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Concise Communication

An outbreak of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) infections among hospital personnel with high mRNA vaccine uptake

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Abstract

Real-world studies have demonstrated impressive effectiveness of the BNT162b2 COVID-19 vaccine in preventing symptomatic and asymptomatic SARS-CoV-2 infection. We describe an outbreak of SARS-CoV-2 infections in a hospital with high vaccine uptake. We found a low secondary attack rate (7%), suggesting low infectivity of vaccinated persons with vaccine breakthrough SARS-CoV-2 infections.

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The Pfizer BNT-162b2 coronavirus disease 2019 (COVID-19) vaccine is the current authorized COVID-19 vaccine in Israel. Similar to the phase 3 clinical trial,[1] real-world studies have demonstrated >94% effectiveness in preventing symptomatic SARS-CoV-2 infection,[1–3] and recently, asymptomatic infection.[4]

One question that arises is the infectivity of vaccinated study participants. A preprint analysis of vaccinated healthcare personnel (HCP) demonstrated a 30% reduction of SARS-CoV-2 infection among household contacts within 14 days after the first vaccine dose.[5]

Here, we report an outbreak of SARS-CoV-2 infections in an HCP population with high vaccine uptake. We evaluated the transmission of SARS-CoV-2 from vaccinated HCP to their household contacts.

Methods

This retrospective observational study was performed at the Tel-Aviv Sourasky Medical Center, a tertiary-level hospital with ~7,500 HCP. Ethics approval for this study was obtained from the institutional review board along with a waiver of written informed consent (no. TLV-0189-21).

During the COVID-19 pandemic, the hospital mandated periodic screening of HCP using nasopharyngeal swabs for RT-PCR of SARS-CoV-2. HCP at high risk of exposure (ie, emergency rooms, dedicated COVID-19 wards, etc) were screened biweekly and HCP at lower risk of exposure (ie, general medical wards) were screened once a month, as described elsewhere.[6]

Vaccination of HCP with the BNT-162b2 mRNA vaccine started on December 20, 2020, and proceeded rapidly. By January 24, 2021, >80% of HCP had been vaccinated with 1 dose and >70% had been vaccinated with 2 doses.

A cluster of positive HCP was identified in a nonclinical department in late January 2021. HCP were divided into 3 groups of vaccination status: fully vaccinated (>7 days after receiving the second vaccine dose), partially vaccinated (received only one vaccine dose or <7 days after the second dose), and unvaccinated. Contact tracing involved an epidemiological interview and SARS-CoV-2 RT-PCR screening of persons who spent >15 minutes closer than 2 m (~6 feet) from the index case.[7]

Microbiological methods

SARS-CoV-2 RT-PCR was performed using the Allplex 2019-nCoV assay (Seegene, Seoul, South Korea) that detects the N, E, and RdRP genes. Cycle threshold values were retrieved and compared among patient groups as a surrogate marker of viral load.[4] All available SARS-CoV-2 RNA specimens were analyzed using whole-genome sequencing on the Illumina MiSeq platform. Enrichment and library construction were performed on extracted total nucleic acids using QIAseq SARS-CoV2 Primer Panel (Qiagen, Denmark) and the QIAseq FX DNA Library Kit (Qiagen). The libraries were sequenced using the Illumina MiSeq reagent kit v3 600 cycles (2X150 bp). Bioinformatics analysis was performed using the CLC Genomics Workbench version 21.02.2 (Qiagen). Viral reads were mapped to the Wuhan SARS-CoV-1 reference genome (MN908947.3).

Serologic testing for anti–spike protein (anti-S) IgG and anti–nucleocapsid protein (anti-N) IgG antibodies was performed using

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Table 1. Description of Infection Healthcare Personnel

Participant No.	Age	Sex	Symptoms	SARS-CoV-2 Cycle Threshold	Vaccine Status	Time From Second Dose (Days)	No. of Positive Contacts	Serology Within 3 Days of Diagnosis AU/mL[a]	Serology Within 3 Days of Diagnosis BAU/mL	Serology After at Least 12 Days of Diagnosis AU/mL[a]	Serology After at Least 12 Days of Diagnosis BAU/mL	NGS Findings
1	26	Female	Mild	16	Unvaccinated		NA	NA				
2	31	Female	Mild	15	Unvaccinated		NA	NA				
3	32	Male	Asymptomatic	16	Unvaccinated		NA	NA				
4	46	Female	Mild	27	Unvaccinated		NA	Anti-S negative Anti-N negative				B.1.1.7/501.v1
5	24	Female	Mild	15	Partially vaccinated		NA	NA				
6	67	Female	Mild	20.5	Partially vaccinated		NA	Anti-S positive, 1554 Anti-N negative	Anti-S positive, 221			B.1.1.7/501.v1
7	32	Female	Asymptomatic	17	Partially vaccinated	4	0/2	Anti-S positive, 14260 Anti-N negative	Anti-S positive, 2025			B.1.1.7/501.v1
8	67	Female	Asymptomatic	23	Fully vaccinated	9	0/0	Anti-S -positive, 11190 Anti-N negative	Anti-S positive, 1589	Anti-S positive, 6808 Anti-N positive	Anti-S positive, 967	B.1.1.7/501.v1
9	58	Female	Mild	22	Fully vaccinated	11	0/7 Only 6 tested	Anti-S positive, 965 Anti-N negative	Anti-S positive, 137	Anti-S positive, 13045 Anti-N negative	Anti-S positive, 1852	B.1.1.7/501.v1
10	49	Male	Asymptomatic	31	Fully vaccinated	16	0/3 Not tested	Anti-S positive, 12479 Anti-N negative	Anti-S positive, 1772			
11	38	Female	Asymptomatic	23	Fully vaccinated	14	0/4 Only 1 tested	Anti-S positive, 4653 Anti-N negative	Anti-S positive, 661	Anti-S positive, 6223 Anti-N positive	Anti-S positive, 884	
12	66	Female	Mild	20	Fully vaccinated	20	0/6	NA		Anti-S positive, 21947 Anti-N positive	Anti-S positive, 3116	
13	60	Female	Mild	29	Fully vaccinated	20	0/2 Not tested	NA		Anti-S positive, 24616 Anti-N positive	Anti-S positive, 3495	B.1.1.7/501.v1
14	54	Female	Asymptomatic	36	Fully vaccinated	14	1/1	NA				
15	41	Male	Asymptomatic	19	Fully vaccinated	10	0/4 Not tested	NA				B.1.1.7/501.v1*

Note. AU/mL; arbitrary units per milliliter; BAU/mL, WHO binding antibody units; NA, not available. NGS, next-generation sequencing

[a]IgG II Quant assay are reported in AU/mL. A conversion factor between AU/mL and BAU/mL has been established as 1 BAU = 0.142 AU. Additional SARS-CoV-2 positive RNA of a seventh employee was also characterized as the same variant based on receptor-binding domain (RBD) sequencing alone without performing whole-genome sequencing (data not shown in the main text)

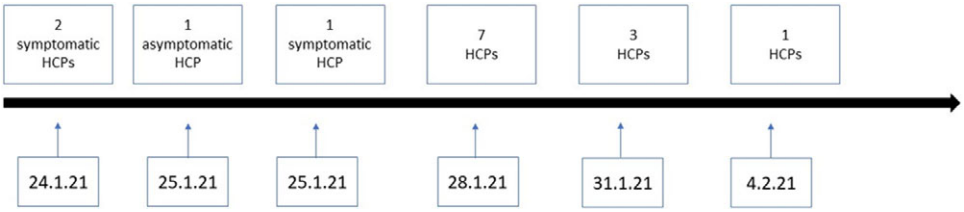

Fig. 1. SARS_CoV-2 detection among healthcare personnel (HCP) over time.

chemiluminescent microparticle immunoassay on the ARCHITECT system (Abbott, Abbott Park, IL) early after SARS-CoV-2 detection and at least 12 days after diagnosis.

Results

Outbreak description

On January 24, 2021, 2 unvaccinated HCP who shared the same work space were found positive for SARS-CoV-2 after reporting symptoms of sore throat and rhinitis that started a day before. They were sent for a furlough the same day. A day later, a third, unvaccinated asymptomatic HCP from the same department was tested as part of the periodic screening program and tested positive. During the following 10 days, the entire department (N = 66) was tested for SARS-CoV-2 and 12 additional HCP tested positive. (Fig. 1) Repeated testing did not identify additional infected HCP.

Of the 15 infected HCP, 4 (26%) were unvaccinated, 3 (20%) were partially vaccinated, and 8 (53%) were fully vaccinated (range, 9–20 days after the second vaccine dose) (Table 1). Of the 8 fully vaccinated HCP, 5 (63%) were asymptomatic and 3 (37%) had mild upper respiratory tract symptoms. A thorough epidemiological investigation revealed only short (<15 minutes) close contacts among 4 of the 15 infected HCP.

Contact tracing

Overall, 27 close contacts of fully vaccinated SARS-CoV-2 positive HCP were traced, 19 of whom were household contacts. Of these 27 contacts, 16 were unvaccinated, 3 were partially vaccinated, and 8 were fully vaccinated. Also, 14 close contacts (8 unvaccinated, 3 partially vaccinated, 3 fully vaccinated) underwent RT-PCR testing for SARS-CoV-2. Among them, 1 contact (7.14%, 1 of 11 unvaccinated contacts, 9%), the unvaccinated spouse of an index HCP, was positive for SARS-CoV-2. This person developed mild symptoms that started 3 days before the HCP tested positive. None of the other 26 close contacts developed symptoms.

Genome sequencing and serology

Whole-genome sequencing was performed on 6 samples that were available for analysis (Table 1). All 6 outbreak sequences were related to the B.1.1.7/501.v1 (α) lineage and were identical or exhibited a maximal difference of 1-2 SNPs. Moreover, 4 of the 8 fully vaccinated study participants and 2 of 4 partially vaccinated study participants who were tested for serology demonstrated anti-S antibodies within 3 days of diagnosis (mean titer 7,517Au/mL; range, 965–14,260Au/mL), and negative anti-N IgG. Also, 5 of the 8 fully vaccinated HCP who were tested for serology after at least 12 days of diagnosis had anti-S antibodies (mean titer 14,528 Au/mL; range 6,223–24,616 Au/mL), and 4 of these 5 also demonstrated anti-N antibodies. The median cycle threshold value of SARS-CoV-2 RNA was 20.5 and was higher among vaccinated HCP than unvaccinated HCP (23 vs 16.5; $P = .01$).

Discussion

In this outbreak among 15 SARS-CoV-2–infected HCP in 1 department, all specimens that were genetically sequenced corresponded to the same lineage (B.1.1.7/501.v1) and clustered together. All vaccinated HCP who were tested for serology within 3 days of SARS-CoV-2 diagnosis had evidence of anti-S antibodies and negative anti-N IgG, whereas most HCP who were tested later in the course of infection had evidence of anti-S as well as anti-N antibodies. These findings suggest a humoral response to the vaccine at the time of COVID-19 diagnosis.

Among the 27 close contacts of the 8 vaccinated HCP (mostly households), only 1 of 14 tested positive, corresponding to an estimated attack rate of 7.14%, which is less than half that reported in a large meta-analysis of 54 studies prior to the introduction of COVID-19 vaccine (16.6%).[8] Notably, the single positive contact of this cohort was symptomatic 3 days prior to the diagnosis of SARS-CoV-2 infection in his spouse. Therefore, it is difficult to estimate the primary source of infection.

Several factors may explain the low attack rate in this study. First, although the overall median cycle threshold value of the cohort was low (20.5), vaccinated HCP had higher median cycle threshold values than unvaccinated HCP. This result, though in small numbers, is in line with other reports that demonstrated lower viral loads among vaccinated compared to unvaccinated persons infected with SARS-CoV-2,[4] possibly making vaccinated persons less likely to transmit the virus to others.[9,10] Second, most of the vaccinated HCP were asymptomatic. Several previous studies have demonstrated a lower attack rate among asymptomatic compared to symptomatic patients.[5]

This study has several limitations. First, only 14 of the 27 high-risk contacts were tested for SARS-Cov2, which might have resulted in overestimation or underestimation of the actual attack rate. Second, our study did not consider covariates that could affect the secondary attack rate (ie, adult or child contacts, crowding, number of contacts in household).

In summary, viewed in the context of encouraging "real-world" data on the effectiveness of COVID-19 vaccines, our findings suggest low infectivity of vaccinated persons with vaccine breakthrough SARS-CoV-2 infections.

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Conflicts of interest. R.B. reports receiving consulting fees from Pfizer, Gilead, and Teva, outside the scope of this study. Other authors report no potential conflict of interest.

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