Original Article

Coronavirus Disease 2019 Frequency After CoronaVac Vaccine: Ascovid Study

Burcu Öztürk Şahin[1] , Şennur Özen[2] , Oya Baydar Toprak[3] , Nurdan Köktürk[1] ,
Mehmet Tevfik Kitapçı[4]

[1]Department of Pulmonary Medicine, Gazi University, Faculty of Medicine, Ankara, Turkey
[2]Department of Pulmonary Medicine, Delta Hospital, İstanbul, Turkey
[3]Department of Pulmonary Medicine, Çukurova University, Faculty of Medicine, Adana, Turkey
[4]Department of Nuclear Medicine, Integra Medical Imaging Center, Ankara, Turkey

Abstract

OBJECTIVE: It is accepted that the only way to end severe acute respiratory syndrome coronavirus 2 epidemic is through community vaccination. The frequency and clinical features of infection after vaccination are not known clearly. The aim of this study is to determine the frequency and clinical features of coronavirus disease 2019 seen after either the first or second dose of CoronaVac vaccination in healthcare workers and their relatives.

MATERIAL AND METHODS: This is a cross-sectional retrospective survey study. The study was carried out in 2013 volunteers, including 1903 (94.5%) healthcare workers and 110 (5.5%) relatives of healthcare workers. The frequency and clinical features of coronavirus disease 2019 before and after the first or second dose of CoronaVac vaccination were retrospectively evaluated using an online questionnaire conducted in July 2021.

RESULTS: A total of 2013 people, 1312 women and 701 men, participated in the study. Of these individuals, 245 (12.1%) were polymerase chain reaction positive for coronavirus disease 2019 before vaccination. Of this group, 185 (75.5% of polymerase chain reaction positives and 9.1% of the whole population) received home-based therapy, while 38 (15.5%) received hospital admission. Asymptomatic polymerase chain reaction positivity before vaccination was seen in 22 (9%) individuals.

There were 177 (8.8%) participants who developed polymerase chain reaction positivity at any time after vaccination. In 129 (72.8%) of these participants, polymerase chain reaction positivity occurred 21 days after the second dose of vaccine. While the number of patients hospitalized before vaccination was 38 (15.5% of the polymerase chain reaction positivity group and 1.89% of the general population), the number of patients hospitalized after the vaccination was 17 (10.1% of the polymerase chain reaction positivity group and 0.80% of the general population). The decrease in hospitalization proportion was statistically significant ($P = .002$).

CONCLUSION: The frequency of coronavirus disease 2019, severe illness, and hospitalization rates were found to be lower in post-vaccination period. The vaccine is effective in preventing coronavirus disease 2019 and severe disease.

KEYWORDS: SARS-CoV-2, COVID-19, vaccines, CoronaVac, safety, PCR positivity

Received: July 24, 2022   *Accepted: September 15, 2022*   *Publication date: February 10, 2023*

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a complex disease caused by the etiological agent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), at the end of 2019, in the city of Wuhan, in China. As of September 2021, according to World Health Organization (WHO) data, 220 million cases and more than 4.5 million deaths were reported due to COVID-19.[1] Severe acute respiratory syndrome coronavirus 2 is accepted as a public health problem all over the world due to its easy and rapid spread, straining health systems, and clinical management.[2] As a result, although important measures have been taken, including social distancing, quarantine, and isolation, SARS-CoV-2 has adversely affected not only the infected people but also the entire population, the global economy, and resources. The only way to control the pandemic is community vaccination. For this purpose, the development of a vaccine against COVID-19 has become an urgent agenda for the whole world for the last 2 years.[3]

Since the outbreak began, researchers have worked to develop a vaccine against COVID-19. As of March 2021, there were 5 vaccines in phase IV trials: Sinovac Research and Development Corporation (CoronaVac), Pfizer/BioNTech–Fosun Pharma (BNT162b2); Moderna–National Institute of Allergic and Infectious Diseases (mRNA-1273), AstraZeneca–University of Oxford (AZD1222); and Janssen Pharmaceutical (Ad26.COV2.S, Johnson and Johnson).[4] Developing and approving effective vaccines during this time has been possible thanks to coordinated work between the scientific and medical communities and government agencies such as the Food and Drug Administration.[5] CoronaVac is an inactivated vaccine against SARS-CoV-2 developed by Sinovac Biotech, China, which was approved by World Health Organization in June 2021. The inactivated SARS-CoV-2 vaccine, CoronaVac, acquired emergency use approval from

Corresponding author: Oya Baydar Toprak, e-mail: oyabaydarr@yahoo.com.tr

the Turkish Medicines and Medical Devices Agency based on the initial efficacy results of a nationwide phase III trial in January 2021; CoronaVac was first administered to healthcare workers in Turkey and afterward, the risk groups were vaccinated as stratified.[6] While information about the safety and effectiveness of vaccines is increasing, unfortunately, we have also started to encounter patients who have had a post-vaccine COVID-19 infection in real life. However, the frequency of reinfection after vaccination and the clinical features of reinfection are not clearly known yet.

The main objective of this study is to make a contribution in determining the frequency and clinical features of COVID-19 infection seen after the first or second dose of CoronaVac in healthcare workers and their relatives.

MATERIAL AND METHODS

Study Design and Population
In order to determine the polymerase chain reaction (PCR) positivity that may occur after vaccination against COVID-19, an online questionnaire was sent via e-mail to those who agreed to volunteer for the research with an informed consent. The study is approved by the Cukurova University Ethical Committee (112/2021). Our target audience in the study is healthcare professionals and their relatives. A total of 2013 volunteers, including 1903 (94.5%) healthcare workers and 110 (4.5%) relatives of healthcare workers older than 18 years of age who received a single or double dose of the CoronaVac vaccine, participated in the cross-sectional survey study. The frequency and clinical features of COVID-19 after the first or second dose of CoronaVac vaccination were retrospectively evaluated using an online questionnaire between 1 and 31 July 2021.

Individuals with positive SARS-CoV-2 nucleic acid amplification test after receiving 1 or 2 doses of CoronaVac were defined as post-vaccine COVID-19-infected participants.

Questionnaire
We designed an online self-administered questionnaire after CoronaVac vaccination. In the survey, primarily the basic demographic characteristics (age, gender, occupation, smoking history, and health status), the history of COVID-19 infection before vaccination, the presence of antibody test in the blood after CoronaVac vaccine, the presence of anti-spike antibodies, the positivity of SARS-CoV-2 PCR, the time of PCR positivity, and the symptoms related to post-vaccine COVID-19 infection were recorded.

MAIN POINTS

- The inactivated coronavirus disease 2019 (COVID-19) Vaccine (CoronaVac) reduces the rate of COVID-19 and hospitalizations due to severe acute respiratory syndrome coronavirus 2.
- The need for hospitalization due to COVID-19 infection was 15.5% before and 10.1% after CoronaVac, respectively.
- The positivity rate anytime in unvaccinated and postvaccination periods was 12.1% and 8.8%, respectively.

Antibody Test
In the questionnaire, a question was asked whether participants had their antibody levels checked voluntarily (since there was no routine use). The participants were required to answer this question as positive if the results are above the positive cut-off value specified in the anti-spike antibody kit used in the laboratory where they checked the antibody level.

Statistical Analysis
The descriptive statistics were presented as frequency and percentages for categorical variables while mean ± standard deviation was given for continuous variables. All statistical analyses were conducted by using the IBM Statistical Package for the Social Sciences version 23 program. Figure 1 was generated using the ggplot2 package in the R programming language.[7]

RESULTS

A total of 2013 volunteers, including 1903 (94.5%) healthcare workers and 110 (4.5%) relatives of healthcare workers, were included in the study. Of the volunteers, 1312 were women and 701 were men. Of the health workers, 893 (44.4%) were specialist physicians, 332 (17.5%) were family physicians, 175 (8.7%) were general practitioners, and 127 (6.3%) were nurses. Four hundred eighty-two participants (24%) had a smoking history. Detailed sociodemographic characteristics are documented in Table 1.

Of the 2013 volunteers, 245 (12.1%) were PCR positive before vaccination. Of this group, 185 (75.5% of PCR positives and 9.1% of the general population) received home-based treatment, while 38 (15.5%) received hospital-based treatment. Asymptomatic PCR positivity before vaccination was seen in 22 (9%) participants (Table 2). There were 177 (8.8%) participants who developed PCR positivity at any time after vaccination. In the group with PCR positive after CoronaVac, in 129 (72.8%) of these participants, PCR positivity occurred 21 days after the second dose of vaccine (Figure 1).

A decrease in hospitalization was observed after vaccination. While the number of patients hospitalized before vaccination was 38 (15.5% of the PCR positivity group and 1.89% of the general population), the number of patients hospitalized after the vaccination was 17 (10.1% of the PCR positivity group and 0.80% of the general population) (Table 2). The most common symptoms during PCR positivity are muscle/joint pain (140, 19.4%), fatigue (135, 18.7%), headache (113, 15.6%), runny nose/sore throat (108, 14.9%), cough (94, 13%), fever (84, 11.6%), shortness of breath (38, 5.3%), and clouding of consciousness (11, 1.5%).

The association between PCR positivity after CoronaVac and gender, age, and smoking status was examined, and no statistically significant correlation was found between PCR positivity and gender, age, and smoking status after vaccination.

Of the 2013 people who answered the question about the antibody test, 689 (34.23%) had an antibody test. Out of 689 people who had antibody tests at least 2 weeks after vaccination, 595 (86.3%) people (29.5% of the general total) were found to be above the positive cut-off value specified in the anti-spike antibody laboratory kit.
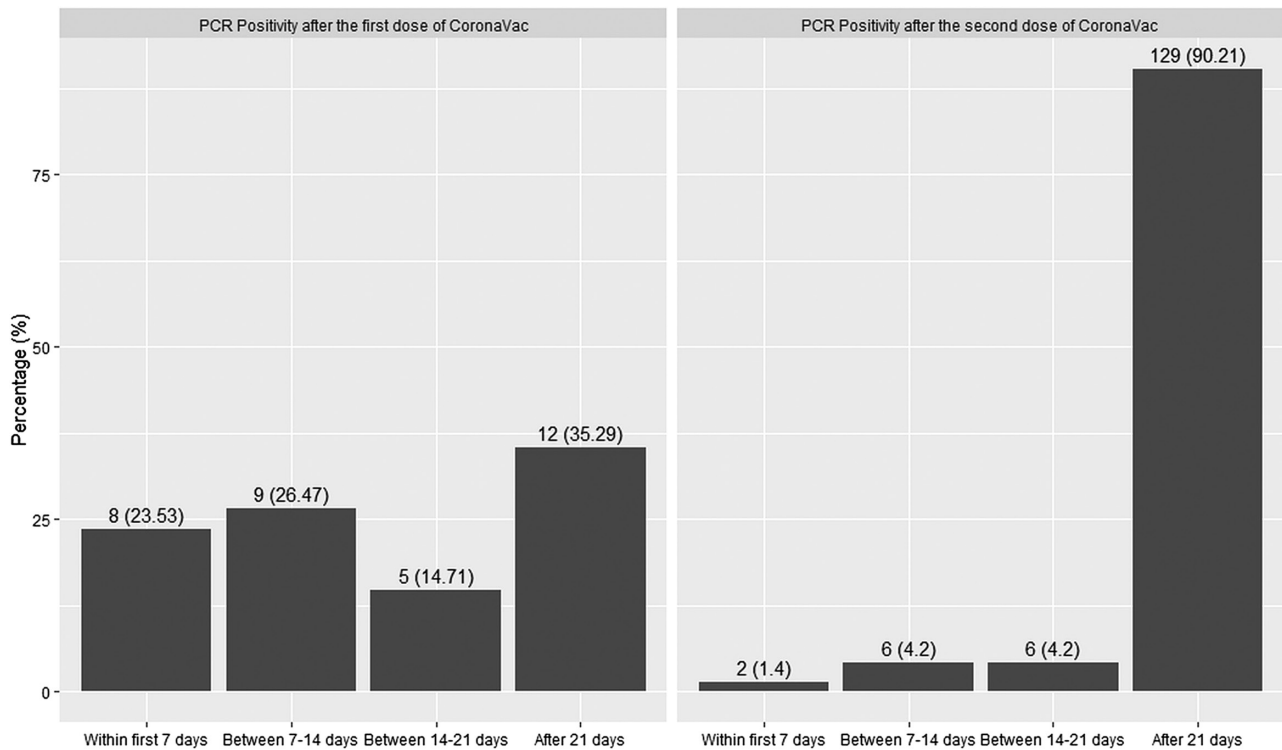
Figure 1. Polymerase chain reaction positivity days after the first and second doses of CoronaVac.

DISCUSSION

Vaccination against COVID-19 started with CoronaVac in January 2021 in healthcare workers in our country and the society stratified later on. This study was conducted in July 2021 and includes the healthcare workers and their relatives as participants. The frequency of COVID-19 was 12.1% and 8.8% before and after vaccination, respectively, based on the self-report of the participants. The need for hospitalization due to COVID-19 was 15.5% before and 10.1% after CoronaVac. An anti-spike antibody value above the labor-atory-determined lower limit was found in 86.3% of participants who had tests at least 2 weeks after vaccination.

A few real-world studies concerning the effectivity of mRNA vaccines against SARS-CoV-2 have been published in the literature.[8,9] A hospital-wide cohort study determined a 71% and 97% decline in acute SARS-CoV-2 infection rates compared to the pre-vaccine period in healthcare workers after the first and second dose, respectively.[8] In another real-life study including 3950 healthcare workers with no previous laboratory documentation of SARS-CoV-2 infection, 1.38 SARS-CoV-2 infections were confirmed by reverse transcription-PCR per 1000 person-days among unvaccinated participants. In contrast, among fully immunized (≥14 days after the

Table 1. Sociodemographic Characteristics of the Participants

Variable	Descriptive Statistics
Gender, n (%)	
Female	1312 (65.18)
Male	701 (34.82)
Profession, n (%)	
Specialist physician	893 (44.36)
Primary care physician	352 (17.49)
General practitioners	175 (8.69)
Research assistants	98 (4.87)
Nurse	127 (6.31)
Dentist	74 (3.68)
Pharmacist	17 (0.84)
Other and unemployed	277 (13.76)
Age (mean ± standard deviation)	46.32 ± 11.65
Presence of smoking history, n (%)	482 (24.39)

Table 2. PCR Positivity and Clinical Characteristics of COVID-19 in Pre- and Postvaccination Periods*

PCR positivity before vaccination	245 (12.17)
Home-based treatment	185 (9.19)
Hospital-based treatment	38 (1.89)
Asymptomatic	22 (1.09)
ICU	3 (0.15)
PCR positivity after vaccination	177 (8.79)
Home-based treatment	129 (6.41)
Hospital-based treatment**	17 (0.84)
Asymptomatic	30 (1.49)
ICU	2 (0.10)

COVID-19, coronavirus disease 2019; ICU, intensive care unit; PCR, polymerase chain reaction.
*All parameters were shown as n (%).
**Hospital-based treatment includes ICU patients.

second dose) persons, 0.04 infections per 1000 person-days were reported, and among partially immunized (≥14 days after the first dose and before the second dose) persons, 0.19 infections per 1000 person-days were reported.[9] A study aimed to determine the early vaccine efficacy concluded that 1.07% of vaccinated healthcare workers had COVID-19 infection, whereas 10.29% of the unvaccinated group had acute COVID-19 infection.[10] A letter concerning healthcare workers in the United States showed that 2.61% of unvaccinated, 1.82% of partially vaccinated, and 0.05% of fully-vaccinated participants had SARS-CoV-2 infection after mRNA vaccines within the first month.[11] The positivity rate of SARS-CoV-2 was 0.05% in healthcare workers approximately in 2 months period after the inoculation of the first dose of mRNA vaccine.[12] An Israel study indicated 0.45% of the vaccinated and 7.26% of the unvaccinated groups were PCR (+) in 63 days period.[13] Severe acute respiratory syndrome coronavirus 2 PCR positivity rate was 0.85% in a comprehensive study enrolling healthcare workers within the first 3 months after inoculation of mRNA vaccine.[14]

To the best of our knowledge, this is the first report emphasizing the postvaccination PCR positivity rate and the clinical characteristics of postvaccine COVID-19 after CoronaVac vaccination. The positivity rates anytime in unvaccinated and postvaccination periods were 12.1% and 8.8%, respectively, in our study. These are relatively higher rates when compared with the studies described earlier. This may be due to the fact that the higher infectious rate in Turkey relates to disease course especially between January and July 2021.[15] Another factor contributing to the high infection rate might be that only inactivated vaccines were available during the first immunization phase. Especially starting from late March until July, the number of daily cases increased to an average of 60 000 new cases per day.[16] Parallel to the normal population, the case and death rates of healthcare workers have also changed; while the deaths of healthcare workers decreased between March 2020 and June 2020, they reached a peak value by climbing after June until December.[17]

Our questionnaire investigated a period between the beginning of the vaccination (June 2021) until end of July 2021. There was only CoronaVac available in the period of June 2021 to April 2021 in Turkey. We included the participants only after the first and second doses of CoronaVac vaccination period for follow-up information. In July, third dose of any vaccine either with BioNTech/Pfizer mRNA vaccine or CoronaVac was officially recommended to prioritize healthcare workers; however, we did not intend to collect any information about the third dose in this study.

The PCR positivity mostly occurred after 21 days of the second dose of CoronaVac. This is too early for diminished antibody response and therefore vaccine efficacy. However, we did not know the exact occurrence time of that positive result. It could have been just after 21 days after vaccination or more depending on follow-up period. Although we did not collect the exact time of SARS-CoV-2 infection, we could comment that the longest period of the second vaccine dose in the study was no longer than 6 months where we know that the efficacy of the vaccine is still acceptable.[18]

We argue that there would be 2 ways to explain the postvaccination high PCR positive rate; either the participants did not take enough precautions since several variants become predominant during the pandemic progress or the positive PCR mostly occurred when the immunity against the virus was diminished by nature after several months of vaccination. Despite all the interpretations, that data shows the vaccination reduces the SARS CoV-2 infection rates from 12.1% to 8.8% which shows statistical significance. The data need further evaluation.

Another important point of this study is that it provided the first data to the literature describing the clinical features of COVID-19 cases after CoronaVac. The need for hospitalization due to COVID-19 infection was 15.5% before and 10.1% after CoronaVac. In some of the limited number of mRNA vaccine studies, it was shown that there was no difference in clinical presentation compared to the pre-vaccine period, while in others, asymptomatic cases were more common in post-vaccine PCR (+) COVID-19 cases. A study including the healthcare workers in Madrid showed that 47% of new infections were symptomatic while the remaining 53% were detected as a part of the screening program.[8] A cohort concerning the incidence of SARS-CoV-2 infection after the first dose of mRNA vaccine determined no significant difference in clinical presentation between vaccinated and unvaccinated participants.[10] Asymptomatic acute COVID-19 infection rate was 70.4% and 30.9% in mRNA vaccinated and unvaccinated groups in a retrospective cohort, respectively.[13] In the literature review, no data were accessible showing the frequency of hospitalization with acute COVID-19 infection in the post-vaccine period. Although a head-to-head comparison could not be established, the dynamics of the epidemic and COVID-19 hospitalization criteria have changed throughout the pandemic; the increment of asymptomatic cases in the post-vaccine period in other similar studies supports the data in our study.

The major limitation of this study is that it is nature of descriptive online survey that questions the retrospective data. Therefore, it carries low reliability due to this design. Although there is participation from all provinces of Turkey, it still does not represent the whole country. The lack of active laboratory surveillance in the study may have resulted in an underestimation of asymptomatic or mild cases. Since the PCR test could not be performed on all patients participating in the study, post-vaccination positivity was of course made according to the person's notification, but it is already known that of Ministry of Health of the Republic of Turkey recommends SARS-CoV-2 PCR testing in the presence of at least 1 symptom during daily screening or by an identified exposure, regardless of vaccination status through the entire period of the pandemic.

CONCLUSION

Although these data need to be validated in prospective larger series, the study is remarkable as it is the first real-world study reporting on the SARS-CoV-2 infection rate and the clinical features of the disease after CoronaVac. In light of these data, CoronaVac emerges as a useful tool in reducing the rate of COVID-19 and the hospitalization due to it.

REFERENCES

1. World Health Organization (WHO). *COVID-19 Weekly Epidemiological Update*, Edition 57. Published 14 September 2021.
2. Doroftei B, Ciobica A, Ilie O-D, Maftei Radu, Ilea C. Mini-review discussing the reliability and efficiency of COVID-19 vaccines. *Diagnostics (Basel)*. 2021;11(4):579. [CrossRef]
3. García-Montero C, Fraile-Martínez O, Bravo C, et al. An updated review of SARS-CoV-2 vaccines and the importance of effective vaccination programs in pandemic times. *Vaccines*. 2021;9(5):433. [CrossRef]
4. Pai SM, Othman AA, Rusch L, et al. Science and evidence-based review and approval of COVID-19 vaccines: a statement of support for the US FDA. *J Clin Pharmacol*. 2021;61(3):277-279. [CrossRef]
5. Zhang Y, Zeng G, Pan H, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect Dis*. 2021;21(2):181-192. [CrossRef]
6. Mallapaty S. China COVID vaccine reports mixed results - what does that mean for the pandemic? *Nature*. 2021. [CrossRef]
7. Wickham H. *ggplot2: Elegant Graphics for Data Analysis*. New York: Springer-Verlag; 2016.
8. Guijarro C, Galán I, Martínez-Ponce D, et al. SARS-CoV-2 new infections among health-care workers after the first dose of the BNT162b2 mRNA COVID-19 vaccine. A hospital-wide cohort study. *Clin Microbiol Infect*. 2021;27(11):1699.e1-1699.e4. [CrossRef]
9. Thompson MG, Burgess JL, Naleway AL, et al. Interim estimates of vaccine effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines in preventing SARS-CoV-2 infection among health care personnel, first responders, and other essential and frontline workers — eight U.S. locations, December 2020–March 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70(13):495-500. [CrossRef]
10. Gupta K, O'Brien WJ, Bellino P, et al. Incidence of SARS-CoV-2 infection in health care workers after a single dose of mRNA-1273 vaccine. *JAMA Netw Open*. 2021;4(6):e2116416. [CrossRef]
11. Daniel W, Nivet M, Warner J, Podolsky DK. Early evidence of the effect of SARS-CoV-2 vaccine at one medical center. *N Engl J Med*. 2021;384(20):1962-1963. [CrossRef]
12. Keehner J, Horton LE, Pfeffer MA, et al. SARS-CoV-2 infection after vaccination in health care workers in California. *N Engl J Med*. 2021;384(18):1774-1775. [CrossRef]
13. Angel Y, Spitzer A, Henig O, et al. Association between vaccination with BNT162b2 and incidence of symptomatic and asymptomatic SARS-CoV-2 infections among health care workers. *JAMA*. 2021;325(24):2457-2465. [CrossRef]
14. Jacobson KB, Pinsky BA, Montez Rath ME, et al. Post-vaccination SARS-CoV-2 infections and incidence of presumptive B.1.427/B.1.429 variant among healthcare personnel at a northern California academic medical center. *Clin Infect Dis*. 2021:ciab554. [CrossRef]
15. T.C. Sağlık Bakalnlığı. *Covid-19 Bilgilendirme Platformu*. Available at: https://covid19.saglik.gov.tr
16. *Worldometer*. Available at: https://www.worldometers.info/coronavirus/country/turkey/#graph-cases-daily.
17. Türkiye'de sağlık çalışanı ölümlerinin anlattıkları. Available at: https://www.ttb.org.tr/userfiles/files/son_son_saglik_emekcileri_olumleri_rapor.pdf.
18. Antibodies from Sinovac's COVID-19 shot fade after about 6 months, booster helps - study. Available at: https://www.reuters.com/business/healthcare-pharmaceuticals/antibodies-sinovacs-covid-19-shot-fade-after-about-6-months-booster-helps-study-2021-07-26/.