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Vaccination plus previous infection: protection during the omicron wave in Brazil

As of May 11, 2022, an estimated 519 million individuals have been infected with SARS-CoV-2, and at least 11 billion COVID-19 vaccine doses have been administered worldwide. Therefore, understanding hybrid immunity (ie, immunity derived from infection plus vaccination) is crucial to guide future vaccination policies. We found that vaccination provided additional protection to that induced by past infection during the gamma (P.1) and delta (B.1.617.2) variant waves of the pandemic in Brazil.[1] With the emergence of the omicron (B.1.1.529) variant, vaccine effectiveness appears to decay,[2,3] but protection in individuals who have been previously infected and vaccinated remains unknown. We analysed the effect of hybrid immunity in preventing infection and severe outcomes during circulation of the omicron variant in Brazil.

Using national databases, we did a test-negative case-control study as previously described.[1] Cases were defined as individuals with positive RT-PCR or lateral-flow tests and controls as individuals with negative RT-PCT or lateral-flow tests between Jan 1 and March 22, 2022—a period during which omicron was the predominant variant in Brazil (appendix pp 2–4). Severe outcomes were defined as a positive test obtained from 14 days before to 3 days after hospital admission or death occurring within 28 days after a positive test. We analysed vaccine effectiveness in individuals who had been previously infected using two references groups: unvaccinated with or without previous infection. Individuals could have more than one test included in these analyses, and each test was separately counted as a case or control. Detailed methods, including full inclusion and exclusion criteria, are in the appendix (p 2).

Of 9 266 235 tests from 8 471 561 individuals registered on surveillance databases during the study period, 918 219 tests from 899 050 individuals were eligible for inclusion in our analyses. 476 901 (51·9%) of 918 219 tests from 468 804 (52·1%) of 899 050 individuals were positive and defined as cases, and 441 318 (48·1%) tests from 430 246 (47·9%) individuals were negative and defined as controls; 323 704 (35·2%) tests were from individuals who were unvaccinated (22 935 [2·4%] with and 300 769 [32·8%] without previous infection; appendix pp 6–7). Compared with those who were unvaccinated without previous infection, the effectiveness of past infection in preventing reinfection during the omicron wave was low (28·9% [95% CI 26·9–30·9]), increasing with vaccination with any vaccine type (Ad26.COV2.S [Johnson & Johnson], BNT162b2 [Pfizer–BioNTech], ChAdOx-1 nCoV-19 [Oxford–AstraZeneca], or CoronaVac [Sinovac Biotech]), especially after a booster dose, although this protection waned over time (appendix pp 5, 8). Protection against severe outcomes after a previous infection was relatively high (85·6% [95% CI 82·7–88·0]), increasing with vaccination (vaccine effectiveness ranging from 88·0% to 100%; appendix pp 5, 8). Compared with unvaccinated individuals with a previous infection, vaccination with previous infection showed a moderate increase in protection against symptomatic infection ranging from 7·3% (95% CI 4·0–10·4) to 62·7% (61·0–64·3), once again waning over time, and substantial protection against severe outcomes after the booster (appendix pp 5, 8–9). Similar results were obtained using a matched analysis by date of test (within 10 days), age (5-year bands), municipality of residence, and sex in a ratio of 1:2 (with replacement; appendix pp 10–12).

In summary, during a period when omicron was the dominant SARS-CoV-2 variant in Brazil, robust protection against severe disease was offered by a previous infection, and this was increased with hybrid immunity. However, against symptomatic infection, even boosted

For **COVID-19 case and vaccination data** see https://coronavirus.jhu.edu/map.html

See **Online** for appendix

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individuals with hybrid immunity had low levels of protection and protection waned over time. Booster doses in previously infected individuals offered a moderate but transient increase in protection against symptomatic infection and a slight improvement against severe outcomes. These data highlight an issue of whether future efforts should focus on preventing symptomatic infection or severe disease, considering the moderate and transient increase in protection offered by boosters against symptomatic infection and the likely endemicity of SARS-CoV-2.

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