

Severe Acute Respiratory Syndrome Coronavirus-2 Breakthrough Infection Among Immunized Healthcare Workers

Aamir Ahmad¹, MRCP, Momin Tahirkheli², MS, Stephanie Hobbs², MS, Nitara Margana², MS, Momna Wazir³, MBBS, Tanzeel Rehman¹, MBBS, Mudassar Zia², MD, Anna Razvi, BS⁴, Muhammad Shah Miran^{2,*}, MD

¹ Hayatabad Medical Complex, Peshawar, Pakistan

² University of Missouri-Kansas City

³ Khyber Medical College, Peshawar, Pakistan

⁴ George Washington University

Abstract

Background— Data is currently evolving regarding incidence and prevalence of breakthrough infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in fully vaccinated healthcare workers (HCWs). In this study, we report upon four immunized HCWs who acquired SARS-CoV-2 infection and examine both their risk factors and disease progression.

Methods— We identified four HCWs from single tertiary care hospital in Peshawar, Pakistan, who were immunized with the Sinopharm vaccine, and were subsequently diagnosed with a SARS-CoV-2 infection by polymerase chain reaction (PCR) test on nasopharyngeal specimen. We examined disease characteristics, duration between vaccine administration and breakthrough infection, and outcomes using a standardized questionnaire.

Results— The mean duration between last dose of vaccine administration and breakthrough infection was 147.5 days \pm standard deviation (SD) 16.3 days. The ages of HCWs were between 20-39 years and all 4 HCWs were men. Mean duration between the first and second dose of vaccine was 25 days \pm standard deviation (SD) 7.1 days. All four vaccinated HCWs experienced fever, body aches, cough, nasal congestion, loss of smell and taste, and post infection fatigue and depression.

Conclusions— Our study highlights the risk of SARS-CoV-2 breakthrough infection among fully vaccinated HCWs and necessity of booster immunization.

Keywords

Healthcare workers (HCWs), Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Reverse Transcriptase Polymerase Chain Reaction (RT-PCR).

BACKGROUND

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) breakthrough infection in fully immunized persons has been reported in several studies.¹ Factors predisposing to breakthrough infection has become a priority for the Centers for Disease Control and Prevention (CDC) due to impact on recommendations regarding booster immunization and public health guidelines. Few cases of breakthrough infection among fully immunized HCWs have been documented.² We report upon four SARS-CoV-2 breakthrough infections seen among HCWs with associated patient risk factors and disease characteristics.

METHODS

We identified four fully vaccinated HCWs from one tertiary care hospital in Peshawar, Pakistan who experienced breakthrough infection with SARS-CoV-2 using HCWs self-reporting system. They were immunized with BBIBP-CorV, an inactivated SARS-CoV-2 vaccine developed by Sinopharm's Beijing Institute of Biological Products. The vaccine is administered by intramuscular injection and the course consists of a two dose series. A questionnaire was completed among 100 fully vaccinated interns and postgraduate trainees in a tertiary care hospital between February 15, 2021 and September 8, 2021. SARS-CoV-2

TABLE 1: Duration between vaccination with two doses of BBIBP-CorV vaccine and breakthrough. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) among healthcare workers (HCWs).

| HCWs | Speciality | Duration between 1st and 2nd Dose | Type of Vaccine | Duration between Vaccination and Break-through Infection |
|-------|-------------------------|-----------------------------------|-----------------|--|
| HCW 1 | Intensive Care Medicine | 21 days | Sinopharm | 165 days |
| HCW 2 | General Surgery | 19 days | Sinopharm | 126 days |
| HCW 3 | Intensive Care Medicine | 35 days | Sinopharm | 146 days |
| HCW 4 | Neurosurgery | 25 days | Sinopharm | 153 days |

Abbreviations used: HCWs Healthcare Workers

breakthrough infections were confirmed by PCR test performed on a nasopharyngeal specimen. Breakthrough infection was defined using the Centers for Disease Control and Prevention (CDC), breakthrough infections which is based on detection of SARS-CoV-2 in a respiratory specimen collected from a person >14 days after they have completed all doses of an FDA-approved vaccine. We determined the duration between vaccine administration and breakthrough infections, severity and characteristics of symptoms, and clinical outcomes. Microsoft Word and Excel were used for data collection and basic statistical analysis.

RESULTS

The average duration between vaccine administration and breakthrough infection was 147.5 days \pm standard deviation (SD) of 16.3 days (Table 2). The age range of the HCWs with breakthrough infection ranged between 20-39 years; all four HCWs were men. Two of the HCWs worked in the Intensive Care Unit, one worked in the Neurosurgery department, and the remaining one HCWs worked in the General Surgery department. None of the HCWs had other comorbidities nor were cigarette smokers. Average duration between the first and second doses of vaccine was 25 days \pm 7.1 days. All four vaccinated HCWs experienced fever, body aches, cough, nasal congestion, loss of smell and taste, post-infection fatigue and depression. One HCW reported dyspnea. Three of the four HCWs experienced moderate illness, while one HCW experienced more severe disease with profound shortness of breath. All four HCWs clinically recovered and had resolution of symptoms after 14 days.

DISCUSSION

Numerous SARS-CoV-2 vaccines have shown efficacy and safety in clinical trials.³ The BNT162b2 messenger RNA (Pfizer–BioNTech) and mRNA-1273 (Moderna) vaccines have shown effectiveness in preventing primary infection, reinfection, and breakthrough infection with SARS-CoV-2 and in preventing the severity of reinfection and breakthrough infections.^{1,2,4} Though these vaccines are largely effective, there have been reported cases of SARS-CoV-2 breakthrough infections. The CDC reports that as of October 2021, there have been 30,177 patients with breakthrough infections.¹

It is important to investigate cases of breakthrough infections, as they may indicate waning immunity and need for booster

vaccination. A study among vaccinated HCWs in Israel reported 39 cases of breakthrough infection among 11,453 fully vaccinated HCWs. They report that 67% of breakthrough infections had mild symptoms and the remainder were asymptomatic, with none requiring hospitalization.² Our case series is consistent with the aforementioned studies that SARS-CoV-2 breakthrough infections are milder and less likely to require hospitalization. These findings support the efficacy of immunization in preventing severe SARS-CoV-2 infection and hospitalization. They also highlight the possible benefit of booster vaccination in healthcare workers and at risk populations. A recently published article by Krause et al., suggested that even if immunity appears to diminish, reductions in efficacy against mild disease do not predict reductions in efficacy against severe disease.⁴ They claim this is due to protection mediated by antibody responses, memory responses, and cell mediated immunity.⁴

In the United States, the Food and Drug Administration (FDA) has approved the use of three SARS-CoV-2 vaccines: Moderna, Pfizer-BioNTech, and Johnson&Johnson. While these are the mainstay for prevention in the United States, vaccines approved outside North America demonstrate similar levels of efficacy. The vaccine, Sinopharm, has been approved for use in sixty-seven countries worldwide. The Sinopharm vaccine is an inactivated coronavirus vaccine, unlike the Moderna and Pfizer vaccines which are mRNA-based. The efficacy of the Sinopharm vaccine can be ascertained based on the number of symptomatic and hospitalized cases of SARS-CoV-2 that it prevents. In a large multi-country Phase 3 trial, it was shown that 2 doses of the Sinopharm vaccine, given 21 days apart, have an efficacy of 79% against symptomatic SARS-CoV-2 infection and hospitalization, two weeks after the second dose.⁵ Furthermore, the administration of the Sinopharm vaccine was found to have a lower prevalence of side effects as opposed to the Pfizer vaccine after each dose.⁶ 40% of participants did not report any adverse symptoms after the Sinopharm vaccine, compared to just 25.71% of Pfizer recipients. Data regarding post-vaccination reinfection rates and immunity is very limited at this time.

Analyzing the rate and clinical features of vaccine breakthrough infections (VBI) is exceedingly important from a public health perspective. As the SARS-CoV-2 pandemic has advanced, research regarding reinfection and VBI is of major importance and it is ever changing. However, data regarding VBI is currently limited. All four HCWs tested positive for

SARS-CoV-2 infection based on the aforementioned criteria and experienced moderate to severe symptoms despite having been fully vaccinated. None of the HCWs received a booster vaccine prior to breakthrough infection. A recently published case series analysis of 6,399 SARS-CoV-2 infections in Washoe County, Nevada found 339 subjects had breakthrough infection despite being fully vaccinated.⁷ Moreover, a recently published CDC report described that vaccinated individuals who had previous PCR-confirmed diagnosis of SARS-CoV-2 had significantly lower reinfection rates when compared to unvaccinated individuals with previous PCR-confirmed diagnosis of SARS-CoV-2.⁸ Despite this reassuring finding, it is important to note that breakthrough infection is still occurring at a significant rate and individuals that are infected after vaccination may still have severe symptoms. Additionally, a case series investigating reinfection among five unimmunized HCWs with natural immunity revealed that all five HCWs experienced more severe symptoms during reinfection in comparison to primary infection.⁹ The findings from our case series in conjunction with the data from these recently published papers supports the approval of booster vaccines for populations that are at a high risk for primary or reinfection. Recently, the CDC updated their guidelines to recommend the use of a booster dose for all individuals 18 years and above.¹⁰ These updated guidelines represent a significant achievement for the prevention of SARS-CoV-2 infection in the United States. However, to effectively end the pandemic, there is a need for providing vaccines in equity to all countries in the world, especially for HCWs and

immunocompromised patients worldwide.^{4,11} Randomized Controlled Trials with large sample sizes need to be done to investigate the prevalence of breakthrough infection as well as antibody titers.

LIMITATIONS

Due to our small sample size we are limited in determining incidence and prevalence of breakthrough infections. Furthermore, because of limited resources, laboratory testing to identify SARS-CoV-2 variants was not performed.

CONCLUSION

Our case series highlights the risk of SARS-CoV-2 breakthrough infection of HCWs despite immunization with Sinopharm vaccines. All HCWs had moderate to severe symptoms despite having no significant comorbidities, as all of them reported experiencing fever, body aches, fatigue, and depression. These findings are of concern, considering the fact that HCWs are persistently at a high risk of SARS-CoV2 exposure. Further studies with large sample sizes of HCWs as well as the general population should be done to determine the incidence of VBI, symptom severity, evidence of waning immunity, and efficacy of booster vaccines. Our study supports the expanding role of booster vaccination in high-risk populations beyond the U.S. to prevent breakthrough infection as well as reinfection to effectively contribute towards ending the ongoing pandemic.¹¹

REFERENCES

1. Covid-19 Vaccine Effectiveness. Centers for Disease Control and Prevention. <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/index.html>. Last Updated November 10, 2021. Accessed November 18, 2021.
2. Bergwerk M, Gonen T, Lustig Y, et al. Covid-19 Breakthrough Infections in Vaccinated Health Care Workers. *New England Journal of Medicine* 2021;385(16):1474–84.
3. Soiza RL, Scicluna C, Thomson EC. Efficacy and safety of COVID-19 vaccines in older people. *Age Ageing* 2021;50(2):279–83.
4. Krause PR, Fleming TR, Peto R, et al. Considerations in boosting COVID-19 vaccine immune responses. *Lancet* 2021;398(10308):1377–80.
5. Interim recommendations for use of the inactivated COVID-19 vaccine BIBP developed by China National Biotech Group (CNBG), Sinopharm. Interim guidance. Available at: <https://apps.who.int/iris/bitstream/handle/10665/352470/WHO-2019-nCoV-vaccines-SAGE-recommendation-BIBP-2022.1-eng.pdf>. Accessed 10 August, 2022.
6. Al Khames Aga QA, Alkhaffaf WH, Hatem TH, et al. Safety of COVID-19 vaccines. *J Med Virol* 2021;93(12):6588–94.
7. Kerwin H, Briggs R, Nair-Desai S, et al. An Analysis of SARS-CoV-2 Vaccine Breakthrough Infections and Associated Clinical Outcomes. medRxiv 2021;2021.09.09.21262448.
8. Cavanaugh AM, Spicer KB, Thoroughman D, et al. Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May–June 2021. *MMWR Morb Mortal Wkly Rep* 2021;70:1081–1083.
9. Ahmad A, Shah Miran M, Kamal O, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Reinfection Among Healthcare Workers. *HealthCare Research Journal*. 2021;2(2):39–42.
10. Centers for Disease Control and Prevention. CDC Expands Eligibility for COVID-19 Booster Shots to All Adults. November 19, 2021. Available at <https://www.cdc.gov/media/releases/2021/s1119-booster-shots.html>. Accessed November 24, 2021.
11. Georgieva K, Ghebreyesus TA, Malpass D, et al. World Health Organization. A New Commitment for Vaccine Equity and Defeating the Pandemic. 31 May, 2021. Available at <https://www.who.int/news-room/commentaries/detail/a-new-commitment-for-vaccine-equity-and-defeating-the-pandemic>. Accessed November 24, 2021.