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Tracking SARS-CoV-2 infection in India with serology

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The rapid spread of COVID-19 across the globe caught most countries off guard, in terms of their ability to detect, track, and contain the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. India, with 462 million of its 1·3 billion people living in densely populated urban settlements with high contact rates, was at risk of catastrophic spread of the virus.[1] Decades of underinvestment in public health, with inadequate diagnostic capacity and programmatic agility, made the implementation of test, trace, and treat strategies at scale challenging. The country's leadership had little choice but to enforce a harsh nationwide lockdown to give themselves time to strengthen capacity. Although the lockdown did result in delaying an exponential increase in infections, when the restrictions on activity and movement were reduced, cases of COVID-19 in hospitals increased, even as testing intensified; first in metropolitan cities and then in smaller cities and towns.[2]

Proceeding with little clinical and laboratory data in the early phase of the pandemic, with inadequate testing infrastructure, the contribution of suppression measures to the slowing or reduction in infection rates was unclear. Case numbers increased steadily with an increase in testing from April, 2020. Reported cases in India surpassed those in Brazil on Sept 6, 2020, with India second highest after the USA in number of cumulative cases; this remains as of Jan 12, 2021, despite India having a population of more than four times that of the USA. During April–September, 2020, reported case numbers increased to more than 90 000 new cases per day, showing widespread community transmission, but the high positivity rate of tests also indicated that the testing strategy was only detecting a small proportion of the total number of infections. A nationally representative seroepidemiological survey was done in May–June, 2020,[3] followed by a second survey in August–September, 2020, with about 30 000 participants in each survey. In this issue of *The Lancet Global Health*, Manoj Murhekar and colleagues[4] describe some of the key insights from the second survey. In the first survey, the same group reported a seroprevalence among adults aged 18 years or older of approximately 0·7% with an assay detecting IgG antibodies to inactivated virus; whereas in this report, they employed the Abbott assay detecting IgG antibodies to the nucleoprotein of SARS-CoV-2 and found that, by August, 2020, the seroprevalence had increased to an estimate of 6·6% (95% CI 5·8–7·4; weighted and adjusted for test performance) in those aged 10 years or older. As expected, seroprevalence was higher in urban areas, particularly in slums.

Both serosurveys were large and designed to be generally representative of India's population. Similar to serosurveys elsewhere, they showed that infections outnumber the cases detected through symptomatic screening and contact tracing strategies.[3–5] Even after tests for SARS-CoV-2 became more widely available, the ratio of infection to cases remained close to 30:1, implying that the ability to gauge the spread of epidemic on the basis of case numbers alone is poor.[4] The exponential growth of the pandemic resulted in a tenfold increase in seroprevalence over just 2 months. A substantial proportion of the population were infected, suggesting that strategies to decrease transmission might not have been uniformly effective. This inference is also supported by other studies from urban areas in India,[6] which have reported much higher seroprevalence than seen in this survey that excluded zones designated as so-called containment zones with higher reporting of cases, more intensive testing, and more stringent restrictions. The study uses the seroprevalence and data from the sampled sites to estimate an infection-fatality ratio of about 0·1%, which is much lower than has been reported in other countries.[7] The age structure of the population and under-reporting of deaths are both proposed as possible reasons for the lower value, but other data from Asia also indicate high rates of asymptomatic infections.[8]

Within the wider context of the pandemic are several local epidemics at different stages of progression. The higher seroprevalence in urban areas and areas with an influx of migrants indicate that high contact rates probably fuelled the rapid spread of the virus. Continued tracking of case accumulation in defined locations together with periodic serosurveys could help identify herd immunity thresholds and help understand whether population immunity attained by infection will have a role in slowing or ending the pandemic. The lower seroprevalence in non-slum urban areas also raises the issue of the risk of a second wave of infections

in cities limited to defined geographical areas and socioeconomic strata.

Seroprevalence studies are dependent on the characteristics of the assays and the sampling strategies used. In the two national serosurveys in India, although different assays were used, the results appear generally plausible, based on case reporting from India. Nonetheless, nucleocapsid antibodies decay and therefore might underestimate seroprevalence, whereas antibodies targeted at the viral spike receptor binding domain seem to persist for longer periods and more closely track neutralising antibodies, thus possibly making them more useful for future serosurveys.[9] At their simplest, serosurveys estimate how much of a population has been exposed to a particular pathogen at a defined time, but repeated serosurveys have much greater value. Such studies in the same population, correlated with the trajectory of reported case counts, will provide insights into the spread of the virus, the potential for herd immunity, and possibly the Asian conundrum of low infection-fatality rates.

GK is vice chair of the board of the Coalition of Epidemic Preparedness Innovations, which is a non-profit organisation supporting vaccine development, and a member of the board of Hilleman Laboratories, which is also a non-profit organisation. JJ declares no competing interests.

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