



CONVENIENCE SAMPLING FOR PANDEMIC SURVEILLANCE OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 IN CHILDREN IN JACKSON, MISSISSIPPI

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Abstract

We assessed severe acute respiratory syndrome coronavirus 2 seroprevalence on residual blood samples for pediatric COVID-19 surveillance: 2263 samples were collected during routine outpatient visits (<18 years, April 2020–August 2021). Seroprevalence increased over time, coinciding with or preceding virus circulation in the community and with or preceding pediatric severe COVID-19 hospitalization peaks. Residual blood sample seroprevalence may be a useful surveillance tool in future outbreaks.

Keywords

pandemic preparedness; coronavirus disease 2019; serology

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Surveillance and transmission mitigation strategies have evolved rapidly during the coronavirus disease 2019 (COVID-19) pandemic. At the beginning of the pandemic, confirming COVID-19 diagnosis was far from adequate due to the strained health systems, limited availability of test kits and insufficient personnel.^{1,2} Because the testing resource was preferentially allocated to adult patients who suffered from more severe disease, testing was rarely performed in children in the first year of the pandemic. In addition, the need for a nasopharyngeal sample, which can be difficult to tolerate for children, and the fears of school or extracurricular activity exclusion may also have contributed to inadequate testing.¹ As a result, passive reporting of COVID-19 in children based on molecular testing underestimates the incidence,² and the kinetics of the epidemiology of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children at the beginning of the pandemic largely remains unclear.

Serology can provide evidence of past infection and therefore population exposure to infectious organisms. It has been used extensively to estimate the exposure to SARS-CoV-2 throughout the pandemic.^{3,4} While molecular testing may be restricted by the scarcity of reagents and test kits during the early pandemic as was the case in the COVID-19 pandemic, serology, which tends to require less resources, on blood samples obtained as part of routine care that would otherwise be discarded may turn out to provide valuable information that can inform public health mitigation strategies, or at least, help understand epidemiology.⁵ In addition, Jackson, Mississippi particularly suffered from the lack of resources and low vaccine acceptance rate in an early pandemic, resulting in high caseloads of COVID-19.⁶ In this study, we assessed the utility of seroprevalence in a community-based pediatric practice based on residual blood samples collected for routine care in assessing the community circulation of an infectious agent (SARS-CoV-2 in this case) in children.

METHODS

This was a retrospective study conducted at the University of Mississippi Medical Center (UMMC), the only children's hospital in the state providing tertiary care, located in Jackson MS, in collaboration with Children's Medical Group Jackson, a major community-based pediatric primary care practice in Jackson MS, and the Centers for Disease Control and Prevention (CDC). This study was approved by the UMMC Institutional Review Board; CDC was determined to be nonengaged and therefore did not undertake a separate institutional review board review.

We used residual blood specimens from children 0–17 years of age during routine medical care (primarily well-child checkups) in the period of April 2020 through August 2021 at Children's Medical Group. Samples were deidentified at Children's Medical Group and were processed at UMMC. SARS-CoV-2 serologic testing was performed at CDC using a multiplex bead assay developed at CDC.⁷ Both S protein and RBD591 antibodies (receptor binding domain of S protein) were required to be above the cutoff values for the result for S to be interpreted as positive.⁷ Cutoff values of the antibody assay using a receiver operator characteristics curve were determined so that both sensitivity and specificity were maximized (>95% and >97%, respectively).

An individual was counted only once (first encounter) when more than one sample was available. Separately, active, population-based surveillance for multisystem inflammatory syndrome in children (MIS-C) and acute COVID-19 hospitalizations meeting clinical and laboratory criteria was conducted by adjudicating clinicians at the UMMC, from April 2020 to August 2021 (data reported in publication ended in February 2021 but surveillance continued through August 2021).⁸ Overall trends in the seroprevalence from residual samples from the community practice were compared with hospitalization data, and community circulation of the SARS-CoV-2 was derived from the data on Hinds County in publicly available CDC data on COVID-19 community levels by county (https://healthdata.gov/dataset/United-States-COVID-19-Community-Levels-by-County/nn5b-j5u9/about_data).

All data analysis and visualization were performed using R software, version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 2263 blood samples from the same number of individuals were included in the analysis. Case counts of SARS-CoV-2 infection in the community showed 2 periods of rapid increase during the study period: July–August 2020 and again in December 2020–February 2021, and the data period also captured the beginning of another rapid increase in June–August 2021 (Fig. 1B). Overall seroprevalence for SARS-CoV-2 increased over time, and higher rates of increase in seroprevalence were seen coinciding with or slightly earlier than the beginning of the rapid increases of circulation of the virus in the community (Fig. 1A). Peaks of pediatric hospitalizations for acute COVID-19 occurred preceding or coinciding with the beginning of the rapid increases in community circulation of SARS-CoV-2, whereas peaks of hospitalizations for MIS-C occurred after the onset of rapid increases in community circulation and seroprevalence (Fig. 1A). We also observed an increased anti-S only seroprevalence (compared with anti-S and anti-N) in May 2021, coinciding with the authorization of COVID-19 vaccine in children 12–15 years of age (Fig. 1A).

DISCUSSION

In this study, we observed that the changes in the serial seroprevalence in a local pediatric practice based on residual blood samples, which would otherwise have been discarded, reasonably coincided with or preceded rapid increases in the community circulation of SARS-CoV-2 and pediatric hospitalizations for COVID-19 at the tertiary care children's hospital. MIS-C cases lagged the increase in seroprevalence from infection, consistent with prior data that MIS-C cases peak 2–6 weeks after community COVID-19 spikes.⁹ This methodology also detected the surge in anti-S-only antibody seroprevalence coinciding with the COVID-19 vaccine rollout in children 12–15 years old.

In the setting of a pandemic of a novel pathogen, society needs to rapidly increase the capacity to assess the spread of the pathogen. Besides molecular testing of individuals, an example of powerful surveillance methodologies that turned out to be effective may include molecular testing on groundwater. However, it still relies on molecular testing which was

limited at the beginning of the pandemic by several factors such as scarcity of resources and the need for extensive validation. Based on our results, residual blood samples collected as part of routine care, which are expected to be available even during future pandemics, are a reasonable, and potentially powerful, public health tool during outbreaks of novel pathogens.

There are limitations to consider in interpreting our results. First, the positivity of both anti-S and anti-N generally correlates with infection-mediated immunity and anti-S-only positivity classically associates with vaccine-induced immunity,¹⁰ although this distinction is not always clear and insufficient information is available in children. Because the specimens are derived only from the first few years of the pandemic, the effect of waning N antibody levels after infection has cleared is likely less prominent. Second, we were able to assess samples only from the first year of the pandemic (to August 2021) although the inclusion of longer time periods may have provided even more useful information. Nonetheless, we believe that the current data are sufficient to support the use of serology on residual blood samples in local community practice as a promising surveillance tool to be considered in future outbreaks or pandemics of novel pathogens, given that this was the time of the pandemic during which there was limited testing.

In conclusion, serological surveillance at a local community-based pediatric clinic using residual blood samples that would have otherwise been discarded reasonably reflected local circulation of SARS-CoV-2 and healthcare utilization at the local tertiary care hospital. In future outbreaks and pandemics caused by novel pathogens in which direct molecular testing methodology may be limited, serology using residual blood samples in local community practices could be useful for informing public health mitigation strategies and describing the epidemiology, either in real-time or retrospectively.

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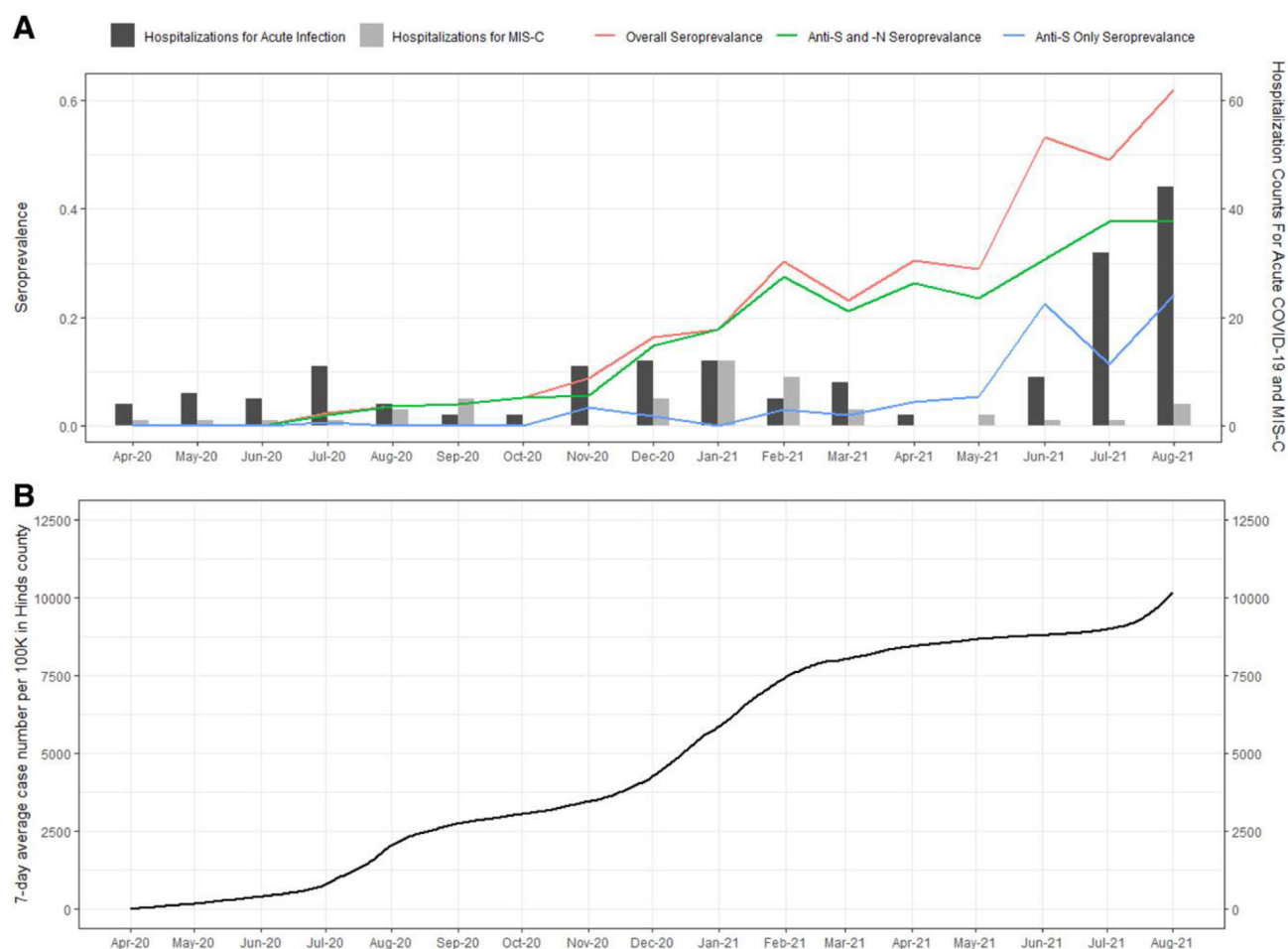
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**FIGURE 1.**

A: Serial seroprevalence at a local pediatric primary care practice and the case counts of pediatric hospitalization for acute COVID-19 and MIS-C at the tertiary care children's hospital. B: Seven-day average case number of SARS-CoV-2 infection per 100,000 population in Hinds County based on molecular testing. Overall seroprevalence: seroprevalence combining both anti-S only and anti-S and anti-N seroprevalence.