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Lower Severe Acute Respiratory Syndrome Coronavirus 2 Viral Shedding Following Coronavirus Disease 2019 Vaccination Among Healthcare Workers in Los Angeles, California

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Among 880 healthcare workers with a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test, 264 (30.0%) infections were identified following receipt of at least 1 vaccine dose. Median SARS-CoV-2 cycle threshold values were highest among individuals receiving 2 vaccine doses, corresponding to lower viral shedding. Vaccination might lead to lower transmissibility of SARS-CoV-2.

Keywords. COVID-19; cycle threshold; SARS-CoV-2; vaccine; viral load.

In the United States (US), 1 vaccine, BNT162b2 (Pfizer-BioNTech), has been fully licensed by the Food and Drug Administration (FDA) for the prevention of coronavirus disease 2019 (COVID-19), while 2 vaccines, mRNA-1273 (Moderna) and Ad26.CoV2.S (Janssen/Johnson & Johnson), have received emergency use authorization [1]. All 3 vaccines demonstrated

high efficacy in the prevention of severe COVID-19 in phase 3 clinical trials [2–4].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral loads in the nasopharynx have been identified as a key driver for transmission [5]. Therefore, in addition to preventing severe COVID-19 disease, vaccines might also decrease viral transmission both by preventing infections and through a reduction of viral shedding in breakthrough infections following vaccination. However, there are limited data regarding postvaccination nasal viral loads of SARS-CoV-2 infections. A small study of 10 asymptomatic nursing home residents found a reduction in nasopharyngeal SARS-CoV-2 viral loads, estimated using the cycle threshold (Ct) values, following 1 dose of vaccine [6]. In 1 study in Israel, increased Ct values were observed among infections occurring ≥ 12 days following the first vaccine dose, which were estimated to correspond to a 4-fold reduction in viral load [7].

The University of California, Los Angeles (UCLA) Health System began a COVID-19 vaccination program on 16 December 2020. Our objective was to determine if SARS-CoV-2 Ct values differed by vaccination status among healthcare workers.

METHODS

Study Design and Population

This was an observational, retrospective study of all UCLA Health employees with a SARS-CoV-2 infection after implementation of a COVID-19 vaccination program. SARS-CoV-2 testing is available to UCLA Health employees and is performed by employee request or recommended based on symptoms, exposures, or contact-tracing efforts. In an effort to increase surveillance testing for SARS-CoV-2, an optional, asymptomatic surveillance testing program that used self-collected anterior nasal samples was launched on 26 December 2020 for all UCLA Health employees. Any employee who was not experiencing symptoms was eligible to participate in the testing program and had the option of testing up to once weekly.

All employees with a positive SARS-CoV-2 test from 16 December 2020 through 31 March 2021 were included. Testing and vaccination data were extracted from the employee health record database. Testing data were extracted from laboratory databases. Only data from the first positive test during the study period were used.

Laboratory Testing

SARS-CoV-2 testing was performed by either the UCLA Clinical Microbiology Laboratory, the UCLA SwabSeq COVID-19 Laboratory, or an external laboratory. The UCLA

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Clinical Microbiology Laboratory performed real-time reverse-transcription polymerase chain reaction (RT-PCR) testing using the following assays: Simplexa COVID-19 Direct (Diasorin Molecular, Cypress, California), cobas 6800 SARS-CoV-2 and Influenza A/B Test and cobas Liat SARS-CoV-2 and Influenza A/B Assay (Roche Molecular Systems, Pleasanton, California), and TaqMan SARS-CoV-2, FluA/B RT-PCR Assay (ThermoFisher Scientific, Carlsbad, California). The asymptomatic surveillance testing program for employees used SwabSeq, an FDA-authorized high-throughput SARS-CoV-2 testing platform that uses next-generation sequencing [8].

The Ct values were extracted from each instrument. One assay did not produce Ct values (cobas Liat), while another assay (TaqMan) generated 1 combined Ct value for 2 targets: N and S gene. Two assays provided Ct values for 2 separate targets: ORF1 and S genes (Diasorin Simplexa) and ORF1 and E genes (Roche cobas 6800). The midpoint between those 2 values were used for analysis. SwabSeq uses the S-ratio, the ratio of virus to in vitro standard, to estimate Ct values based on the following equation: $40 - [\log(S\text{-ratio} \times 250) / \log(1.6)]$ [9]. Testing data from external laboratories were not available.

Analysis

The outcomes were classified into several categories based on vaccination status. Positive tests that were detected on or prior to a first dose of vaccine were considered to have occurred prior to vaccination. A 12-day cutoff following the first vaccine dose was used based upon a prior report and vaccine efficacy data, suggesting early onset of protection by the vaccine [2, 7]. Following the second vaccine dose, outcomes were separated into those that were detected within the first week and those that were detected after the first week in order to capture tests that might have occurred prior to an increased immune response to the second dose.

Counts and percentages are presented for descriptive variables. Medians and interquartile ranges (IQRs) are presented for nonnormally distributed variables. The Kruskal-Wallis test was used to measure differences in Ct values by vaccination categories. A *P* value < .05 was considered significant. All statistical analyses were done in Stata version 16 (Stata Corporation, College Station, Texas).

Patient Consent Statement

Ethical review and approval were obtained by the UCLA Institutional Review Board (#21-000373). The study did not include factors that necessitated written patient consent.

RESULTS

Between 16 December 2020 and 31 March 2021, there were 43 516 SARS-CoV-2 tests done among 11 930 employees with 880 employees having a positive SARS-CoV-2 test. Among those employees with a positive test, 594 (67.5%) received at

least 1 vaccine dose during the study period and 286 (32.5%) were not vaccinated. Among the vaccinated employees, 368 (62.0%) received BNT162b2, 205 (34.5%) received mRNA-1273, and 21 (3.5%) received Ad26.CoV2.S.

The UCLA Clinical Microbiology Laboratory performed 672 (76.4%) of the SARS-CoV-2 tests, SwabSeq performed 77 (8.8%), and 131 (14.9%) were performed by external laboratories. In total, 616 (70.0%) of the infections were detected among unvaccinated employees, which included 3 infections that were detected on the same day as the first vaccine dose, and 264 (30.0%) of the infections were detected in employees after receiving their first vaccine dose. Among infections detected after the first vaccine dose, 223 (84.5%) occurred prior to the second vaccine dose, with a median of 9 days following the first dose (IQR, 5–14 days). Forty-one (15.5%) infections occurred after the second dose, with a median of 16 days (IQR, 4–35 days).

Ct values were available for 742 tests: 82.8% (510/616) of the tests on or prior to the first vaccine dose and 88.9% (232/264) of the tests done after first vaccine dose. The median Ct value was 20.1 (IQR, 16.9–25.1) for tests done prior to the first vaccine dose, 20.6 (IQR, 16.9–26.3) for tests done within 11 days following the first vaccine dose, 21.9 (IQR, 17.5–27.1) for positive tests ≥ 12 days following the first vaccine dose and before the second dose, 24.9 (IQR, 16.4–32.4) for tests done on or within 6 days after the second dose, and 30.4 (IQR, 20.8–34.1) for tests done 7 or more days following the second dose. The median Ct values differed by vaccination category (*P* < .01). The median Ct values according to vaccination status are shown in Figure 1.

Ct values by days following the first vaccine dose are shown in Supplementary Figure 1. Data regarding Ct values according to the different vaccine and assay types are shown in Supplementary Table 1. The Ct values for individual gene targets (ORF1, E, and S genes) for the 2 assays that separately reported these values are shown in Supplementary Figure 2. Supplementary Figure 3 shows Ct values by date of positive test, stratified by vaccination status at the time of testing.

DISCUSSION

This is a single-center retrospective study of healthcare workers who had a positive SARS-CoV-2 test following the implementation of a COVID-19 vaccination program. Testing was performed either based on symptoms and exposures or through participation in an asymptomatic surveillance testing program. SARS-CoV-2 Ct values were shown to be significantly higher among vaccinated individuals compared to unvaccinated individuals. There is an inverse relationship between Ct values and quantity of viral RNA, with higher Ct values being associated with lower viral loads [10]. SARS-CoV-2 viral loads are known to be a critical driver of transmission [5]. Thus, our findings using real-world data suggest that COVID-19 vaccination

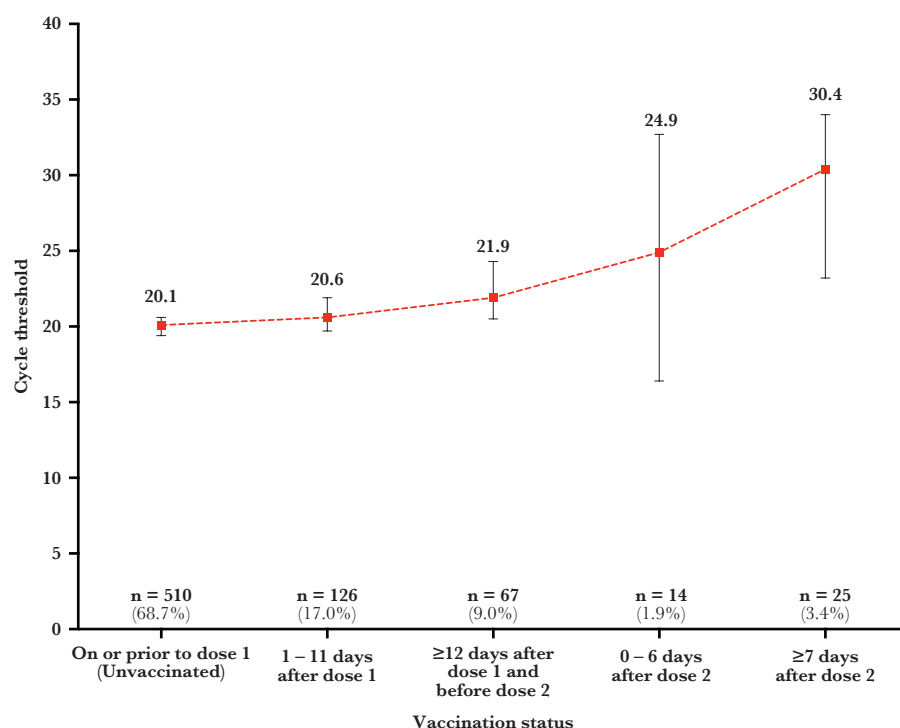


Figure 1. Severe acute respiratory syndrome coronavirus 2 cycle threshold (Ct) values by vaccination status at the time of testing. Median Ct values are shown with 95% confidence intervals.

might translate into decreased transmissibility of SARS-CoV-2 infections.

We found an increase in Ct values following vaccination, and the median Ct values were highest among those who received their second vaccine dose. Our findings are consistent with data showing increased Ct values ≥ 12 days following vaccination with BNT162b2 in Israel [7], as well as with a study from the US showing increased Ct values among nursing home residents who received 1 vaccine dose [6]. In a cohort of healthcare personnel, first responders, and other essential and frontline workers in the US, lower SARS-CoV-2 viral loads were observed among vaccinated and partially vaccinated individuals, compared to unvaccinated individuals [11]. Additionally, data have also demonstrated the reduction of symptomatic and asymptomatic COVID-19 infections following vaccination, which might be associated with decreased viral loads [11–13].

The findings presented here occurred prior to the widespread transmission of the B.1.617.2 (Delta) variant in Los Angeles County, which did not become the predominant strain in Los Angeles County until May–June 2021 [14]. Recent data suggest that viral loads among vaccinated and unvaccinated individuals infected with the Delta variant are higher than with prior variants [15]. In addition, studies have found that unvaccinated and vaccinated individuals infected with the Delta variant have similar viral loads, especially in early infection, suggesting similar risk for viral transmission [16, 17]. However, emerging data have also found that vaccinated

individuals clear infections quicker and have a more rapid decline in viral loads, which might be associated with decreased transmission [17, 18]. While our findings are consistent with other studies done prior to the emergence of the Delta variant, they should be interpreted with caution, as they might not be generalizable in the current setting of widespread Delta variant transmission.

The strengths of our study include access to vaccination records and SARS-CoV-2 testing data from a large cohort of healthcare workers. However, this was a retrospective observational study, and several limitations should be considered. First, data regarding the reason for SARS-CoV-2 testing or symptoms at the time of testing were not accessible; therefore, we were not able to assess the association of Ct values with symptom status. Given the nonsystematic nature of testing, those with asymptomatic infections or with mildly symptomatic infections might have been undercounted, which could have contributed to overall lower Ct values across categories. Second, while Ct values are associated with viral loads, many variables can impact the determination of Ct values, including age, onset and severity of symptoms, and collection and testing methods. Our study aggregated Ct values, which might lessen the impact of Ct value variation. One potential limitation is that few individuals had a positive SARS-CoV-2 test following the second vaccine dose, which resulted in wide confidence intervals due to the small sample. While it is possible that employees could have received a vaccination outside of the health system, potentially

leading to misclassification bias, we suspect this was very rare, as vaccine supply was limited during the study period.

In conclusion, prior to the emergence of the Delta variant, we found that SARS-CoV-2 Ct values were significantly higher following vaccination among healthcare workers. This report contributes to the emerging body of evidence suggesting lower SARS-CoV-2 viral shedding following vaccination. Our data support the idea that people who develop SARS-CoV-2 infections after vaccination have reduced transmissibility.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Potential conflicts of interest. All authors: No potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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