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# SARS-CoV-2 antibody seroprevalence in patients receiving dialysis in the USA

Published Online
September 25, 2020
https://doi.org/10.1016/
S0140-6736(20)32006-7

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Antibody serosurveillance is an essential tool for monitoring the COVID-19 pandemic, offering a more comprehensive picture of who has been infected than swab testing of symptomatic individuals alone. In recent months, several countries have done large-scale seroprevalence surveys, including the USA,[1,2] China,[3] Brazil,[4] England,[5] and Spain.[6] These studies have confirmed that the world is still in the early stages of the COVID-19 pandemic, with the majority of the populations surveyed testing negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies.

The surveys carried out so far have two major limitations. The first is the use of sampling strategies prone to selection bias, including non-random, unrepresentative sampling,[3,4] postal sampling with substantial dropout,[2,6] or convenience sampling.[1] This is problematic for an infection that disproportionately affects some ethnic groups and deprived communities who are less likely to participate in research.[5,7] The second is the use of antibody tests with inadequate performance characteristics. Most large surveys have sought to avoid costly laboratory testing by using point-of-care lateral flow assays.[2,4-6] These tests are often poorly validated on a handful of samples,[2] can be subject to inter-batch variation, and even when thoroughly assessed have inferior sensitivity to laboratory assays (<90%).[8] This adds uncertainty and necessitates substantial adjustment of raw data to account for false-negative results.[9]

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In *The Lancet*, Shuchi Anand and colleagues describe an inventive, practical, and scalable strategy for conducting SARS-CoV-2 seroprevalence surveys, which overcomes these limitations.[10] By testing the remainder plasma of 28 503 randomly selected patients receiving dialysis in the USA, they were able to test an unbiased sample of an important patient group across the entire country.

Importantly, Anand and colleagues chose a good test for their survey. The Siemens lab-based spike-protein-receptor-binding domain total antibody chemiluminescence assay adopted by the authors was the best-performing platform in the largest external appraisal of commercial assays to date, in terms of both sensitivity and specificity.[11] Their choice negates the need for major adjustment of the raw data to obtain reliable prevalence estimates.

The authors standardised data by age, sex, region, and race and ethnicity to provide the first nationally representative estimates of SARS-CoV-2 seroprevalence in the US dialysis and US adult populations, with samples taken in July, 2020. Using anonymised demographic data, residence, postal codes, census data, and publicly available COVID-19 burden and community mobility data, the authors provide estimates for differences in seroprevalence by neighbourhood, race and ethnicity, poverty, population density, and mobility restriction.

The findings are striking. 2292 dialysis participants had SARS-CoV-2 antibodies, comprising 970 (42·3%) women and 1322 (57·7%) men, the majority of whom (1765 [77·0%]) were aged 45–79 years. This translated to a seroprevalence of 8·0% (95% CI 7·7–8·4) in the sample, rising to 9·3% (8·8–9·9) when standardised to the US adult population. There was a remarkable variation in seroprevalence by state in the sampled participants, with early pandemic hotspots such as New York (33·6%, 95% CI 31·7–35·6), Louisiana (17·6%, 10·8–28·7), and Illinois (17·5%, 15·2–20·2) recording substantially higher seroprevalence than their respective neighbouring states of Pennsylvania (6·4%, 4·7–8·8), Arkansas (1·9%, 1·0–3·5), and Missouri (1·9%, 0·9–3·8).

By comparing sample seroprevalence data from July, 2020, with Johns Hopkins University estimates of cumulative PCR-diagnosed cases as of June 15, 2020,

the authors estimate just 9·2% (95% CI 8·7–9·8) of seropositive cases were diagnosed. Given antibodies take days rather than weeks to appear, this might underestimate the true proportion of patients diagnosed by swab testing. However, this finding still points to a high number of people with the virus never being tested. In the absence of clinical data, it is not clear whether this is because of asymptomatic infection or difficulty accessing testing, or other reasons.

The study also estimated substantially higher seroprevalence in residents of predominantly Hispanic (11·3%, 95% CI 9·8–12·9), non-Hispanic Black (13·9%, 12·1–16·0), and Hispanic and Black (16·3%, 14·3–18·5) neighbourhoods compared with predominantly non-Hispanic white neighbourhoods (4·8%, 4·1–5·5), when standardised to the US adult population. This alarming discrepancy is in keeping with trends identified in the largest survey from Europe[5] and demands urgent attention.

As the authors point out, patients receiving dialysis might be considered an ideal sentinel population in which to study the evolution of the pandemic, given the guarantee of regular blood tests, established vascular access, and a high proportion of patients with multiple risk factors for SARS-CoV-2 infection and COVID-19, including older age, non-white ethnicity, hypertension, diabetes, and poverty. Importantly, end-stage kidney disease is considered a qualifying condition for Medicare in the USA, such that patients effectively enter a universal health-care system.

Extrapolation of seroprevalence in the dialysis population to the general population is inevitably problematic. Despite adjustments for age, sex, region, and race and ethnicity, the dialysis population's risk of exposure to SARS-CoV-2 is unlikely to be representative of the general population: attending a health-care facility three times a week would seem like a good way to encounter SARS-CoV-2, as has been shown elsewhere.[11]

However, concerns over sample applicability are bidirectional: patients with end-stage kidney disease and associated comorbidities might be less likely to mount a detectable antibody response.[12] They are also more likely to die from COVID-19,[13] increasing the chance of unexposed, seronegative survivors being over-represented in the sample. Although general population estimates from dialysis sampling are imperfect, they at least remain consistent across the country and from one survey to the next, permitting longitudinal surveillance.

Despite the massive burden of COVID-19 in the USA, Anand and colleagues show that a small minority of the population has evidence of humoral immunity to SARS-CoV-2. Questions remain around the longevity of the immune response and correlates of protection, but high-quality longitudinal serosurveillance with accompanying clinical data can help to provide the answers. Anand and colleagues deserve credit for pioneering a scalable sampling strategy that offers a blueprint for standardised national serosurveillance in the USA and other countries with a large haemodialysing population.

We declare no competing interests.

*Barnaby Flower, Christina Atchison
**b.flower@imperial.ac.uk**

Department of Infectious Disease, Faculty of Medicine, Imperial College London, London W2 1NY, UK (BF); and School of Public Health, Imperial College London, London, UK (CA)

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