# Coronavirus Pandemic

# COVID-19 infection among healthcare workers in an oncology hospital

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#### Abstract

Introduction: Healthcare workers are at high risk for acquiring COVID-19 and transmitting it to the patients especially to cancer patients in whom the risk of severe COVID-19 is high. We determined the rate of COVID-19 infection among healthcare workers in an oncology hospital and their epidemiological characteristics.

Methodology: Data of infected workers from March 11, 2020, to February 28, 2022 were obtained via Infection Control Committee COVID-19 Surveillance Records and evaluated retrospectively.

Results: During this period 58.34% of 2,355 workers were vaccinated with > 3 doses of COVID-19 vaccines. A total of 1,294 COVID-19 attacks developed in 1,181 (50.14%) workers; mean age was  $38.08 \pm 9.52$  years, 744 (63%) were female. Re-infection occurred in 112 (9.5%) workers. Source of infection in 858 attacks (66.31%) was unknown. Hospitalization was needed in 24 (2%) and intensive care unit admission in 1 (0.08%), no death occurred. In the first attacks, 587 (49.70%) were unvaccinated; in re-infections 66 (58.92%) were  $\geq$  3 doses vaccinated. Hospitalizations were predominantly in the pre-Delta period (16/24: 66.7%, p < 0.05). Re-infections occurred mostly in the Omicron variant period (p < 0.05). Relationship between hospitalization and male gender, age  $\geq$  50 years, "doctor" profession and presence of chronic diseases were significant (p < 0.05).

Conclusions: During the study period, half of the healthcare workers in our hospital developed COVID-19 infection of whom 9.5% re-infected, predominantly during the Omicron variant period. Our findings highlight the importance of taking preventive measures and administering booster vaccine doses even after initial vaccination/infection.

Key words: COVID-19; healthcare workers; oncology hospital.

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#### Introduction

Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the causative agent of Coronavirus disease 2019 (COVID-19), has infected more than 500 million people worldwide and caused more than 6 million deaths (as of May 1, 2022) since its emergence in Wuhan, China in late 2019 [1]. On the days when the pandemic was declared, the first case of COVID-19 was detected in Turkey (March 11, 2020) and the first death was recorded on March 15, 2020 [2].

SARS-CoV-2 is transmitted through respiratory droplets, aerosols generated during medical procedures, and contact with surfaces contaminated with secretions of patients [3]. For the viral transmission routes, the risk is higher at home, workplace, and hospitals where there is close and frequent contact with the patient. Healthcare workers (HCWs) are at the frontlines in the war against COVID-19 and are at high risk of contracting the disease and transmitting the virus to patients and colleagues through close contact [4]. Before the introduction of COVID-19 vaccines, 14% of the COVID-19 cases reported to the WHO were among HCWs [5]. Especially in the early days of the pandemic, many HCWs lost their lives due to the difficulties in obtaining protective equipment and the lack of effective vaccines [6]. The most critical ways of protection from this infection in HCWs are the appropriate use of protective equipment, early diagnosis, isolation, and vaccination [5].

Our center is an oncology training and research hospital where patients with hematological and solid organ malignancies are followed and treated. The COVID-19 infection of the HCWs attending to oncologic patients who are prone to infections brings the risk of transmission to these unique patients. It has been reported that oncologic patients have a high risk of severe COVID-19, admission to intensive care units, and death [7]. Since the pandemic was declared, all personnel in our hospital have been provided with periodic training on COVID-19 symptoms and protective measures. They have been strongly recommended to apply to the pandemic outpatient clinic for SARS-CoV-2 PCR testing when suspicious symptoms develop.

This study was carried out to determine the rate of symptomatic and SARS-CoV-2 PCR-positive COVID-19 infection among HCWs in our hospital and evaluate epidemiological characteristics of them since the pandemic's beginning. The clinical course of the disease, source of infection, vaccination status, and development of COVID-19 re-infections were evaluated.

# Methodology

This study evaluated HCWs of our hospital who had SARS-CoV-2 PCR positive symptomatic COVID-19 between March 11, 2020, and February 28, 2022.

Since the beginning of the pandemic, the SARS-CoV-2 PCR results of HCWs, with the decision of the Infection Control Committee of our hospital are followed daily by the nurses and physicians appointed for COVID-19 surveillance from the Public Health Management System (online). HCWs with positive PCR results are followed up during the isolation period through the online tracking system if they are hospitalized or by phone if they are being followed at home and their information is recorded in the surveillance follow-up form. HCWs who met the confirmed case definition of COVID-19 from surveillance records were evaluated retrospectively.

## Definitions

Healthcare worker

Any individual working in the hospital.

## Confirmed case

The presence of at least two of the suspected symptoms of COVID-19, per the guidelines of the General Directorate of Public Health of the Turkish Ministry of Health (prepared per the definitions made by ECDC and WHO) or the presence of at least one of these symptoms alongside a history of > 15 minutes of close contact ( $\leq$  1m) with confirmed COVID-19 patient without using appropriate personal protective equipment or who has SARS-CoV-2 PCR positive in the nasopharyngeal and/or oropharyngeal sample [2].

# Re-infection

In accordance with the definition of CDC, these are the cases that develop COVID-19 compatible

symptoms and PCR positivity again > 45 days after the symptoms of the first infection have completely healed and the PCR has become negative [8].

# Laboratory values indicating poor prognosis

Lymphocyte count < 800 cells/ $\mu$ L, CRP (C-reactive protein) > 10 mg/L × upper limit of normal, Ferritin > 500 ng/mL, D-Dimer > 1000 ng/mL [9].

# Diagnosis period

Classification of date of diagnosis according to the periods in which SARS-CoV-2 variants appeared

- pre-Delta: from the start of the pandemic to May 31, 2021

- Delta: June - end of November 2021

- Omicron and its sub-variants: December 2021-the end of the study (February 28, 2022).

The data was evaluated using the COVID-19 surveillance records;

- SARS-CoV-2 PCR positivity date and diagnosis period

- Age

- Gender

- Occupation [doctor, nurse, nursing assistant, general worker (non-clinical staff who are not directly attending to medical care of the patients)]

- Concomitant chronic diseases (hypertension, diabetes mellitus, cardiovascular diseases, chronic lung, liver, kidney disease, malignancies, autoimmune diseases)

- Admission to hospital/intensive care unit due to COVID-19

- Re-infection

- Time between first attack and re-infection

- COVID-19 vaccination history and dose of vaccinations

- Time between COVID-19 first attack/re-infection and last vaccine dose (for personnel who have had at least two doses of vaccination and  $\geq$  14 days past the last dose)

- Source of infection (history of contact with a confirmed COVID-19 patient without using appropriate personal protective equipment)

- Blood tests (if done): lymphocyte count and percentage, D-dimer, CRP, ferritin.

The study design was approved by the Ministry of Health of the Turkish Republic (Date: 09.09.2021, Application No:2021-09-09-T11-07-21) and the Clinical Research Ethics Committee (Date: 10.02.2022, Decision No: 2021-12-10).

## Statistical analysis

The Statistical Package for the Social Sciences (SPSS) 24.0 IBM package program was used for analysis. Frequency tables and descriptive statistics were used to interpret the results. "Pearson- $\chi^2$  crosstabs" were used to evaluate the relationships between two qualitative variables. A *p* value < 0.05 was considered significant.

# Results

Between March 11, 2020, and February 28, 2022, a total of 2,355 personnel worked in our hospital, including 1,438 (61.06%) women HCWs. Occupational distribution was as follows: physicians: 502 (21%), nurse/nursing assistants: 995 (42%), general workers: 858 (37%). As of the 28<sup>th</sup> of February, 2022, 1,374 personnel (58.34%) received at least three doses of COVID-19 (2 doses of primary vaccination + 1 dose of a booster) vaccine (CoronaVac /Pfizer-BioNTech).

1,294 COVID-19 attacks (first attack + reinfection) occurred in 1,181 (50.14%) HCWs in our hospital during the study period. According to the diagnosis period classification, 606 (46.83%) of the COVID-19 attacks developed during the pre-Delta, 144 (11.13%) Delta, and 544 (42.04%) Omicron variants periods. According to occupational groups, 544 (46.00%) were in the nurse/nursing assistant group. It was determined that 933 (79%) personnel did not have a chronic disease (Table 1).

The source of COVID-19 infection was unidentified in 858 attacks (66.31%); the probable source was household/out of the hospital in 273 (21.10%) attacks, other HCWs in 111 (8.58%), and infected patients in 52 (4.01%) attacks (Table 1).

Re-infection was developed in 112 (9.5%) personnel, one of them had a third attack of infection. Of re-infections; 67 (59.82%) cases occurred 12-17 months after the first attack (12.60  $\pm$  4.72 months) (Table 1). The risk of the first COVID-19 attack was 50.14% (1181/2355) and the risk of re-infection was 9.5% (112/1181), that is, the risk is reduced by 5.27 times.

Hospitalization occurred in 24 personnel (2%), 23 (95.83%) of them during the first attack, and one during re-infection. One personnel (0.08%) was followed up in the intensive care unit with noninvasive ventilation, and no death was detected (Table 1). In terms of SARS-CoV-2 diagnosis periods, 16 of the hospitalizations (16/24: 66.7%) were in the pre-Delta period, which was statistically significantly higher than the other periods ( $\chi^2 = 10.654$ ; p = 0.005). Hospitalized personnel were predominantly male (14/24 = 58.3%,  $\chi^2 = 4.782$ ; p =

0.029) and  $\geq$  50 age group (8/24 = 33.3%,  $\chi^2$  = 13.545; p = 0.004). The non-hospitalized personnel was mostly in the 40-49 age group, and these findings were statistically significant. The relationship between hospitalization and occupational groups was strong; 50% (12 people) of those hospitalized were doctors ( $\chi^2$ = 21.91; p = 0.000). A significant relationship was also found between hospitalization and the presence of chronic diseases; It was determined that 50% (12/24) of those who were hospitalized had chronic disease, and those who were not hospitalized were predominantly free of chronic disease (79.6%) ( $\chi^2 = 12.42$ ; p = 0.000). Re-infection developed in 6 (6/24 = 25%) of those who were hospitalized at the first attack, this rate was found to be higher than those who were not hospitalized (106/1157 = 9.2%) (Table 2).

In the Pre-Delta, Delta, and Omicron variants periods; 7 (6.3%), 7 (6.3%), and 98 (87.4%) reinfections developed respectively (Table 1). Reinfections occurred mostly in the period of the Omicron variant; this finding was statistically significant ( $\chi^2 =$ 106.013; *p* = 0.000). During re-infection, one personnel

**Table 1.** Characteristics of the study population.

Variables	HCW, $n = 1181$ (%)
Gender	
Female	744 (63.0)
Male	437 (37.0)
Age (year)	
< 30	296 (25.1)
30-39	343 (29.0)
40-49	409 (34.6)
$\geq 50$	133 (11.3)
Occupation	
Doctor	192 (16.3)
Nurse/Nursing Assistant	544 (46.0)
General worker	445 (37.7)
Source of infection [Attacks, n = 12	294 (%)]
Unknown	858 (66.31)
HCWs*	111 (8.58)
Patients	52 (4.01)
Family/out of hospital	273 (21.10)
Hospitalization	
No	1157 (98.0)
Yes	24 (2.0)
Re-infection	
No	1069 (90.5)
Yes	112 (9.5)
<b>Re-infection period</b>	
Pre-Delta	7 (6.3)
Delta	7 (6.3)
Omicron	98 (87.4)
Time to re-infection (month)	
< 6	14 (12.5)
6-11	21 (18.8)
12-17	67 (59.8)
$\leq 18$	10 (8.9)

\*HCWs: Healthcare workers.

(1/112: 0.89%) was hospitalized, and this person was not vaccinated. There was no statistically significant relationship between re-infection status and gender, age groups, occupation, and presence of chronic diseases (p > 0.05).

Regarding the relationship between the first COVID-19 attack and re-infections with vaccination; in the first attack 587 personnel (49.70%) were unvaccinated/1 dose vaccinated, while in those who had re-infection only 21 (18.75%) personnel were unvaccinated/1 dose vaccinated whereas 25 (22.32%) had 2 doses, 32 (28.57%) had 3 doses and 34 (30.35%) had  $\geq$  4 doses vaccination, so 66 (58.92%) personnel were vaccinated with  $\geq$  3 doses. The first attack and re-infections primarily developed in the first six months after the last vaccination (Table 3).

In terms of poor prognostic laboratory values in patients with laboratory results at the first attack of COVID-19, Lymphocyte < 800 cells/UL, Ferritin > 500 ug/mL, and D-Dimer > 1000 pg/L were detected at rates of; 7.5% (30/398), 1.3% (5/374) and 2.6% (10/389) respectively. Sufficient laboratory results were not available in re-infections for statistical analysis. Regarding the relationship between hospitalization and laboratory tests, the CRP level was high in 79 (21.2%) non-hospitalized personnel during the first attack and 13 (59.1%) personnel who were hospitalized; the difference was significant ( $\chi^2 = 16.712$ ; p = 0.000), ferritin level was high in 3 (0.9%) personnel who were

**Table 3.** COVID-19 vaccination data of the study population.

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	n (%)
Vaccine doses at first COVID-19 attack (n	= 1181)
Unvaccinated/1 dose vaccine	587 (49.7)
2 doses	199 (16.8)
3 doses	210 (17.8)
$\geq$ 4 doses	185 (15.7)
First attack-last vaccine dose interval* (mor	nth) (n = 594)
< 3	233 (39.2)
3-6	235 (39.6)
> 6	126 (21.2)
Vaccine doses in COVID-19 re-infection (n	= 112)
Unvaccinated/1 dose vaccine	21 (18.75)
2 doses	25 (22.32)
3 doses	32 (28.57)
$\geq$ 4 doses	34 (30.35)
COVID-19 re-infection-last vaccine dose in	terval *(month)
(n = 95)	
< 3	33 (34.7)
3-6	36 (37.9)
> 6	26 (27.4)

\*Calculated in healthcare workers who have had at least 2 doses of vaccine and  $\geq$  14 days past the last dose.

not hospitalized and in 2 (9.1%) who were hospitalized, the difference was also statistically significant ( $\chi^2 =$  10.655; p = 0.001). For lymphocyte count and percentage and D-dimer levels, there was no significant difference between the hospitalized and nonhospitalized personnel. The differences in laboratory test results at the re-infection between those who were hospitalized and those not hospitalized were not significant (lack of sufficient data) (Table 4).

Table 2. Analysis of association b	etween hospitalization and	study nonulation characteristics
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Hospitalization	No (n = 1157)		Yes (	n = 24)	1 4
	n	%	n	%	<i>p</i> value*
Diagnosis period					
Pre-Delta	582	50.3	16	66.7	
Delta	131	11.3	6	25.0	$\chi^2 = 10.654; p = 0.005$
Omicron	444	38.4	2	8.3	
Gender					
Female	734	63,4	10	41.7	2 4 792
Male	423	36.6	14	58.3	$\chi^2 = 4.782; p = 0.029$
Age (year)					
< 30	294	25,5	2	8.3	
30-39	336	29.0	2 7	29.2	2 12 545
40-49	402	34.7	7	29.2	$\chi^2 = 13.545; p = 0.004$
$\geq$ 50	125	10.8	8	33.3	
Occupation					
Doctor	180	15.6	12	50.0	
Nurse	366	31.6	3	12.5	2 21 010 0 000
Nursing Assistant	174	15.0	1	4.2	$\chi^2 = 21.910; p = 0.000$
General worker	437	37.8	8	33.3	
Chronic diseases					
No	921	79.6	12	50.0	$\chi^2 = 12.420; p = 0.000$
Yes	236	20.4	12	50.0	
Re-infection					
No	1051	90.8	18	75.0	$\chi^2 = 6.871; p = 0.009$
Yes	106	9.2	6	25.0	

\*Pearson-x2 crosstabs" were used to examine the relationships between two qualitative variables.

#### Discussion

Our study showed that 58.34% of HCWs in our hospital had at least three doses of COVID-19 vaccine during the study period. Symptomatic PCR-positive COVID-19 infection developed in 50.14% of the workers, of whom 9.5% developed re-infection predominantly in the omicron variant period.

HCWs are at high risk for SARS-CoV-2 infection due to the nature of their work. Many studies demonstrated that a higher rate of COVID-19 cases occurs in HCWs who attended face-to-face care of patients compared to the general population, nurses and doctors are the HCWs at the highest risk [10-12]. Similarly, in our study, most of the COVID-19 cases were diagnosed in the nurse/nursing assistant group (46%). Regarding the source of COVID-19 infection in HCWs, reports from China and Italy inform that one patient can be a source of infection for ten HCWs. In the study by Hartmann et al, the source of infection could not be detected in 45% of the cases, contact with hospitalized patients or other personnel in 44%, and suspected contact outside the hospital in 11% could be the source of infection [11]. Mandic-Rajčevićet al. pointed out the most common source of infection (49%) as other positive HCWs [12]. On the other hand, studies have confirmed that asymptomatic COVID-19 cases are similar to symptomatic cases in terms of viral load, with an emphasis on asymptomatic carriers (healthcare workers or patients) being an essential transmission source, which explains the difficulty in identifying the possible source of COVID-19 [13]. In our study, the source of infection could not be identified in 66.31% of COVID-19 attacks, and the household/out-of-thehospital and social contacts were the important identified possible sources. We believe that this situation is due to the more protective measures in the

**Table 4.** Analysis of associations between hospitalization and laboratory findings.

Hospitalization	No (n = 1157)		Yes (	n = 24)	<i>p</i> value*
	n	%	n	%	<i>p</i> value.
Lymphocyte count					
First COVID-19 attack					
Low	44	11.7	2	9.1	
Normal	330	87.8	20	90.9	$\chi^2 = 0.263$
High	2	0.5	-	-	$\chi = 0.203$ p = 0.877
Re-infection					p = 0.877
Low	-	-	-	-	
Normal	11	100.0	-	-	
Lymphocyte (%)					
First COVID-19 attack					
Low	62	16.6	7	31.8	
Normal	307	82.3	15	68.2	$\chi^2 = 3.491$
High	4	1.1	-	-	p = 0.175
Re-infection					-
Normal	11	100.0	2	100.0	
D-dimer					
First COVID-19 attack					$\chi^2 = 2.970$
Normal	316	86.1	16	72.7	
High	51	13.9	6	27.3	<i>p</i> = 0.085
Re-infection					$\chi^2 = 0.430$
Normal	9	81.8	2	100.0	
High	2	18.2	-	-	p = 0.512
CRP					
First COVID-19 attack					$\chi^2 = 16.712$
Normal	294	78.8	9	40.9	$\chi^2 = 16.712$ p = 0.000
High	79	21.2	13	59.1	p = 0.000
Re-infection					$w^2 = 1.051$
Normal	7	63.6	2	100.0	$\chi^2 = 1.051$
High	4	36.4	-	-	<i>p</i> = 0.305
Ferritin					
First COVID-19 attack					$w^2 = 10.655$
Normal	349	99.1	20	90.9	$\chi^2 = 10.655$
High	3	0.9	2	9.1	<i>p</i> = 0.001
<b>Re-infection</b>					$x^2 = 0.107$
Normal	1	9.1	-	-	$\chi^2 = 0.197$
High	10	90.9	2	100.0	p = 0.657

\*"Pearson- $\chi^2$  crosstabs" were used to examine the relationships between two qualitative variables.

hospital environment in conjunction with the inspections and training compared to the external environment.

Literature reveals that certain demographic factors are associated with severe COVID-19 and mortality. The most prominent factors are advanced age ( $\geq 60$ ) and male gender. Furthermore, comorbidities such as cardiovascular diseases, chronic kidney and lung disease, diabetes mellitus, hypertension, sickle cell anemia, and immunosuppression come to the fore concerning poor prognosis and mortality [14]. In a systematic review, the average rate of severe COVID-19 requiring hospitalization in HCWs was 5% (95% CI; 3%-8%), and the mortality rate was 0.5% (95% CI; 0.02%-1.3%). In cases that resulted in death, the mean age was higher (mean age 60 vs. 42 years), and the comorbidity rate was higher (86.6%) [10]. In our study, the rate of hospitalization was 2%, the rate of admission to the intensive care unit was 0.08% and no death was reported. It was determined that hospitalization was primarily seen in the occupational group of doctors, and those admitted to the hospital were predominantly male and  $\geq$  50 years old. Chronic disease was present in half of those hospitalized. The low rate of hospitalization and admittance to the intensive care unit and the absence of mortality may be due to the average young age of our personnel  $(38.08 \pm 9.52)$  and the low rate of chronic diseases.

Some laboratory markers help predict the prognosis of COVID-19, and using these markers in patient triage has been recommended [14]. In the guideline of the General Directorate of Public Health of the Ministry of Health of Turkey (last updated April 12, 2022), poor prognostic criteria were described in the initial evaluations performed upon admission to the hospital [9]. In our study, in terms of poor prognostic criteria in patients who underwent laboratory tests; lymphopenia, ferritin, and D-dimer elevation rates were determined as 7.5%, 1.3%, and 2.6%, respectively. Relating to the relationship between hospitalization and laboratory tests, ferritin and CRP levels were statistically significantly higher in hospitalized patients than in nonhospitalized ones.

Vaccination is an important method of protection against COVID-19. Since the emergence of the pandemic, studies have been started for the production of effective vaccines against SARS-CoV-2 in many countries. With the worldwide approval of the use of vaccines by countries and authorities, priority has been given to the vaccination of HCWs to prevent the disruption of services in the field of health and to prevent the spread of the disease on a global scale [15,16]. With the COVID-19 vaccines first approved in Turkey, the vaccination of HCWs started as the priority group. The vaccination program first started with CoronaVac vaccine (inactivated-vero cell vaccine) from January 2021. The BNT162b2 (Pfizer-BioNTech, mRNA) vaccine has been available since April 2021. Although protection against hospitalization and severe illness continues as time passes after the first vaccination (90-95%), due to the decreasing immunity over time. CDC recommended a booster dose 5 months vaccination after the first months (3 in immunocompromised patients) with mRNA vaccines for individuals over 12 years of age [17]. The protection rates vary according to the production technology, the applied antigen dose, or the vaccination calendar. Still, none of the vaccines are fully protective against SARS-CoV-2 infections. Although the COVID-19 vaccination has significantly reduced SARS-CoV-2 infections in HCWs, cases occur in full-dose vaccinated personnel [18]. Among the vaccines administered in Turkey, the efficacy of CoronaVac was found to be 70-83.5% (95% CI 65.4-92.1) in preventing COVID-19 disease and 86-88% in preventing hospital admission or death [19,20]. In a large placebo-controlled trial, the efficacy of the Pfizer-BioNTech vaccine in preventing symptomatic COVID-19 (for individuals  $\geq 16$  years of age) at a median two-month follow-up after a two-dose primary series was 95%, and at longer follow-ups, it has been shown to decrease to 90% at 2-4 months and to 84% 4-6 months post-vaccination [21,22]. Our study determined that in the first COVID-19 attack, 49.7% of the personnel were unvaccinated/1 dose vaccinated, while 58.92% of those who had re-infection were  $\geq 3$ doses vaccinated. In terms of hospitalization; 95.83% of hospitalizations occurred during the first attack, while during re-infection only one unvaccinated personnel hospitalized. was It indicated that vaccination/immunity from the previous infection protected from severe disease and hospitalization, although not fully protective against re-infection and symptomatic disease.

Since the pandemic outbreak, genetic variants of the virus have emerged. The new variants are more contagious than the initial version, and the severity and lethality of the developing disease differ between variants. Neutralizing antibody activity formed by infection or vaccine is lower against the latest Delta (B.1.617.2) and Omicron variants (B.1.1.529) and the risk of new infection (re-infection) increases [23,24]. Although variants may partially evade vaccine-induced immunity, it has been observed that vaccination significantly reduces the risk of severe/critical illness

and hospitalization and death rates [25,26]. The effectiveness of two doses of BioNTech vaccine against infection with the Omicron variant was around 30%, against severe disease it was 70% in the Omicron variant and 93% in the Delta variant. The effectiveness against severe disease has increased to 90% with the booster doses of mRNA vaccines [27,28]. In our center, COVID-19 attacks mainly occurred during the pre-Delta and Omicron variants periods (46.83% and 42.04%, respectively). Hospitalizations mainly were (66.7%) in the pre-Delta period, when most of the personnel were unvaccinated/not fully vaccinated.

Since the first documented case of re-infection of COVID-19 was recorded in August 2020, similar cases have been reported with increasing frequency worldwide [29,30]. In our study, the first COVID-19 attack occurred in 50.14% of our personnel and 9.5% of them re-infected. Thus, the risk of re-infection appears to be reduced by 5.27 times after the first COVID-19 attack. It seems that factors such as; first-attack-induced immunity, increased vaccination rates, and applying appropriate isolation and protection precautions may be responsible for this decline during the course of the pandemic. In terms of clinical course, it has been observed that SARS-CoV-2 re-infection is similar to the first infection attack and sometimes more severe. The mean time between two infections was reported as 5.7 months (172 days) in Brouqui's study [31,32]. We found that re-infections developed predominantly during the Omicron variant period (87.4%) and 12-17 months after the first attack (59.8%). The rate of severe illness/hospitalization in re-infections was also very low (0.89%). These findings suggest that vaccination and/or previous infection is less protective against the Omicron variant than the other variants, but can be protective against severe disease.

There are limitations to our study; since most of the HCWs do not perform laboratory tests, especially in reinfection attacks, data on this subject are lacking. In addition, diagnosis of re-infection is difficult. Since genomic data on initial and re-infection could not be obtained in our study, it could not be confirmed that they belong to different strains.

## Conclusions

In pandemics, improper use of personal protective equipment and loss of concentration may develop in HCWs due to long shifts and heavy working conditions, which increases the viral transmission risk. COVID-19 infection in HCWs causes a decline in their work performance and increased mortality and morbidity in case of transmission to patients, especially those with immunodeficiency. SARS-CoV-2 re-infections in HCWs show that it is crucial to comply with protective measures even after infection/vaccination. Previously infected personnel should be vaccinated and booster doses of vaccines should be administered.

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### References

1. Worldometer (2022) COVID-19 Coronavirus pandemic. Available:

https://www.worldometers.info/coronavirus/#countries. Accessed: 15 July 2022.

- Republic of Turkey Ministry of Health General Directorate of Public Health (2020) COVID-19 general information, epidemiology and diagnosis, Available: https://covid19.saglik.gov.tr/Eklenti/39551/0/covid19rehberig enelbilgilerepidemiyolojivetanipdf.pdf. Accessed: 1 June 2022.
- World Health Organization (2020) Transmission of SARS-CoV-2: Implications for infection prevention precautions. Available: https://www.who.int/newsroom/commentaries/detail/transmission-of-sars-cov-2implications-for-infection-prevention-precautions. Accessed: 9 July 2022.
- 4. Centers for Disease Control and Prevention (2022) Interim US guidance for assessment and public health management of healthcare personnel with potential exposure in a healthcare setting to patients with coronavirus disease (COVID-19). Available: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html. Accessed: 21 January 2022.
- World Health Organization (2020) Prevention, identification and management of health worker infection in the context of COVID-19. Available: https://www.who.int/publications/i/item/10665-336265. Accessed: 6 June 2022.
- Bandyopadhyay S, Baticulon RE, Kadhum M, Alser M, Ojuka 6 DK, Badereddin Y, Kamath A, Parepalli SA, Brown G, Iharchane S, Gandino S, Markovic-Obiago Z, Scott S, Manirambona E, Machhada A, Aggarwal A, Benazaize L, Ibrahim M, Kim D, Tol I, Taylor EH, Knighton A, Bbaale D, Jasim D, Alghoul H, Reddy H, Abuelgasim H, Saini K, Sigler A, Abuelgasim L, Moran-Romero M, Kumarendran M, JamieNA, Ali O, Sudarshan R, Dean R, Kissyova R, Kelzang S, Roche S, Ahsan T, Mohamed Y, Dube AM, Gwini GP, Gwokyala R, Brown R, Papon MRKK, Li Z, Ruzats SS, Charuvila S, Peter N, Khalidy K, Moyo N, Alser O, Solano A, Robles-Perez E, Tariq A, Gaddah M, Kolovos S, Muchemwa FC, Saleh A, Gosman A, Pinedo-Villanueva R, Jani A, Khundkar R (2020) Infection and mortality of healthcare workers worldwide from COVID-19: a systematic review. BMJ Glob Health 5: e003097. doi: 10.1136/bmjgh-2020-003097.
- 7. Rüthrich MM, Giessen-Jung C, Borgmann S, Classen AY, Dolff S, Grüner B, Hanses F, Isberner N, Köhler P, Lanznaster

J, Merle U, Nadalin S, Piepel C, Schneider J, Schons M, Strauss R, Tometten L, Vehreschild JJ, vonLilienfeld-Toal M, Beutel G, Wille K; LEOSS Study Group (2021) COVID-19 in cancer patients: clinical characteristics and outcome-an analysis of the LEOSS registry. Ann Hematol 100: 383-393. doi: 10.1007/s00277-020-04328-4.

- Centers for Disease Control and Prevention (2020) Investigative criteria for suspected cases of SARS-CoV-2 reinfection (ICR). Available: https://www.cdc.gov/coronavirus/2019-ncov/php/investcriteria.html. Accessed: 30 October 2020.
- Republic of Turkey Ministry of Health General Directorate of Public Health (2022) COVID-19 (SARS-CoV-2 infection) adult patient treatment. Available: https://covid19.saglik.gov.tr/Eklenti/43095/0/covid-19rehberieriskinhastayonetimivetedavi-12042022pdf.pdf. Accessed: 12 April 2022.
- Gómez-Ochoa SA, Franco OH, Rojas LZ, Raguindin PF, Roa-Díaz ZM, Wyssmann BM, Guevara SLR, Echeverría LE, Glisic M, Muka T (2021) COVID-19 in Health-Care Workers: A living systematic review and meta-analysis of prevalence, risk factors, clinical characteristics, and outcomes. Am J Epidemiol 190: 161-175. doi: 10.1093/aje/kwaa191.
- Hartmann S, Rubin Z, Sato H, O Yong K, Terashita D, Balter S (2021) Coronavirus disease 2019 (covid-19) infections among healthcare workers, Los Angeles County, February-May 2020. Clin Infect Dis73: e1850-e1854. doi: 10.1093/cid/ciaa1200.
- Mandić-Rajčević S, Masci F, Crespi E, Franchetti S, Longo A, Bollina I, Velocci S, Amorosi A, Baldelli R, Boselli L, Negroni L, Zà A, OrfeoNV, Ortisi G, Centanni S, Colosio C (2020) Source and symptoms of COVID-19 among hospital workers in Milan. Occup Med (Lond) 70: 672-679. doi: 10.1093/occmed/kqaa201.
- Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, Yu J, Kang M, Song Y, Xia J, Guo Q, Song T, He J, Yen HL, Peiris M, Wu J (2020) SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med 382: 1177-1179. doi: 10.1056/NEJMc2001737.
- Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, Salazar-Mather TP, Dumenco L, Savaria MC, Aung SN, Flanigan T, Michelow IC (2021) Predictors of COVID-19 severity: A literature review. Rev Med Virol 31: 1-10. doi: 10.1002/rmv.2146.
- 15. Dooling K, McClung N, Chamberland M, Marin M, Wallace M, Bell BP, Lee GM, Talbot HK, Romero JR, Oliver SE (2020) The Advisory Committee on Immunization Practices' interim recommendation for allocating initial supplies of COVID-19 vaccine United States, 2020. MMWR Morb Mortal Wkly Rep 69: 1857-1859. doi: 10.15585/mmwr.mm6949e1.
- 16. Weber DJ, Al-Tawfiq JA, Babcock HM, Bryant K, Drees M, Elshaboury R, Essick K, Fakih M, Henderson DK, Javaid W, Juffras D, Jump RLP, Lee F, Malani AN, Mathew TA, Murthy RK, Nace D, O'Shea T, Pettigrew E, Pettis AM, Schaffzin JK, Shenoy ES, Vaishampayan J, Wiley Z, Wright SB, Yokoe D, Young H (2022) Multi society statement on coronavirus disease 2019 (COVID-19) vaccination as a condition of employment for healthcare personnel. Infect Control Hosp Epidemiol 43: 3-11. doi: 10.1017/ice.2021.322.
- CDC Newsroom (2021) CDC expands eligibility for COVID-19 booster shots to all adults media statement for immediate release, Friday, 19 November 2021. Available:

https://www.cdc.gov/media/releases/2021/s1119-boostershots.html. Accessed: 12 April 2022.

- Bergwerk M, Gonen T, Lustig Y, Amit Sh, Lipsitch M, Cohen C, Mandelboim M, Levin EG, Rubin C, Indenbaum V, Tal I, Zavitan M, Zuckerman N, Bar-Chaim A, Kreiss Y, Regevyochay G (2021) Covid-19 breakthrough infections in vaccinated healthcare workers. N Engl J Med 385: 1474-84. doi: 10.1056/NEJMoa2109072.
- 19. Tanriover MD, Doğanay HL, Akova M, Güner HR, Azap A, Akhan S, Köse Ş, Erdinç FŞ, Akalın EH, Tabak ÖF, Pullukçu H, Batum Ö, Şimşek Yavuz S, Turhan Ö, Yıldırmak MT, Köksal İ, Taşova Y, Korten V, Yılmaz G, Çelen MK, Altın S, Çelik İ, Bayındır Y, Karaoğlan İ, Yılmaz A, Özkul A, Gür H, Unal S; CoronaVac Study Group (2021) Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. Lancet 398: 213-222. doi: 10.1016/S0140-6736(21)01429-X.
- Jara A, Undurraga EA, González C, Paredes F, Fontecilla T, Jara G, Pizarro A, Acevedo J, Leo K, Leon F, Sans C, Leighton P, Suarez P, Garcia-Escorza H, Araos R (2021) Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. N Engl J Med 385: 875-84. doi: 10.1056/NEJMoa2107715.
- Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Marc GP, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group (2020) Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 383: 2603-15. doi: 10.1056/NEJMoa2034577.
- 22. Thomas SJ, Moreira ED Jr, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Marc GP, Polack FP, Zerbini C, Biley R, Swanson KA. Xia Xu X, Roychoudhury S, Koury K, Bouguermouh S, Kalina WV, Cooper D, Frenck RW ,Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Yang Q, Liberator P, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Gruber WC, Jansen KU; C4591001 Clinical Trial Group (2021) Safety and Efficacy of the BNT162b2 mRNA Covid-19 vaccine through 6 Months. N Engl J Med 385: 1761-1773. doi: 10.1056/NEJMoa2110345.
- 23. Edara VV, Pinsky BA, Suthar MS, Lai L, Davis-Gardner ME, Floyd K, Flowers MW, Wrammert J, Hussaini L, Ciric CR, Bechnak S, Stephens K, Graham BS, Bayat Mokhtari E, Mudvari P, Boritz E, Creanga A, Pegu A, Derrien-Colemyn A, Henry AR, Gagne M, Douek DC, Sahoo MK, Sibai M, Solis D, Webby RJ, Jeevan T, Fabrizio TP (2021) Infection and vaccine-induced neutralizing-antibody responses to the SARS-CoV-2 B.1.617 variants. N Engl J Med 385: 664-666. doi: 10.1056/NEJMc2107799.
- 24. Planas D, Veyer D, Baidaliuk A, Staropoli I, Guivel-Benhassine F, Rajah MM, Planchais C, Porrot F, Robillard N, Puech J, Prot M, Gallais F, Gantner P, Velay A, GuenJL, Kassis-Chikhani N, Edriss D, Belec L, Seve A, Courtellemont L, Pere H, Hocquelloux L, Fafi- Kremer S, Prazuck T, Mounquet H, Bruel T, Simon-Loriere E, A.Rey F, Schwarts O (2021) Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature 596: 276-280. Doi: https://doi.org/10.1038/s41586-021-03777-9
- 25. Thompson MG, Stenehjem E, Grannis S, Ball SW, Naleway AL, Ong TC, DeSilva MB, Natarajan K, Bozio CH, Lewis N, Dascomb K, Dixon BE, Birch RJ, Irving SA, Rao S, Kharbanda

E, Han J, Reynolds S, Goddard K, Grisel N, Fadel WF, Levy ME, Ferdinands J, Fireman B, Arndorfer J, Valvi NR, Rowley EA, Patel P, Zerbo O, Griggs EP, Porter RM, Demarco M, Blanton L, Steffens A, Zhuang Y, Olson N, Barron M, Shifflett P, Schrag SJ, Verani JR, Fry A, Gaglani M, Azziz-Baumgartner E, Klein NP (2021) Effectiveness of Covid-19 vaccines in ambulatory and inpatient care settings. N Engl J Med 385: 1355-1371. doi: 10.1056/NEJMoa2110362.

- 26. Haas EJ, Angulo FJ, McLaughlin JM, Anis E, Singer SR, Khan F, Brooks N, Smaja M, Mircus G, Pan K, Southern J, Swerdlow DL, Jodar L, Levy Y, Alroy-Preis S (2021) Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet 397: 1819-1829. doi: 10.1016/S0140-6736(21)00947-8.
- Collie S, Champion J, Moultrie H, Bekker LG, Gray G (2022) Effectiveness of BNT162b2 vaccine against Omicron variant in South Africa. N Engl J Med 386: 494-496. doi: 10.1056/NEJMc2119270.
- 28. Thompson MG, Natarajan K, Irving SA, Rowley EA, Griggs EP, Gaglani M, Klein NP, Grannis SJ, DeSilva MB, Stenehjem E, Reese SE, Dickerson M, Naleway AL, Han J, Konatham D, McEvoy C, Rao S, Dixon BE, Dascomb K, Lewis N, Levy ME, Patel P, Liao IC, Kharbanda AB, Barron MA, Fadel WF, Grisel N, Goddard K, Yang DH, Wondimu MH, Murthy K, Valvi NR, Arndorfer J, Fireman B, Dunne MM, Embi P, Azziz-Baumgartner E, Zerbo O, Bozio CH, Reynolds S, Ferdinands J, Williams J, Link-Gelles R, SchragSJ, Verani JR, Ball S, Ong TC (2022) Effectiveness of a third dose of mRNA vaccines against COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and Omicron variant predominance -

VISION Network, 10 States, August 2021-January 2022. MMWR Morb Mortal Wkly Rep 71: 139-145. doi: 10.15585/mmwr.mm7104e3.

- Tillett RL, Sevinsky JR, Hartley PD, Kerwin H, Crawford N, Gorzaski A, Laverdure C, Verma SC, Rossetto C, Jckson D, Farrell MJ, Hooser SV, Pandori M (2020) Genomic evidence for reinfection with SARS-CoV-2: a case study. Lancet Infect Dis 21: 52–58. doi: 10.1016/S1473-3099(20)30764-7.
- Wang J, Kaperak C, Sato T, Sakuraba A (2021) COVID-19 reinfection: a rapid systematic review of case reports and case series. J Investig Med 69: 1253-1255. doi: 10.1136/jim-2021-001853.
- Cohen JI, Burbelo PD (2021) Reinfection with SARS-CoV-2: implications for vaccines. Clin Infect Dis73: e4223-e4228. doi: 10.1093/cid/ciaa1866.
- Brouqui P, Colson P, Melenotte C, Houhamdi L, Bedotto M, Devaux C, Gautret P, Million M, Parola P, Stoupan D, La Scola B, Lagier JC, Raoult D (2021) COVID-19 re-infection. Eur J Clin Invest 51: e13537. doi: 10.1111/eci.13537.

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