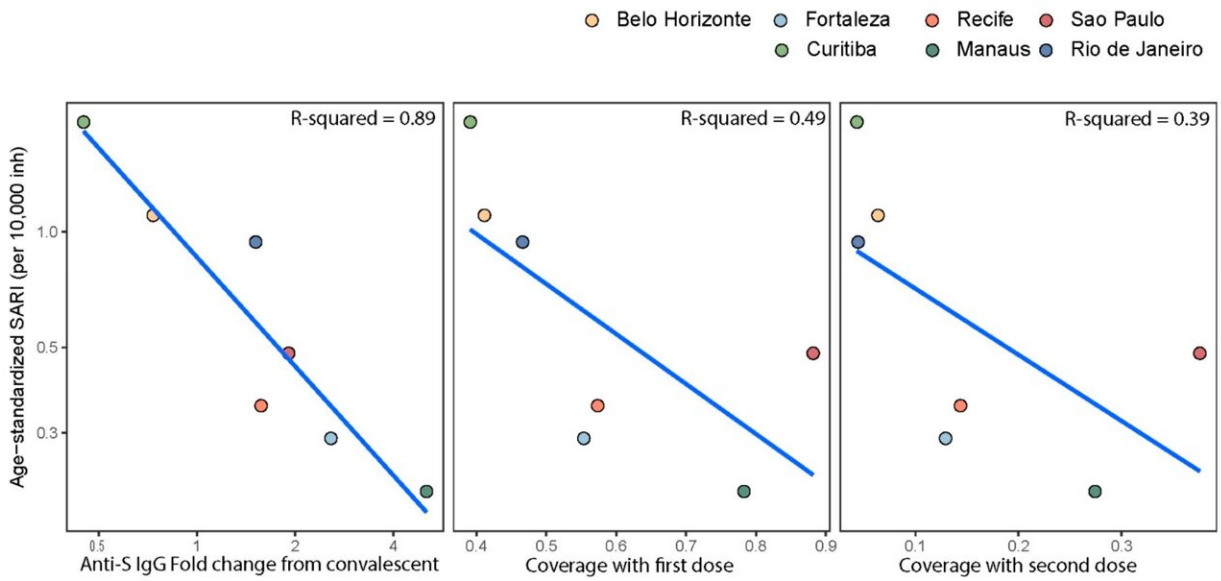
A novel method to predict the behavior of different COVID-19 waves in the vaccinated or previously infected

September 22 2022, by Luciana Constantino



Predictors of epidemic size of the Delta growth phase across seven Brazilian cities. Convalescent-normalized mean anti-S IgG signal to cut-off was calculated for the month when Delta reached 10% dominance in each of the cities (range 19 June 2021 in Curitiba to 16 August 2021 in Manaus). Percentage coverage with the first and second doses was also calculated up to (and inclusive of) the month of 10% dominance in each city. Total severe acute respiratory syndrome (SARI) cases, within the age range of blood donors (15–65 years) were age-standardized using the direct method and the age structure of São Paulo as the reference population. A two-month period starting from the date of 10% dominance was used to calculate epidemic size. R-squared terms are from separate simple linear models fit to the seven points shown on the figure. Credit:

Vaccines (2022). DOI: 10.3390/vaccines10091437

Researchers at the Brazil-UK Center for Arbovirus Discovery, Diagnosis, Genomics and Epidemiology (CADDE) have developed a faster, more affordable method of analyzing serological data to monitor and predict the epidemiological behavior of COVID-19.

A study conducted by the scientists showed that the method predicted the arrival in Brazil of the delta variant first detected in India in 2020 and originally named B.1.617.2. They now aim to validate its use in epidemiological surveillance to detect and to assure a faster response to novel variants of SARS-CoV-2 as well as other viruses.

Using samples from blood donors in the capitals of seven Brazilian states—São Paulo, Rio de Janeiro, Manaus, Recife, Fortaleza, Curitiba and Belo Horizonte—the researchers conducted anti-spike protein microparticle assays to measure levels of immunoglobin G (IgG) antibodies, which bind to the virus's S protein and prevent it from infecting cells. The main aim was to assess the protection afforded by vaccination against delta.

At the start of the pandemic, seroprevalence studies were important to estimate the proportion of the population that was infected, but their significance declined as more and more people acquired immunity via vaccination or infection. In this context, novel methods of analyzing and predicting the behavior of the virus became increasingly important to track case numbers per region and help formulate public policy.

"In this study, instead of calculating the proportion of the population with antibodies, which was close to 100%, we analyzed blood antibody levels and how these correlated with the morbidity caused by delta. In

this manner, we demonstrated the value of collecting, analyzing and sharing this kind of data," Lewis Buss, a researcher at Imperial College London (UK), told Agência FAPESP.

A former graduate student at the Institute of Tropical Medicine Tropical (IMT), part of the University of São Paulo's Medical School (FM-USP) in Brazil, Buss is the first author of an article on the study published in the journal *Vaccines*.

The results of the study showed that while cases of COVID-19 caused by the delta variant were on the rise in Brazil, low numbers of cases of severe acute respiratory infection (SARI) correlated strongly with levels of antibodies measured in donor blood samples.

The risk of infection by delta was found to be lower for subjects who had already been infected by SARS-CoV-2 or vaccinated. Hybrid immunity (due to vaccination plus prior infection) produced a higher level of protection.

"Vaccines are very important to boost immunity. Infection alone isn't sufficient. We saw from our study that antibody levels rose very quickly after the first dose of the vaccine in cities where case numbers were highest in the first wave of COVID-19, such as Manaus and Fortaleza. The second dose had a stronger effect in cities where case numbers rose at a later stage, such as Curitiba and Rio de Janeiro. Their populations were better protected, and this helps explain why delta's effects in Brazil weren't as bad as in other countries," said Ester Sabino, last author of the article. Sabino is a professor at FM-USP and principal investigator for CADDE in Brazil.

Marker

The study showed that, boosted by vaccination, which began in Brazil in

January 2021, the average number of antibodies rose by a factor of 16 in the period analyzed—between March and November of that year. Among eligible blood donors aged 15-69, first dose coverage reached 75% in all cities by the end of the period. Second dose coverage was also high.

"We looked for a marker that could facilitate the analysis and could be used routinely to infer the degree of protection provided by vaccination," Sabino said. "In epidemics we have to use simple tools that can provide answers quickly. Testing the entire population is costly and hard to do."

Previous research showed that levels of neutralizing antibodies are strong predictors of protection against symptomatic infection by SARS-CoV-2. However, complex and expensive tests are required to detect these antibodies, which effectively stop the virus from entering human cells. Not all anti-S antibodies are necessarily neutralizing, but in this study the researchers found that high levels of anti-S antibodies could predict lower incidence of severe cases caused by a novel variant introduced into a seropositive population. They used semi-quantitative tests, which provide an estimate of the levels of antibodies produced in a subject against infection by SARS-CoV-2.

The group then conducted different kinds of analysis of samples collected in 2021, when the gamma, delta and omicron variants emerged in rapid succession, estimating the extent to which vaccination and prior infection contributed to levels of anti-S IgG in the population and how far these variables predicted the incidence of severe cases of COVID-19 caused by delta.

The tests were performed on 850 samples per month. In the second week of each month, samples were selected from donated blood or from the city neighborhoods analyzed, in order to ensure they were representative. Chemiluminescent microparticle immunoassays were conducted to

detect IgG antibodies against the SARS-CoV-2 spike protein. Vaccine dose administration statistics were taken from OpenDataSUS, the database maintained by Brazil's unified health service (SUS).

Three sources were consulted to obtain case numbers: records of SARI and deaths from the Ministry of Health's Flu Epidemiological Surveillance System (SIVEP-Gripe); the total number of confirmed cases from the Ministry of Health; and a SARS-CoV-2 test positivity time series from a chain of pharmacies in the city of São Paulo.

They also used metadata for all genomes of the virus posted to the GISAID platform between March 2020 and March 2022 by the seven Brazilian states.

Context

The cities analyzed in the study experienced distinct moments of the epidemic. The cumulative attack rate (inferred from seroprevalence) in December 2020, before the second wave caused by the gamma variant and before vaccination began in Brazil, ranged from 20.3% in Curitiba to 76.3% in Manaus. Attack rate is a term used in epidemiology to refer to the number of new cases divided by the total population.

While all seven cities saw a sharp gamma-dominated surge in cases and deaths, the ensuing period, dominated by delta, had different characteristics, with low levels of cases and deaths in Manaus, Fortaleza and Recife, and declining levels in Belo Horizonte and São Paulo.

The analysis of omicron showed varying rises in case numbers in the cities. Deaths rose only 3.7%. There was a modest surge in SARI cases except in Fortaleza, where omicron-associated SARI rose more sharply, although this appears to have been due to inconsistent reporting.

In sum, the authors conclude that antibodies acquired via infection and vaccination were sufficiently high in Brazil to prevent a significant public health impact from the emergence of omicron and other novel variants at that time.

Access to the data used in the study is open via GitHub.

More information: Lewis Buss et al, Predicting SARS-CoV-2 Variant Spread in a Completely Seropositive Population Using Semi-Quantitative Antibody Measurements in Blood Donors, *Vaccines* (2022). DOI: 10.3390/vaccines10091437

Github: github.com/CADDE-CENTRE

Provided by FAPESP