Received: 1 November 2022 | Accepted: 6 November 2022

DOI: 10.1111/irv.13070

LETTER TO THE EDITOR

WILEY

A comparative immune response to COVID-19 vaccination between children and adults

Epidemiological evidence has consistently shown milder course of disease and reduced mortality in children upon infection with SARS-CoV-2 compared to adults; however, the potential mechanisms remain unclear. Recent studies have focused on the profiles of SARS-CoV-2-specific immune responses in children and adults after natural infection and revealed that children generated a strong anti-viral response compared to adults.[1,2] On this background, we consider there are also two issues required to be explored. It remains unclear whether children respond differently to SARS-CoV-2 vaccination compared to adults, and if yes, how should the vaccine deployment be modified in children?

On October 29, 2021, the Food and Drug Administration issued an emergency use authorization amendment for Pfizer-BioNTech COVID-19 (BNT162b2) vaccine for use in children aged 5–11 years; as of October 2022, approximately 11.13 million children aged 5–11 years have received at least one dose of COVID-19 vaccine in the United States.[3] There have been little data on the comparison of immune response to COVID-19 vaccine between children and adults to date. In two recent multi-center, placebo-controlled, observer-blinded trials,[4,5] the immunological profile showed that the serum-neutralizing geometric mean titer (GMT) 1 month after two doses of BNT162b2 vaccine was 1,198.0 in the 5-to 11-year-old cohort (10 μg/dose), 1,283.0 in the 12- to 15-year-old cohort (30 μg/dose), and 730.8 in the 16- to 25-year-old cohort (30 μg/dose), indicating a greater antibody response to vaccine in participants aged 5–15 years than that in those aged 16–25 years (Figure 1). However, the authors did not record the attenuation of antibody response and detect the cross-reactive antibody response to human coronaviruses (HCoVs). To date, no clinical trial has been carried out comparing the cellular immunological response between children and adults after COVID-19 vaccination, despite studies have showed that younger adults consistently kept higher T-cell response rate than the older (Th1 response 76–83% vs. 60–67%; CD8 + T-cell response 51–64% vs. 24–36%).[6] On the basis of the current preliminary data above, we speculate that children may also develop stronger immune response to COVID-19 vaccine compared to adults, in parallel with the immunologic profile after natural infection.

In children, the individualized vaccination strategies should be formulated according to the age-related immune response. First, the dynamic monitoring of both humoral and cellular immune response is

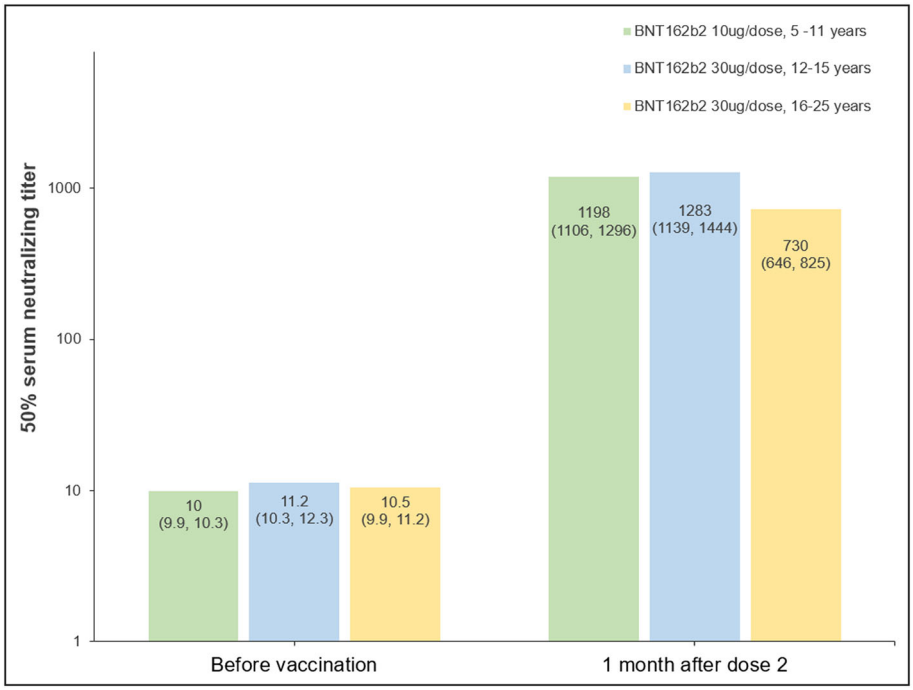

FIGURE 1 Serum-neutralizing geometric mean titer for participants 5–11, 12–15, and 16–25 years old

required in children after COVID-19 vaccination to design the optimal vaccination dosage and interval. Second, future studies are warranted to identify the potential consequence of antibody cross-reactivity between seasonal hCoVs and SARS-CoV-2 on children after vaccination. Ng et al.[7] revealed that hCoVs seroconversion in SARS-CoV-2 uninfected health cohort aged 1–16 years was significantly higher than that in adults and correlated with relative protection from COVID-19; thus, the detection of cross-reactive immunity to SARS-COV-2 may have implications in the deployment of COVID-19 vaccination in children. Third, a booster dose of COVID-19 vaccine should be recommended to elder children and adolescents with suboptimal response after two-dose primary vaccine series to aid in the generation of an immune response. Bar-On et al.[8] found that the rate of confirmed SARS-COV-2 infection was significantly lower in the booster group aged 16–29 years than that in the nonbooster group by a factor of 17.2 (95% CI, 15.4 to 19.2) in Poisson regression analysis. Last, heterologous vector/mRNA vaccination regimen should be also attempted as another candidate in children after primary vaccinations. In a randomized, double-blind, placebo-controlled trial from China, Zhu et al.[9] confirmed that adenovirus type-5-vectored COVID-19 vaccine with a single dose in children aged 6–17 years induced robust immune responses, with GMTs of 1091.6 in ELISA antibody and 96.6 in neutralizing antibody, respectively.

KEYWORDS

adult, children, COVID-19 vaccination, immune response

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Qi Jiang: Data curation; investigation; methodology; validation; visualization; writing-original draft. **Yue Cao:** Data curation; investigation; methodology; software; writing-original draft. **Jin Wei Ruan:** Data curation; resources; validation; writing-original draft; writing-review and editing. **Peng Hu:** Conceptualization; methodology; supervision; writing-review and editing.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/irv.13070.

DATA AVAILABILITY STATEMENT

Data are available on reasonable request from the corresponding author.

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