Hospitalisation among vaccine breakthrough COVID-19 infections

Lancet Infect Dis 2021
Published Online
September 7, 2021
https://doi.org/10.1016/
S1473-3099(21)00558-2

Emergency use authorisations granted by the US Food and Drug Administration for three SARS-CoV-2 vaccines represent an important milestone in the response to the COVID-19 pandemic. Data presented from the VIVALDI study by Shrotri and colleagues[1] and other phase 3 clinical trials[2–4] have shown robust vaccine efficacies (>85%) at preventing severe symptomatic disease. Although rare, emerging reports describe breakthrough SARS-CoV-2 infections in fully vaccinated individuals.[5] We describe the impact of vaccination on admission to hospital in patients with confirmed SARS-CoV-2 infection using real-world data collected by the Yale New Haven Health System. We did a systematic review of patients admitted to hospital with SARS-CoV-2 (confirmed by a positive PCR test at the time of admission) between March 23 and July 1, 2021. SARS-CoV-2 vaccination status was recorded, including the specific vaccine type (mRNA-1273 [elasomeran; Moderna], BNT162b2 [tozinameran; Pfizer–BioNTech], or Ad.26.COV2.S [Janssen]) and vaccination dates. Patients were considered fully vaccinated if the final dose (either second dose of BNT162b2 or mRNA-1273, or first dose of Ad.26.COV2.S) was administered at least 14 days before symptom onset or a positive PCR test for SARS-CoV-2. In total, we identified 969 patients who were admitted to a Yale New Haven Health System hospital with a confirmed positive PCR test for SARS-CoV-2. Severity of COVID-19 infection was determined on the basis of established guidelines.[6]

172 (18%) of 969 patients had received at least one dose of a COVID-19 vaccine at the time of admission to hospital. Among these patients, 103 had received a partial vaccine course (one dose of BNT162b2 or mRNA-1273), 15 had received a complete course (two doses of BNT162b2 or mRNA-1273 or one dose of Ad.26.COV2.S within 14 days before symptom onset or a positive PCR test), and 54 were fully vaccinated (appendix pp 1–2). Patients deemed to have a breakthrough SARS-CoV-2 infection—ie, the 54 patients who were fully vaccinated—were evaluated for illness severity. Among this cohort, we found that 25 (46%) patients were asymptomatic (admitted to hospital for a non-COVID-19-related diagnosis but with an incidental positive PCR test for SARS-CoV-2), four (7%) had mild disease, 11 (20%) had moderate disease, and 14 (26%) had severe or critical illness. Among those with severe or critical illness, the median age was 80·5 years (IQR 76·5–85·0); four of 14 patients required intensive care, one required mechanical ventilation, and three died. Pre-existing comorbidities in the 14 patients with severe or critical illness included overweight (body–mass index >25 kg/m^2; n=9), cardiovascular disease (n=12), lung disease (n=7), malignancy (n=4), type 2 diabetes (n=7), and use of an immunosuppressive agent (n=4; appendix pp 3). 13 of 14 patients had received BNT162b2 (appendix p 1–2).

Vaccination for SARS-CoV-2 is highly effective against infection with SARS-CoV-2 or hospitalisation with COVID-19. In our real-world assessment of patients admitted to hospital with a positive SARS-CoV-2 PCR test, we found that nearly a fifth of patients had received at least one dose of the vaccine, and we observed that many patients had not completed the full vaccine course. The finding that more than a quarter of fully vaccinated patients admitted to hospital with SARS-CoV-2 were severely or critically ill with COVID-19 could be reflective of numerous factors, including the emergence of SARS-CoV-2 variants that might confer decreased vaccine effectiveness and an ineffective immune response mounted against vaccines among those with comorbidities—eg, older age, overweight, and use of immunosuppressive agents. Although the incidence of severe or critical COVID-19 illness remains low in those who are fully vaccinated, we observed a higher number of patients with severe or critical illness in those who received the BNT162b2 vaccine than in those who received mRNA-1273 or Ad.26.COV2.S (total number of vaccine doses distributed in Connecticut [USA] until May 17, 2021, was 1 358 175 for BNT162b2, 1 044 420 for mRNA-1273, and 267 000 for Ad.26.COV2.S).[7] This finding would benefit from further investigation. Overall, although vaccines have undoubtedly conferred widespread protection against SARS-CoV-2 infection worldwide, future studies are needed to identify and mitigate factors that are associated with inadequate vaccine response in those with breakthrough infections.

See Online for appendix

We declare no competing interests. PVJ, AG, and KAB contributed equally to this Comment. The Yale University institutional review board approved the study (2000027792) and waived the need for informed consent.

*Prerak V Juthani, Akash Gupta, Kelly A Borges, Christina C Price, Alfred I Lee, Christine H Won, *Hyung J Chun*
hyung.chun@yale.edu

Department of Internal Medicine (PVJ, AG), Yale Center for Clinical Investigation (KAB), Section of Immunology (CCP), Section of Haematology (AIL), Section of Pulmonary, Critical Care, and Sleep Medicine (CHW), Yale Cardiovascular Research Center, Section of Cardiovascular Medicine (HJC), Yale School of Medicine, New Haven, CT 06511, USA

1 Shrotri M, Krutikov M, Palmer T, et al. Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study. *Lancet Infect Dis* 2021; published online June 23. https://doi.org/10.1016/S1473-3099(21)00289-9.

2 Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA COVID-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med* 2021; **384:** 1412–23.

3 Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384:** 403–16.

4 Sadoff J, Le Gars M, Shukarev G, et al. Interim results of a phase 1–2a trial of Ad26.COV2.S COVID-19 vaccine. *N Engl J Med* 2021; **384:** 1824–35.

5 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:** 1774–75.

6 National Institutes of Health. Clinical spectrum of SARS-CoV-2 infection. 2021. https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/ (accessed May 2, 2021).

7 Connecticut Department of Public Health. COVID-19 vaccine distribution in Connecticut. 2021. https://data.ct.gov/stories/s/CoVP-COVID-Vaccine-Distribution-Data/bhcd-4mnv/ (accessed July 5, 2021).