

Neutralizing antibodies against the SARS-CoV-2 Omicron variant following two CoronaVac vaccinations and a Pfizer/BioNTech mRNA vaccine booster

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Dear Editor

In a previous study conducted by our group, we evaluated 41 subjects who were vaccinated with two doses of the CoronaVac SARS-CoV-2 vaccine, with an interval of 28 days between doses, and subsequently received a booster of the mRNA vaccine from Pfizer/BioNTech¹. We determined the neutralizing capacity against the SARS CoV-2 Omicron variant 62.7 days following the administration of the booster.

In this investigation, we extended our initial findings on the same study subjects by reporting levels of neutralizing antibodies against the Omicron variant at a mean of 151.5 days after the booster vaccine.

Neutralizing antibodies against Omicron decreased in the subjects, since the first result showed a 85.3% positivity, whereas at day 151.5 ($p = 0.0336$), this percentage fell to 60.5%. The virus neutralization titer (VNT) also decreased at day 151.5 post-booster as opposed to day 62.7 VNT ($p = 0.0256$).

There is very limited knowledge about the activity and duration of neutralizing antibodies in vaccinated people after a two-dose vaccine schedule with an inactivated vaccine (CoronaVac) followed by a booster dose with an mRNA vaccine, as currently recommended by the Brazilian Ministry of Health²⁻⁴. To the best of our knowledge, this is the first report of anti-Omicron neutralizing antibodies in sera following a protracted period (day 151.5) post-mRNA vaccine booster. Our parallel findings from other studies suggest that vaccine effectiveness wanes over time following a booster vaccination^{5,6}. In one study conducted during the Omicron variant outbreak in our country, vaccine effectiveness against COVID-19-associated hospitalization was 91% versus 78% among those who received the third dose of mRNA vaccine in periods equal to or less than two months in comparison with periods of more than four months after the second dose of vaccine, respectively⁶.

The post-vaccination sera with virus neutralization activity and the virus neutralization titer (VNT) against the SARS-CoV-2 Omicron variant at two different time frames are shown in **Table 1**. This prospective study recruited 41 subjects who have never been infected with SARS-CoV-2 and were vaccinated with two doses of the CoronaVac (Sinovac Life Sciences, Beijing, China) SARS-CoV-2 vaccine. Thirty-eight of these individuals received a booster immunization with

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Table 1 – Neutralizing antibody activity against the Omicron SARS-CoV-2 variant in sera from subjects who received two doses of the CoronaVac vaccine followed by a Pfizer mRNA vaccine booster.

Mean days post-booster	Nº tested	Nº with neutralizing activity (%)	Median VNT (IQR)
62.7	34	29 (85.3%) ^a	1: 40 (0, 1: 320) ^b
151.5	38	23 (60.5%)	1: 20 (0, 1: 160)

The presence of virus neutralization activity was defined as the absence of cytopathic activity at a serum dilution $\geq 1:20$. VNT, virus neutralization titer; IQR, interquartile range); ^a $p = 0.0336$; ^b $p = 0.0256$

the Pfizer mRNA vaccine. The vaccination protocol, immunization dates and quantification of neutralizing antibodies against the Omicron variant using the Cytopathic Effect-based Virus Neutralization Test had been previously reported⁵. Most subjects (90.2%) were female and their ages ranged from 30 to 77 years old with a median of 54 years. The majority (65.9%) were <60 years old. The presence of virus neutralization activity was defined as the absence of cytopathic activity at a serum dilution $\geq 1:20$. The statistical analysis was performed by means of the Fisher's exact test and the paired Wilcoxon test.

It should be noted that measurement of the *in vitro* VNT is not the only determinant of the level of protection against SARS-CoV-2. Anamnestic humoral and cell-mediated immune responses against a new infection also influence viral persistence and disease severity.

Despite this limitation, we believe that the findings of our study contribute to a better understanding of the effectiveness of the current Brazilian SARS-CoV-2 vaccination schedule, as it supports the current Brazilian guideline, which recommends a booster dose of a Covid-19 mRNA vaccine for the general population after completion of the primary vaccination series².

We conclude that this vaccination schedule provides limited protection against the Omicron SARS-CoV-2 variant as it wanes significantly over five months. Our findings of decreased immunity over time also suggest that a second booster dose may be beneficial and should be recommended for specific populations².

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AUTHORS' CONTRIBUTIONS

Conceptualization, writing and review, and supervision: ARSJ, LSVB, MCMC, and SSW; data curation: ARSJ, TRTM, LH, AP, and LSVB; laboratory assays, analysis, and interpretation of data: ARSJ, AP, LSVB, and MCMC; formal analysis: MCMC, SSW.

CONFLICT OF INTERESTS





The authors declare to have no conflict of interests.

ETHICS

This study was approved by the Brazilian National Research Ethics Commission (*Comissão Nacional de Ética em Pesquisa – CONEP*), registration N° 30419620.1.0000.0068. All subjects signed written informed consents.

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