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LETTER TO THE EDITOR

# Delayed kinetics of SARS-CoV-2 IgG antibody production in kidney transplant recipients following the third dose of COVID-19 vaccination

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## To the Editor

Effective vaccination is crucial for the management of coronavirus disease 2019 (COVID-19). A weak immune response to the second dose of vaccine (V2) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been observed in patients undergoing renal replacement therapy (RRT), particularly in kidney transplantation (KTx) recipients [1, 2].

Few studies have evaluated the immune response kinetics observed in patients undergoing hemodialysis (HD), patients undergoing peritoneal dialysis (PD), and KTx recipients after several months following the third dose (V3) of vaccination with mRNA vaccines [3, 4]. To the best of our knowledge, no data are available on the antibody kinetics at 6 months after V2 in KTx recipients.

Herein, we report the humoral response kinetics in patients undergoing RRT who received three doses of the Comirnaty mRNA vaccine (BioNTech–Pfizer BNT162b2). This study included 78 patients undergoing HD (mean ± SD age, 72.6 ± 9.1 years; 65.3% were males), 35 undergoing PD (74.5 ± 9.5 years; 62.8% males), and 32 KTx recipients (56.6 ± 12.3 years; 68.7% males).

The first dose (V1) and V2 were administered at a 3-week interval as per recommendations; V3 was administered at least 6 months after V2. Serum samples were collected 4–8 weeks following V3 and tested for SARS-CoV-2 antibodies using Elecsys® Anti-SARS-CoV-2 S RUO (Roche Diagnostics, Basel, Switzerland), which measured immunoglobulin G (IgG) levels against SARS-CoV-2 spike S1 subunit. Antibody titers > 0.8 U/mL were considered a positive immune response to vaccination.

At 2 months after V2, the median antibody titers (interquartile range [IQR]) were significantly lower in the KTx group than in the HD and PD groups ($p < 0.0001$). However, at 6 months after V2 there was no significant difference in the antibody titers among the three groups (Fig. 1).

Studies have reported waning humoral response after V2 administration in healthy controls and patients undergoing HD [5], which support our findings. However, in KTx recipients, the median antibody titer increased from 1.3 [0.4–107.5] U/mL 2 months after V2 to 42.7 [0.4–275.3] U/mL 6 months after V2 and subsequently to 1216 [19.6–7,651] U/mL 2 months after V3 ($p < 0.001$). At 6 months after V2, the antibody titer tended to be higher in the KTx group than in the HD and PD groups (Fig. 1).

In this study, during the 6-month follow-up after V2, a serological response was observed in four KTx recipients who were seronegative for the second dose. This antibody seroconversion indicates possible asymptomatic or subclinical infection; however, all patients tested negative for SARS-CoV-2 nucleocapsid (N) protein. Therefore, we speculated slower antibody formation owing to certain factors associated with immunosuppression-related impairments. Although the antibody titer test results were negative at 2 months, sufficient quantities of antibodies were subsequently produced, and seroconversion could, therefore, be confirmed at 6 months.

Furthermore, the prevalence of anti-SARS-CoV-2 antibodies was 53.3%, 2 months after V2; 65.6%, 6 months after V2; and 77.2%, 2 months after V3. Although a similar

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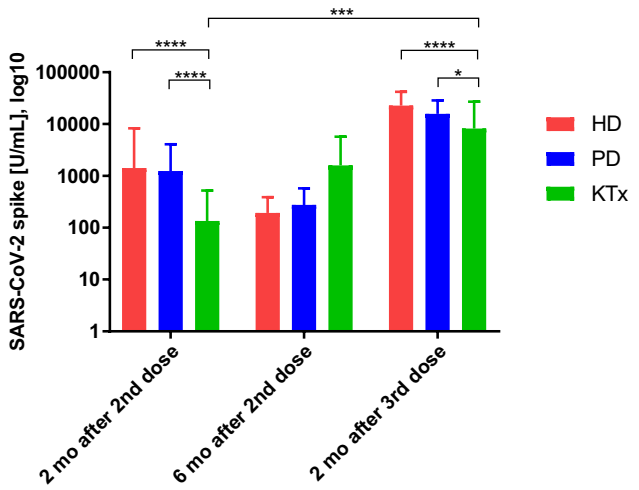


**Fig. 1** Antibody response kinetics following the second and third doses of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine in 78 patients undergoing hemodialysis (HD), 35 patients undergoing peritoneal dialysis (PD), and 32 kidney transplant (KTx) recipients. The data from the non-normally distributed samples were analyzed using the non-parametric Kruskal–Wallis and post hoc Dunn's tests, using GraphPad Prism 7.0 (GraphPad Software, San Diego, CA) (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$)

significant difference was found 2 months after V3 administration among the three groups, the extent of difference was not as much as that observed after V2 administration. This implies that SARS-CoV-2 IgG production in KTx recipients is delayed and that future vaccination may induce similar IgG kinetics as that observed in patients undergoing HD or PD.

Study limitations include the small sample size, short follow-up period, and lack of cellular immunity testing. Further studies are necessary to clarify the mechanism of delayed kinetics of SARS-CoV-2 IgG production and to provide a better estimate of antibody response in KTx recipients.

In conclusion, our findings regarding delayed kinetics are important in understanding the immune response against SARS-CoV-2 in immunosuppressed KTx recipients. This study may provide insights into developing strategies to monitor antibody responses to additional vaccination and help in the better management of COVID-19.

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**Author contributions** MM designed and drafted the manuscript. TS and KM contributed to protocol design. JY and HK contributed to the patient follow-up and data management. MM, TS, and KM analyzed the data and drafted the manuscript. All authors have read and approved the final manuscript.

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**Availability of data and materials** All data supporting our findings are contained within the manuscript.

## Declarations

**Conflict of interest** The authors have declared that no conflicts of interest exist.

**Ethics approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of Kameda Medical Center (Approval Number 21–025) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

**Informed consent** This ethics committee waived the requirement for written informed consent due to the retrospective nature of this study.

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