disease, the clinical and pathological characteristics of the disease are still uncertain and constantly evolving with more studies being undertaken. [2,3] While the diagnosis and symptoms are becoming more apparent, there are still many unknowns such as treatment and immunization efforts. Other characteristics of the disease, possibility of reinfection, although thought not likely in the beginning has changed. Scientific community is receiving evidence more and more on not just the possibility of reinfection but also mortality and morbidity associated with a second course of disease. Yet, international consensus on definition and diagnosis of reinfection is still unclear. How long the acquired immunity due to past infection is unknown and it is hypothesized that mild course of infection may cause decrease in antibody levels and lead to reinfection. [4,5] In addition, PCR tests that utilize nasopharyngeal swab samples collection procedures vary and might lead to misdiagnosis, due to sensitivity and specificity of test kit, collection methods or collectors experience issues ,and to false negative results. [6-8]

For these reasons, it is unsure whether the the positive PCR results of the patients are genuine reinfection or viral shedding of RNA fragments. In addition, there are evidence in the literature showing people of older age or with comorbidities might be reinfected with different strains of Corona Virus, even after two negative PCR results. [9] Our study aims to describe the progression of disease and characteristics of disease inhealthcare workers who are reinfected in İstanbul.

## Methods

### *Definitions*

Confirmed case: Turkey uses WHO's case definition of at least one PCR positivity for COVID-19. Cases that have a clinical presentation or radiological signs of COVID-19 are not accepted as confirmed cases and are not included in our study population.

Reinfected case: For our study, reinfected COVID-19 case was defined as having two consecutive PCR negative results after having a PCR test confirmed COVID-19 infection.

### *Data Collection*

Data was collected from a central COVID-19 database of the country. Study population was healthcare workers who were tested with PCR between August 1, 2020 and September 11, 2020 who also had a positive PCR result for COVID-19 in the last six months. Healthcare workers who did not have 2 consecutive negative PCR results after the first positive result were eliminated. All of the participants were contacted by phone and asked for their consent. Questionnaires were distributed online, through various mediums. The questionnaire included sociodemographic information (age, sex, profession, comorbidities, medication use), first and second infection durations, progression, severity, symptoms, hospitalization status and contact with COVID-19 patients. In addition, participants were asked questions about the treatment they received, when they went back to work, possible factors that could have affected transmission and if they cared for COVID-19 patients, the interventions (including aerosol producing intervention) and their contact time, place and protection tools used caring for these patients. The questions about frequency of use and practice of hygiene and personal protection were also included.

### *Ethical Approval*

This study is approved by Üsküdar University Non-Interventional Research Studies Ethical Review Board with decree number 61351342/2020-475. All participants who consented to take part were shared the online questionnaire.

### *Statistical Analysis*

Continuous variables are presented as median, maximum and minimum while categorical variables are in absolute frequency (n) relative frequency (%). McNemar's test was used to analyze the difference between first and reinfection characteristics for dependant variables and significance level was set at  $p < 0.005$  with %80 power calculation. All analysis are done in SPSS version 22.0.

## **Findings**

31 participants were eligible for the study. Three of the participants were unable to be reached and one participant lacked the technical infrastructure to fill the questionnaire online. 23 participants out of 27 accepted to participate and filled the questionnaire (85%).

### *Demographics*

Median age was 29 (min. 23-max.52) and 69.6% (n=16) were women. Median time between two negative PCR results (end of first episode) to a new positive PCR (reinfection) without any symptoms were 106,4 days (min. 27 – max 174). Participants occupation distribution is 30.4% (n=7) nurse, 21.7% (n= 5) physician, 13.0% (n= 3) data entry personnel and 13.0% (n= 3) health officer. 2 were cleaning personnel, 2 anesthesia technician, 1 hospital security. 26.1% (n=6) were working in clinical departments, 17.4% (n=4) were in COVID-19 ward, 13.0% (n=3) were in emergency unit and 13.0% (n=3) were in intensive care unit. Three participants were employees of municipal health directorate, one was from a primary care center, one from surgical ward and one from dental practice.

34.8% (n=8) had a chronic disease (Hypertension, COPD, Diabetes Mellitus or Hepatitis B) and all participants but one with a chronic disease reported using at least one drug for their condition. Smoking prevalence was 43.5% (n=10).

### *Characteristics and progression of first COVID-19 infection*

73.9 (n=17) of the participants were treated as outpatients while 26.1% (n=6) were hospitalized. 47.8% (n=11) were symptomatic when diagnosed. 41.7% of the asymptomatic participants developed symptoms between two to five days of diagnosis. Most frequent symptom was headache with 56.5% (n=13) with malaise following (52.1%, n=12) and sore throat (52.1%, n=12).

One participant took Plaquenil after contact with a patient. 57.1% of participants (n=12) received Hydroxychloroquine as treatment (Table 1), while two of them did not receive any treatment. 63.6% (n= 13) of treatment receivers started their treatment in the first two days of diagnosis. 39.1% (n=9) of participants went back to work on 14<sup>th</sup> day of diagnosis (min.10 – max.25).

Participants were asked about risk of transmission due to attending to COVID-19 patients. 26.1% (n= 6) treated COVID-19 patients, 39.1% (n=9) had contact face to face with a patient, 26.1% (n= 6) applied aerosol producing intervention to COVID-19 patients and 39.1% (n=9) spent time in COVID-19 patient treatment units (Table 2).

52.2% of participants (n= 12) indicated that their patients were using a disposable mask during contact and 65.2% (n=15) of the participants used appropriate personal protective equipment (PPE) during contact. 94.1% (n=16) were using masks all the time before diagnosis, 64.7% (n= 11) were using surgical gloves and 17.6% (n=3) were using protective shield or glasses and 23.5% (n=4) were using surgical gown all the time (Table 2).

### *Characteristics and progression of reinfection*

95.7% (n= 22) of the participants were followed as outpatients after the new PCR positive result. 78.3% (n=18) had symptoms during diagnosis. 73.3% (n =11) developed symptoms in the first three days of diagnosis (min 1 – max 7), however 5 participants did not answer this question. Most frequent symptom was malaise (65.2%, n=15), headache following with 60.8% (n=14) and fever in 47.8% (n= 11) and sore throat in 47.8% (n=11) (Table 1).

76.5% (n=11) of the participants started treatment in two days after the diagnosis. 39.1% (n=6) went back to work on 14<sup>th</sup> day (min.1 – max.30). 34.7% (n=8) of the participants used Favipiravir. Six of the participants did not receive any treatment.

Participants were asked about risk of transmission due to attending to COVID-19 patients before the second positive PCR result. 39.1% (n=9) treated COVID-19 patients, 30.4% (n=7) had contact face to face with a patient, 13.0% (n=3) applied aerosol producing intervention to COVID-19 patients and 39.1% (n=9) spent time in COVID-19 patient treatment units (Table 3).

56.5% of participants (n= 13) indicated that their patients were using a disposable mask during contact and 69.9% (n=16) of the participants used appropriate personal protective equipment (PPE) during contact. Among respondents for this question, 94.1% (n=16) were using masks all the time before diagnosis, 72.2% (n= 13) were using surgical gloves and 94.4% (n=17) were using protective shield or glasses and 33.6% (n=6) were using surgical gown all the time (Table 2).

## **Discussion**

Defining the criteria of reinfection is important to understand the disease progress and create epidemiological and clinical control and treatment protocols. In our study with 23 participants, the median time between two infections was 106.4 days. In a guideline report by European Center for Disease Control (ECDC) about the COVID-19 infection

characteristics, false PCR positivity, or decreased sensitivity due to swab methodology, contamination due to transport or analysis are shown as possible factors for wrong diagnosis. In addition, it is possible to misdiagnose the length of time between two infections that is only due to suppressed immunity or low levels of antibody as a reinfection. Genome sequencing can alleviate this issue by providing information about phylogenetic differences in infecting agent. [10] In addition, many reinfection cases are associated with false negative PCR results, continuing viral shedding or ceasing the treatment due to no symptoms in patients leading to increased viral replication. [11] PCR diagnosis, still regarded as the cornerstone of COVID-19 diagnosis, has been used for all participants in our study to confirm the episodes. Only 6 participants stayed asymptomatic after the diagnosis of COVID-19 first time while 4 participants stayed asymptomatic after the reinfection was confirmed. Most prevalent symptom during both courses were headache, fatigue and sore throat. Less commonly participants experienced chills, sweating and eye pain/ blurriness.

It is likely that the participants who were not experiencing any symptoms during testing for the first time could have only tested due to contact with a high-risk patient. In addition, only half of asymptomatic participants developed any symptoms after diagnosis.

While 6 participants were treated as inpatients in the first infection, most of them were treated as outpatients during reinfection, even though symptoms did not change between two episodes. It could be that mortality and morbidity was estimated higher due to COVID-19 being a emerging disease with a lot unknowns or using novel drugs that have higher efficacy. In addition, using any treatment during reinfection was lower. While these can be interpreted as less severe disease progression during reinfection, it is also possible that more we understand the disease, treatment and follow-up protocols change.

Majority of reinfection cases are diagnosed after being tested for having symptoms in the literature. In our study population, there were participants who were tested without any symptoms likely due to a contact with a high-risk patients or sporadic institutional screenings. For estimating the population level reinfections, testing of asymptomatic persons is important. [12]

Studies show the swab methodology plays a role in diagnosing reinfections of COVID-19 and also the sensitivity and specificity varies on the swab collector: While in nasopharyngeal samples rates were 7.3%, it went up to 21.4% in oropharyngeal and fecal samples. [11] In our study all swab samples were nasopharyngeal for PCR testing.

In a meta-analysis study, the required time elapsed between first and second positive results are accepted as 35.4 days [13]. However, there is evidence that shedding of SARS-COV-2 RNA can last until 53,65 or 83 days. [14,15] In our study, minimum time between two infections was 27 days while half of the patients were reinfected before day 102. Studies with larger sample sizes with phylogenetic and RNA analysis of SARS-COV-2 infections are needed to understand the underlying mechanism and discriminate between recurring infections, prolonged viral clearance and reinfections.

World Health organization recommends medical masks, surgical gloves, long sleeved gowns and eye protection (shields or glasses) for aerosol producing procedures for healthcare workers treating COVID-19 patients. [16]. The use of PPE's was less common during the first infection than reinfection. It could mean that being infected lead to more caution in our group. However, use of disposable mask and surgical gloves stayed around 60% both before two episodes. WHO recommends use of risk appropriate PPE since 2014 with additional recommendations of N95 masks, long sleeved gowns, eye protection and surgical gloves for healthcare personnel working with COVID-19. [17,18] Using face masks are also shown to protect against infections both in healthcare workers and the population, while addition of eye protection provides extra protection. [19] Therefore, the recommendations also include non-healthcare

personnel (cleaning, kitchen, security personnel) in the hospital to use the same protection protocols. [20] In our study usage of all protection equipment was below desired levels for all profession groups.

While participants were questioned about their contact with possible transmission, nature and length of these were not questioned, a risk stratification therefore cannot be made. However, it is known that physical distancing of 2 meters is very effective in preventing transmission. [21] Half of the participants had clinical duties as doctor, nurse or technician which put them into closer contact with COVID-19 patients, while others likely only shorter and more distant contact as cleaning personnel or health officer. Due to the nature of work, it is highly difficult for healthcare workers to maintain that distance.

### *Limitations*

This study enrolled a small sample of healthcare workers, who are usually under higher risk than normal population for both COVID-19 and reinfection due to nature of their work. In addition, the questionnaire was done online, leading to multiple participants being unable to fill, decreasing the sample. Data collected were through a centralized platform, however no genome sequencing, viral culture or sub genomic RNA detection was done. Since the diagnostic criteria for reinfection are still limited, it is possible that some of the participants were having a recurrent or reactivated disease rather than a reinfection.

## **Conclusion**

This study aims to describe disease characteristics and progression of 23 reinfected healthcare workers. Median time between two infections was 106.4 days. 73.9% of participants experienced symptoms during the first infection while this rate went up to 82% during reinfection. In this relatively young population, it should also be noted that immune suppression and extended exposure due to the nature of the work and increasing workload due to pandemic could have played an important role. Our study population seems to have experienced first infection more severely than the reinfection, considering almost all were treated as outpatient during their reinfection while less received any treatment. Even though the rates of reinfection in general population is unknown, increasing the capacity for testing, including asymptomatic persons could lead to increased rates. Genome testing is also vital to confirm whether cases are actual reinfections. While there are still much to learn about COVID-19 pandemic, hygiene, physical distancing and protective equipment are still the best measures for preventing cases around the world.

## **Declarations**

### **Funding**

There was no funding for this study.

### **Conflicts of Interest / Competing Interests**

The authors declare that they have no conflict of interest.

### **Ethics approval**

This study is approved by Üsküdar University Non-Interventional Research Studies Ethical Review Board with decree number 61351342/2020-475.

### **Consent to Participate**

All participants were asked for oral consent to participate.

### Consent for Publication

All participants were asked for oral consent to participate.

### Availability of data and material

Data used in this study is not publicly available.

### Code availability

Not applicable.

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## Tables

**Table 1. Symptoms and treatment regimens during both infection durations**

	First Infection		Reinfection		P value <sup>[1]</sup>
	n (23)	%	n (23)	%	
<b>Follow-up</b>					
Outpatient	17	73.9	22	95.7	0.12
Hospital Service	6	26.1	1	4.3	0.06
<b>Symptoms<sup>[2]</sup></b>	n (17)	%	n (19)	%	
Malaise	13	76.4	14	73.7	1.00
Headache	12	70.6	15	78.9	1.00
Fever	12	70.6	11	57.9	1.00
Sore throat	8	47.1	6	31.6	0.37
Loss of smell and taste	6	35.3	11	57.9	0.25
Myalgia	6	35.3	5	26.3	0.62
Cough	4	23.5	3	15.8	1.00
Diarrhea	4	23.5	8	42.1	0.21
Respiratory Distress	3	17.6	11	57.9	0.70
Vomiting	1	5.9	5	26.3	0.25
Chills	1	5.9	2	10.5	1.00
Arthralgia	1	5.9	1	5.3	1.00
Back pain	-	-	2	10.5	
Sweating	-	-	1	5.3	
Eye pain/ Blurrines	-	-	1	5.3	
No Sypmtoms	<b>6</b>	<b>26.0</b>	<b>4</b>	<b>17.3</b>	
<b>Treatment</b>	-	-	-		
Favipiravir	7	33.3	11	64.7	7
Hydroxychloroquine	17	80.9	8	47.0	17
No treatment	2	8.6	6	26.0	

[1] P-values of McNemar test.

[2] Among respondents.

Table 2. Frequency of PPE use during both infection durations

Frequency of PPE use[1]		First Infection		Reinfection	
		n (17)	%	n (18)	%
<b>Disposable Mask</b>	Always	16	94.1	17	94.4
	Most of the time	1	5.9	1	5.6
<b>Surgical Glove</b>	Always	11	64.7	13	56.5
	Most of the time	1	5.9	2	8.7
	Sometimes	3	17.6	2	4.3
	Rarely	1	5.9	1	8.7
	Never	1	5.9	-	-
<b>Protective Shield / Glasses</b>	Always	3	17.6	17	94.4
	Most of the time	7	41.2	1	5.6
	Sometimes	5	29.4	-	-
	Rarely	1	5.9	-	-
	Never	1	5.9	-	-
<b>Medical Gown</b>	Always	4	23.5	6	33.3
	Most of the time	5	29.4	4	22.2
	Sometimes	4	23.5	4	22.2
	Rarely	1	5.9	1	5.6
	Never	3	17.6	3	16.7

[1] Only among responders.

Table 3. Clinical characteristics of individual participants during first infections and reinfections[i]

Age	Time between diagnosis (days)	Sex	Chronic Disease	First infection			Reinfection	
				Hospitalization[1]	Symptoms	Treatment	Symptoms	Treatment
23	105	F		O	F, H, ST, M, My	HCL	L	HCL
23	67	F		H	F, ST, M, H, H, V	F	F, ST, M, H, M, V	None
23	96	F		H	F, ST, M, H, H, V	F	F, ST, M, H, V	None
24	143	F		H	F, C	HCL	F, L	F
25	119	M	Hernia	O	H, M, ST, My, L	HCL	ST, M, H, V	None
25	64	F		H	F, C, ST, H, M, D	HCL	F, C, SoB, ST, M, H	HCL+F
26	92	F		O	C, M, H, My	F	C, M, H, My, L, ST	F
27	80	F		O	No symptoms	HCL	F, C, SoB, M, H, L	None
28	140	F		H	ST, L	HCL	ST, L	HCL
29	146	F		O	M, G, D, My	HCL+F	M, H, V, D, My	F
29	77	F	COPD	O	F, ST, M, H, V, D, C	None	F, M, H	None
29	147	F	COPD	O	C, SOB, M, H, A	HCL	F, C, SOB, ST, H, M	F
35	110	F		O	ST, M, H, D	F	V, H, KTK, EA	F
44	134	F	HTN	O	L, A	HCL	My, A	HCL
52	75	M	HTN	O	C, ST	HCL	F, SOB, ST, L, A	F
52	97	M	DM+HTN	O	F, ST, M, H, D	HCL+F	F, ST, M, H, D	F
26	124	F		O	No symptoms	HCL	No symptoms	HCL
30	132	M		O	ST, M, H	HCL	F, C, SOB, ST, M, H, L	HCL
40	78	F	HEPB	O	No symptoms	HCL	No symptoms	HCL
45	174	F	DM+HTN	O	No	HCL+F	F, M, H, D,	HCL+F

					symptoms	L		
51	106	M		O	No symptoms	None	No symptoms	None
52*	116	M	HTN	H	No symptoms	HCL	No symptoms	F
43	27	F		O	C, ST, M, H, D	HCL	C, ST, M, H, L	F

[1] \* All participants other than one was hospitalized during the second time.

**[i] Legend for Table 3**

**Hospitalization:**

O: Outpatient H: Hospitalized

**Symptoms:**

F: Fever, C: Cough, ST: Sore throat, H: Headache, A: Arthralgia, My: Myalgia , L: Loss of Smell and Taste , B: Back Pain SOB: Shortness of Breath, M: Malaise, V: Vomiting, D: Diarrhea

**Treatment:**

HCL: Hydroxychloroquine, F: Favipiravir