


## BRIEF RESEARCH REPORT

## Infectious Disease

# Seroprevalence of SARS-CoV-2 antibodies in front-line pediatric health care workers

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**ABSTRACT**

**Objective:** The goal of this study was to determine the prevalence of SARS-CoV-2 infections in pediatric front-line health care workers (HCWs) using SARS-CoV-2 serum antibodies as an indicator of infection.

**Methods:** In this cross-sectional study, we collected blood samples and survey responses from HCWs in a 38-bed pediatric emergency department. Serum antibodies to SARS-CoV-2 (IgM and/or IgG) were measured using a 2-step enzyme-linked immunosorbent assay (ELISA) to detect antibodies against the Spike protein receptor binding domain (RBD), the ectodomain of Spike (S), and the nucleoprotein (N).

**Results:** We collected survey responses and serum samples from 54 pediatric front-line HCWs from October 2020 through April 2021. Among the 29 unvaccinated HCWs, 4 (13.7%) had antibodies to SARS-CoV-2. For the 25 vaccinated HCWs, 10 (40%) were seropositive; 3 were <10 days from the first vaccine dose and 7 were ≥10 days after the first dose. Two of the 10 seropositive vaccines had a prior positive reverse transcription polymerase chain reaction test. Individuals ≥10 days from receiving the first vaccine dose were 37.5 (95% CI: 3.5–399.3) times more likely to have SARS-CoV-2 antibodies than unvaccinated individuals or those <10 days from first vaccine dose.

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**Conclusions:** Evidence of widespread SARS-CoV-2 infections was not found in unvaccinated front-line HCWs from a pediatric ED as of April 2021. Future work will be required to determine the reasons underlying the lower SARS-CoV-2 antibody prevalence compared to adult HCWs.

**KEYWORDS**

COVID, COVID-19, healthcare workers, pediatric emergency department, SARS-CoV-2 antibodies, vaccine response

## 1 | INTRODUCTION

### 1.1 | Background

As the global SARS-CoV-2 pandemic progressed, it became clear that health care workers (HCWs) were at risk for infection due to workplace exposures. Seroprevalence studies indicate that emergency department (ED) and other front-line HCWs have an increased infection risk that is nearly equivalent to those working in dedicated COVID-19 units; however, the risk can vary by region.<sup>1,2</sup> One study of emergency medicine attending physicians, resident physicians, and physician assistants at a high-volume ED found a seroconversion rate of 46%, which was more than twice the estimated community seroprevalence.<sup>3</sup>

### 1.2 | Importance

Little is known about the risks of SARS-CoV-2 exposure for pediatric front-line HCWs. Studies of adult front-line HCWs may not be generalizable to pediatric HCWs for several reasons. First, adult and pediatric ED visits sharply declined during the pandemic and remained below prior years' baseline for several months, but the decline among pediatric ED visits was more significant and prolonged than for adult visits.<sup>4</sup> Additionally, children might be less likely to transmit the virus than adults.<sup>5</sup> Together, these factors could lower the risk for pediatric HCWs compared to their adult counterparts. Conversely, it is also possible that the higher rate of mild or asymptomatic infections in children<sup>6</sup> could lead to more opportunities for pediatric frontline HCW exposures, especially in situations where full personal protective equipment was conserved for use with symptomatic patients. Also, very young children or those with special needs may not be able to safely comply with masking guidelines that could increase pediatric HCW exposures, even in the absence of high-risk aerosol-generating procedures. A better understanding of the exposure risks specific for pediatric ED HCWs would help inform staffing decisions and future screening methods, potentially protecting not only HCWs themselves but also their more vulnerable patients.

### 1.3 | Goals of this investigation

This study aims to determine the seroprevalence of SARS-CoV-2 antibodies in front-line HCWs employed at a large pediatric tertiary care

ED. Because SARS-CoV-2 vaccines became available during the enrollment period, secondary goals were to compare the serologic profiles of those with and without vaccination and determine a role for multiantigen antibody screening.

## 2 | METHODS

### 2.1 | Study design and setting

This cross-sectional study with convenience sampling was approved by the Institutional Review Board (IRB) of the University of Arkansas for Medical Sciences (UAMS) (IRB No: 261206). The study setting is the 38-bed pediatric ED of a freestanding tertiary care children's hospital. It is the state's only Level I pediatric trauma center and averages more than 60,000 ED visits per year.

### 2.2 | Participants

Volunteers were recruited between October 2020 and April 2021 from HCWs in the pediatric ED of Arkansas Children's Hospital (Little Rock, AR), with inclusion criteria extending to any HCW working any shift in the ED at time of enrollment. Recruitment took place during both day and night shifts. Participants were approached in person and via department-wide emails seeking volunteers. The only exclusion criterion was inability to ensure follow-up. Per hospital administration request, enrollment was limited to 2 employees per week. In order to comply, research assistants approached only 2 employees weekly. In the case where more than 2 employees requested to be part of the study during a given week, a wait-list was formed, and subjects were enrolled first-come, first-served. Vaccination efforts for HCWs began in December 2020, and all vaccinated participants received the Pfizer BioNTech vaccine.

### 2.3 | Measures

After enrollment, participants were provided a questionnaire requesting basic demographic information; underlying medical condition(s); COVID-19 symptom(s) in the last 6 months, last 2 months, and/or last

### The Bottom Line

Front-line health care workers—particularly the unvaccinated—are vulnerable to COVID-19 infection. In this study of 54 pediatric emergency department staff, 4 of 29 (13.7%) unvaccinated and 10 of 25 (40%) vaccinated individuals tested seropositive for SARS-CoV-2 antibodies. These results highlight gaps in our understanding of COVID-19 transmission among health care workers.

2 weeks; COVID-19 exposure(s) histories; vaccination status (added December 2020); and their role in the ED. Serum samples were obtained for antibody testing for the SARS-CoV-2 receptor binding domain, spike protein, and nucleoprotein.

## 2.4 | Outcome

The primary outcome of this study is to determine the presence or absence of SARS-CoV-2 antibodies in pediatric front-line health care workers.

## 2.5 | Procedures

Venipuncture was performed on all subjects after completion of the informed consent. One BD Vacutainer® serum separator tube (Becton Dickinson, Franklin Lakes, NJ, USA) per participant was filled and centrifuged for serum per manufacturer's instructions. Serum was aliquoted and stored at -80°C until antibody testing could be performed.

## 2.6 | Laboratory methods

A 2-tier enzyme linked immunoabsorbent assay (ELISA) assay was designed and used to evaluate participants' sera for SARS-CoV-2 antibodies, as suggested by the Centers for Disease Control and Prevention guidelines.<sup>7</sup> As previously described, all sera were initially tested for IgG and IgM antibodies to the SARS-CoV-2 receptor binding domain (RBD). Samples scoring positive for RBD binding were confirmed with a 4-antigen confirmation test (FACT).<sup>8,9</sup> The FACT consisted re-screening for antibodies against SARS-CoV-2 RBD and testing for antibodies to the full-length Spike (S) protein and nucleoprotein (N), and bovine serum albumin (BSA) (specificity control). The final optical density (OD)<sub>450</sub> reading for each antigen was calculated by subtracting the mean absorbance of BSA from the mean OD<sub>450</sub> for each antigen. A positive score required at least 2 antigens to reach a threshold of 0.3 after subtracting the BSA value. Pre-COVID-19 sera and sera from polymerase chain reaction (PCR)-confirmed SARS-CoV-

2 patients were used as negative and positive controls, respectively. Sensitivity and specificity were 100% and 94.6%, respectively.

## 2.7 | Data Analysis

The raw seroprevalence of SARS-CoV-2 was calculated by determining the frequency of positive antibody responses and then dividing by the total number in the study sample. Demographic characteristics of the overall sample are displayed as means and SDs for continuous variables and frequencies and percentages for categorical variables. Additionally, these characteristics are distributed by vaccination status. To determine if age differed across vaccination status, assumptions of normality and equal variances were confirmed. A *t* test was conducted to determine if mean values differed across status. Chi-square or Fisher's exact tests were performed to determine if categorical variables differed across vaccination status. Differences in seroprevalence of SARS-CoV-2 between vaccination statuses were ascertained with a Fisher's exact test. To assess the association between a positive antibody response and early versus post vaccination status, a simple logistic regression model was run and an odds ratio with 95% confidence interval (CI) was computed. Statistical significance was set at the 0.05 level. All analyses were conducted in SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

## 3 | RESULTS

Demographic data are represented in Table 1. A total of 54 participants were recruited. An additional 30 HCWs were approached but declined to participate. To respect the privacy of those individuals who declined to participate, no information was collected on them. Of those who did participate, 46 (85%) were female with a median age 34.7 years. Study participants consisted of physicians and advanced practice registered nurses (*n* = 25, 46.2%), registered nurses (*n* = 19, 35.1%), and other (*n* = 10, 18.5%). Twenty-nine (53.7%) participants enrolled before vaccine availability or were not yet vaccinated at time of enrollment, and 25 participants (46.3%) had received at least 1 vaccine dose at the time of enrollment. Seven of the 25 vaccinated subjects (28%) had received at least 1 vaccine more than 10 days before enrollment. Three vaccinated subjects had received both vaccine doses (Table 2).

The observed raw seroprevalence of SARS-CoV-2 antibodies in this population was 26% (14 of 54 enrollees). Because of the timing of vaccine distribution, we divided the study population into 3 distinct groups of HCWs: unvaccinated (either prevaccine availability or unvaccinated), those who were <10 days from the first vaccine dose, and those who were ≥10 days from the first vaccine dose. For those considered unvaccinated, the seroprevalence was 14% (4 of 29 individuals) of the sample of HCWs, compared to 40% among those who were vaccinated (Figure 1). HCWs who were ≥ 10 day from first vaccination were 37.5 times (CI: 3.5–399.3) more likely to have a positive antibody response compared to unvaccinated HCWs or those <10 days from first vaccine. There was not a statistically significant difference in sero-

**TABLE 1** Demographic characteristics of study participants

Characteristic	No. of Patients (%)
<b>Age group (year)</b>	
<20	0 (0)
20–29	12 (22.2)
30–39	26 (48.1)
40–49	9 (16.6)
50–59	4 (7.4)
60–69	3 (5.6)
≥70	0 (0)
<b>Sex</b>	
Female	46 (85.2)
Male	8 (14.8)
<b>Race</b>	
White	51 (94.4)
Black	2 (3.7)
Asian	1 (1.9)
<b>Role</b>	
Physician/APRN	25 (46.2)
Nurse	19 (35.1)
Other <sup>a</sup>	10 (18.5)
<b>Seroprevalence<sup>b</sup></b>	14 (25.9)
<b>Vaccination Status</b>	
Unvaccinated	29 (53.7)
<10 days vaccinated <sup>c</sup>	18 (33.3)
>10 days vaccinated <sup>d</sup>	7 (13)
<b>Comorbidities<sup>e</sup></b>	
Type 1 diabetes	2 (3.7)
Asthma	6 (11.1)
Autoimmune disorder	4 (7.4)
Other immune system disorder	3 (5.6)
Pregnancy	1 (1.9)

<sup>a</sup>The “Other” category includes patient care techs (n=2), paramedics (n=2), respiratory therapists (n=1), registered nurse patient care managers (n=1), social workers (n=1), child life workers (n=1), and unit secretaries (n=2).

<sup>b</sup>The seroprevalence variable is the prevalence of positive antibody response in overall study sample.

<sup>c</sup>Individuals received 1 vaccination <10 days before enrollment.

<sup>d</sup>Individuals received 1 vaccination ≥10 days before enrollment.

<sup>e</sup>Each comorbidity is expressed as a percentage of the total N in the sample. Abbreviation: APRN, advanced practice registered nurse.

prevalence between the unvaccinated and those <10 days from their first vaccine ( $P>0.05$ ). In addition, there was not a statistically significant difference in seroprevalence among the roles of the HCWs.

The questionnaire identified that 3 participants had previously been diagnosed with COVID-19 by PCR before enrollment in the study. These 3 HCWs had symptoms consistent with the diagnosis at least 6 months before enrollment in this study, including fever, cough, and loss of smell. Two were <10 days after first vaccination and 1

was unvaccinated at the time of enrollment. All 3 had antibodies to SARS-CoV-2 RBD, S, and N, which is likely indicative of prior infection because current vaccines should stimulate antibody only to the S protein. The questionnaire also identified subjects who suspected they were exposed to SARS-CoV-2 at work or in the community but were never PCR tested. These subjects also had symptoms consistent with SARS-CoV-2 infection 6 months before enrollment, specifically fever (57%), cough (48%), loss of smell (19%), runny nose/congestion (62%), headache (62%), and nausea, vomiting, and diarrhea (52%). Eight of these subjects had received at least 1 dose of vaccine at enrollment with only 1 receiving both vaccinations. In these subjects, we found that 42.8% (9/21) had antibodies to S and 23.8% (5/21) had N-specific antibodies.

#### 4 | LIMITATIONS

The small sample size limits the power of our study and the inferences that can be drawn from the data. This is most obvious (eg, the wide CI) in the odds ratio (OR) for the presence of antibodies in the vaccinated compared to the unvaccinated (OR 37.5, [CI:3.5–399.3]). Second, the study design is cross-sectional with an inherent inability to make causal inferences. As such, we cannot determine whether detection of SARS-CoV-2 antibodies in unvaccinated HCWs reflects workplace or community exposure. Our convenience sampling may not accurately reflect the demographics of our ED staff and may introduce selection bias. However, it is important to note that the ED staff currently consists of 50 physicians and physician extenders and 100 other staff. The population in this study represents ~33% of the total ED staff. Additionally, asymptomatic HCWs at risk of SARS-CoV-2 exposure may have declined to participate owing to fear of being quarantined based on test results. These factors could have caused sampling bias. Finally, using N antibodies alone as a marker for natural infection may be problematic as N antibodies have been recently shown to wane more quickly than S antibodies.<sup>10</sup>

#### 5 | DISCUSSION

We found that 14% of our sample of pediatric ED HCWs who were unvaccinated or <10 days from first vaccine dose had antibodies to SARS-CoV-2 approximately 11 months after the start of the pandemic. Our findings are similar to the meta-analysis conducted by Hossain et al.<sup>2</sup> in which the pooled seroprevalence in 12 US studies was 12.4% in HCWs. However, these studies included data from much earlier in the pandemic as well as HCWs in low- or intermediate-risk occupations and were not specific to pediatric personnel. In contrast, Jeong et al found a 46% seroprevalence in front-line adult HCWs, although this study was from a hospital in a large urban setting with a high baseline community seroprevalence (19.9%).<sup>3</sup> In the state of Arkansas, studies suggest the seroprevalence of the general population was approximately 7% (December 2020), whereas pediatric patients had a higher seroprevalence, approaching 25% (December 2020).<sup>8,9</sup>

**TABLE 2** Characteristics by COVID-19 vaccination status

Vaccination Status	Unvaccinated (n=29)	<10 days vaccinated <sup>a</sup> (n=18)	≥10 days vaccinated <sup>b</sup> (n=7)	P value <sup>d</sup>
Age, mean (SD)	38.1 (9.5)	37.4 (11.1)	32.6 (9.2)	0.430
Sex, n (%)				
Female	26 (89.7)	17 (94.4)	6 (85.7)	0.366
Male	3 (10.2)	3 (16.7)	2 (28.6)	
Race, n (%)				
White	28 (96.6)	17 (94.4)	6 (85.7)	0.303
Black	1 (3.4)	0 (0.0)	1 (14.3)	
Asian	0 (0.0)	1 (5.6)	0 (0.0)	
Role, n (%)				
Physician/APRN	15 (51.7)	6 (33.3)	4 (57.1)	0.615
Registered nurse	8 (27.6)	9 (50.0)	2 (28.6)	
Other	6 (20.7)	3 (16.7)	1 (14.3)	
Seroprevalence <sup>c</sup>	4 (13.7)	4 (22.2)	6 (85.7)	<b>0.0005</b>

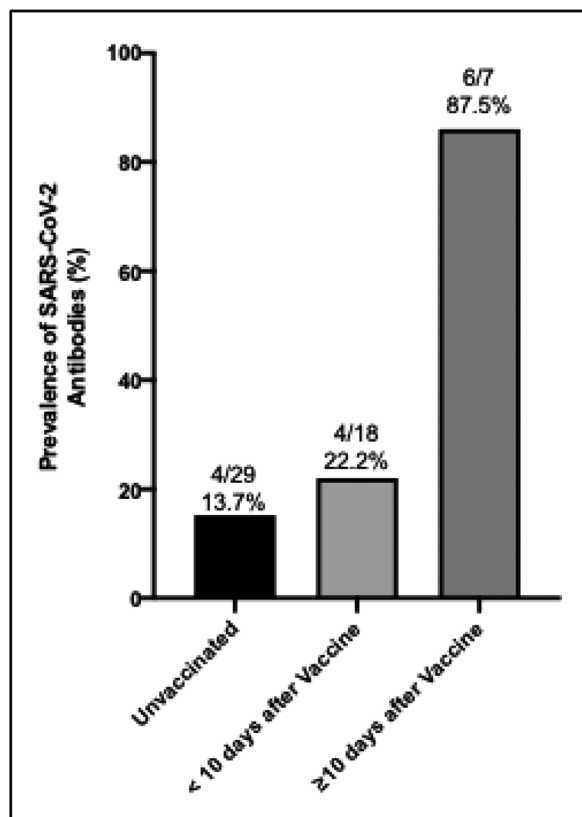
Abbreviation: APRN, advanced practice registered nurse.

<sup>a</sup>Individuals who received 1 vaccination <10 days before enrollment.

<sup>b</sup>Individuals who received 1 vaccination ≥10 days before enrollment. *P* values are based on a *t* test for age and chi-square or Fisher's exact test for categorical variables.

<sup>c</sup>Seroprevalence variable is the prevalence of positive antibody response.

<sup>d</sup>Bold text indicates statistically significant *p* value.

**FIGURE 1** Seroprevalence of SARS-CoV-2 antibodies for front-line pediatric health care workers in Arkansas

As expected, vaccine administration was associated with increased antibodies to S and RBD. However, this was evident only if the participant was ≥10 days after their first vaccination. We found that 6 of 7 (86%) participants who were ≥10 days after first vaccination had antibodies. Antibodies to SARS-CoV-2 were found in only 22.2% of those <10 days from first vaccination, suggesting care should be taken for exposures to the virus during this time. Further, our study suggests the use of a multiantigen screen to possibly discriminate between those with natural and vaccine acquired immunity. N antibodies were found in many enrollees who had previously tested positive by PCR for SARS-CoV-2, a response that would not be expected with vaccination. Despite working in a high-risk environment, our small sampling indicates that pediatric front-line HCWs had a low seroprevalence of SARS-CoV-2 antibodies.

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#### CONFLICTS OF INTEREST

The authors have none to disclose.

## AUTHOR CONTRIBUTIONS

Study concept and design: Bobby L. Boyanton, Joshua L. Kennedy, Lawrence Quang, David M. Spiro, Hannah Wilkins. Acquisition, analysis, or interpretation of the data: Lee Crawley, Ebaa Jastaniah, Joshua L. Kennedy, Catherine Kirkpatrick, Lawrence Quang, David M. Spiro, Hannah Wilkins, Karl W. Boehme, James C. Forrest. Draft of the manuscript: Ebaa Jastaniah, Joshua L. Kennedy, Hannah Wilkins. Critical revision of the manuscript for important intellectual content: Bobby L. Boyanton, Ebaa Jastaniah, Joshua L. Kennedy, Lawrence Quang, David M. Spiro, Hannah Wilkins, Karl W. Boehme, James C. Forrest. Statistical analysis: Beverly Spray. Obtained funding: Joshua L. Kennedy, Lee Crawley, David M. Spiro, Hannah Wilkins. Administrative, technical, or material support: Karl W. Boehme, Bobby L. Boyanton, Lee Crawley, James C. Forrest, Catherine Kirkpatrick.

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