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Letter to the Editor

LETTER TO THE EDITOR

Antibody maintenance and breakthrough infections 6 months after complete COVID-19 vaccination with the mRNA-1273 and BNT162b2 vaccines in hemodialysis patients

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Given that in-center hemodialysis patients have a high severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection risk and a higher mortality rate than the general population [1], several groups have published their immunization experience with messenger RNA (mRNA) vaccines in this group of patients [2, 3]. Currently there is extensive data on short- and medium-term vaccination efficacy, measured in terms of seroconversion, with both BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines in hemodialysis patients [4, 5]. However, despite the known poor immune response of this population experienced in other immunization programs (e.g. influenza, hepatitis B) [6, 7], there are scant data on long-term serological maintenance in response to mRNA vaccination [8]. Therefore we decided to determine the persistence of anti-S1-RBD immunoglobulin G (IgG), its blood levels and its degree of decline 6 months after receiving two doses of an mRNA vaccine, complementing our previous study at 3 months with new information [5].

As of April 2021, 201 patients had completed their two-dose vaccination scheme. Ninety-one patients received the BNT162b2 vaccine and 110 received the mRNA-1273 vaccine. The methodology and results of the immediate humoral and cellular response to vaccination are reported in detail in a previous work [4]. In the present study we were able to test for anti-S1-RBD IgG presence and blood levels in 160 patients 6 months after vaccination, 91 with the mRNA-1273 and 69 with the BNT162b2 vaccine. Forty-one subjects were lost during follow-up, 19 died, 16 received a kidney transplant, 3 were transferred to another hemodialysis center, 2 were vaccinated outside the center and the remaining patient was on vacation when blood tests were obtained. A total of 130 patients (81.25%) had a positive anti-S1-RBD test (Figure 1A). Those with negative anti-S1-RBD IgG titers were significantly older (76.9 ± 11 versus 70.6 ± 15 years; $P = 0.012$), had lower immediate post-vaccination levels than those who did not (22.8 ± 29.5 versus 106 ± 52.4; $P < 0.001$), were more likely to have been SARS-CoV-2 naive before the initial vaccination was completed [26 patients; relative risk (RR) 2.58; $P = 0.042$] and had received the BNT162b2 vaccine rather than the mRNA-1273 vaccine (22 patients; RR 3.28; $P = 0.001$). Of the 30 subjects with negative anti-S1-RBD IgG titers, 4 were on immunosuppressive treatment, 5 had never presented a positive result to the vaccine and 5 had an initially positive response but lost detectable levels 3 months after vaccination [5]. Also, there was a statistically significant median decrease in anti-S1-RBD IgG levels of 56.3% [interquartile range (IQR) 25.3] between 3 and 6 months after vaccination (Figure 1B and C) and the median anti-S1-RBD IgG levels were significantly greater in those vaccinated with the mRNA-1273 than

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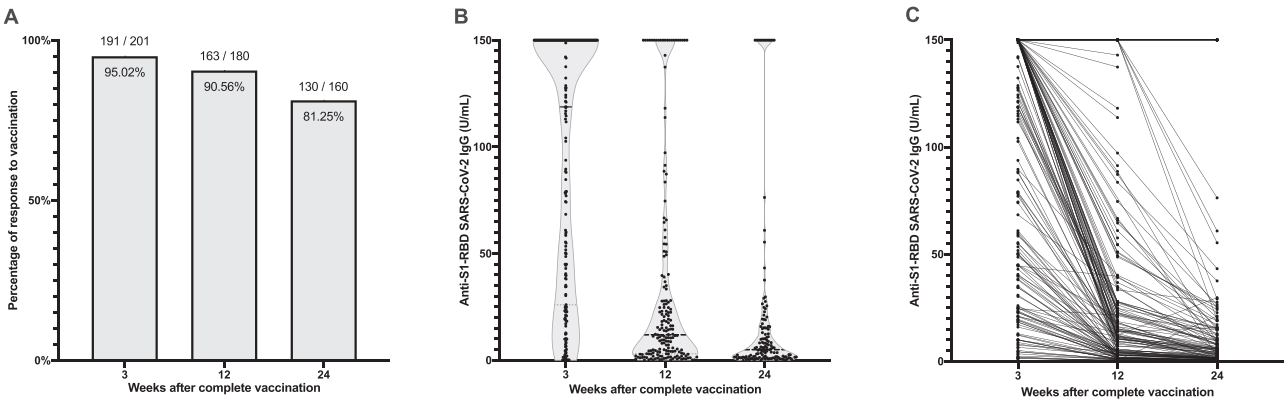

FIGURE 1: (**A**) The proportion of seropositive (i.e. anti-S1-RBD IgG >1 U/mL) patients at 3, 12 and 24 weeks after completing vaccination with either mRNA-1273 or BNT162b2. (**B**) Violin plot of anti-S1-RBD IgG levels in patients who have not been infected with SARS-CoV-2 postvaccination at 3, 12 and 24 weeks after the second vaccine dose. (**C**) Variation of anti-S1-RBD IgG in every individual who has not been infected with SARS-CoV-2 postvaccination from anti-S1-RBD IgG measurement at 3, 12 and 24 weeks after the second vaccine dose.

in those with BNT162b2 [8.33 (IQR 21.35) versus 1.79 (IQR 12.63); P = 0.001].

Moreover, nine vaccinated patients with positive antibodies and one who seroreverted at 3 months postvaccination were infected with SARS-CoV-2. Among them, there was only one case of severe coronavirus disease 2019 (COVID-19) that required intensive care unit admission, another patient was admitted to the hospital for COVID-19 pneumonia, while the remaining cases were mild and did not require hospital admission. None of these patients died.

The persistence of a positive anti-S1-RBD IgG test up to 6 months after vaccination has been reported in healthy adult subjects with both mRNA-1273 and BNT162b2 [9, 10], and there are only data in a small cohort of hemodialysis patients vaccinated with the BNT162b2 that report a decrease in seroconversion from 97.9% to 65.8% 4 weeks after vaccination. In contrast, our cohort went from an initial seroconversion of 95.4% [4] to 81.25%. Also, antibody levels continued to decrease following the decrease already observed 3 months after vaccination [5]. Despite this decrease, no COVID-19 deaths were observed in vaccinated patients. None of them had a fatal outcome related to COVID-19, unlike in the pre-vaccination era, where around one-third of hemodialysis patients died [1]. Given these results, we believe that hemodialysis patients will benefit from a third vaccine dose as a booster to maintain antibody levels in those who have them and restimulate an immune response in those who have lost them. We will continue to monitor their response to vaccination and report their effectiveness in response to new viral strains.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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