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Seroprevalence of COVID-19 IgG Antibody in Resident and Fellow Physicians in Milwaukee, Wisconsin: Analysis of a Cross-Sectional Survey

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Purpose	Medical trainees are likely at differential risk of exposure to COVID-19 per respective clinical activity. We sought to determine the seroprevalence of COVID-19 antibody (Ab) among resident and fellow physicians with varying degrees of exposure to COVID-19.
Methods	A cross-sectional study of Milwaukee-based resident and fellow physicians, encompassing December 2019–June 2020, was conducted. Relevant variables of interest were ascertained by survey and payroll data, and Abbott ARCHITECT Ab test (index cut-off of ≥ 1.4) was performed. Descriptive statistics were generated, with 95% CI calculated for the study's primary outcome of seroprevalence.
Results	Among survey respondents (92 of 148, 62%), 61% were male, 44% were non-White, mean age was 31 years, 94% had no underlying conditions, and 52% were either family or internal medicine residents. During the study period, $\geq 32\%$ reported cough, headache, or sore throat and 62% traveled outside of Wisconsin. Overall, 83% thought they had a COVID-19 exposure at work and 33% outside of work; 100% expressed any exposure. Of those exposed at work, 56% received COVID-19 pay, variously receiving 69 mean hours (range: 0–452). Ultimately, 82% (75 of 92) had an Ab test completed; 1 individual (1.3%; 95% CI: 0.0–3.9) tested seropositive, was not previously diagnosed, and had received COVID-19 pay.
Conclusions	The low Ab seroprevalence found in resident and fellow physicians was similar to the concurrently reported 3.7% Ab-positive rate among 2456 Milwaukee-based staff in the same integrated health system. Ultimately, COVID-19 seroconversion may be nominal in properly protected resident and fellow physicians despite known potential exposures. (<i>J Patient Cent Res Rev.</i> 2022;9:75-82.)
Keywords	coronavirus infections; SARS-CoV-2; COVID-19; education, medical, graduate; antibodies, viral

As of December 2021, the COVID-19 infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in approximately 50 million cases and 800,000 deaths in the United States.¹ Early on, the etiologic virus was challenging to predict, control, and track.²⁻⁴ For obvious reasons, health care workers, including physicians, are at higher risk for acquisition of COVID-19.⁵ These individuals also can be exposed outside of the work environment, especially given the significant percentage of spread from presymptomatic and asymptomatic individuals.^{6,7}

In most integrated health systems, resident and fellow physicians provide frontline care to inpatients and outpatients in many departments, and their safety is the responsibility of the institution.⁸ Similar to other health care workers, residents and fellows are likely at differential risk of exposure to COVID-19 based on the specific clinical activities in which they engage.⁷ The impact of the COVID-19 pandemic on operations and continuing accreditation of residencies and fellowships is already observed to be substantial.^{cf.8-14} Current and future protection of these trainees, as well as their co-workers and family, is vitally important.

The role of serology is essential for understanding COVID-19 past exposure and future planning.^{15,16} Currently, it is still being determined what level of antibody response confers immunity and how long it may last.¹⁷⁻¹⁹ In Wisconsin, at the time of study initiation, limited testing

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for acute COVID-19 infection had been positive in 9% of all individuals tested and 12% of all health care workers tested; 10.5% of statewide COVID-19 immunoglobulin G (IgG) antibody (Ab) tests performed for various reasons were positive (internal data on file May 11, 2020). The percentage of our own institution's residents and fellows who had contracted COVID-19 infection (including asymptomatic, presymptomatic, and minimally symptomatic disease) was also unknown at the time.

Therefore, this study's primary aim was to determine the overall seroprevalence of COVID-19 IgG Ab in relatively young, healthy adults who are resident and fellow physicians. We also wished to determine the seroprevalence of Ab in these individuals by specialty type, associations of positive Ab tests by degree and types of clinical activities, and number of known exposures to COVID-19 patients or persons outside of the work setting. We hypothesized that the overall seroprevalence of COVID-19 IgG Ab among residents and fellows would be higher than that of the general population of similar age in the surrounding community and that the seroprevalence would differ by type of clinical activity subjects were involved. As this study was set in a city (Milwaukee, Wisconsin) during a time of medium risk (June 2020), we believe the results to be generalizable to other U.S.-based training sites and hence may inform graduate medical education program directors, institutional officials, and oversight bodies such as the Accreditation Council for Graduate Medical Education (ACGME) of the (perhaps differential) risk of trainee infection with COVID-19.

METHODS

Study Population, Design, Data Sources

This targeted, cross-sectional study aimed to estimate the seroprevalence of COVID-19 viral infection²⁰ among all residents and fellows employed by a single integrated health system and based in Milwaukee, Wisconsin (n=148). Similar to other institutions, many of the medical trainees in generalist or specialty programs were redeployed to cover or perform extra inpatient duties, including care of COVID-19 patients.^{8,10} These individuals were afforded appropriate personal protective equipment (PPE), including gowns, face shields, and N95 respirators.

Subjects were asked to voluntarily participate in the study, irrespective of training program, primary clinical setting, and relevant demographics. This study received local institutional review board approval, and subjects acknowledged informed consent information embedded within the initial pages of the survey.

Participants were invited by the manager of research for our system's graduate medical education department via

email on June 5, 2020, to complete the online survey using REDCap, a mature, secure web application for building and managing online surveys and databases.^{21,22} Those among the 148 residents and fellows who did not acknowledge consent for participation, who indicated they were not based in Milwaukee, or who did not participate in a program within the last 8 training program block intervals were excluded. The survey queried respondents regarding the 8 4-week duration curriculum rotation block intervals within the time period of December 2019 to June 2020 and collected demographic characteristics, working conditions, household size, previous clinical symptoms, preexisting medical conditions, working conditions by time period, household size, known COVID-19 exposures, acute COVID-19 testing history and results, subject Ab test result prediction, desires for a positive versus negative test result, and reasons for desiring a particular result. Additionally, the timing by rotation block and number of hours of special COVID-19 pay received during the survey time period was linked to each completed survey by the research manager for the last 4 blocks.

Antibody Assay

Following survey completion, participants were sent a requisition to complete an Ab test if they had not already completed one. Willing subjects had a SARS-CoV-2 (nucleocapsid protein) IgG Ab test (ARCHITECT®, Abbott) performed on their serum in our health system laboratory per manufacturer protocol. Tests were drawn during June–July 2020. Results and the index value (numerical test result) were recorded for each test; a value of ≥ 1.4 was considered seropositive per manufacturer specifications. All test results regardless of positivity were reported to the appropriate health department and to the subjects.

Statistical Analysis

The primary outcome of interest for this study was to estimate seroprevalence of COVID-19 antibodies among all eligible and willing resident and fellow physicians. The minimum sample size was determined by the previous surveillance of COVID-19 within our health system at study onset. Using the then-estimated seroprevalence of 10.5% (internal data on file May 8, 2020), we needed to enroll an estimated minimum of 78 participants in order to estimate the true population proportion of COVID-19 seroprevalence, with a required margin of error of 5% and a confidence level of 95%. A finite population correction was applied to the sample size formula. Descriptive statistics were performed to describe the demographic characteristics and outcome of study participants. Frequencies were calculated with 95% CI, as appropriate by variable type and the distribution of values, and potential associations analyzed by simple linear regression.

RESULTS

Survey Results

The overall survey response rate was 62% (92 of 148, Figure 1). Survey responses varied by program type and training year (Table 1). Demographic details of the surveyed residents and fellows are presented in Online Supplemental Table S1. Most subjects had no underlying chronic illnesses, and the minority reported symptoms typical of acute symptomatic COVID-19 infection,²³ none of which were apparently severe (Online Supplemental Table S2).

Table 2 details the exposure histories of those surveyed. Only one individual reported a history of positive polymerase chain reaction test results for COVID-19. All reported some type of exposure, with the majority (83%) reporting patient exposures, and fewer reporting

household (22%) or other exposures (33%). Travel outside of Wisconsin was common during the time period; 61% of participants traveled during blocks before the state-issued lockdown (November 18, 2019–March 8, 2020) and 26% during blocks after the lockdown.

Table 3 describes the number of encounters with COVID-19–positive patients by training program. Special duty COVID-19 pay was used as a proxy for patient exposure, and it was variously received by 40 trainees in this study between March 9, 2020, and June 30, 2020. Online Supplemental Table S3 depicts aggregate receipt of hours of this special pay by trainee specialty; unsurprisingly, internal medicine residents accumulated the most hours. Figure 2 illustrates hours of COVID-19 pay by the number of reported COVID-19–positive patient encounters for the 40 subjects who received it. The association was statistically significant but explains a minority of the variation.

Of 92 survey respondents, 16 (17%) believed they had COVID-19 sometime during the study period. In addition, 18 of 92 (19%) were previously tested for acute COVID-19, of which 1 tested positive (this person

Figure 1. Breakdown of resident and fellow physicians approached to participate.

Table 1. Response Rate to Survey Invitation by Postgraduate Year and Training Program (N=148)

Respondent status	n (%)
Postgraduate year (PGY)	
1	33 (36%)
2	17 (18%)
3	24 (26%)
4	8 (9%)
5	5 (5%)
6	2 (2%)
7	3 (3%)
Training program ^a	
Family medicine	25 (80.6%)
Internal medicine	23 (60.5%)
Radiology	13 (65.0%)
Transitional year	10 (71.4%)
Cardiology fellowship ^b	11 (40.7%)
Obstetrics and gynecology	7 (62.2%)
Hospice/palliative care fellowship	2 (100%)
Gastrointestinal fellowship	1 (33.3%)
Surgical oncology fellowship	0 (0%)
Total	92 (62.2%)

^aPercentages, other than for “Total,” were calculated within each program group.

^b“Cardiology fellowship” includes all cardiology subspecialty fellowship programs.

Table 2. Previous COVID-19 Testing and Exposure Among All Respondents Throughout Any Time Period in Study (N=92)

Known testing and exposure to COVID-19	n (%)
Previous testing	
Tested for acute COVID-19	17 (18.5%)
Tested positive for acute COVID-19	1 (1.1%)
Household exposure	
Had a household member with known exposure	20 (21.7%)
Exposed by a confirmed positive household member ^a	4 (4.5%)
Patient exposure by training program ^b	
Family medicine	23 (92.0%)
Internal medicine	20 (87.0%)
Radiology	6 (46.2%)
Transitional year	10 (100%)
Cardiology fellowship ^c	9 (81.8%)
Obstetrics and gynecology	6 (85.7%)
Hospice/palliative care fellowship	1 (50.0%)
Gastrointestinal fellowship	1 (100%)
Total	76 (82.7%)
Other exposure	
Outside work and home	30 (32.6%)
Any exposure ^d	
Household member or patient or other	92 (100%)
Travel	
International	14 (15.2%)
Domestic	55 (59.8%)

^aA confirmed positive household member was determined by clinical signs and symptoms only. There were no cases of household exposure to a COVID-19–positive person where the positive status was confirmed by a COVID-19 test.

^bPercentages, other than for “Total,” were calculated within each program group.

^c“Cardiology fellowship” includes all cardiology subspecialty fellowship programs.

^dFor “Any exposure,” household exposure was defined as any household member with a known exposure.

did not take the Ab test). When asked if they wished to be seropositive, 59 of 92 (64%) responded affirmatively. Primary reasons for wanting to test seropositive (open-ended question) included having immunity to COVID-19 (n=42, 71%), peace of mind (n=17, 29%), and concern about an asymptomatic infection or possible transmission (n=14, 24%). Other reasons included lower risk of transmission (n=8, 14%), protect family (n=7, 12%), ability to donate plasma (n=4, 7%), comfort treating patients (n=4, 7%), confirmation of previous COVID-19 symptoms (n=3, 5%), and exemption from vaccination (n=1, 2%).

Seroprevalence

Ab testing was performed on 75 individuals (51% of all potential subjects, 82% of those surveyed) (Figure 1). One individual tested seropositive (1.3%; 95% CI:

0.0–3.9). This trainee had not been previously diagnosed with COVID-19, was not previously tested for acute COVID-19, reported no COVID-19–related symptoms for the duration of the study period, and had no underlying health conditions (as defined in Table 3). Approximately 64 hours of COVID-19 pay was given to this participant during March 9, 2020, to April 5, 2020. There was no known domestic or international travel for this participant, who lived in a household with 3 other persons who had not tested positive for COVID-19 during the study period. There was no known exposure outside of work and home.

All remaining 74 Ab-tested subjects had index values well below the cut-off of 1.4 (Figure 3). The association analysis planned in the study design was not performed due to there being a single positive test result.

Table 3. Patient Encounters With COVID-19–Positive Patients by Training Program

Training program	Mean encounters per respondent (SD)	Total encounters within program (%)
Family medicine	10.1 (8.9)	252 (19.5%)
Internal medicine	29.7 (30.2)	653 (50.6%)
Radiology	3.7 (7.7)	48 (3.7%)
Transitional year	15.8 (10.8)	158 (12.2%)
Cardiology fellowship ^a	7.5 (8.8)	82 (6.4%)
Obstetrics and gynecology	11.1 (6.4)	78 (6.0%)
Hospice/palliative care fellowship	9.5 (13.4)	19 (1.5%)
Gastrointestinal fellowship	-	1 (0.10%)
<i>Total encounters</i>		<i>1291 (100%)</i>

^a“Cardiology fellowship” includes all cardiology subspecialty fellowship programs.

SD, standard deviation.

Figure 2. Total COVID-19 pay by number of COVID-19–positive patient encounters (n=40). Note: n=40 includes only those who were exposed to a COVID-19 patient and received COVID-19 pay. *Logarithmic transformation performed on values of total COVID-19 pay and total patient encounters as data was highly skewed.

DISCUSSION

At the time of this writing, we found no published reports of COVID-19 seroprevalence solely among resident and fellow physicians based in the United States. COVID-19 IgG seroprevalence was quite low in our population of residents and fellows (1.3%; 95% CI: 0.0–3.9) despite various and universal self-report of exposures. There are many possible explanations for this prevalence rate, which was similar to the reported 3.7% Ab-positive rate among 2456 Milwaukee-based staff in our same integrated health system.²⁴ Ab rates among

those with clinical roles (residents and fellows not delineated) from the combined Wisconsin and Illinois portions of our health system was 3.5%, compared to 3.0% in nonclinical staff,²⁴ both of which are similar to our study’s findings. Our study population’s Ab prevalence rate was lower than the 6.5% reported for systemwide staff deemed “COVID-19 clinical”²⁴ and (nonsignificantly) lower than the 7.0% (95% CI: 2–20) prevalence found in 43 echocardiography and stress laboratory staff at the primary medical center that also hosts our study’s medical trainees.²⁵

Figure 3. *Negative IgG values by training program for all participants who received an antibody test. *Cardiology includes all cardiology subspecialty fellowship programs. Gastrointestinal fellowship was excluded as there was only 1 participant.*

Our results are similar to the <1% seroconversion (utilizing the IgG ELISA [EUROIMMUN] and Elecsys® [Roche Diagnostics] assays) among well-protected health care workers not known to have had acute COVID-19 infection following an outbreak in a German perinatal center²⁶ and to the 2.9% seroconversion among internal/family medicine physicians and 0% conversion among pulmonary/critical care physicians in Chicago.²⁷ The latter study was performed during a similar time period as ours and used the same Ab test (index value cut-off not reported), but it did not differentiate residents and fellows. That study had an overall Ab positivity rate among all patient-facing and non-patient-facing health care workers of 4.3%, among whom 17.5% believed they had experienced nonhospital COVID-19 exposure.²⁷ Therefore, COVID-19 seroconversion may be low in properly protected residents and fellows and proportional to other protected health care workers.

Our seroprevalence rate was below that of physicians (6.1%, not specific for trainees) in 27 hospitals in the Detroit, Michigan, area tested during a similar time period utilizing VITROS (Ortho Clinical Diagnostics).²⁸ Of various units, seroprevalence was highest among physicians in hospital emergency departments (8.2%). Consistent use of N95 and surgical facemasks decreased the likelihood of seropositivity among hospital workers in this study, with household COVID-19–positive exposures increasing likelihood of seropositivity.²⁸

Talbot and colleagues performed a cross-sectional study of 474 health care workers at a single New York hospital utilizing a survey and nucleocapsid-detecting COVID-19 IgM/IgG Ab assay (DPP®, Chembio Diagnostics, Inc.).²⁹ Various physicians were included, but residents and fellows were not delineated. Seroprevalence was lower (12.7%) in physicians with “frontline” potential COVID-19 patient exposure than in “other” physicians (16.5%). Overall, Ab prevalence was lower (14.2%) among health care workers with high time exposure to COVID-19 patients than in those with minimal time exposure (18.9%). The authors concluded that their overall seropositivity (16.9%) was similar to the general population of New York during that time (14%) and that COVID-19 infection among health care workers may result from community rather than occupational exposure.²⁹ A recent systematic review indicated that COVID-19 seroprevalence is generally higher among those 1) working in a COVID-19 unit, 2) having shortage of PPE, and 3) having known or suspected household COVID-19 contact.⁷ It is unclear if our study’s comparatively lower prevalence rate was due to relatively lower COVID-19 patient census, fewer COVID-19 patient contact hours, better or more familiar PPE usage, different physician habits, or other factors. A minority of our subjects reported household contact exposure. While estimates vary widely,³⁰ a study of Wisconsin and Tennessee households during the approximate time of our study showed an overall secondary household infection rate of 53%.³¹

Another possible explanation for our study’s low prevalence is that some number of our subjects had become acutely infected with COVID-19 but did not have significant Ab levels at the time of testing (perhaps as much as 4 months following exposure). While there are reports of waning IgG Ab beyond 3 months from acute illness onset, especially in milder disease,^{17,18} a study of 1215 COVID-19 patients in Iceland suggests that Ab levels do not decline within 4 months of diagnosis.¹⁹ Studies from Portugal and New York report Ab detection for up to 5–6 months.^{32,33} Thus, it is likely that Ab would persist in previously infected subjects until the time of assay in our study. Conversely, subjects who had become infected with COVID-19 within 2–3 weeks prior to the Ab test, particularly with mild disease, may have yielded a negative result for this IgG test.³⁴ Based on our health system’s COVID-19 pay data, this would be expected to be a small number of potential subjects.

Regarding attitudes held by residents and fellows on prior infection, more than half of the respondents noted they hoped their Ab test would come back positive. Most of those reportedly hoping for a positive test explained that stance as wanting evidence of personal immunity, even though national COVID-19 guidance advised that Ab testing not be considered a reliable measure of immunity status.

Regarding the specific ARCHITECT Ab assay employed in this study, it compares favorably to other commercial assays in prior studies,³⁵⁻³⁹ with up to 98.9% agreement for consensus negative and 99.7% for consensus positive tests, as compared to other assays.^{36,39}

Limitations

In addition to the aforementioned discussion points, limitations of our study include a relatively modest sample of resident and fellow physicians in a single metropolitan area, reliance on subject recall, and inability to perform subset analysis due to having only a single positive subject. Additionally, not all ACGME program disciplines were represented in our institution. These issues limit generalizability. Acute COVID-19 testing was not performed on most subjects in order to correlate with our very low Ab prevalence. Therefore, our results must be put in context of the local community prevalence (approximately 1% cumulative acute cases) at the time of the study.⁴⁰ An updated study by the Survey of the Health of Wisconsin revealed that Ab prevalence among Wisconsin participants increased 4–5-fold between summer (1.6%) and fall (6.8%) of 2020, with reported prevalence of 9.2% in southeastern Wisconsin in the latter time period.⁴¹

CONCLUSIONS

COVID-19 IgG seroprevalence was quite low in this population of U.S. Midwest, urban-based resident and fellow physicians despite all subjects reporting various potential exposures to infectious patients. As these findings were similar to those of other reported regional Ab rates among well-protected hospital staff, it appears that secondary acquisition of COVID-19 may remain low (and similar to community levels, as previously suggested²⁹) in properly protected residents and fellows regardless of clinical activities.

Patient-Friendly Recap

- Physicians-in-training, such as residents and specialty fellows, are variously exposed to patients with COVID-19 and must be protected from catching the disease.
- The authors surveyed resident and fellow physicians about their risk factors and potential exposures to COVID-19 during early months of the pandemic in Milwaukee, Wisconsin.
- Only 1 of 75 tested residents and fellows had evidence of prior COVID-19 disease based on a serum antibody (nucleocapsid protein) test.

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Author Contributions

Study design: all authors. Data acquisition or analysis: Baumgardner, Schwank, Kram, La Fratta. Manuscript drafting: Baumgardner, Schwank, Kram. Critical revision: all authors.

Conflicts of Interest

None.

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