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Humoral Response to BNT162b2 and CoronaVac in Patients Undergoing Maintenance Hemodialysis: A Multicenter Prospective Cohort Study

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Keywords
COVID-19 · Dialysis · Hemodialysis · SARS-CoV-2 · Vaccine

Abstract

Introduction: Data regarding inactivated vaccines for SARS-CoV-2 in patients undergoing maintenance hemodialysis (MHD) are limited. We aimed to investigate humoral responses induced by CoronaVac compared to BNT162b2 in this population. ***Methods:*** In this multicenter prospective cohort study, adult patients undergoing MHD who lacked a history of COVID-19 and decided to get vaccinated with BNT162b2 or CoronaVac were enrolled. Participants provided serum samples before, 1 and 3 months after 2 doses. Anti-SARS-CoV-2 IgG antibodies against receptor-binding domain of the virus were measured, and levels ≥50 AU/mL were considered as positive. Breakthrough infections and adverse events were recorded. ***Results:*** Ninety-two patients were included, 68 (73.9%) of whom were seronegative at baseline. BNT162b2 and CoronaVac were administered in 38 (55.9%) and 30 (44.1%) patients. At 1 month, seropositivity was 93.1% in BNT162b2 and 88% in CoronaVac groups ($p = 0.519$). Quantitative antibody levels were significantly higher in BNT162b2 ($p < 0.001$). At 3 months, both seropositivity (96.4% and 78.3%, $p = 0.045$) and antibody levels ($p = 0.001$) remained higher in BNT162b2 compared to CoronaVac. Five patients (7.4%) experienced breakthrough COVID-19. Adverse events were more frequent with BNT162b2, although all of them were mild. Multiple linear regression model showed that only vaccine choice (BNT162b2) was related to the humoral response ($\beta = 0.272$, $p = 0.038$). Seropositive patients at baseline ($n = 24$) had higher antibody levels at any time point. ***Conclusions:*** BNT162b2 and CoronaVac induced humoral responses in naïve patients undergoing MHD, which were more robust and durable for 3 months after BNT162b2. Both vaccines created high antibody levels in patients who were seropositive at baseline.

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Introduction

More than 2 years earlier, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the infamous pandemic of coronavirus disease 2019 (COVID-19) which became the third leading cause of death in the USA in 2020 [1]. Mortality rates have been found as high as 20–25% in patients undergoing maintenance hemodialysis (MHD) due to their serious comorbidities, immunodeficient states caused by kidney disease, and logistical aspects of the treatment sessions [2–4].

Starting from December 2020, several vaccines developed using different techniques have become available throughout the world. mRNA-based BNT162b2 vaccine (Pfizer Inc., New York, NY, USA; BioNTech SE, Mainz, Germany) was initially shown to have an efficacy of 95% [5], whereas inactivated CoronaVac (Sinovac Biotech, Beijing, PR China) had an efficacy of 65–83% in different healthy populations [6, 7]. However, patients with chronic kidney disease (CKD) were excluded from these trials. Various observational studies after implementation of these vaccines reported that mRNA vaccines had an efficacy of 70–96% in patients undergoing MHD [8]. Nevertheless, data are scarce when it comes to the inactivated virus vaccines. Only a handful of articles demonstrated 50–88% rates of antibody production against the receptor-binding domain of SARS-CoV-2 1 month after two doses without any longitudinal follow-up [9–11]. A study investigated the durable humoral responses for 6 months, yet there was no comparison with an mRNA-based vaccine [12]. A very recent observational cohort from Chile compared the efficacy of CoronaVac with BNT162b2, but serologic responses were not included in this analysis [13]. Therefore, in this prospective cohort study, we aimed to evaluate longitudinal humoral responses against SARS-CoV-2 induced by BNT162b2 and CoronaVac in patients undergoing MHD.

Materials and Methods

Patient Selection and Data Collection

Starting from April 2021, all patients of at least 18 years of age undergoing MHD twice or thrice weekly in participating centers were screened and included in this study if they lacked a history of COVID-19 diagnosed by nucleic acid amplification tests or clinical symptoms and radiological signs despite negative results of nucleic acid amplification tests. Patients with a history of immunosuppressive treatment in the last 3 months, undergoing hemodialysis due to acute kidney injury, vaccinated before enrollment in the study, did not complete a course of at least 2 doses of vaccines or unable to give consent were excluded.

Baseline demographics, primary kidney diseases, comorbidities, medications, and data regarding dialysis (dialysis duration [years], type of vascular access, number of weekly sessions, weight [kg], dialysis adequacy calculated by Kt/V and urea reduction ratio, surface area of dialysis membrane, average ultrafiltration volume per session, residual urine output) were collected. Results of routine laboratory tests (complete blood count, serum urea, creatinine, electrolytes, calcium and phosphorus, alanine aminotransferase [ALT], serum albumin, C-reactive protein [CRP], ferritin, parathormone) at the last visit before vaccination were recorded, as well.

For the purposes of this study, participants provided serum samples before, 1 and 3 months after the administration of two doses of any vaccines. Also, a sample 1 month after the booster dose was collected from patients who chose to get the booster injections. COVID-19 infections after two doses of vaccination were recorded. All participants provided written informed consent. The study was approved by our Ministry of Health (2021-04-05T06_07_56), Ethical Committee of one institution (2021-9/2) and administration of each participating center, and complied with the Declaration of Helsinki and its later amendments. Reporting was carried out in line with the STROBE guidelines [14].

Vaccines

CoronaVac (Sinovac Biotech, Beijing, PR China) and BNT162b2 (Pfizer Inc.; BioNTech SE) were approved for emergency use in Turkey in January 2021 and April 2021, respectively. Both vaccines were administered in two doses at least 4 weeks apart, and in each case, patient choice and availability determined the vaccine to be applied. Data of any adverse events (AEs) following injections were collected. Starting in July 2021, a booster option at least 3 months after the second dose was provided by national authorities according to vaccine preferences: BNT162b2 or CoronaVac for recipients of two doses of CoronaVac and BNT162b2 for recipients of two doses of BNT162b2. Patients who opted to have booster injections were recorded, as well.

Measurement of Anti-SARS-CoV-2 IgG Levels

Serum specimens were collected from participants at baseline, 1 and 3 months after the administration of second dose. Patients who chose to get booster injection provided another serum sample 1 month after the booster dose. Samples were centrifuged at 3,000 rpm for 10 min, and aliquots were prepared and stored at −80°C until further analyses. A chemiluminescent microparticle immunoassay was used to measure serum levels of anti-SARS-CoV-2 IgG antibodies directed against the receptor-binding domain of the virus (SARS-CoV-2 IgG II Quant on an ARCHITECT analyzer; Abbott, Abbott Park, IL, USA) by the same expert. Results were reported as arbitrary unit per milliliter (AU/mL), and levels ≥50 AU/mL were considered as positive.

Statistical Analyses

Parametric and nonparametric tests were used according to the distribution pattern of the data. Results were expressed as mean ± standard deviation (SD) when normally distributed or as median (interquartile range [IQR], 25–75%) otherwise. Categorical variables were shown as frequency (%). Comparisons of continuous variables between two groups (BNT162b2 and CoronaVac)

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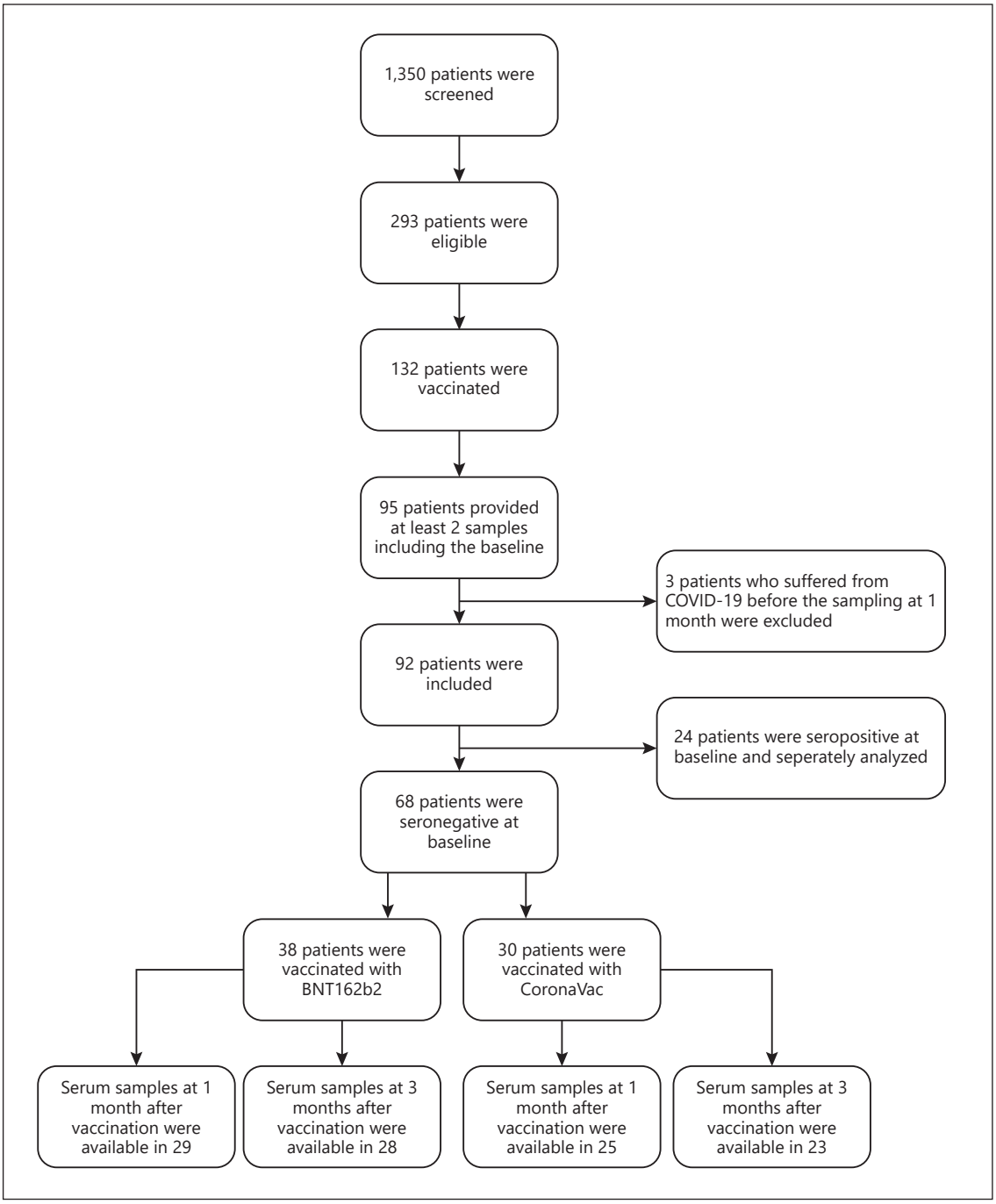


Fig. 1. Flowchart of the study.

were evaluated by using *t* tests or the Mann-Whitney U test. Differences in proportions of different patient groups were compared using the χ^2 test. For multiple linear regression analysis, variables were selected according to their statistical significance ($p < 0.10$) in simple linear regression. Age and sex were also included in the final regression model in which $\log_{10}$-transformed antibody levels were used to meet the normal distribution. Missing data were considered as pairwise missing in the analyses and were not imputed. All analyses were two sided, and a p value of 0.05 or less was considered as statistically significant. Statistical analyses were performed with SPSS for Windows (SPSS version 25.0; IBM Corp., Armonk, NY, USA), and graphics were generated using MedCalc for Windows (MedCalc version 19.0; MedCalc Software, Ostend, Belgium).

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Table 1. Demographic, clinical, and laboratory features of patients who were seronegative at baseline according to their vaccines (*n* = 68)

Characteristics	BNT162b2 (*n* = 38)	CoronaVac (*n* = 30)	*p* value
Male sex, *n* (%)	23 (60.5)	16 (53.3)	0.552
Age, mean ± SD, years	51.6±11.1	50.6±17.1	0.778
Primary kidney disease, *n* (%)			
Hypertension	13 (34.2)	6 (20)	0.073
Diabetes mellitus	11 (28.9)	5 (16.7)	
Polycystic kidney disease	1 (2.6)	7 (23.3)	
Glomerulonephritis	2 (5.3)	2 (6.7)	
Others or unknown	11 (28.9)	10 (33.3)	
Comorbidities, *n* (%)			
Diabetes mellitus	13 (34.2)	8 (26.7)	0.504
Hypertension	29 (76.3)	17 (56.7)	0.085
COPD	6 (15.8)	2 (6.7)	0.246
Coronary artery disease	14 (36.9)	7 (23.3)	0.231
Heart failure	10 (26.3)	1 (3.3)	0.011
Cerebrovascular disease	3 (7.9)	1 (3.3)	0.427
Cancer	3 (7.9)	0 (0)	0.115
Chronic liver disease	2 (5.3)	1 (3.3)	0.700
Autoimmune and/or autoinflammatory disorders	5 (13.2)	4 (13.3)	0.983
Medications, *n* (%)			
ACE inhibitors	3 (7.9)	3 (10)	0.761
Angiotensin receptor blockers	2 (5.3)	0 (0)	0.202
Calcium channel blockers	13 (34.2)	12 (40)	0.623
Beta blockers	14 (36.9)	11 (36.7)	0.988
Antiplatelets	18 (47.4)	14 (46.7)	0.954
Anticoagulants	18 (47.4)	9 (30)	0.146
Erythropoietin	28 (73.7)	19 (63.3)	0.359
Intravenous iron	20 (52.6)	22 (73.3)	0.081
Intravenous vitamin D or analogues	24 (63.2)	16 (53.3)	0.414
Calcium containing phosphate binders	24 (63.2)	21 (70)	0.554
Lanthanum carbonate	2 (5.3)	0 (0)	0.202
Cinacalcet	6 (15.8)	6 (20)	0.651
Insulin	7 (18.4)	7 (23.3)	0.619
Statins	4 (10.5)	1 (3.3)	0.259
Dialysis duration, median (IQR), years	5 (3–9.5)	3.3 (1.5–7.3)	0.124
AV fistula as the vascular access, *n* (%)	34 (89.4)	19 (63.3)	0.010
Thrice weekly hemodialysis, *n* (%)	37 (97.3)	29 (96.7)	0.865
Weight, mean ± SD, kg	67.4±15.3	68.6±14.6	0.742
Kt/V, median (IQR)	1.64 (1.5–1.94)	1.76 (1.48–1.99)	0.608
URR, mean ± SD, %	75.7±7.2	76.6±7	0.581
Surface area of dialysis membranes, median (IQR), m^2	1.8 (1.6–1.9)	1.8 (1.7–1.9)	0.512
Average UF volume per session, median (IQR), L	2.7 (2–3.8)	2.9 (2–3.5)	0.960
Residual urine output, median (IQR), mL/day	150 (100–500)	300 (100–800)	0.482
Serum urea*, mean ± SD, mg/dL	120.9±31.2	120.9±28.5	0.997
Serum creatinine*, mean ± SD, mg/dL	7.9±2.5	7.7±1.7	0.710
Sodium*, mean ± SD, mmol/L	138.8±2.9	138.9±2.9	0.905
Potassium*, mean ± SD, mmol/L	5.2±0.5	4.8±0.7	0.008
Calcium, mean ± SD, mg/dL	8.7±0.9	8.8±0.7	0.628
Phosphorus, mean ± SD, mg/dL	4.9±1.3	5±1.1	0.996
Parathormone, median (IQR), pg/mL	411 (261–651)	487 (319–770)	0.429
Albumin, mean ± SD, g/dL	4±0.4	3.8±0.4	0.068
ALT, median (IQR), U/L	10 (7–19)	9.9 (7–13.2)	0.561
Ferritin, median (IQR), ng/mL	670 (465–909)	464 (215–901)	0.126
CRP, median (IQR), mg/L	4.5 (2.3–14.6)	7.3 (4.5–18.4)	0.149

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Table 1 (continued)

Characteristics	BNT162b2 (n = 38)	CoronaVac (n = 30)	p value
Hemoglobin, mean ± SD, g/dL	11.3±1.3	10.8±2.1	0.211
White blood cells, mean ± SD, per mm^3	7,100±2,358	6,537±2,004	0.301
Neutrophils, median (IQR), per mm^3	4,200 (3,718–5,398)	4,085 (3,255–5,678)	0.525
Lymphocytes, mean ± SD, per mm^3	1,471±458	1,483±655	0.928

ACE, angiotensin-converting enzyme; ALT, alanine aminotransferase; AV, arteriovenous; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; IQR, interquartile range; SD, standard deviation; URR, urea reduction ratio; UF, ultrafiltration. * Before the dialysis session.

Table 2. Serum anti-SARS-CoV-2 spike IgG levels of patients who were seronegative at baseline according to their vaccines (n = 68)

Anti-SARS-CoV-2 spike IgG, AU/mL	BNT162b2 (n = 38)	CoronaVac (n = 30)	p value
1 month after two doses			
Seropositivity, n (%)	27/29 (93.1)	22/25 (88)	0.519
Quantitative levels, median (IQR)	3,826.9 (814.3–8,997.5)	311.1 (71.8–1,194.4)	<0.001
3 months after two doses			
Seropositivity, n (%)	27/28 (96.4)	18/23 (78.3)	0.045
Quantitative levels, median (IQR)	1,289.6 (687.6–4,275.7)	125.7 (52.9–947.8)	0.001

IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Results

Baseline Characteristics of Patients

In 8 participating centers, 1,350 prevalent patients undergoing MHD were screened for the study and 293 of them were found to be eligible. Of these patients, 132 patients (45%) chose to receive vaccination. At least 2 serum samples including the one at baseline were collected from 95 patients. Three patients who suffered from COVID-19 before the sampling at 1 month were excluded. Twenty-four (26%) of 92 were seropositive at baseline, hence were considered to have recovered from COVID-19 and separately analyzed. Flowchart of the study is shown in Figure 1.

Overall 68 seronegative patients at baseline were included. Thirty-nine (57.4%) were male, and mean age was 51.2 ± 13.9 years. Hypertension (27.9%) and diabetes mellitus (23.5%) were the leading causes of primary kidney diseases, followed by autosomal dominant polycystic kidney disease (11.8%) and glomerulonephritis (5.9%). Primary disease was unknown in 13 patients (19.1%), and remaining causes were as follows: AA amyloidosis (n = 2), congenital hypoplastic kidneys (n = 1), drug-induced kidney failure (n = 1), ischemic nephropathy following acute coronary syndrome (n = 1), neurogenic bladder due to spina bifida (n = 1), urolithiasis (n = 1), and vesicoureteral reflux (n = 1).

BNT162b2 and CoronaVac were administered in 38 (55.9%) and 30 (44.1%) patients, respectively. Heart failure was more common in BNT162b2 (26.3%) as compared to CoronaVac (3.3%, p = 0.011). Vascular access was arteriovenous fistula in 89.4% and 63.3% of patients in BNT162b2 and CoronaVac groups, respectively (p = 0.010). Serum potassium levels before dialysis were higher in BNT162b2 (p = 0.008), as well. Remaining baseline demographic, clinical, and laboratory features were comparable between groups (Table 1). Time spent between two doses was 6 (6–6.25) weeks in BNT162b2 and 4 (4–4.25) weeks in CoronaVac groups (p < 0.001).

Serum Anti-SARS-CoV-2 Spike IgG Levels

One month after completing two doses, seropositivity was 93.1% (27/29) and 88% (22/25) in BNT162b2 and CoronaVac groups, respectively (p = 0.519). However, quantitative antibody levels were significantly higher in BNT162b2 (3,826.9 [814.3–8,997.5] AU/mL) than CoronaVac (311.1 [81.8–1,194.4] AU/mL, p < 0.001). At 3 months,

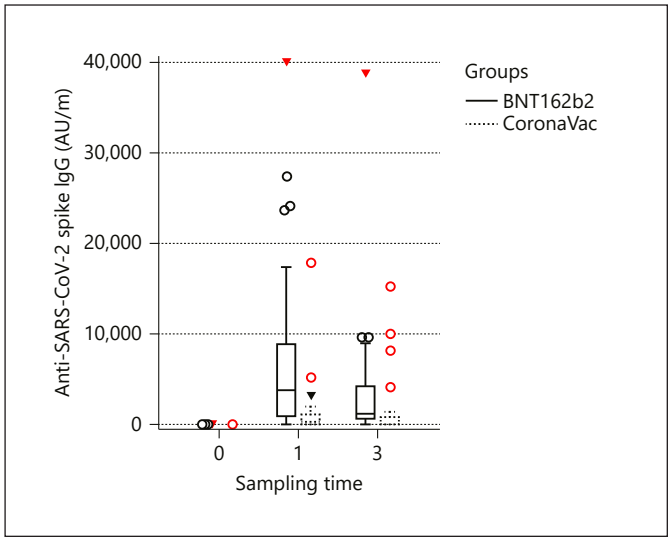


Fig. 2. Anti-SARS-CoV-2 spike IgG levels (AU/mL) before (0), 1 month (1), and 3 months (3) after vaccination with two-dose regimen in seronegative patients at baseline (n = 68).

seropositivity remained high in BNT162b2 (27/28, 96.4%) when compared to CoronaVac (18/23, 78.3%; p = 0.045). Antibody levels were significantly higher in BNT162b2, as well (p = 0.001) (Table 2) (Fig. 2).

Seven patients in CoronaVac group received a booster 14.3 ± 1.5 weeks after the second dose. As boosters, BNT162b2 and CoronaVac were chosen by 3 and 4 patients, respectively. Six patients (85.7%) were seropositive at 1 month after the second dose with a median antibody level of 72.1 (50.3–196.1) AU/mL of 7 patients. At 3 months, 3 out of 4 patients remained seropositive (63.1 [18.2–82.5] AU/mL) and serum samples could not be obtained in 3 patients. One month after the booster, all patients became seropositive and median antibody level was 719.2 (251.5–4,761.2) AU/mL.

Breakthrough COVID-19

In total, 5 patients (7.4%) experienced breakthrough COVID-19 23 ± 3.4 weeks after the second dose. Four patients (80%) were vaccinated with CoronaVac, two of whom remained seronegative after vaccination even though one patient had a booster with BNT162b2. All patients recovered well without any known sequelae.

Adverse Events

AEs were more common in BNT162b2 group. After the first dose, 16 patients (42.1%) in BNT162b2 and 1 patient (3.3%) in CoronaVac had AEs (p < 0.001), most of which were injection site pain. Following the second dose, 20 patients (52.6%) in BNT162b2 had similar AEs, as well (p < 0.001). There were no serious AEs (online suppl. Table S1; for all online suppl. material, see www.karger.com/doi/10.1159/000528170).

Linear Regression Model

Since antibody levels of the patients in both groups were more robust at 1 month after vaccination, we evaluated the factors in relation to the humoral response at this time. Final multiple linear regression model revealed that only vaccine choice (BNT162b2) was related to the humoral response (β = 0.272, p = 0.038) (Table 3).

Seropositive Patients at Baseline

In total, 24 seropositive patients at baseline were included. Fifteen (62.5%) were male, and median age was 54 (44–60.8) years. Hypertension (41.7%) and diabetes mellitus (29.2%) were the leading causes of primary kidney diseases, followed by glomerulonephritis (8.3%). Primary kidney disease was unknown in 1 patient, and remaining causes were as follows: autosomal dominant polycystic kidney disease (n = 1), congenital hypoplastic kidneys (n = 1), ischemic nephropathy following valve replacement surgery (n = 1), and preeclampsia (n = 1).

BNT162b2 and CoronaVac were administered in 14 (58.3%) and 10 (41.7%) patients, respectively. Baseline demographic, clinical, and laboratory features were comparable between groups (online suppl. Table S2). Time spent between two doses was 6 (5.5–7) weeks in BNT162b2 and 4 (4–5.25) weeks in CoronaVac groups (p = 0.023).

Quantitative antibody levels at baseline were higher in CoronaVac group (1,030.6 [180.4–1,523.3] AU/mL) compared to BNT162b2 group (460.9 [94.8–679.5] AU/mL), yet this difference was not significant (p = 0.069). Of 24 patients, 19 (10 in BNT162b2 and 9 in CoronaVac) and 20 patients (12 in BNT162b2 and 8 in CoronaVac) had serum samples at 1 and 3 months after vaccination, respectively. All patients with sera remained seropositive throughout the 3-month period. At 3 months, antibody levels were significantly higher in BNT162b2 group (10,105.8 [4,250.3–37,559.9] AU/mL) than CoronaVac group (1,407.4 [397.1–2,075.8] AU/mL, p < 0.001) (online suppl. Table S3; online suppl. Fig. S1). One patient in CoronaVac group received a CoronaVac booster 13 weeks after the second dose. Median antibody level increased from 848.6 AU/mL at 1 month after two doses to 1,157.2 AU/mL 1 month after the booster. None of the seropositive patients at baseline experienced COVID-19 after vaccination. Antibody levels were significantly higher at both 1 month and 3 months after vaccination when compared to seronegative patients at baseline (p = 0.001 for both).

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Table 3. Multiple linear regression model of the factors related to the antibody levels at 1 month after vaccination in patients who were seronegative at baseline ($n = 68$)

Variables	B	SE	β	*p* value
Age	−0.010	0.010	−0.131	0.335
Male sex	0.062	0.275	0.031	0.822
Comorbidities				
Heart failure	−0.144	0.424	−0.050	0.737
Cancer	0.804	1.221	0.113	0.515
Medications				
ACE inhibitors	0.732	0.403	0.221	0.077
Anticoagulants	0.469	0.261	0.223	0.080
Statins	0.981	0.521	0.235	0.067
Weight	−0.012	0.011	−0.159	0.278
Surface area of dialysis membranes	−0.938	0.694	−0.199	0.185
Potassium	0.177	0.203	0.115	0.389
Albumin	0.098	0.315	0.040	0.759
ALT	−0.001	0.017	−0.011	0.951
Ferritin	<0.001	<0.001	0.202	0.176
BNT162b2 as the vaccine	0.528	0.245	0.272	0.038

Variables with a p value <0.10 in simple linear regression were selected for multiple linear regression model. Age and sex were also included. Log_{10}-transformed antibody levels 1 month after two doses of the vaccines were the dependent variable. $R^2 = 0.582$ and adjusted $R^2 = 0.428$. ACE, angiotensin-converting enzyme; ALT, alanine aminotransferase; SE, standard error.

AEs were again more common in BNT162b2 group. After the first dose, 5 patients (35.7%) in BNT162b2 while no patients in CoronaVac had AEs ($p = 0.034$), most of which were injection site pain and myalgia. Following the second dose, 7 patients (50%) in BNT162b2 and 1 patient (10%) in CoronaVac experienced AEs, as well ($p = 0.040$). No serious AEs were recorded (online suppl. Table S4).

Discussion

In the beginning of a development of new pharmaceutical agents like drugs and vaccines, patients with CKD are generally excluded from trials; hence, observational data after application of these agents become quite important. Although various articles have reported humoral and cellular immune responses after vaccination for SARS-CoV-2 in patients undergoing MHD [8, 15], long-term data on inactivated vaccines are hard to come by in this population [12, 13]. We found that both BNT162b2 and CoronaVac induced humoral responses in naïve patients undergoing MHD, and these responses were more robust and durable for 3 months after BNT162b2. Also, we demonstrated that both vaccines created high antibody levels in patients who were seropositive at baseline.

Patients with CKD generally generate a reduced immunological response to various stimuli. Different aspects of immune system are affected by uremia and consequent metabolic disturbances, including but not limited to impaired function of innate immunity, reduced antigen presenting of macrophages and dendritic cells to T and B cells, disrupted T-cell maturation, poor memory B-cell response, and decreased antibody production [16, 17]. Seroconversion rates after vaccination were diminished in patients with kidney disease [17]. For instance, median humoral response rate to standard 3-dose recombinant hepatitis B vaccine was 64% in patients undergoing MHD compared to 90–95% in healthy population [16]. Moreover, those responses were found out to be transient [18]. On the other hand, recent evidence also suggests that vaccines for SARS-CoV-2 could induce robust cellular and humoral responses in patients undergoing MHD [19–26]. We showed that both BNT162b2 and CoronaVac elicited good humoral responses in a naïve MHD population, yet the antibody levels started to wane over time. Breakthrough infections were quite low (7.4%) and mostly seen in CoronaVac group. Seropositive patients at baseline produced more robust antibody levels at any time point compared to naïve patients as expected [27].

mRNAs are recognized by various pattern recognition receptors, thereby inducing innate and consequently adaptive immune responses [28]. mRNA-based vaccines

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were recently developed and firstly used for COVID-19 with a great success [5, 29, 30]. An immunogenicity analysis revealed better response rates with an mRNA vaccine compared to an inactivated vaccine in health care workers [31]. We demonstrated that it produced more robust and durable antibody responses against the virus in MHD patients, as well.

Humoral responses to vaccines in patients undergoing MHD tend to wane rapidly which can be undetectable in up to 40% of patients after a year [16]. Therefore, a booster dose can be particularly useful in this population which was demonstrated again for hepatitis B with a 4-dose vaccine regimen producing better seroconversion rates [16, 18]. In this study, 7 patients who were initially vaccinated with CoronaVac had a booster injection. One month after the booster, all patients showed robust humoral responses. Of course, number of patients in this group was too low to draw firm conclusions but the results were in line with previous findings [21, 32, 33]. Despite the limited number of patients with boosters, considering the previous data suggesting that overall decay trajectory of humoral responses is similar between patients undergoing MHD and healthy population, we think that booster doses will elicit robust humoral responses in this susceptible population, as well [34]. Beyond booster regimens, higher vaccine doses might elicit better responses like previous examples [18], whereas no results have been published for SARS-CoV-2 so far.

We observed that AEs were mild after both BNT162b2 and CoronaVac injections, but more frequent with BNT162b2. Injection site pain was the most common AE followed by myalgia. No patients experienced serious AEs including myocarditis. Our findings regarding the safety of these vaccines were in line with the previous reports [5, 6].

Only half of the eligible patients in our centers decided to get vaccinated during the study period, which was an alarming but maybe an overestimated finding. Most of the patients who opted for a SARS-CoV-2 vaccine started their vaccination schedules before the study enrollment. Remaining patients might have mostly represented a hesitant niche. Holt and colleagues reported a much lower but still an important level of hesitancy (20%) for the vaccination [11]. Scientific community must overcome this barrier considering the future risk of pandemics.

Our study has suffered from several limitations. First of all, we reported only 3-month data of humoral responses. Evolution of these responses over a longer period would have been nice to follow, although booster injection schedule starting after 3 months could have implicated the results. Second, we included a moderate number of patients since a lot of patients got the first dose of vaccines before the enrollment. Third, our study lacked a healthy control group. Fourth, cell-mediated immune responses were not the subject of our investigation.

On the other hand, the study has various strengths. It was performed as a multicenter prospective study. To the best of our knowledge, this is the first report comparing the humoral responses of an inactivated vaccine with an mRNA-based vaccine for SARS-CoV-2 with a longitudinal design in MHD patients.

In conclusion, BNT162b2 and CoronaVac induced humoral responses in naïve patients undergoing MHD, which were more robust and durable for 3 months after BNT162b2. Both vaccines created high antibody levels in patients who were seropositive at baseline.

Statement of Ethics

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee at which the studies were conducted (IRB approval number 2021-9/2) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Conflict of Interest Statement

The authors declare no competing interests.

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Author Contributions

Safak Mirioglu participated in data collection, data analyses, and manuscript preparation. Rumeyza Kazancioglu participated in study design and data collection. Egemen Cebeci, Necmi Eren, Tamer Sakaci, Selma Alagoz, Murat Tugcu, Serhan Tuglular, and Nurhan Seyahi participated in data collection. Bilge Sumbul carried out serologic tests. Savas Ozturk participated in study design, data analyses, and manuscript preparation. All authors approved the final version to be submitted.

Data Availability Statement

Deidentified data are available upon reasonable request.

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