Open Forum Infectious Diseases

BRIEF REPORT

Prevalence and Factors Associated With Antigen Test Positivity Following SARS-CoV-2 Infection Among Health Care Workers in Los Angeles

Paul C. Adamson,[1] Judith S. Currier,[1] Daniel Z. Uslan,[1] and Omai B. Garner[2]

[1]Division of Infectious Diseases, David Geffen School of Medicine, University of California, Los Angeles, California, USA, and [2]Department of Pathology and Laboratory Medicine, David Geffen School of Medicine, University of California, Los Angeles, California, USA

Surges of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections among health care workers (HCWs) have led to critical staffing shortages. From January 4 to February 4, 2022, we implemented a return-to-work antigen testing program for HCWs, and 870 HCWs participated. Antigen test positivity was 60.5% for those ≤5 days from symptom onset or positive polymerase chain reaction (PCR), and 47.4% were positive at day 7. Antigen positivity was associated with receiving a booster vaccination and being ≤6 days from symptom onset or PCR test, but not age or a symptomatic infection. Rapid antigen testing can be a useful tool to guide return-to-work and isolation precautions for HCWs following infection.

Keywords. COVID-19; SARS-CoV-2; antigen test; health care workers; infection control; occupational health.

In December 2021, a surge of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections among health care workers (HCWs), primarily driven by the Omicron (B.1.1.529) variant, contributed to staffing shortages in health systems across the United States [1]. Following SARS-CoV-2 infection, a period of isolation is recommended to decrease onward viral transmission; the duration of isolation has changed over the course of the coronavirus disease 2019 (COVID-19) pandemic based on individual factors including symptoms, vaccination status, and occupation. On December 23, 2021, the US Centers for Disease Control and Prevention modified the isolation guidance for health care personnel with SARS-CoV-2 infections, shortening the duration during times of contingency staffing shortages to 5 days from symptom onset, with or without a negative test [2].

Antigen tests for SARS-CoV-2 detect viral protein, can provide rapid results, and can be performed at the point of care or used for at-home testing [3]. Positive antigen tests correlate with higher viral loads and culturable virus [3–7]. As such, antigen test positivity has been used as a proxy to estimate infectiousness, though data evaluating culture positivity and antigen test positivity in relation to transmission are limited. Nevertheless, antigen tests might be useful in identifying those who are more likely to be infectious and have been proposed as a way to discontinue isolation precautions following SARS-CoV-2 infections [8].

The use of antigen testing to guide return to work for health care workers might be an important tool to reduce the risk for viral transmission to patients and other health care workers. This may be especially important during times of high SARS-CoV-2 transmission leading to staffing shortages of health care personnel. The aim of this study was to report findings from the implementation of a return-to-work rapid antigen testing program within a large health system, including data on prevalence and factors associated with antigen positivity following COVID-19.

METHODS

On January 4, 2022, University of California, Los Angeles (UCLA) Health implemented an optional rapid antigen testing program, whereby employees with SARS-CoV-2 infections who were asymptomatic, or mildly symptomatic with improving symptoms, could return to work after 5 days of isolation with a negative antigen test obtained ≥5 days after their positive polymerase chain reaction (PCR) test. This is a retrospective analysis of all UCLA Health employees with a positive SARS-CoV-2 PCR test from December 25, 2021, to February 4, 2022, who participated in the return-to-work testing program.

UCLA Health employees access SARS-CoV-2 PCR testing through asymptomatic surveillance testing or based on exposures or self-reported symptoms. Reverse transcriptase PCR testing was performed by the UCLA Clinical Microbiology Laboratory using the following assays: Simplexa COVID-19 Direct (Diasorin Molecular, Cypress, CA, USA), 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, CA, USA), and TaqMan SARS-CoV-2, FluA/B RT-PCR Assay (ThermoFisher Scientific, Carlsbad, CA, USA). Cycle threshold (Ct) values were extracted and analyzed as previously described [9]. The asymptomatic

Received 20 May 2022; accepted 06 September 2022

Correspondence: P. C. Adamson, MD, MPH, Division of Infectious Diseases, David Geffen School of Medicine, University of California, 10833 Le Conte Ave, CHS 52-215, Los Angeles, CA 90095 (padamson@mednet.ucla.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofac462

surveillance testing program used SwabSeq, a Food and Drug Administration–authorized high-throughput SARS-CoV-2 testing platform [10]. For the antigen testing program, trained laboratory staff supervised the self-collection of nasal specimens and performed all antigen testing using the Sofia SARS Antigen Fluorescent Immunoassay (Quidel Corporation, Athens, OH, USA).

Employee demographic, vaccination, testing, and symptom data were extracted from electronic employee health records. Symptoms were self-reported using daily symptom surveys. COVID-19 vaccination status at the time of positive PCR test was defined as follows: unvaccinated—if no vaccination was recorded; partially vaccinated—only 1 vaccine dose was received; fully vaccinated—primary vaccination series completed >2 weeks prior; fully vaccinated and boosted—primary vaccination and booster dose were completed >2 weeks prior.

The primary outcome was antigen test positivity by day following symptom onset for those reporting symptoms or date of positive PCR for those without symptoms or survey data. Characteristics including age, symptoms, vaccination status, and Ct values were compared between those with positive and negative antigen tests in bivariate and multivariate logistic regression modeling.

Patient Consent

The study was reviewed and approved by the UCLA Institutional Review Board (#21-000373). The study did not include factors that necessitated written patient consent.

RESULTS

From December 25, 2021, through February 4, 2022, 2316 HCWs had a positive SARS-CoV-2 PCR result. Among those, 870 participated in the return-to-work antigen testing program. The median age was 36 (interquartile range: 31–45) years. Symptoms were reported by 78.4% (682/870) of those with antigen testing, 9.0% (78/870) reported no symptoms, and symptom data were missing for 12.6% (110/870). COVID-19 vaccination was received by 93.9% (817/870), and 67.4% (586/870) were fully vaccinated and boosted. Initial PCR Ct values were available for 45.5% (396/870) of HCWs, of which 82.6% (327/396) of Ct values were <30 and 17.4% were ≥30 (Table 1).

Overall, there were 478 (54.9%) negative results, 385 (44.3%) positive results, and 7 (0.8%) indeterminate results. Symptom onset was available for the 78.4% (682/870) of all participants who reported symptoms and was used to determine days to antigen testing; date of positive PCR was used for the remaining

Table 1. SARS-CoV-2 Antigen Test Results and Characteristics Associated With Positivity Among 870 Health Care Workers Participating in a Return-to-Work Antigen Testing Program in January–February 2022

Characteristic	Antigen Test Results (n = 870) Positive/Total	% Positivity	OR	95% CI	*P* Value	aOR	95% CI	*P* Value
Symptomatic								
No	27/74	36.5	Ref	-	-	Ref	-	-
Yes	313/686	45.7	1.45	0.88–2.39	.145	2.18	0.56–8.42	.259
Missing	45/110	40.9	-	-	-	-	-	-
Age group								
18–44 y	276/659	41.9	Ref	-	-	Ref	-	-
45–60 y	91/183	49.7	1.35	0.97–1.87	.075	1.21	0.69–2.11	.502
≥60 y	18/28	64.3	**2.45**	**1.11–5.39**	**.026**	1.65	0.44–6.16	.456
COVID-19 vaccination status								
Unvaccinated	13/43	30.2	Ref	-	-	Ref	-	-
Partially vaccinated[a]	1/1	100.0	-	-	-	-	-	-
Fully vaccinated, not boosted	105/298	35.2	1.16	0.63–2.15	.64	2.44	0.65–9.23	.189
Fully vaccinated, boosted	221/418	52.9	**2.35**	**1.28–4.29**	**.006**	**4.94**	**1.32–18.43**	**.018**
Cycle threshold values of initial PCR[b]								
<30	150/327	45.9	Ref	-	-	Ref	-	-
≥30	36/69	52.2	1.28	0.76–2.15	.352	1.1	0.61–1.98	.74
Days since onset or test								
≤5 d	159/263	60.5	**7.33**	**4.26–12.61**	**<.001**	**3.70**	**1.68–8.22**	**.001**
6 d	85/183	46.4	**4.16**	**2.37–7.31**	**<.001**	**2.82**	**1.26–6.28**	**.011**
7 d	72/152	47.4	**4.38**	**2.46–7.82**	**<.001**	2.34	0.99–5.50	.053
8 d	32/93	34.4	**2.62**	**1.37–5.01**	**.004**	1.48	0.55–3.97	.44
9 d	17/64	26.6	1.72	0.82–3.58	.149	0.82	0.28–2.42	.712
≥10 d	20/115	17.4	Ref	Ref	-	Ref	-	-

Abbreviations: aOR, adjusted odds ratio; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. Bold - results with *p*-value <0.05.

[a]Only 1 observation, logistic regression not performed.

[b]Cycle threshold values available for Diasorin Simplexa, Roche cobas 6800, and ThermoFisher Taqman assays.

21.6% (188/870) without symptoms or survey data. Antigen test positivity following symptom onset or positive PCR test was 61.3% (57/93) for <5 days, 46.5% (308/662) for 5–9 days, and 17.4% (20/115) for ≥10 days. Figure 1 shows the number of antigen tests performed and the test positivity by day.

In multivariate analysis, a positive antigen test was more likely among boosted compared with unvaccinated individuals (adjusted odds ratio [aOR], 4.94; 95% CI, 1.32–18.43). A positive antigen test was also associated with days following symptom onset or positive PCR test, with those presenting at ≤5 days (aOR, 3.70; 95% CI, 1.68–8.2) and on day 6 (aOR, 2.82; 95% CI, 1.26–6.28) being more likely to have a positive test. There was no association between reporting symptoms and antigen positivity (Table 1).

DISCUSSION

In this retrospective, observational study during a time when nearly all SARS-CoV-2 infections were the Omicron variant [11], 60% of asymptomatic or mildly symptomatic HCWs participating in the return-to-work antigen testing program were positive 5 days following symptom onset or positive PCR, and 50% were positive on day 7. Being fully vaccinated and boosted was associated with increased odds of a positive antigen test. Testing ≤6 days following symptom onset or a positive PCR was also associated with increased odds of a positive antigen test. Antigen test positivity was not associated with initial PCR Ct values <30 or with symptomatic infections.

We found a high proportion of antigen positivity among HCWs on days 5–7 following onset of symptoms or a positive PCR. Data on the use of rapid antigen testing among health care workers following COVID-19 are limited, and estimates vary. In one study of 290 HCWs, 49% of those testing on day 5 after COVID-19 diagnosis were antigen positive, and there was no difference among those who were unvaccinated compared with fully vaccinated and/or boosted [12]. In a larger sample of 1661 HCWs, 88.1% were antigen positive on day 5, and antigen positivity was associated with symptomatic infections and vaccinations being up to date [13]. Our findings on antigen positivity fall between these 2 prior reports and show that a majority of HCWs might continue to be infectious at 5 days.

Similar to Tande et al., we found that being fully vaccinated and boosted was associated with antigen positivity compared with being unvaccinated [13]. While data demonstrate that boosted individuals are less likely to be infected with

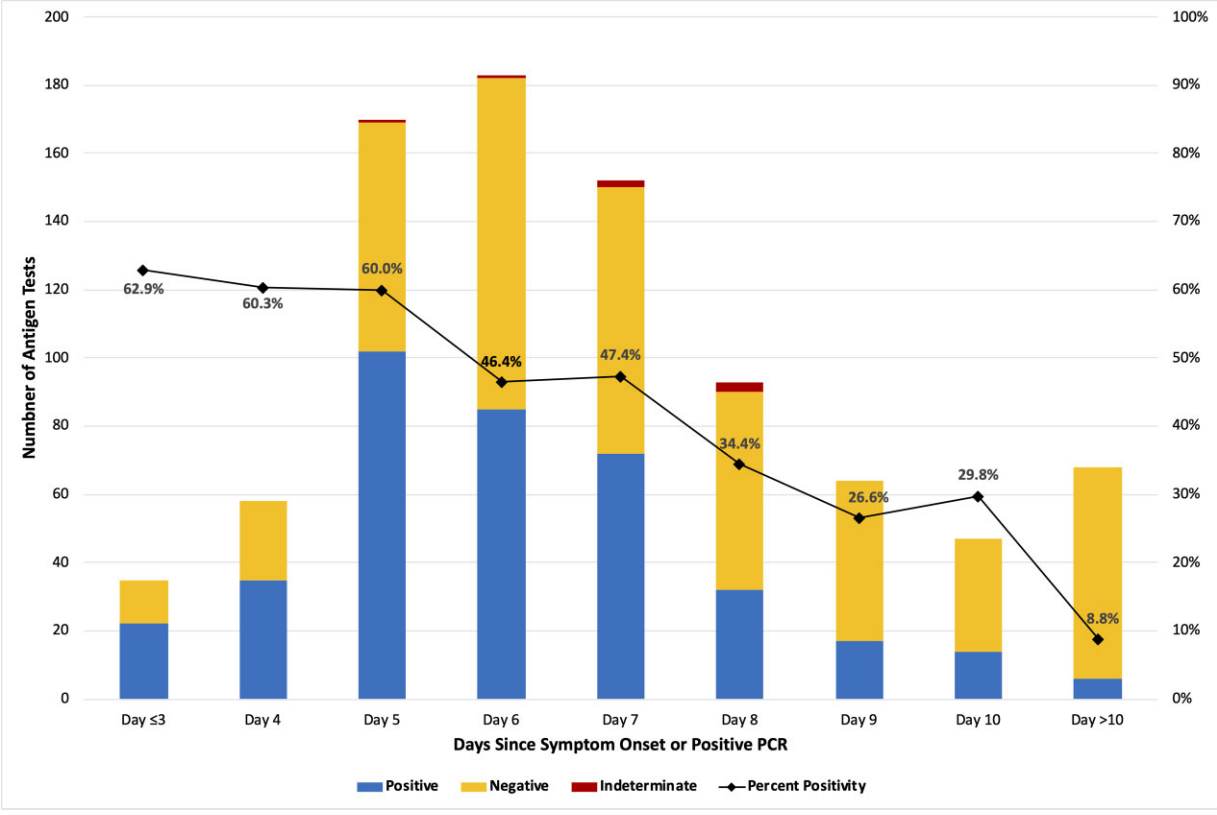

Figure 1. Total number of SARS-CoV-2 antigen tests and positivity by days since symptom onset or positive PCR among health care workers. Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Omicron [14], emerging data suggest that those with breakthrough infections might have delayed viral decay and a longer time to viral clearance, which might explain our findings [15, 16]. A longitudinal study evaluating viral load and culture positivity of the Omicron variant found a median time to culture conversion of 8 days and did not show differences in the median duration of viral shedding between those who were unvaccinated, fully vaccinated, and fully vaccinated and boosted, also suggesting that while vaccinations reduce the risk of infection, there might not be differences in viral kinetics during breakthrough infections with Omicron [17]. In that study, the number of individuals with Omicron infections was relatively small (n = 34), and antigen testing was not performed.

Data linking SARS-CoV-2 culture positivity with confirmed transmission are lacking, though it is often used as a marker of infectiousness. Although antigen test positivity correlates well with culture positivity and higher viral loads [3–7], it is not a perfect proxy. A study by Cosimi et al. found that only half of participants with a positive antigen test had a positive viral culture on day 6 following symptom onset [18]. Interestingly, that study, and another by Bouton et al., both report 100% negative predictive values for antigen testing with relationship to culture positivity [16, 18]. Those studies provide reassuring data that those with a negative antigen test on day 6 are unlikely to be shedding viable virus.

Our results should be interpreted in light of the following limitations. We did not perform viral culture or repeat PCR testing as part of this study. In addition, data on any possible occupational or nosocomial transmissions among HCWs were not available; however, given universal masking procedures at our institution and that HCWs were only allowed to return to work following a negative antigen test, the risk is expected to be very low. Return-to-work antigen testing was implemented as an optional program, and 37% of those with a positive PCR test during the study period participated. There might be a number of reasons why HCWs chose not to participate, but these reasons were not collected as part of this study. Still, data on real-world uptake of antigen testing are important for health systems planning to implement similar programs. It is also possible that unvaccinated HCWs were more likely to have severe infections or a longer duration of symptoms that made them less likely to participate in the optional return-to-work testing, so findings should be interpreted within this context.

This report on antigen test positivity among HCWs participating in a return-to-work testing program within a large health system provides important data for health care settings. UCLA Health continues to use the optional return-to-work antigen testing program described here, in accordance with guidance for hospitals from the California Department of Public Health [19]. Antigen testing before shortening the duration of isolation can help to risk-stratify HCWs before returning to work, which might be particularly helpful during staffing shortages, allowing for interventions to mitigate viral transmission in health care settings, including the use of high-filtration masks, repeat antigen testing, or extending the duration of isolation.

Acknowledgments

The authors thank Alex Gelvezon, Alexey Knyazev, and Russ Smith at the Office of Health Informatics and Analytics at UCLA Health for their assistance on the project.

Financial support. This work was supported by the National Institutes of Health, Fogarty International Center (K01TW012170 to P.C.A).

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.

References

1. Centers for Disease Control and Prevention. CDC releases emergency guidance for healthcare facilities to prepare for potential Omicron surge. Available at: https://www.cdc.gov/media/releases/2021/s1223-emergency-guidance-prepare-for-omicron.html. Accessed December 23, 2021.
2. Centers for Disease Control and Prevention. Interim guidance for managing healthcare personnel with SARS-CoV-2 infection or exposure to SARS-CoV-2. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html. Accessed December 23, 2021.
3. Drain PK. Rapid diagnostic testing for SARS-CoV-2. N Engl J Med **2022**; 386: 264–72.
4. Ford L, Lee C, Pray IW, et al. Epidemiologic Characteristics Associated With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antigen-Based Test Results, Real-Time Reverse Transcription Polymerase Chain Reaction (rRT-PCR) Cycle Threshold Values, Subgenomic RNA, and Viral Culture Results From University Testing. Clin Infect Dis **2021**; 73:e1348–55.
5. Pekosz A, Parvu V, Li M, et al. Antigen-based testing but not real-time polymerase chain reaction correlates with severe acute respiratory syndrome coronavirus 2 viral culture. Clin Infect Dis **2021**; 73:e2861–6.
6. Buder F, Bauswein M, Magnus CL, et al. Contribution of high viral loads, detection of viral antigen and seroconversion to severe acute respiratory syndrome coronavirus 2 infectivity. J Infect Dis **2022**; 225:190–8.
7. Killingley B, Mann AJ, Kalinova M, et al. Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge in young adults. Nat Med **2022**; 28:1031–41.
8. Lefferts B, Blake I, Bruden D, et al. Antigen test positivity after COVID-19 isolation Yukon-Kuskokwim Delta Region, Alaska, January–February 2022. MMWR Morbid Mortal Wkly Rep **2022**; 71:293–8.
9. Adamson PC, Pfeffer MA, Arboleda VA, et al. Lower severe acute respiratory syndrome coronavirus 2 viral shedding following coronavirus disease 2019 vaccination among healthcare workers in Los Angeles, California. Open Forum Infect Dis **2021**; 8:XXX–XX.
10. Bloom JS, Sathe L, Munugala C, et al. Massively scaled-up testing for SARS-CoV-2 RNA via next-generation sequencing of pooled and barcoded nasal and saliva samples. Nat Biomed Eng **2021**; 5:657–65.
11. Los Angeles County Public Health Department. Public health COVID-19 media briefing - February 24, 2022. Available at: http://publichealth.lacounty.gov/media/Coronavirus/media-briefings.htm. Accessed February 28, 2022.
12. Stiefel U, Bhullar D, Zabarsky TF, et al. Healthcare personnel frequently have positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antigen tests 5 days or more after diagnosis of coronavirus disease 2019 (COVID-19). Infect Control Hosp Epidemiol. **2022**:1–2. Available at: https://doi.org/10.1017/ice.2022.21.
13. Tande AJ, Swift MD, Challener DW, et al. Utility of follow-up coronavirus disease 2019 (COVID-19) antigen tests after acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among healthcare personnel. Clin Infect Dis. **2022**; 75(1): e347–49. Available at: https://doi.org/10.1093/cid/ciac235.
14. Accorsi EK, Britton A, Fleming-Dutra KE, et al. Association between 3 doses of mRNA COVID-19 vaccine and symptomatic infection caused by the SARS-CoV-2 Omicron and Delta variants. JAMA **2022**; 327:639–651.
15. Hay JA, Kissler SM, Fauver JR, et al. The impact of immune history and variant on SARS-CoV-2 viral kinetics and infection rebound. medRxiv 2022.01.13.22269257 [Preprint]. June 23, **2022**. Available at: https://doi.org/10.1101/2022.01.13.22269257.
16. Bouton TC, Atarere J, Turcinovic J, et al. Viral dynamics of Omicron and Delta SARS-CoV-2 variants with implications for timing of release from isolation: a longitudinal cohort study. Clin Infect Dis. **2022**. Available at: https://doi.org/10.1093/cid/ciac510.

17. Boucau J, Marino C, Regan J, et al. Duration of shedding of culturable virus in SARS-CoV-2 Omicron (BA.1) infection. N Engl J Med **2022**; 387:275–7.
18. Cosimi LA, Kelly C, Esposito S, et al. Duration of symptoms and association with positive home rapid antigen test results after infection with SARS-CoV-2. JAMA Netw Open **2022**; 5:e2225331.
19. California Department of Public Health. Guidance on quarantine and isolation for Health Care Personnel (HCP) exposed to SARS-CoV-2 and return to work for HCP with COVID-19. **2022**. Available at: https://www.cdph.ca.gov/Programs/CHCQ/LCP/Pages/AFL-21-08.aspx. Accessed August 18, 2022.