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CORRESPONDENCE

Breakthrough Infection by SARS-CoV-2 Delta and Omicron Variants Elicited Immune Response Comparable to mRNA Booster Vaccination

To the Editor—We would like to thank Zhigang Ren and colleagues [1] for the additional valuable information on the immune response after breakthrough infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Delta and Omicron variants. Their results showed that at day 10 postdiagnosis, Omicron-infected individuals possessed lower immunoglobulin G (IgG) and immunoglobulin M (IgM) antibody levels than Delta-infected individuals. Another recent study showed that Omicron infections were less severe with a 2-fold lower mortality rate compared to Delta infections [2]. In addition, the percentages of asymptomatic infection or mild symptoms were higher in Omicron than Delta breakthrough infections, resulting in 10.83 times lower neutralizing antibody titers in Omicron- than Delta-infected individuals after 2 doses of BNT162b2 [3]. Our previous study also showed that nucleocapsid- and spike-specific IgG response to SARS-CoV-2 infection depends on disease severity, with higher responses in individuals with more severe symptoms [4]. Therefore, the comparison of immune response should be classified by disease severity.

In Thailand, numerous variants of concern have been detected during the spread of coronavirus disease 2019 (COVID-19) and they have caused multiple waves of the pandemic. The Delta (B.1.617.2) variant was predominant between August and November 2021. The Omicron (B.1.1.529) variant has been the predominant variant in Thailand since December 2021. Although more than 75% of the Thai population has been vaccinated with at least 2 doses of the COVID-19 vaccine, the vaccine-induced immunity has declined over time and breakthrough infections were increasingly reported. Nevertheless, the antibody responses after Delta or Omicron breakthrough infection are still limited.

In accordance with the study of Zhigang Ren et al [1], our previous study demonstrated that individuals who had been vaccinated with 2 doses of CoronaVac and subsequently infected with the Delta variant elicited high levels of total receptor-binding domain (RBD) Ig with geometric

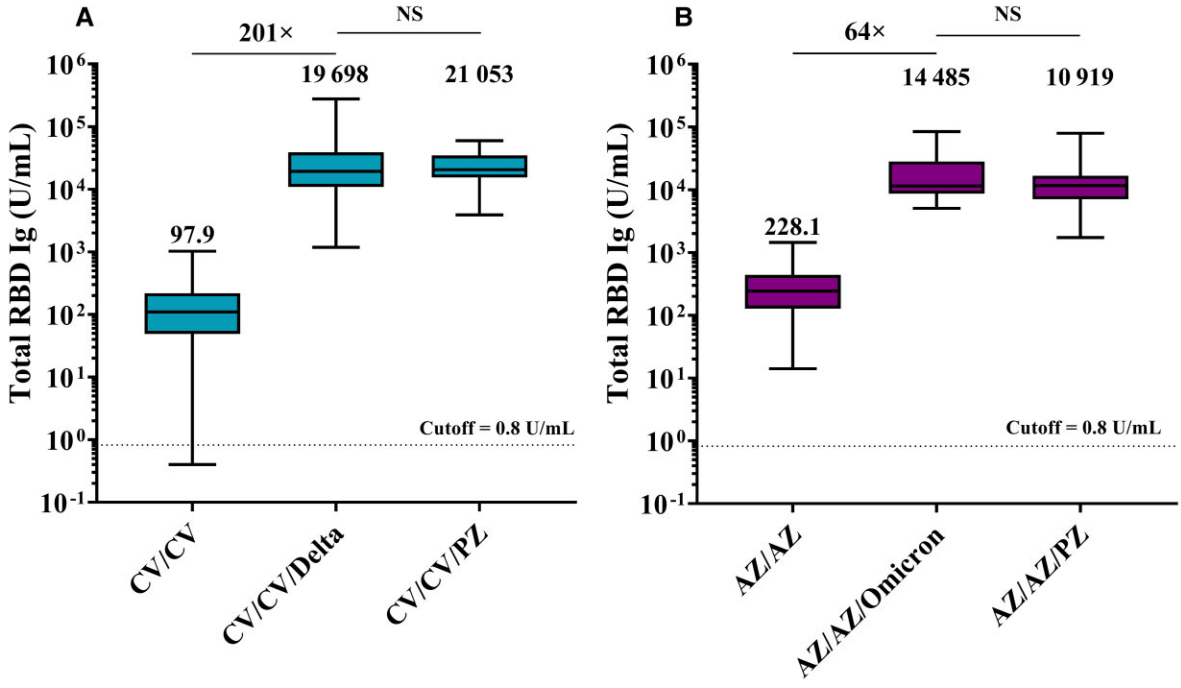

Figure 1. Total RBD Ig of SARS-CoV-2 (U/mL). *A*, Total RBD Ig in Delta-infected individuals after 2-dose CoronaVac (CV/CV/Delta) were compared to those receiving 2-dose CoronaVac (CV/CV) and those who primed with 2-dose CoronaVac plus BNT162b2 as a booster dose (CV/CV/PZ). *B*, Total RBD Ig of Omicron-infected individuals after 2-dose AZD1222 (AZ/AZ/Omicron) were compared to those receiving 2 doses of AZD1222 (AZ/AZ) and those who primed with 2-dose AZD1222 plus BNT162b2 as a booster dose (AZ/AZ/PZ). Lines indicate geometric mean titer and the error bars indicate 95% confidence intervals. The cutoff value is indicated by the dotted line. Abbreviations: Ig, immunoglobulin; NS, not significant; RBD, receptor-binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

mean titer 19 698 U/mL (95% confidence interval [CI], 15 335–25 302 U/mL) at 1 month after infection [5]. The levels of total RBD Ig in the breakthrough group were 201-fold higher than in those who received 2 doses of CoronaVac, and were comparable to those who received the booster dose with BNT162b2 (Figure 1*A*) [6]. Interestingly, another group vaccinated with 2 doses of AZD1222 and subsequently infected with the Omicron variant showed lower levels of total RBD Ig response, with GMT 14 485 U/mL (95% CI, 6886–30 468 U/mL). The levels of total RBD Ig in the AZD1222-vaccinated individuals who subsequently had Omicron breakthrough infection were only a 64-fold increase compared to the AZD1222-primed, but comparable to those who received the booster dose with BNT162b2 (Figure 1*B*). A robust immune response in individuals with breakthrough infection may occur due to the combination of vaccination and natural infection, known as hybrid immunity [7]. The increase in antibody titers after natural infection was similar to that obtained with heterologous mRNA booster vaccination [6, 8]. Regarding the cellular immune response after breakthrough infection, a previous study reported that the levels of secreted interferon-γ (IFN-γ) were similar in individuals infected with the Omicron and Delta variant [9]. These results may indicate no significant difference in memory T-cell response between Delta- and Omicron-infected groups.

In conclusion, both Delta and Omicron breakthrough infection elicited markedly high levels of serum total RBD Ig and neutralizing antibody, as well as T-cell responses in individuals who previously completed 2-dose vaccination. The levels of immune response were comparable to those receiving the heterologous mRNA booster vaccination.

Notes

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