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Letter to the Editor

Antibody titers and breakthrough infections with Omicron SARS-CoV-2

Editor: Prof. R. Read

Dear Editor,

Recent studies indicated that the strong immune evasion potential of the most recent SARS-CoV-2 variant, Omicron, results in more frequent reinfections and breakthrough infections despite the widespread delivery of mRNA vaccine booster doses .[1,2] Antispike antibody titers greater than 141 binding antibody units (BAU) per milliliter are correlated with the presence of neutralizing antibodies (the most widely accepted marker of protection) against wild-type virus and the Alpha variant,[3] but neutralization of the Delta and Omicron variants probably requires higher antibody titers. Recent results showed that there was evidence of significant waning of antibody reactivity against Delta and Omicron six months after the second dose of vaccine.[4] In this complementary study, we compared the concentrations of binding antibodies before breakthrough infections with Delta or Omicron SARS-CoV-2 variants.

We measured the antibody titers in 1169 vaccinated individuals shortly before their breakthrough infection with the Omicron SARS-CoV-2 variant (1 November – 31 December 2021). Total SARS-CoV-2 antibodies were measured with a quantitative enzyme-linked immunosorbent assay (ELISA) (Wantai Biological Pharmacy Enterprise Co., Ltd, China).[5] Symptomatic and asymptomatic infections were detected between 15 November 2021 and 12 January 2022 using a nucleic-acid amplification method (Aptima™ SARS-CoV-2 assay, Panther™ system, Hologic, USA).[6] Viral genotyping was performed using Pacific Biosciences Technology.[7] We matched for age, gender and vaccination status (1, 2 or 3 doses) each Omicron-infected individual with a person infected with the Delta variant identified between September 1 and December 1, 2021 for whom we had a total antibody titer 15 days to 2 months before infection. The antibody concentrations at the time of infection were estimated with an exponential decay model.[8] These analyses were part of the national SARS-CoV-2 surveillance. French law (CSP Art.L1121–1.1) does not require institutional review board approval for anonymous non-interventional studies.

The median age of the 1169 individuals (602; 51.5 males) was 45 years (interquartile range [IQR] 29–71). 258 (22.1%) had been given one, 859 (73.5%) two, and 52 (4.4%) three doses of mRNA vaccine. The ELISA analyses indicated that 90% of the Omicron infections occurred in people whose total antibody concentration was less than or equal to 6967 BAU/ml. In contrast, 90% of the Delta infections involved people with binding antibody concentrations below 2905 BAU/ml (Fig. 1, $p<0.01$, Wilcoxon signed rank test).

These figures suggest that infections with the Omicron SARS-CoV-2 variant can occur despite high binding antibody concentrations, even at concentrations 2.4 higher than infections with the Delta SARS-CoV-2 variant. This is consistent with a recent study indicating that a booster Pfizer dose as well as vaccination of previously infected individuals generated an anti-Omicron neutralizing response, with titers 6 - 23 times lower against Omicron than those against Delta.[9] This is also consistent with another study showing that the neutralization titers of anti-Omicron antibodies in the serum of plasma donors were 17 to 22 times lower than they are against the Delta variant.[10] The antibody thresholds found in our study should be compared to those obtained in further studies on other populations.

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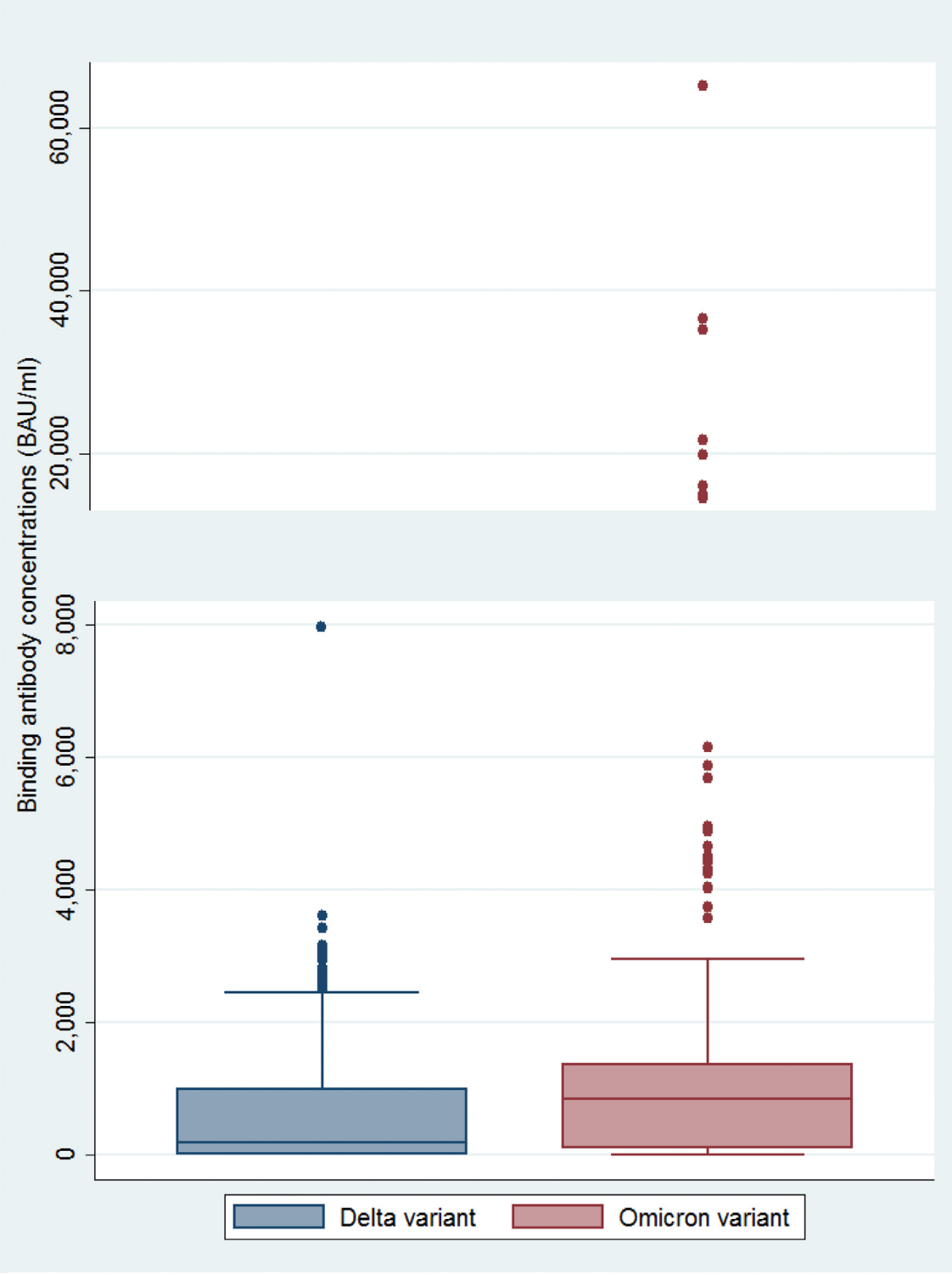

Fig. 1. : Distributions of binding antibody concentrations before infection with Delta or Omicron Sars-CoV-2 variants.

Declaration of Competing Interest

The authors declare no conflict of interest

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