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Concise Communication

Estimating severe acute respiratory coronavirus virus 2 (SARS-CoV-2) seroprevalence from residual clinical blood samples, January–March 2021

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Abstract

We describe severe acute respiratory coronavirus virus 2 (SARS-CoV-2) IgG seroprevalence and antigenemia among patients at a medical center in January–March 2021 using residual clinical blood samples. The overall seroprevalences were 17% by infection and 16% by vaccination. Spent or residual samples are a feasible alternative for rapidly estimating seroprevalence or monitoring trends in infection and vaccination.

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Traditional serosurveys are time- and resource-intensive, making them challenging to conduct repeatedly in short periods to evaluate trends in seroprevalence.[1] Spent or residual clinical blood samples, which are collected for clinical testing and then routinely discarded, provide an alternative method for conducting serosurveys and have been conducted on a large scale, particularly early in the coronavirus disease 2019 (COVID-19) pandemic.[2] To understand population immunity to severe acute respiratory coronavirus virus 2 (SARS-CoV-2), however, serosurveys must differentiate individuals with infection and vaccine-induced immunity.[3] After deployment of SARS-CoV-2 vaccines, individuals in a population may have detectable antibodies to the SARS-CoV-2 receptor binding domain (RBD) from either infection or vaccination. Spent samples offer a readily available source of specimens for testing of multiple targets such as antibodies to the RBD or nucleocapsid or, alternatively, SARS-CoV-2 antigens to identify prior infection, active infection, or vaccination. The objective of this study was to determine SARS-CoV-2 antibody prevalence and antigenemia in spent samples from an urban medical center during the initial stages of vaccine implementation.

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Methods

Spent samples were collected weekly from January 22 to March 12, 2021, from the clinical laboratory of a medical center in Atlanta composed of a 500-bed hospital and multispecialty outpatient clinics. The clinical laboratory processed all blood specimens from inpatient and outpatient laboratory collection, including from medical-surgical wards, intensive care units, obstetrics units, the emergency department, and infusion centers. After processing, blood chemistry specimens were stored up to 5 days prior to being discarded. The same day weekly, a convenience sample of discarded specimens representing ~400 unique patients from that day was transported to the research laboratory for SARS-CoV-2 testing. Patient samples were matched to clinical data from the electronic medical record and assessed for both SARS-CoV-2 antigen and antibody. Antigenemia was assessed on the Quanterix platform by ultrasensitive quantitative immunoassay for SARS-CoV-2 nucleocapsid protein.[4] SARS-CoV-2 RBD and nucleocapsid antibodies were detected by single-dilution serological assays that were developed and validated using prepandemic and polymerase chain reaction (PCR)–confirmed COVID-19 patient serum and plasma samples.[5] ELISA optical density cutoffs for seroconversion were chosen using receiver

Table 1. Estimated Seroprevalence of SARS-CoV-2 IgG in Spent Samples From a Clinical Laboratory by Sampling Week and Comparison With CDC Laboratory Surveillance Estimates for the Preceding Week for the State of Georgia in January–March 2021

Sampling Week[a]	1 Jan 22 (N = 301)	2 Jan 29 (N = 338)	3 Feb 5 (N = 243)	4 Feb 12 (N = 336)	5 Feb 19 (N = 371)	6 Feb 26 (N = 291)	7 Mar 5 (N = 426)	8 Mar 12 (N = 100)
IgG RBD+, N+ (infected), no. (%)	57 (18.9)	81 (24.0)	34 (14.0)	61 (18.2)	36 (9.7)	39 (13.4)	84 (19.7)	17 (17.0)
CDC lab surveillance estimate, % (95% CI)	21.0 (18.0–24.1)	26.3 (23.0–29.8)		17.1 (14.9–19.6)		17.3 (14.9–19.9)	17.8 (15.4–20.4)	
IgG RBD+, N-(vaccinated), no. (%)	23 (7.6)	15 (4.4)	20 (8.2)	32 (9.5)	110 (29.7)	93 (32.0)	81 (19.0)	16 (16.0)

Note. RBD, receptor binding domain; N, nucleocapsid; CDC, Centers for Disease Control and Prevention.
[a]Average of 4-day lag from date of blood sample draw from patient to date of collection for study.

operating characteristic analysis with areas under the curve >0.95 after 14 days after symptom onset. IgG profiles were defined as natural infection when both RBD and nucleocapsid antibodies were positive or vaccinated when RBD antibody was positive but nucleocapsid antibody was negative. SARS-CoV-2 antigenemia was measured in serum and plasma samples initially at 1:3 dilution, with retesting at higher sample dilutions triggered if the nucleocapsid protein concentration was outside the linear range of the assay. Statistical methods included the χ^2 test and Clopper-Pearson confidence limits for proportions. Serosurvey data are available via the Emory Dataverse (https://dataverse.unc.edu/dataverse/Emory). The study was approved by the Emory University Institutional Review Board.

Results

Among 2,406 samples collected, 1,186 (49%) originated from inpatient units, 586 (24%) originated from outpatient labs, 403 (17%) originated from the emergency department, and 231 (10%) originated from infusion centers. Matching with the medical record identified 2,132 unique patients: 55% were female; the median age was 58 years (IQR, 40–70); and 36% were aged >65 years. Also, 63% self-reported as Black or African American, 27% as white, and 3% as Hispanic or Latino. For this cohort overall, the median body mass index was 25 kg/m^2 and the median Elixhauser comorbidity index was 6. Clinical data indicated that 210 (9.9%) ever had SARS-CoV-2 detected by PCR and that 191 (9.0%) had received a COVID-19 vaccine within the health system.

Among 2,406 samples, 409 (17%, 95% confidence interval [CI], 15.5%–18.6%) had serologic evidence of natural infection and 390 (16%; 95% CI, 14.7%–17.7%) had evidence of vaccination without infection. These estimates were consistent when excluding resampled patients. Inpatients (21%) were more likely than patients from other settings to have evidence of infection (14% for outpatients, 11% for infusion center, 15% for emergency department, χ^2 P <0.001). Outpatients (20%) and those in the infusion center (20%) were more likely to have evidence of vaccination (15% for inpatients, 12% for emergency department; P = .001).

Seroprevalence and antigenemia were reported by week from January 22 to March 12 (Table 1 and Fig. 1). Over the sampling period, estimates of serologic evidence of vaccination varied but generally increased from 7.6% in January to 16% in March. Estimates of serologic evidence of infection ranged from 9.7% to 24%, and the prevalence of antigenemia, suggestive of current infection, gradually decreased from 18% to 4%.

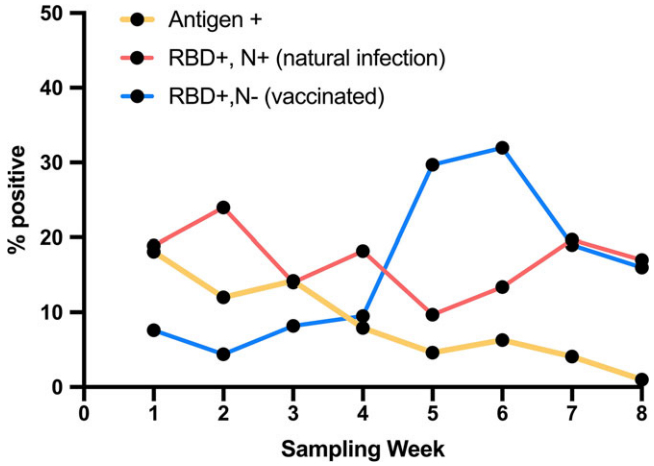

Fig. 1. Estimated prevalence of SARS-CoV-2 IgG and antigenemia in spent samples from a clinical laboratory, January–March 2021. Note. RBD, receptor binding domain; N, nucleocapsid.

Discussion

In this serosurvey, spent samples were used to estimate SARS-CoV-2 IgG seroprevalence from infection and vaccination as well as antigenemia among patients at a medical center early in the COVID-19 pandemic. Our study demonstrates that spent samples are a feasible alternative for obtaining a rapid estimate of seroprevalence or for monitoring trends in a population during periods of disease spread or vaccine implementation. As might be expected, the estimated IgG seroprevalence due to infection was more common in inpatients, whereas vaccination was more common in patients presenting to outpatient settings. The increasing prevalence of the vaccination signature likely reflects vaccine uptake early in the implementation of SARS-CoV-2 vaccines in the first months of 2021 as community vaccine coverage increased from ~5% to 20%.[6,7] In contrast, the infection seroprevalence is fairly stable over the sampling period, consistent with IgG antibody remaining detectable for months after infection.[8] This estimate of infection prevalence is comparable to CDC-reported laboratory surveillance estimates for Georgia during the study period (Table 1).[9] A household-based survey from August to December 2020 estimated a seroprevalence of 7.8% (95% CI, 5.1–11.7) in the core Atlanta counties of Fulton and DeKalb.[10] The higher estimate in our study likely reflects incident infections during the winter 2020–2021 surge.

Spent or residual samples represent a feasible alternative serosurvey sample method, particularly for obtaining repeated estimates over time in a defined population. As demonstrated by the analysis of antigenemia, the same samples can be used for multitarget surveillance, improving detection of acute infections.[4] This rapidly available information could inform infection control practices at the healthcare facility or system level by capturing data from

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patients seeking care in both inpatient and outpatient settings without additional sample collection. This would be useful as a surveillance method both during periods of presumed low SARS-CoV-2 transmission, to potentially identify an increase in infections in the patient population, and during periods of influenza-like illness activity to target patient testing, care, and isolation resources. The spent sample approach could also be applied to public-health case-finding and vaccination activities, including monitoring for waning vaccine-induced antibody response in a vaccinated population. The limitations of this study include the convenience sampling method that yielded a varying number of unique patients per week, a study period before breakthrough infections were common, and a care setting distribution that may not reflect the actual distribution of patients seeking care at the medical center.

In conclusion, spent samples provide a feasible alternative for a rapid estimate of seroprevalence or for monitoring trends in infection and vaccination over time in a defined population. This approach has potential impactful applications for patient care, infection control, and public health to monitor epidemiologic changes as the COVID-19 pandemic persists.

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Conflicts of interest. All authors report no conflicts of interest relevant to this article.

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