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Prevalence, Distribution and IgG Antibody Levels Associated with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Among Health-System and Community-Based Employees and Patients



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ABSTRACT

Background: Following the high morbidity and mortality due to Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infections in New Orleans, Louisiana, we sought to assess progress toward herd immunity.

Methods: Ochsner Health employees and patients who volunteered for Abbott SARS-CoV-2 immunoglobulin G (IgG) antibody test between March 1 and May 1, 2020 were included. We estimated IgG prevalence and used logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) for variables associated with IgG test status.

Results: Of the 13,343 participants with IgG test results, 78.6% were women, 70.6% were non-Hispanic White, 21.1% non-Hispanic Black, 2.9% Hispanic Americans and 5.4% belonged to other races. Overall, 7.99% (95% CI: 7.53-8.45%) of the participants tested IgG positive. In age-, sex- and body mass index (BMI)-adjusted analyses, non-Hispanic Blacks were 2.7times more likely to test positive than non-Hispanic Whites (OR=2.72; 95% CI: 2.33-3.19). Corresponding ORs (95% CIs) were 1.29 (0.84-1.99) for Hispanic Americans and 1.22 (0.85-1.75) for Other race/ethnicities. Compared to participants in administrative occupations, physician assistants (OR=7.14; 95% CI: 1.72-29.6) and therapists (OR=4.74; 95% CI: 1.49-15.03) were significantly more likely to have IgG antibodies while the association among nurses was not significant (OR=2.35; 95% CI: 0.96-5.77). Relative to 1.40, the test threshold for positivity, our measurements indicate a strong immune response (5.38 \pm 1.69), especially among those with a higher BMI.

Conclusions: SARS-COV-2 IgG antibodies were prevalent only in 8% of the participants. IgG prevalence was highest among non-Hispanic Blacks and participants with higher BMI but was lower among older participants.

Key Indexing Terms: SARS-COV-2; COVID-19; IgG antibodies; Non-Hispanic Blacks; Prevalence. [Am J Med Sci 2022;363(1):18-24.]

INTRODUCTION

any cities, including New Orleans in Louisiana, have experienced a large morbidity and mortality burden from Coronavirus disease-2019 (COVID-19), the disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The greatest impact was observed among non-Hispanic Blacks in which more than 70% of New Orleans's COVID-19 hospitalizations and deaths occurred.¹ Greater COVID-19 burden among blacks compared to other race/ethnicities has also been observed among other populations including the US veterans.² While interventions such as "stay-at-home" orders have had a significant reduction in the disease burden, questions still remain on how to safely return people to their normal activities including patient care. One aspect of the evolving strategy for safe return to normal activities is to determine the level and distribution of SARS-CoV-2 antibodies that can be used as a proxy for immunity. As for other viral diseases with an R₀ of 2.5-3.0, herd immunity is attained when 60-70% of the population develops protective antibodies to the virus.³ Emerging community studies have shown that individuals who have recovered from COVID-19 develop an immunoglobulin G (IgG) response^{4,5} but the value and reliability of the results have been questioned due to multiple tests that vary in their sensitivity and specificity^{6,7} and by presence of convalescent individuals without detectable IgG.⁸ Furthermore, it remains unclear as to whether development of immunity, as measured by IgG response, varies by factors such as age, sex, race, body mass index (BMI), and other social determinants that have been associated with immune response, COVID-19 incidence and health outcomes.^{1,9-11}

We hypothesized that individuals in occupations that involve close contact with other people will be more likely to get infected and develop IgG antibodies to COVID-19. We further hypothesized that some individuals, especially the elderly, immunosuppressed, obese and those with certain comorbidities will fail to mount a strong immune response despite being exposed to COVID-19. Indeed some studies among donors of convalescent plasma show that some PCR positive patients fail to maintain an IgG response.⁸

In this study we sought to (a) estimate the prevalence and distribution of SARS-CoV-2 IgG antibodies across race and other variables associated with COVID-19 incidence and outcomes, (b) determine the magnitude of IgG antibody response across various social demographic characteristics, and (c) determine whether there are variables that are independently associated with SARS-CoV-2 IgG response. This information will guide administrators in estimating the progress the Ochsner community is making toward attaining herd immunity and therefore inform plans for bringing more employees and patients back on campuses.

METHODS

Study sample

Participants in this study were 13,343 Ochsner Health employees and patients who volunteered to take a blood test for SARS-CoV-2 IgG antibodies and had records available in the EPIC Electronic Health Records (EHR). Any employee or patient volunteer from any of the Ochsner facilities was eligible for inclusion in the study if they took the IgG test on or before May 1, 2020. The study was reviewed and approved by Ochsner IRB (protocol # 2020.179). Most data was obtained from an existing Ochsner COVID-19 Research database (IRB #: 2020.089) that has been described elsewhere.¹ Additional data on IgG response was obtained from our existing pathology laboratory database.

SARS-COV-2 IgG antibody testing

Qualitative IgG blood test (serum) was performed on the ARCHITECT i2000SR system from Abbott Laboratories (Abbott Park, IL, USA). The test is approved for use under the Federal Drug Administration Emergency Use Authorization (FDA-EUA) program.¹² A sample is considered positive for SARS-COV-2 IgG antibody when the signal to calibrator (S/C) ratio or index is 1.4 or higher. The test has 99.63% (95% CI: 99.05, 99.90) specificity and for specimens collected at 14 or more days after symptom onset, the antibody test has 100.00% (95% CI: 95.89, 100.00) sensitivity.^{5,12} The published test performance parameters have been verified at Ochsner.

SARS-COV-2 PCR tests

Qualitative Real-Time reverse transcriptase PCR tests for SARS-Cov-2 (Nasopharyngeal Swab) mRNA were performed on the Abbott M2000 or Cepheid Xpert Xpress Real Time system. All tests are approved under the FDA-EUA. The analytical sensitivity of nucleic acid test for Abbott M2000 and Cepheid Xpert Xpress are 100 Copies/mL and 250 Copies/mL, respectively. No cross-reaction with other coronaviruses and common respiratory viruses is expected.

Statistical analysis

SAS software was used for all statistical analyses (SAS Institute, Cary, NC). From 13,343 unique participants with complete data on sex and IgG result, we excluded 2 for missing data on age and additional 251 participants for race leaving 13,090 observations. For regression analyses, we lost 2650 additional participants for missing data on BMI leaving a total of 10,440 participants with complete data. We computed descriptive statistics for participants who tested positive and those who tested negative on IgG test and used the Chi-squared test (for categorical variables) and the Student's t-test or Wilcoxon rank sum test to determine the significance of the differences between groups. Differences were considered statistically significant at P<0.05. Associations between IgG test status (positive/negative) and independent variables (age, sex, race/ethnicity and BMI) were assessed using unconditional logistic regression. We created cumulative distribution plots to study IgG levels across demographic characteristics and used ANOVA to determine associations between IgG response (as measured by the S/C ratio) and age, sex, race/ethnicity and BMI. Measures of association and corresponding 95% confidence intervals were estimated before and after adjustment for potential confounders like age and sex. In additional analyses, we used a spline regression to assess whether IgG levels varied by the number of days between a positive PCR test and an IgG test performed after the PCR test (n = 312).

In a subgroup analysis among 588 participants who had data on occupation, we created 11 occupational categories in which we combined related occupations (e. g., physician, dentist and resident physician) if the number of participants in each occupation was small (n<10) or if there was quasi-complete separation. The 11 categories were administration (n = 66), medical assistant (n = 23), nurse (n = 247), nurse practitioner (n = 14), students (n = 34), physician/dentist/resident (n = 64), physician assistant (n = 12), support staff (n = 29), technicians (n = 21), therapists (n = 28), and other occupations (n = 50). We then used unconditional logistic regression to test whether occupational categories are associated with IgG test status before and after adjusting for age, sex and race/ethnicity among 582 participants with complete data.

To further explore relationships among variables, we tested for two-way interactions between age, race/ethnicity and BMI in models with IgG status as the dependent variable. For interaction analyses, the P for significance was set at 0.10.

RESULTS

Study sample and overall SARS-COV-2 IgG prevalence

Among the 13,343 employees and patients who took SARS-COV-2 IgG test, 78.6% were women, 70.6% were non-Hispanic White, 21.1% non-Hispanic Black, 2.9% Hispanic American and 5.4% belonged to other races. In all race/ethnic groups, women tended to be younger than men. Among non-Hispanic Blacks, the mean age (\pm SD) for women was 43.3 \pm 11.9 years while it was 45.3 \pm 12.6 years for men. Corresponding mean ages (\pm SDs) for women vs men were 43.0 \pm 12.5 years vs 46.0 \pm 13.3 years for non-Hispanic Whites, 40.6 \pm

11.9 years vs 45.3 \pm 12.3 years for Hispanic Americans, and 38.6 \pm 10.7 vs 41.3 \pm 11.8 for other races.

Of the 13,343 participants with an IgG test result, 7.99% (95% CI: 7.53, 8.45%) tested positive for SARS-COV-2 IgG antibody. Among them, 1320 also had at least one type of PCR test for SARS-COV-2 RNA and 29.2% (95% CI: 27.2, 32.1%) tested positive. Among the 391 PCR positive participants, 34 (8.7%) did not illicit an immune response above the 1.4 S/C ratio threshold set by Abbott^{5,12} and were classified as IgG negative while the 870 (93.7%) participants among the 929 who tested negative on any PCR test, also tested negative on the SARS-COV-2 IgG antibody test.

Participant characteristics by SARS-COV-2 IgG test

In the analytic sample with complete data on age, sex, race/ethnicity and body mass index (n = 10,440), we describe the characteristics of study participants by SARS-COV-2 IgG test status (Table 1). Participants with a positive IgG test were significantly (P<0.05) younger (42.7 vs 44.7 years), mostly women (84.0 vs 80.1%), more likely to be non-Hispanic Black (41.1 vs 19.9%), higher BMI (31.4 vs 29.7 kg/m²), and more likely to have hypertension (11.4 vs 4.1%) and type 2 diabetes (2.7 vs 1.2%) when compared to those who tested negative. Those who tested positive were less likely (P<0.001) to be current or past smokers when compared to those who tested negative.

Associations between social determinants and IgG test status (binary variable)

In univariable associations, we observed statistically significant associations between IgG test status and

TABLE 1. Characteristics of study participants by SARS-COV-2 immunoglobulin G (IgG) antibody status.

	SARS-COV-2	IgG test status*			
Variable	Positive (<i>n</i> = 854)	Negative (<i>n</i> = 9586)	Р		
Age, years	42.7 ± 12.8	44.2 ± 12.6	0.001		
Sex, % female	84.0	80.9	0.03		
Race, %			<0.0001		
Non-Hispanic Black	41.1	19.9			
Non-Hispanic White	52.0	72.5			
Hispanic American	2.8	2.9			
Other	4.1	4.7			
Smoking status, % [†]			0.001		
Current smoker	2.0	6.7			
Past smoker	13.9	16.5			
Never smoker	84.1	76.7			
Body mass index, kg/m ²	31.4 ± 7.9	29.7 ± 7.3	<0.0001		
IgG response (S/C ratio) ‡	5.38 ± 1.69	0.07 ± 0.13	<0.0001		
Hypertension, %	11.4	4.1	<0.0001		
Type 2 diabetes, %	2.7	1.2	0.0001		

Abbott Architect SARS-COV-2 IgG test.

[†] Analysis done only among 2082 participants with data on smoking.

[‡] S/C = signal to calibrator ratio. A value of 1.4 or higher indicates a positive result.

TABLE 2. Odds and 95% confidence intervals for variables associated with a positive SARS-COV-2 antibody status.

	Odds ratio (95% CI)				
Variable	Unadjusted models	* Adjusted model [†]			
Race					
Black	2.89 (2.49, 3.35)	2.72 (2.33, 3.19)			
Hispanic	1.33 (0.87, 2.04)	1.29 (0.84, 1.99)			
Other	1.22 (0.85, 1.74)	1.22 (0.85, 1.75)			
White	1.00	1.00			
Age in quintiles					
5 th (57-88 years)	0.77 (0.62, 0.96)	0.75 (0.60, 0.94)			
4 th (48-56 years)	0.74 (0.59, 0.92)	0.68 (0.54, 0.86)			
3rd (39-47 years)	0.77 (0.62, 0.96)	0.69 (0.55, 0.86)			
2nd (32-38 years)	0.97 (0.79, 1.20)	0.93 (0.75, 1.15)			
1st (17-31 years)	1.00	1.00			
Sex					
Female	1.23 (1.02, 1.49)	1.00 (0.83, 1.22)			
Male	1.00	1.00			
BMI in quintiles					
5 th (≥35.3 kg/m²)	1.89 (1.51, 2.36)	1.41 (1.13, 1.79)			
4 th (30.3-35.3 kg/m ²)	1.38 (1.09, 1.74)	1.17 (0.91, 1.49)			
3rd (26.8-30.3 kg/m ²)	1.20 (0.95, 1.53)	1.09 (0.85, 1.39)			
2nd (23.6-26.8 kg/m ²)) 1.15 (0.91,1.47)	1.10 (0.86, 1.41)			
1st (≤23.6 kg/m²)	1.00	1.00			
* Each variable entered in the model individually.					

[†] All variables entered in the model individually.

race, age, sex and BMI (Table 2). When all variables were modeled simultaneously, sex became non-significant while race, age and BMI remained statistically significant (P<0.05). The strongest association was observed for race in which non-Hispanic Blacks had a 2.7-fold increase in odds of testing positive when compared to Non-Hispanic Whites. Hispanic Americans and Other races were not significantly different (P>0.05) from Non-Hispanic Whites. While there were no significant differences across lower BMI groups, participants in the highest BMI quintile (BMI \geq 35.3 kg/m²) were 1.4-times (95% CI: 1.13-1.79) more likely to test positive when compared to those in the lowest quintile (BMI \leq 23.6 kg/m²). Compared to the lowest quintile of age (17-31 years), we observed significant inverse associations between age and having a positive IgG test. Participants above 38 years of age showed 25-32% lower odds of testing positive when compared to those less than 32 years of age (*P*<0.05). None of the interactions tested attained statistical significance (*P*>0.10).

Magnitude of IgG response across race/ethnicity

We observed a strong IgG response among those who tested positive (5.38 ± 1.69 relative to the threshold S/C ratio of 1.4) and this was evident in all race/ethnic groups (Table 3). Regardless of sex, Non-Hispanic Blacks tended to have a significantly higher (P>0.05) IgG response than Non-Hispanic Whites. We also observed an inverse association between the magnitude of IgG response and age but a positive association with BMI.

IgG response and days since the first positive PCR test

In the absence of repeated IgG measurements to determine whether IgG levels increase or wane with time, we plotted IgG levels against the number of days between the first positive PCR test and an IgG test. As shown in Fig. 1, the average level of IgG response attained around day 14 remained stable up to around day 40, the longest period of observation for most participants.

Associations between occupational categories and IgG test status (binary variable)

In exploratory analyses with a limited dataset of 582 participants, we observed significant associations between occupational categories and IgG test status (Table 4). Physician assistants (OR=7.14; 95% CI: 1.72, 29.6) and therapists (OR=4.74; 95% CI: 1.49, 15.03)

Sex	Race/ethnicity	N	S/C ratio median (25 th , 75 th percentile)*	Р
Women	Non-Hispanic Black	366	6.24 (4.79, 6.85)	0.003
	Non-Hispanic White	403	5.40 (3.83, 6.60)	
	Hispanic American	22	6.02 (4.57, 6.85)	
	Other	34	6.37 (4.04, 7.05)	
Men	Non-Hispanic Black	38	5.59 (4.42, 6.40)	0.02
	Non-Hispanic White	124	4.92 (3.42, 6.45)	
	Hispanic American	5	6.19 (5.91, 6.48)	
	Other	19	6.31 (5.74, 6.83)	

TABLE 3. Association between race/ethnicity and magnitude of immunoglobulin G (IgG) response among participants with signal to calibrator (S/C) ratio of 1.4 or higher, the threshold for a positive IgG test.

*Values are medians (25th and 75th percentiles) for signal to calibrator ratios, a proxy for magnitude of the immune response as measured by Abbott Architect SARS-COV-2 IgG test.



FIGURE 1. The number of days between first positive COVID-19 PCR test and immunoglobulin G (IgG) test is not associated with the magnitude of the antibody response as measured by the Abbott Architect SARS-COV-2 IgG test.

were significantly more likely to have IgG antibodies than participants in administrative occupations (referent group). In the same model, nurses also showed higher odds for being IgG positive relative to those in administrative positions, but the association did not attain statistical significance (OR=2.35; 95% CI: 0.96, 5.77).

DISCUSSION

In this large SARS-COV-2 seroprevalence study among 13,343 employees and patients at Ochsner, we found that 8% of the participants in the first 6 months of the pandemic had SARS-COV-2 IgG antibodies. Non-Hispanic Blacks were 2.7-times more likely to test IgG positive than non-Hispanic Whites. Although the prevalence of IgG in Hispanic Americans and other races were higher than that in non-Hispanic Whites, the differences did not reach statistical significance. The prevalence of IgG positivity also varied by occupation with physician assistants (7.1-fold), therapists (4.7-fold) and nurses (2.4-fold) showing the highest fold increase in odds of having IgG antibodies when compared to participants in administrative positions. Higher age (32+ years vs <32 years) was associated with lower odds of testing IgG positive but higher BMI was associated with increased odds for IgG positivity, an observation consistent with data from Iceland showing a positive correlation between BMI and antibody levels.¹³ Although high IgG antibody levels were generally found in positive cases, responses among non-Hispanic white men and women were lower than those of other race/ethnic groups. The reason for this disparity in the magnitude of response may be due to differences in the timing of exposure to the virus or

TABLE 4. Associations between occupation and SARS-COV-2 immunoglobulin G (IgG) positivity.

Occupation	n*	IgG positive (%)	Odds ratio (95% CI)		
Physician assistants	12	41.7	7.14 (1.72, 29.60)		
Therapists	28	32.1	4.74 (1.49, 15.03)		
Nurses	247	19.0	2.35 (0.96, 5.77)		
Students	34	14.7	1.72 (0.49, 6.12)		
Medical assistants	23	8.7	0.95 (0.18, 5.09)		
Nurse practitioners	14	14.3	1.67 (0.30, 9.27)		
Other occupations	50	12.0	1.36 (0.41, 4.51)		
Physicians/Dentists/Resident physicians	64	12.5	1.43 (0.47, 4.38)		
Support staff	29	13.8	1.60 (0.42, 6.16)		
Technicians	21	4.8	0.50 (0.06, 4.41)		
Administrative staff (referent group)	60	9.1	1.00		
Data on occupation and covariates were available only for 582 participants who also had a SARS-COV-2 IoG test.					

other host, environment or viral characteristics. We speculate that non-Hispanic white participants were exposed later than the minority populations as has been suggested in other studies.¹⁴

Our observed prevalence of 8% is consistent with prevalence estimates of 4.8-10.9% observed in population surveys in Switzerland¹⁵ but are higher than those reported from studies in Santa Clara and Los Angeles County in California⁴ and Boise, Idaho⁵ where prevalence estimates were less than 5% early in the pandemic. These differences may in part be due to the early timing of the study relative to the spread of the epidemic or may also be due to the differences in the sensitivity and specificity of the diagnostic tests used. Except for the Boise, Idaho study⁵ that used the same Abbott test as the one used in our study, all the other studies used other tests and testing was done before major outbreaks in the study sites.

Unlike the studies in Wuhan and Germany¹⁶ where SARS-COV-2 IgG prevalence was generally <5% among healthcare workers, we observed prevalence estimates of 10% or higher among physician assistants, therapists, nurses, nurse practitioners, and physicians, dentists, and resident physicians. These prevalence estimates are consistent with the prevalence of 13.7% observed among healthcare providers from New York City hospitals.^{17,18} It is not clear why physician assistants and therapists have the highest odds for testing positive for SARS-COV-2 IgG compared to other providers. It is possible that 'therapists' category may have included respiratory therapists that would be expected to handle more patients with COVID-19 and therefore have a higher risk for exposure to the virus. Health care providers other than physician assistants and therapists had prevalence estimates that were not statistically different from those obtained from participants who worked in occupations not related to direct patient care. Lack of significant differences in IgG prevalence across job categories in healthcare has also been reported in another study in New York City.¹⁷ These data may indicate that COVID-19 preventive measures put in place in our healthcare facilities are overall effective in mitigating disease transmission. This finding is further supported by the finding that IgG prevalence levels in patients / healthcare workers are similar to those from the general population e.g., the prevalence estimates in the study sample vs randomly selected community participants were 8% vs 6.9% in New Orleans¹⁹ and 13.7% vs 14.0% in New York City.¹⁷

Our study confirms the high burden of COVID-19 among minority populations and shows that once exposed, the infection elicits a strong immune response within about 14 days after the first positive PCR test and that regardless of race/ethnicity the response remains stable at least up to 40 days, the longest duration between results from PCR tests and the IgG test in our study. This finding is consistent with observations from

other populations e.g., in China and the US in which the antibody responses became stable 6-14 days after mRNA detection^{5,20} and in Iceland where antibodies increased up to 2 months after the PCR test and remained stable for 4 months.^{13,21} Newer studies in Sweden show that the antibodies against SARS-COV-2 are detectable 9 months after the infection.²² The strong immune response after a natural infection with SARS-COV-2 is also supported by the low incidence of breakthrough infections among seropositive compared to seronegative individuals across various age groups.^{23,24} For example, in large cohort in England (n = 2111), seropositive individuals tested at least monthly were 41-85% less likely to have a positive PCR test for SARS-COV-2 when compared to seronegative individuals.²⁴ Thus, the immune response induced by natural infection with SARS-COV-2 should augment the COVID-19 vaccine efforts to attain herd immunity assuming that new SARS-COV-2 variants retain significant overlap in epitopes with currently circulating variants.

Our study has several strengths including (a) use of quantitative data on IgG response compared to only binary data (positive vs negative) in most COVID-19 seroprevalence studies, (b) having a large diverse sample of men and women from various race/ethnic groups, and (c) adjustment of various confounders. However, our study based on existing data from electronic health records had some limitations including lack of repeated IgG measurements to fully assess IgG trajectories, missing data on occupational categories for some participants, and lack of data on specific work assignments during the pandemic. The latter, together with the small sample of participants with occupational data, could have biased estimates of associations between occupation and IgG status and precluded detailed analyses that would stratify participants by professional assignment and location during the pandemic.

In summary, our data confirm that exposure to SARS-COV-2 induces a strong immune response regardless of race/ethnicity or sex and that the response remained stable up to 40 days after a positive PCR test. The observed higher IgG positivity observed among non-Hispanic blacks, Hispanic Americans and other race/ethnicities compared to non-Hispanic Whites may indicate differences in the timing of exposure to the virus, being earlier in minority populations. The similarity in prevalence levels in samples recruited from healthcare facilities compared to those from general populations (e.g., in New Orleans and New York City)^{17,19} support the effectiveness of COVID-19 preventive measures such as wearing facial masks. Our data also show that the 8% SARS-COV-2 IgG prevalence estimate is below the 60-70% level needed for effective community / herd immunity, an observation that underscores the need for an effective vaccine and the need to continue using facial masks and physical distancing approaches in the fight against COVID-19.

AUTHOR CONTRIBUTIONS

Conceived the study (EKK, WMR, LS), designed the study (EKK, GS, QW, WMR, MH, YL, EPH and LS), prepared IRB application and literature searches (MH, EKK), obtained data (DF, QW, CV-G, EPH), conducted statistical analyses (CV-G and EKK), interpreted the data (all), drafted the manuscript (EKK, QW), reviewed, improved and approved the manuscript (all).

CONFLICTS OF INTEREST

The authors have no financial or other conflicts of interest to disclose.

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