Immune response after COVID-19 vaccination among patients with chronic kidney disease and kidney transplant

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ABSTRACT

Background: Vaccination of patients with chronic kidney disease (CKD) and kidney transplants (KTs) may achieve a less robust immune response. Understanding such immune responses is crucial for guiding current and future vaccine dosing strategies.

Methods: This prospective, observational study estimated the immunogenicity of humoral and cellular responses of two SARS-CoV-2 vaccines in different patient groups with CKD compared with controls. Secondary outcomes included adverse events after vaccination and the incidence of COVID-19 breakthrough infection, including illness severity.

Results: In total, 212 patients received ChAdOx1 nCoV-19 (89.62 %) or inactivated vaccines (10.38 %).The antibody response against the S protein was analyzed at T0 (before the first injection), T1 (before the second injection), and T2 (12 weeks after the second injection). Seroconversion occurred in 92.31 % of controls at T2 and in 100 % of patients with CKD, 42.86 % undergoing KT, 80.18 % of hemodialysis (HD), and 0 % of patients undergoing continuous ambulatory peritoneal dialysis (CAPD) at T2 of the ChAdOx1 nCoV-19 vaccine. Neutralizing antibody levels by surrogate virus neutralization test were above the protective level at T2 in each group. The KT group exhibited the lowest neutralizing antibody and T cell response. Blood groups O and vaccine type were associated with good immunological responses. After the first dose, 14 individuals (6.6 out of the total population experienced COVID-19 breakthrough infection.

Conclusion: Immunity among patients with CKD and HD after vaccination was strong and comparable with that of healthy controls. Our study suggested that a single dose of the vaccine is not efficacious and delays may result in breakthrough infection. Some blood groups and types of vaccine can affect the immune response.

1. Introduction

Patients with chronic kidney disease (CKD), including kidney transplant (KT) recipients, and those on dialysis represent a special subgroup of patients requiring protection during the severe coronavirus disease 2019 (COVID-19) pandemic [1,2]. Patients with CKD usually have a compromised immune response [3,4], require higher dosages of vaccine and more frequent dosing because the vaccine response is short lived and achieves a lower response, especially among patients undergoing dialysis [5,6].

Related reports of vaccination among patients with CKD mainly considered mRNA vaccines [8,7]. Recent reports describing seroconversion rates among patients undergoing dialysis receiving two doses of the BNT 162b2 vaccine (Pfizer BioNtech) were lower than those of controls [9,10]. One study reported a weak antibody response of patients with HD to the viral vector COVID-19 vaccine [11]. In Thailand, the main vaccines available are Coronavac (Sinovac Life Science, Beijing, China), BBIBP-Cor V vaccine (Sinopharm) and ChadOx1 nCoV-19 (Oxford-Astra Zeneca). Zhang et al. conducted a pilot, prospective study to survey the safety and humoral response to inactivated SARS-CoV-2 vaccine among 45 patients with CKD receiving a 2-dose immunization of inactivated (Sinovac and Sinopharm). They showed that the majority (84 %) of patients with CKD acquired detectable neutralizing antibody lower than those of controls [12]. Bruminhent et al. studied immune responses among 31 patients with KT, 28 with PD, 31 with HD and 16 controls with two-dose inactivated SARS-CoV-2 vaccine (V2) and a third dose of ChAdOx1 nCoV-19 vaccine (V3) at 1–2 months after V2. The anti-receptor binding domain antibody levels significantly increased from V2 across all groups (p < 0.05). Seroconversion and
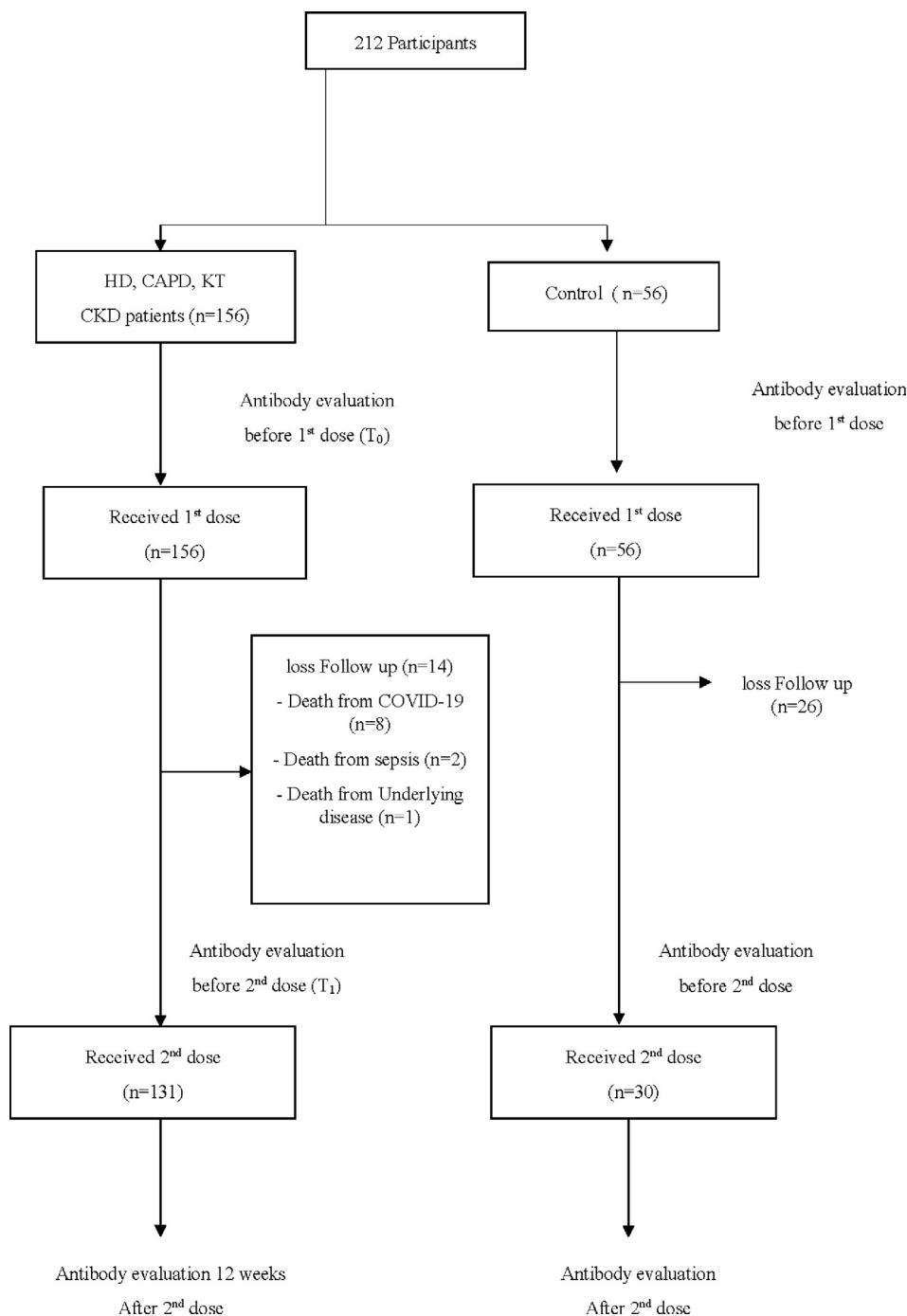
Fig. 1. Study flowchart.

neutralization positivity rates were impaired among patients with KT in contrary to the other groups [13]. This study aimed to measure the antibody and cellular responses among patients with CKD, including those undergoing dialysis therapy and kidney transplantation, and to monitor the adverse events (AEs) after the first and second doses of vaccination. The incidence rate of SARS-CoV-2 postvaccination was also observed.

2. Materials and methods

This prospective cohort study included four different patient groups: patients with CKD, those on hemodialysis (HD) and contin-

uous ambulatory peritoneal dialysis (CAPD), recipients of KT, and a control group without kidney failure from the Faculty of Medicine, Vajira Hospital, Navamindradhiraj University. Participants were enrolled between July and December 2021. The inclusion criteria were CKD stages 3–5 (eGFR $\leq$ 60 mL/min/1.73 m^3), patients with stage 5 CKD undergoing HD, CAPD and KT > 3 months. The healthy control group consisted of volunteer healthcare workers that had eGFR $\geq$ 60 mL/min/1.73 m^3. Participants in every group were 18–90 years old. Every participant received the same vaccine type in both first and second doses. The exclusion criteria included allergy to the components of the vaccines, inability to receive the vaccine according to their schedule, fever or concomitant serious illnesses and side effects from the first dose of vaccination. Patients

Table 1
Baseline characteristics of patients.

	Overall (n = 212)		Control (n = 55)		CKD (n = 12)		KT (n = 7)		HD (n = 134)		CAPD (n = 4)		P-value
	n	n (%)	n	n (%) |	n	n (%)	n	n (%)	n	n (%)	n	n (%)	
Sex													0.159[a]
M		104 (49.06)		22 (40.00)		3 (25.00)		4 (57.14)		73 (54.48)		2 (50.00)	
F		108 (50.94)		33 (60.00)		9 (75.00)		3 (42.86)		61 (45.52)		2 (50.00)	
Age (years) (mean ± SD)	208	54.8 ± 16.07	52	46.69 ± 17.65	12	63.08 ± 13.66	7	50.86 ± 11.11	133	57.34 ± 14.84	4	58 ± 11.66	<0.001[b]
Weight (kg) (mean ± SD)	205	62.76 ± 14.49	51	64.3 ± 13.89	12	57.4 ± 15.43	7	71.39 ± 14.8	131	61.97 ± 14.44	4	69.75 ± 16.9	0.198[b]
Height (cm) (mean ± SD)	205	162.08 ± 9.31	51	163 ± 9.04	12	158.58 ± 9.86	7	165.29 ± 11.43	131	161.85 ± 9.34	4	162.5 ± 7.14	0.544[b]
BMI (kg/m^2) (mean ± SD)	205	23.75 ± 4.49	51	24.12 ± 4.35	12	22.52 ± 3.84	7	26.13 ± 5.58	131	23.52 ± 4.53	4	26.14 ± 4.38	0.322[b]
Dialysis vintage (year) [median (IQR)]		-0		-0 0		-0 -0	7	9.83 (5.08–20.5)	124	3.04 (1.42–5.29)	3	1.58 (0.58–2.92)	
Kidney disease													<0.001[a]
No		49 (23.9)		46 (95.83)		0		1 (14.29)		2 (1.49)		0	
Yes		156 (76.1)		2 (4.17)		12 (100.00)		6 (85.71)		132 (98.51)		4 (100.00)	
Diabetes mellitus													<0.001[a]
No		144 (70.59)		45 (95.74)		7 (58.33)		7 (100)		82 (61.19)		3 (75)	
Yes		60 (29.41)		2 (4.26)		5 (41.67)		0 (0)		52 (38.81)		1 (25)	
Heart disease													0.013[a]
No		173 (84.80)		46 (97.87)		11 (91.67)		6 (85.71)		106 (79.1)		4 (100.00)	
Yes		31 (15.20)		1 (2.13)		1 (8.33)		1 (14.29)		28 (20.9)		–	
Hypertension													<0.001[a]
No		98 (48.04)		43 (91.49)		5 (41.67)		3 (42.86)		46 (34.33)		1 (25.00)	
Yes		106 (51.96)		4 (8.51)		7 (58.33)		4 (57.14)		88 (65.67)		3 (75.00)	
Lung disease													NA
No		204 (100.00)		47 (100.00)		12 (100.00)		7 (100.00)		134 (100.00)		4 (100.00)	
Yes		0		0		0		0		0		0	
Liver disease													NA
No		204 (100.00)		47 (100.00)		12 (100.00)		7 (100.00)		134 (100.00)		4 (100.00)	
Yes		0		0		0		0		0		0	
Cancer													0.554[a]
No		200 (98.04)		45 (95.74)		12 (100.00)		7 (100.00)		132 (98.51)		4 (100.00)	
Yes		4 (1.96)		2 (4.26)		0		0		2 (1.49)		0	
Blood group													0.842[a]
A		40 (19.70)		11 (23.4)		0		2 (28.57)		26 (19.40)		1 (25.00)	
B		66 (32.51)		14 (29.79)		5 (45.45)		1 (14.29)		44 (32.84)		2 (50.00)	
AB		21 (10.34)		5 (10.64)		2 (18.18)		1 (14.29)		13 (9.70)		–	
O		76 (37.44)		17 (36.17)		4 (36.36)		3 (42.86)		51 (38.06)		1 (25.00)	
BUN [median (IQR)]		45 (27–59)		14 (11–16.5)		27 (23.5–36.5)		21 (17–33)		51 (37–65)		36 (30–55)	<0.001[c]
Creatinine [median (IQR)]		7.83 (3.37–10.3)		0.75 (0.64–0.9)		1.63 (1.23–2.02)		1.28 (1.04–1.86)		8.91 (7–11.4)		10.1 (6.84–11.4)	<0.001[c]
eGFR [median (IQR)]		6 (4.54–11)		97.9 (87.3–100.8)		32 (25–47)		57 (39–65)		5 (4–7)		5 (4–9)	<0.001[c]
CKD Staging													
G1 (≥90)		17 (10.43)		16 (72.73)		0		0		0		0	
G2 (60–89)		8 (4.91)		6 (27.27)		1 (9.09)		2 (40.00)		0		0	
G3a (45–59)		4 (2.45)		0		3 (27.27)		1 (20.00)		0		0	
G3b (30–44)		4 (2.45)		0		2 (18.18)		1 (20.00)		0		0	
G4 (15–29)		4 (2.45)		0		3 (27.27)		1 (20.00)		0		0	
G5 (<15)		126 (77.30)		0		2 (18.18)		0		122 (100)		3 (100.00)	
Hb [median (IQR)]		10.7 (9.3–12.5)		13.25 (12.6–14.05)		11.9 (11.4–12.05)		11.5 (11.5–12.5)		9.95 (8.7–11.2)		9.4 (7.9–11.3)	<0.001[c]
Hct [median (IQR)]		33.1 (29–38.5)		40.35 (38.35–41.85)		36.45 (34.35–37.95)		38 (35.3–39.5)		31.1 (27.9–34.4)		28 (25.1–34.5)	<0.001[c]
WBC [median (IQR)]		6,275 (4,700–7,760)		6,065 (,5055–7,215)		6,250 (5,080–9,715)		7,130 (5,630–7,760)		6,295 (4,495–7,990)		6980 (6490–8570)	0.636[c]
Platelet [median (IQR)]		227,500 (180,500–286,500)		246,500 (28,900–328,500)		260,000 (185,000–2770,00)		187,000 (179,000–256,000)		220,000 (184,000–282,500)		287,000 (251000–335000)	0.544[c]
SGOT [median (IQR)]		21 (17–26)		23 (21–32)		23 (20–26)		0		19 (14–21)		0	0.008[c]
SGPT [median (IQR)]		10 (7–24)		22.5 (10–30)		14.5 (5–24)		0		10 (6–19)		0	0.033[c]
Bilirubin [median (IQR)]		0.48 (0.3–0.57)		0.57 (0.29–0.68)		0		0		0.4 (0.3–0.55)		0	0.216[c]
Albumin [median (IQR)]		4.1 (3.8–4.3)		4.3 (4.2–4.7)		4.3 (4.1–4.5)		4.2 (4.1–4.3)		4.1 (3.8–4.3)		2.6 (2.5–4.10)	0.010[c]

Table 1 (continued)

	Overall (n = 212)		Control (n = 55)		CKD (n = 12)		KT (n = 7)		HD (n = 134)		CAPD (n = 4)		P-value
	n	n (%)	n	n (%)	n	n (%)	n	n (%)	n	n (%)	n	n (%)	
Globulin [median (IQR)]		3.3 (2.9–3.7)		3.1 (2.9–3.35)		3.4 (3.2–4.1)		3 (2.6–3.3)		3.3 (2.9–3.8)		3.4 (3.3–3.6)	0.261[c]
ALP [median (IQR)]		71 (57–88.5)		65 (49–72)		104.5 (49–160)		0		74.5 (58–92.5)		0	0.369[c]
FBS [median (IQR)]		108 (93–137)		99.5 (89.5–126)		109.5 (95–130)		97 (91–101)		112 (94–139)		109 (83–362)	0.585[c]
Cholesterol [median (IQR)]		158 (135–185.5)		192 (161–206)		162 (130–174.5)		181 (175–206)		154.5 (132–176)		177 (131–282)	0.015[c]
Triglyceride [median (IQR)]		98 (69–138)		91 (64–147.5)		129.5 (104–183)		96 (81–130)		98 (69–134)		47 (45–245)	0.297[c]
Uric acid [median (IQR)]		5.85 (4.85–7.4)		5.7 (3.9–7.2)		6.6 (5.7–9)		9.3 (6.4–9.7)		5.8 (4.8–7.4)		5.5 (5.1–6)	0.288[c]
Vaccine type													0.003[a]
AstraZeneca		190 (89.62)		41 (74.55)		11 (91.67)		7 (100.00)		127 (94.78)		4 (100.00)	
Sinovac		20 (9.43)		14 (25.45)		1 (8.33)		0		5 (3.73)		0	
Sinopharm		2 (0.94)		0-		0		0		2 (1.49)		0	

Chi-square test.
ALP, Alkaline phosphatase; BMI, Body mass index;CKD,Chronic kidney disease; Hb, FBS,Fasting blood sugar;Haemoglobin; Hct; HaematocriT;SGOT,Aspartate aminotransferase. SGPT,Alanine transaminase.
[a] Fisher exact test.
[b] One-way ANOVA.
[c] Kruskal-Wallis H test.

or individuals contracting COVID-19 (diagnosed via patient history and serological tests to detect the nucleocapsid [NCP] antibody) were excluded from the study. The study protocol was approved by the Vajira Ethics Committee, approval number 94/2564, and the participants were enrolled after obtaining written informed consent. This study was conducted following the principles of the Declaration of Helsinki and Good Clinical Practice. The vaccine used was authorized by the Thai Food and Drug Administration and Department of Medical Sciences. Each type of vaccine was allocated by patient's preference. Vaccine response was defined as anti-SARS-CoV-2 S1 (IgG) antibody titer ≥35.2 BAU/ml. Seroconversion means that levels of antibody titers to be significantly higher in serum of recipients after vaccination. The reference levels as detailed in Appendix.

2.1. Trial procedure

The enrolled patients received the COVID-19 vaccine according to the vaccination protocol approved in Thailand, that is, two doses of ChAdox-1 nCOV-19 vaccine, 12-week interval, Coronavac, 3-week interval or BBIBP-Cor V, 4-week interval. All participants provided a blood sample for antibody and cellular immunity measurement at the following time periods: T0 (before the first injection), T1(before the second injection) and T2 (12 weeks after the second injection). Immunogenicity analysis was performed at one and three months post-infection.

2.2. Assessment of antibody responses

We classified responses as negative anti-SARS-CoV2-NCP IgG (NCP, Euroimmun, Hausen Bernsten CO; Ltd, Germany); (index value < 0.8), borderline (index value 0.8–1.1) and positive (index value > 1.1). We chose anti-SARS-CoV2 Spike S1/receptor binding domain (RBD) IgG < 25.6 binding antibody unit/mL BAU/mL as the negative cut-off point, values between 25.6 and 35.2 were considered borderline, and levels ≥35.2 BAU/mL were considered positive. A percent inhibition (%IH) > 35 for SARS CoV2 neutralizing antibodies (NA) was considered positive, index values ranging 20–25 % IH were defined as borderline, and values <20 % were considered negative.

2.3. Determination of antibodies against SARS-CoV-2

All SARS-CoV-2 antibody assays were performed and analyzed using the EUROIMMUN Analyzer I-2P® (Euroimmun Medizinische Labordiagnostika, Lubeck, Germany) at the Central Laboratory and Blood Bank, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University. Controls and calibrators were used in the test kit for each run. The ratios of diluted serum, optical density and cut-off values in this study were used according to the manufacturer's instructions.

2.4. Detecting anti-SARS-CoV-2 nucleocapsid protein IgG

The IgG antibody against the nucleocapsid protein of SARS-CoV-2 in plasma samples was detected using an enzyme-linked immunosorbent assay (ELISA) (Euroimmun, Lübeck, Germany) (see Appendix).

2.5. Quantitative determination of anti-SARS-CoV-2 S1 (IgG)

The anti-SARS-CoV-2 S1/ (RBD) IgG QuantiVac ELISA IgG (Euroimmun, Lübeck, Germany) Kit was used for quantitative determination of human antibodies against immunoglobulin class IgG against the S1 domain of the SARS-CoV-2 spike protein of in serum samples (see Appendix).

2.6. Determining neutralizing antibodies against SARS-CoV-2

To detect the presence of NA against the S1 receptor-binding domain (RBD) of SARS-CoV-2 to ACE2 receptors in the plasma samples, the ELISA-based surrogate virus neutralization test was used (SARS-CoV-2 NeutraLISA (Euroimmun, Lübeck, Germany) (see Appendix).

2.7. Assessment of the T cell response by quantitative determination of interferon-γ release by SARS-CoV-2-specific T cells

Cellular immunogenicity was measured by calculating the secretion of interferon gamma (IFN-γ) using peripheral blood mononuclear cells upon SARS-Co-V2 glycoprotein stimulation and subsequent determination of released IFN-γ by ELISA (Euroimmun, Lübeck, Germany) (see Appendix).

2.8. Participants

Demographic information, including age, sex and body mass index, was obtained at the first enrolment. The vaccine type, date of vaccination, use of immunosuppressed agents, number and types of comorbidities and history of transplantation were recorded. Primary outcomes included humoral and cellular responses after COVID-19 vaccination at T0, T1 and T2, as measured by SARS-CoV2 spike S1-specific IgG antibody levels and the viral neutralization test by surrogate virus neutralization test. The percentages of responders in different cohorts (CKD, HD, CAPD and KT) were compared with the controls, within and between cohorts to define the seropositivity rate (individuals who developed detectable anti-SARS-Co-V antibodies). The secondary outcomes were rates of AEs after vaccination and the incidence of

COVID-19 breakthrough infection after vaccination, including illness severity.

2.9. Statistical analysis

The sample size calculation is provided in detail in the Appendix. Values are presented as median (interquartile range) for con-
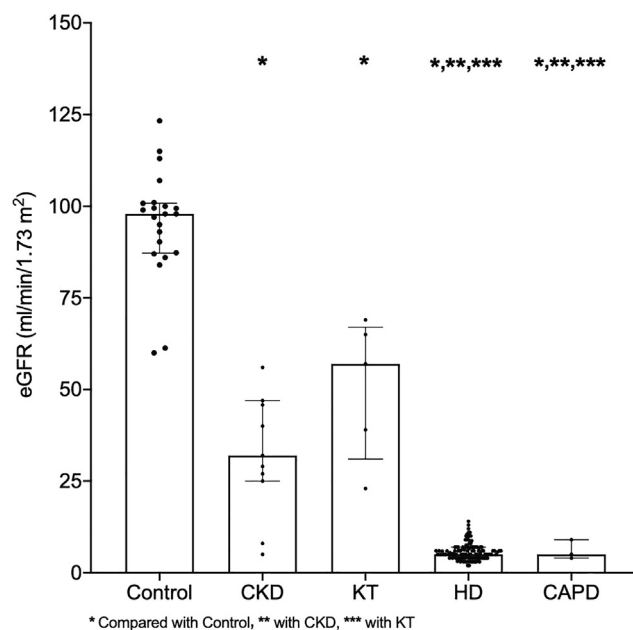

Fig. 2. Estimated glomerular filtration rate (eGFR) according to different patient groups.
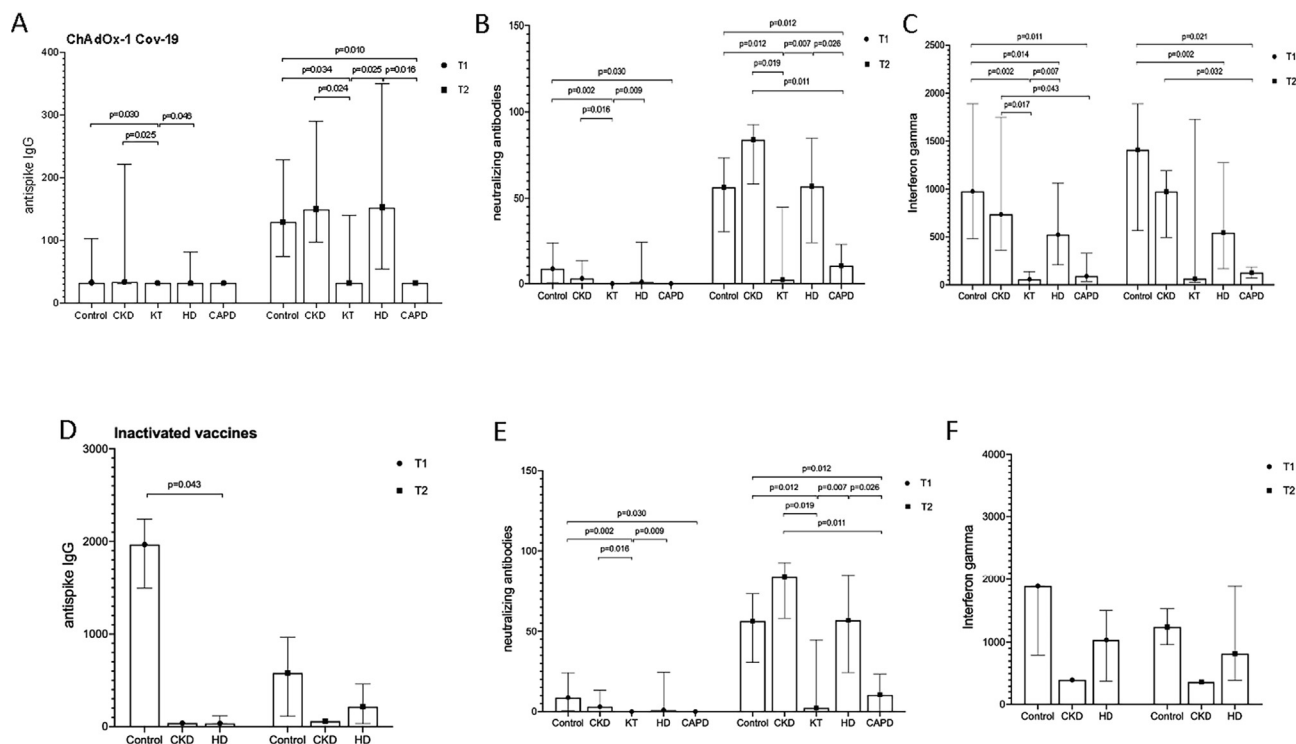
Fig. 3. (A–B) Humoral immune responses against SARS-CoV-2 was assessed by Euroimmune ELISA for (A) antispike IgG antibodies and (B) neutralizing activities level in different groups of CKD patients compared to controls receiving ChAdOx1 nCoV-19 vaccine at T1 and T2 (C) Cellular immune response was assessed by interferon-gamma levels in different groups of patients compared to controls at T1 and T2. (D–F) Humoral and cellular responses to inactivated vaccines in different groups of CKD patients compared to controls at T1 and T2.

tinuous variables. Antibody levels were compared between time-points and analyzed using the paired sample *t*-test or Wilcoxon matched-pairs signed-ranks test. Categorical variables were reported as frequencies and percentages. Proportions were compared using Fisher's exact test (or the Kruskal-Wallis test as appropriate). Correlation between two continuous parameters was calculated using Spearman's correlation. Logistic regression models were used in both univariate and multivariate analyses, and statistical significance was set at p < 0.05. Statistical analysis was
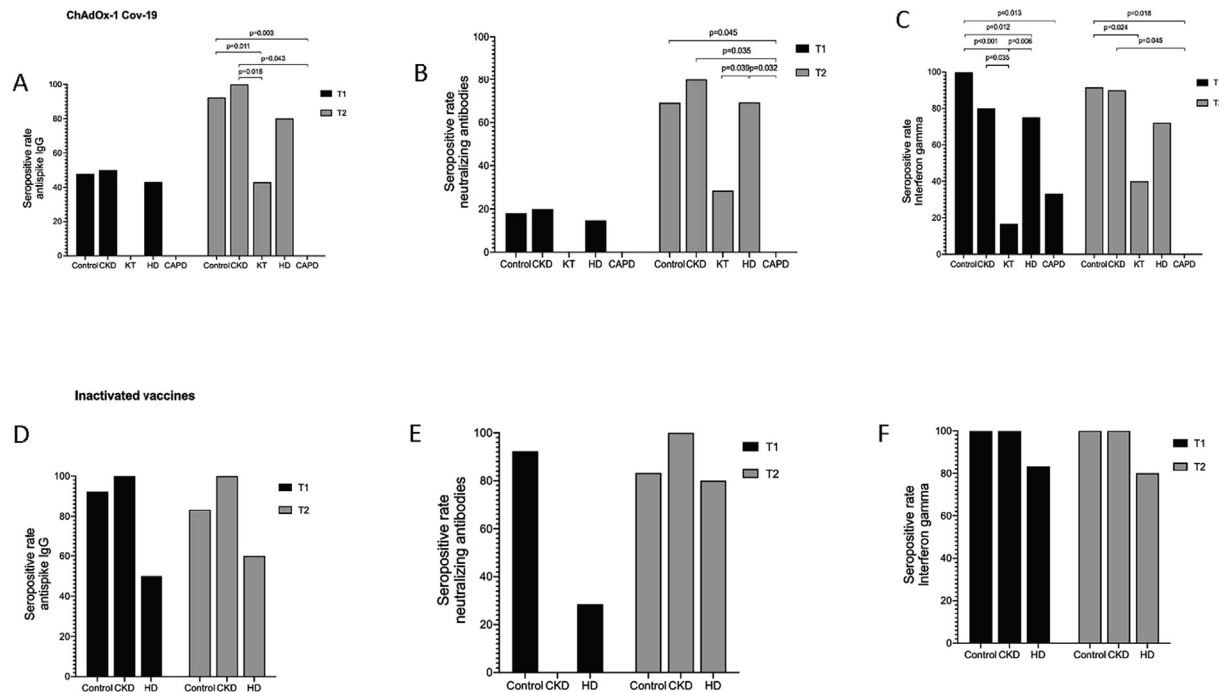
Fig. 4. (A–C) Seropositivity rates in vaccine serum samples elicited by ChAdOx1 nCoV-19. (D–F) Seropositivity rates in vaccine serum samples elicited by inactivated vaccines in different groups of patients at T1 and T2.

Table 2
Proportion of rat seroconversion of anti-spike IgG antibody response, neutralizing capacity, and gamma-interferon among patients receiving dialysis, CKD, kidney transplantation, and healthy controls after vaccination with ChAdOx1 nCoV-19 and inactivated vaccines.

	Control		CKD		KT		HD		CAPD		P-value
	n	%	n	%	n	%	n	%	n	%	
ChAdOx1 nCoV-19 vaccine											
Antispike IgG											0.153
Increase <35	5	29.41	4	40.00	4	66.67	42	40.38	3	100.00	
Increase 35+	12	70.59	6	60.00	2	33.33	62	59.62	–		
NeutraLISA											0.270
Increase <35.2	9	52.94	4	40.00	5	71.43	50	45.45	3	100.00	
Increase 35.2+	8	47.06	6	60.00	2	28.57	60	54.55	–		
Interferon											0.529
Increase ≤ 200	11	68.75	7	70.00	2	50.00	73	77.66	2	100.00	
Increase > 200	5	31.25	3	30.00	2	50.00	21	22.34	0		
Inactivated Vaccines											
Antispike IgG											0.545
Increase <35	5	100.00	1	100.00	0		3	60.00	0		
Increase 35+	0		0		0		2	40.00	0		
Neutralizing Abs											0.545
Increase <35.2	5	100.00	1	100.00	0		3	60.00	0		
Increase 35.2+	0		0		0		2	40.00	0		
Interferon											0.583
Increase ≤ 200	3	100.00	1	100.00	0		3	60.00	0		
Increase ≤ 200	0		0		0		2	40.00			

Fisher's exact test.
Significant if p <0.05.
CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; HD, haemodialysis; KT, kidney transplantation.
For quantitative determination of anti-SARS-CoV-2 S1 (IgG), samples with a ratio of<25.6 BAU/mL were interpreted as negative. Ratios of 25.6–35.2 BAU/mL was considered borderline, and a ratio ≥35.2 BAU/mL was considered positive.
For the SARS-CoV-2 neutralizing antibody, the interpreting results were as follows: % inhibition (IH) <20: Negative, % IH ≥20 to <35: Borderline % IH ≥35: positive.
For the SARS-CoV-2 interferon-gamma ELISA, the interpreting results were as follows: negative:<100 mIU/mL, Borderline: 100–200 mIU/mL, Positive: >200 mIU/mL.

performed using STATA (Version 13.0; StataCorp College Station, TX, USA).

2.10. Monitoring of adverse events

AE assessments, including vaccine and drug side effects after the first and second vaccine doses, were monitored.

3. Results

3.1. Baseline characteristics

Between June 2021 and December 2021, 212 patients with CKD at various stages and controls were vaccinated with COVID-19 vaccines, CoronaVac, BBIBP-Cor V, or ChAdOx1 nCoV-19 vaccine (AZD 1222). Totally, 31 patients (15.20 %) had underlying heart problems and none of the patients had either lung or liver diseases. Fourteen patients were lost to follow-up. Eleven patients died during the study period (COVID-19, eight;underlying diseases, two; sepsis,one:underlying disease). Finally, 212 patients (104 men, 49.06 %) with a mean age 54.8 ± 16.07 years were enrolled in the study (Fig. 1). The vaccination distribution was as follows: 190 patients (89.62 %) received ChAdOx1 nCoV-19, 20 (9.43 %) Corona-Vac and two (0.94 %) BBIBP-Cor V. One hundred and thirty-four (63.20 %) patients were undergoing HD, four (1.88 %) were undergoing CAPD and seven (3.30 %) were KT recipients, twelve (5.66 %) were nondialysis patients with CKD, and 55 (25.94 %) were the controls. The median duration of HD was 3.04 years (IQR 1.42–5.29 years). Almost all patients and the control group received the ChAdOx1 nCoV-19 vaccine being the main vaccine scheme adopted in our country at the time of the study; the baseline characteristics of the population are detailed in Table 1.

The KT recipient group revealed an average age of 50.86 ± 11. 11 years; 42.86 % were women; and median time since transplantation was 9.83 years (IQR 5.08–20.5) The maintenance immunosuppressant regimens included calcineurin inhibitors (87 %), corticosteroids (45.4 %), antimetabolites (82.4 %) and mTor inhibitors (10.4 %). The antimetabolite treatments used included mycophenolate mofetil (85.2 %), mycophenolic acid (11.5 %) and azathioprine (3.3 %). The mean age in the HD group was 57.34 ± 1 4.84 years, 45.52 % were women.Subjects in the control group were aged 46.69 ± 17.65 years and 60 % were women. Only four patients were treated with peritoneal dialysis, with a mean age of 58.00 ± 11.66 years. None of the patients had a prior or current diagnosis of COVID-19 and all tested negative for the anti-SARS-CoV-2 NCP IgG.

Diabetes is the most common cause of end-stage renal disease (ESRD). The median eGFR in the control group was 97.90 [IQR 87.30–100.80] mL/min/1.73 m^2 compared with 32.0 [IQR 25–47] mL/min/1.73 m^2 in the CKD group (p = 0.001). The median eGFR in the KT group was 57.0 [IQR 39–65] mL/min/1.73 m^2. As expected, the eGFR in the HD and CAPD groups was the lowest, with a median eGFR of 5.00 [IQR 4–9] mL/min/1.73 m^2 (Table 1, Fig. 2).

3.2. Anti-SARS-CoV-2 antibody response

Patients on HD and nondialysis patients with CKD exhibited nonsignificant different antibody responses compared with those in the control group. In the CKD group, the median antibody titer was 3.20 BAU/mL [IQR 3.2–3.2] at T0, 34.10 BAU/mL [IQR 32.00–221.70] at T1 and 150.13 BAU/mL [IQR 97.12–290.65] at T2 (Fig. 3).The antibody levels in the CAPD group at T2 were significantly lower than those in the control and HD groups (p = 0.01;

CAPD vs control, p = 0.016 CAPD vs HD). A positive antibody level was detected in only one KT recipient at T2.

Vaccine response was evaluated for 151 patients after the second dose in vaccine types. The response rate was 70.59 % in the control group of the ChAdOx1 nCoV-19 vaccine. The CKD and dialysis group had similar response rates of 60 and 59.62 % respectively. The KT group revealed a weak response of 33.33 % (Fig. 4). The CAPD group also showed a poor immunological response, with none being seropositive at T2. The NA and IFNγ seropositive rates followed a similar pattern to anti-SARS-CoV-2 antibodies with the lowest response rate in the KT and CAPD groups, and the level of immunity and response rate in the inactivated vaccine groups were satisfactory in CKD, HD, and KT groups compared with controls (Table 2).
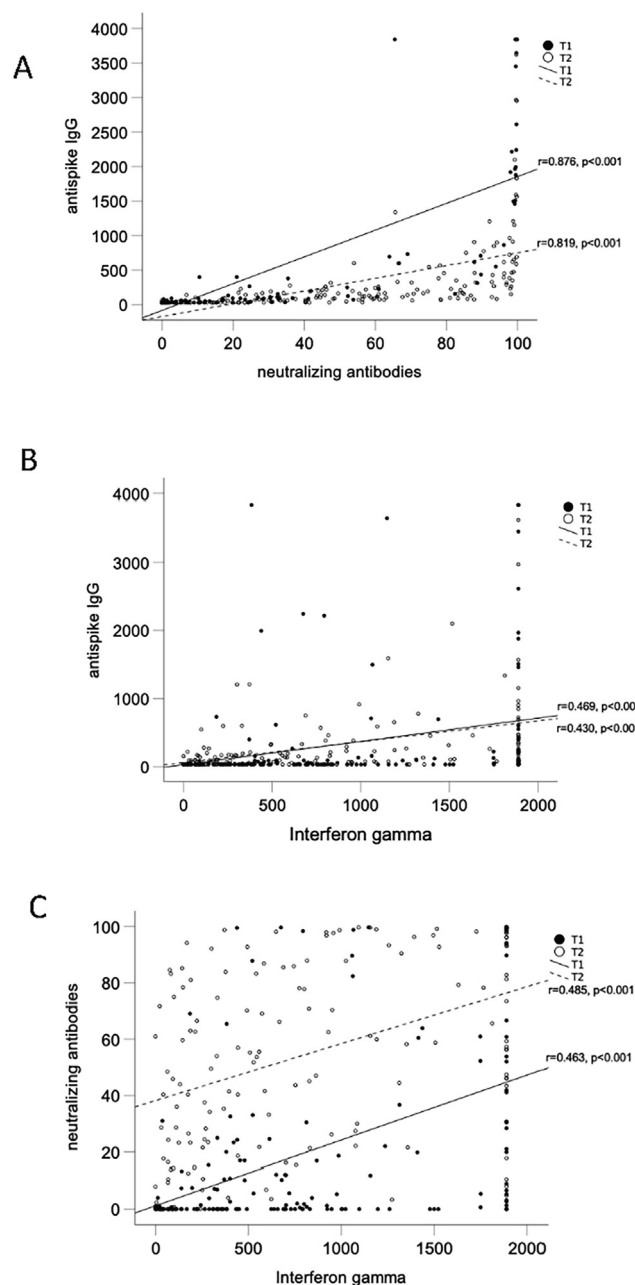

Fig. 5. (A) Correlation of anti-spike IgG levels with neutralizing antibodies. (B) Correlation of anti-spike IgG levels with interferon-gamma. (C) Correlation of neutralizing antibodies with interferon-gamma.

3.3. Neutralizing antibodies test (NA)

NA showed a good correlation with levels of anti-spike IgG antibodies at T1 and T2 (r = 0.876 at T1, r = 0.819 at T2, p <0.001) (Fig. 5).The median NA in the control group was 8.7 % [IQR 0.51– 24.24] at T1 and 56.34 % [IQR 30.61–73.47] at T2. NA levels in the CKD and dialysis groups overlapped with those of controls (Table 3). The NA level in the KT was lowest with a median level of 2.31 % [IQR 0–44.46].

Table 3
Comparison of neutralizing antibodies between different groups of patients and the control group.

	n	Median (IQR)	n	Median (IQR)	P-value
Neutralizing antibody (%Inhibition)					
Control vs CKD					
T0	30	1.1 (0–3.53)	10	0 (0–3.86)	0.336
T1	22	8.7 (0.51–24.24)	10	3.1 (0–13.36)	0.388
T2	26	56.34 (30.61–73.47)	10	83.93 (58.22–92.73)	0.148
ΔT0–T1	20	5.5 (0–16.96)	10	1.17 (0–13.36)	0.627
ΔT1–T2	17	34.33 (21.19–70.37)	10	59.07 (32.22–82.21)	0.228
Control vs KT					
T0	30	1.1 (0–3.53)	7	0 (0–7.78)	0.692
T1	22	8.7 (0.51–24.24)	7	0 (0–0)	0.002
T2	26	56.34 (30.61–73.47)	7	2.31 (0–44.76)	0.012
ΔT0–T1	20	5.5 (0–16.96)	7	0 (−7.78 to 0)	0.003
ΔT1–T2	17	34.33 (21.19–70.37)	7	2.31 (0–44.76)	0.053
Control vs HD					
T0	30	1.1 (0–3.53)	124	0 (0–0.89)	<0.001
T1	22	8.7 (0.51–24.24)	115	1.01 (0–24.59)	0.121
T2	26	56.34 (30.61–73.47)	111	56.93 (24.26–84.89)	0.906
ΔT0–T1	20	5.5 (0–16.96)	115	0.63 (0–22.54)	0.429
ΔT1–T2	17	34.33 (21.19–70.37)	110	39.33 (10.65–62.69)	0.453
Control vs CAPD					
T0	30	1.1 (0–3.53)	4	0 (0–0)	0.021
T1	22	8.7 (0.51–24.24)	3	0 (0–0)	0.030
T2	26	56.34 (30.61–73.47)	3	10.5 (0–23.3)	0.012
ΔT0–T1	20	5.5 (0–16.96)	3	0 (0–0)	0.096
ΔT1–T2	17	34.33 (21.19–70.37)	3	10.5 (0–23.3)	0.064
CKD vs KT					
T0	30	1.1 (0–3.53)	7	0 (0–7.78)	0.743
T1	22	8.7 (0.51–24.24)	7	0 (0–0)	0.016
T2	26	56.34 (30.61–73.47)	7	2.31 (0–44.76)	0.019
ΔT0–T1	20	5.5 (0–16.96)	7	0 (−7.78 to 0)	0.036
ΔT1–T2	17	34.33 (21.19–70.37)	7	2.31 (0–44.76)	0.040
CKD vs HD					
T0	30	1.1 (0–3.53)	124	0 (0–0.89)	0.394
T1	22	8.7 (0.51–24.24)	115	1.01 (0–24.59)	0.879
T2	26	56.34 (30.61–73.47)	111	56.93 (24.26–84.89)	0.120
ΔT0–T1	20	5.5 (0–16.96)	115	0.63 (0–22.54)	0.963
ΔT1–T2	17	34.33 (21.19–70.37)	110	39.33 (10.65–62.69)	0.074
CKD vs CAPD					
T0	30	1.1 (0–3.53)	4	0 (0–0)	0.156
T1	22	8.7 (0.51–24.24)	3	0 (0–0)	0.098
T2	26	56.34 (30.61–73.47)	3	10.5 (0–23.3)	0.011
ΔT0–T1	20	5.5 (0–16.96)	3	0 (0–0)	0.297
ΔT1–T2	17	34.33 (21.19–70.37)	3	10.5 (0–23.3)	0.011
KT vs HD					
T0	7	0 (0–7.78)	124	0 (0–0.89)	0.291
T1	7	0 (0–0)	115	1.01 (0–24.59)	0.009
T2	7	2.31 (0–44.76)	111	56.93 (24.26–84.89)	0.007
ΔT0–T1	7	0 (−7.78 to 0)	115	0.63 (0–22.54)	0.005
ΔT1–T2	7	2.31 (0–44.76)	110	39.33 (10.65–62.69)	0.066
KT vs CAPD					
T0	7	0 (0–7.78)	4	0 (0–0)	0.149
T1	7	0 (0–0)	3	0 (0–0)	1.000
T2	7	2.31 (0–44.76)	3	10.5 (0–23.3)	0.814
ΔT0–T1	7	0 (−7.78 to 0)	3	0 (0–0)	0.207
ΔT1–T2	7	2.31 (0–44.76)	3	10.5 (0–23.3)	0.814
HD vs CAPD					
T0	124	0 (0–0.89)	4	0 (0–0)	0.214
T1	115	1.01 (0–24.59)	3	0 (0–0)	0.084
T2	111	56.93 (24.26–84.89)	3	10.5 (0–23.3)	0.026
ΔT0–T1	115	0.63 (0–22.54)	3	0 (0–0)	0.240
ΔT1–T2	110	39.33 (10.65–62.69)	3	10.5 (0–23.3)	0.116

Mann-Whitney *U* test.
CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; HD, haemodialysis; KT, kidney transplantation.
T0: Before the first vaccination.
T1: Before the second vaccination.
T2: After T1 for 3 months.
For the SARS-CoV-2 neutralizing antibody, the interpreting results were as follows: % inhibition (IH) <20: negative, % IH ≥20 to <35: borderline, % IH ≥35: positive.

3.4. T cell responses

The median INFγ level in the CKD group was lower than that in the control group at T2 (973 mIU/mL, IQR 494.48–1191.11), while the level decreased by one half among patients on HD (median value 544.36 mIU/mL IQR 168.96–1273.58). Patients on CAPD and KT recipients indicated the lowest median INFγ value at 127.99 mIU/mL [IQR 68.46–187.52]. <50 % seropositive individuals were detected in our cohort (Tables 2 and 4).

3.5. Factors affecting the immune response

Variables significantly associated with vaccine response from multivariate regression analysis (anti-spike IgG and NA) included blood group O (OR.8.21;95 % CI,2.12–31.78; p = 0.012) (Table 5) and vaccine type (OR, 9.02; 95 % CI, 2.00–50.10; p = 0.002). The ChAdOx1 nCoV-19 vaccine was associated with higher levels of antispike IgG while the NA and IFNγ did not differ.

3.6. Sars-CoV2 infection

After the first dose, 14 patients (6.6 %) experienced break-through COVID −19 infection and 57.14 % of these patients died.

Of these, 13 (92.85 %) received only one dose of a vaccine, with a median interval of 52 [IQR 44–61] days after the first vaccination. One patient developed COVID-19 after completing the second dose on day 64. Infection in two controls was resolved uneventfully. Overall, 85.17 % of cases were in the HD group. Factors associated with SARS-CoV2 infection were male sex and blood group (p = 0.005 and p = 0.039, respectively) (Supplementary Table 1). Only one patient received an inactivated vaccine. Among the patients diagnosed with COVID-19 during follow-up, the median anti-spike IgG, NA and IFNγ levels significantly increased at 1one and three months after diagnosis, and natural immunity was robust and significantly higher than vaccine-induced immunity for as long as three months (Table 6).

3.7. Vaccine type and immune response

Of the 20 patients receiving inactivated vaccines, seven, one and 14 were in the HD, CKD and control groups, respectively. Antibodies were detected at a positive level (>35 BAU/mL) at T1 and increased progressively to a median of 217.27 [IQR 32–460] at T2 among patients with HD. NA levels were detected at low titers at T2 in both CKD and HD groups. All patients in the control group responded to the inactivated vaccine with an antibody titer above

Table 4
Comparison of interferon gamma levels between different groups of patients and the control group.

Interferon-gamma (mIU/mL)	n	Median (IQR)	n	Median (IQR)	P-value
Control vs CKD					
T1	19	975.82 (480.06–1890)	10	736.02 (358.53–1749.45)	0.345
T2	24	1409.76 (565.84–1890)	10	973 (494.48–1191.11)	0.209
ΔT1–T2	16	61.2 (0–239.38)	10	77.78 (−452.89 to 251.48)	0.711
Control vs KT					
T1	19	975.82 (480.06–1890)	6	57.1 (0–137.58)	0.002
T2	24	1409.76 (565.84–1890)	5	64.94 (25.15–1728.22)	0.088
ΔT1–T2	16	61.2 (0–239.38)	4	481.44 (−23.75 to 1391.01)	0.297
Control vs HD					
T1	19	975.82 (480.06–1890)	109	523.8 (208.25–1062.24)	0.014
T2	24	1409.76 (565.84–1890)	99	544.36 (168.96–1273.58)	0.002
ΔT1–T2	16	61.2 (0–239.38)	94	0 (8130.98 to 166.56)	0.248
Control vs CAPD					
T1	19	975.82 (480.06–1890)	3	91.5 (36.62–329.75)	0.011
T2	24	1409.76 (565.84–1890)	2	127.99 (68.46–187.52)	0.021
ΔT1–T2	16	61.2 (0–239.38)	2	63.93 (31.84–96.02)	1.000
CKD vs KT					
T1	10	736.02 (358.53–1749.45)	6	57.1 (0–137.58)	0.017
T2	10	973 (494.48–1191.11)	5	64.94 (25.15–1728.22)	0.426
ΔT1–T2	10	77.78 (−452.89 to 251.48)	4	481.44 (−23.75 to 1391.01)	0.396
CKD vs HD					
T1	10	736.02 (358.53–1749.45)	109	523.8 (208.25–1062.24)	0.472
T2	10	973 (494.48–1191.11)	99	544.36 (168.96–1273.58)	0.252
ΔT1–T2	10	77.78 (−452.89 to 251.48)	94	0 (−130.98 to 166.56)	0.834
CKD vs CAPD					
T1	10	736.02 (358.53–1749.45)	3	91.5 (36.62–329.75)	0.043
T2	10	973 (494.48–1191.11)	2	127.99 (68.46–187.52)	0.032
ΔT1–T2	10	77.78 (−452.89 to 251.48)	2	63.93 (31.84–96.02)	0.830
KT vs HD					
T1	6	57.1 (0–137.58)	109	523.8 (208.25–1062.24)	0.007
T2	5	64.94 (25.15–1728.22)	99	544.36 (168.96–1273.58)	0.341
ΔT1–T2	4	481.44 (−23.75 to 1391.01)	94	0 (−130.98 to 166.56)	0.166
KT vs CAPD					
T1	6	57.1 (0–137.58)	3	91.5 (36.62–329.75)	0.604
T2	5	64.94 (25.15–1728.22)	2	127.99 (68.46–187.52)	0.699
ΔT1–T2	4	481.44 (−23.75 to 1391.01)	2	63.93 (31.84–96.02)	1.000
HD vs CAPD					
T1	109	523.8 (208.25–1062.24)	3	91.5 (36.62–329.75)	0.072
T2	99	544.36 (168.96–1273.58)	2	127.99 (68.46–187.52)	0.130
ΔT1–T2	94	0 (−130.98 to 166.56)	2	63.93 (31.84–96.02)	0.572

Mann-Whitney *U* test.
CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; HD, haemodialysis; KT, kidney transplantation.
T0: Before the first vaccination.
T1: Before the second vaccination.
T2: After T1 for 3 months.
For the SARS-CoV-2 interferon-gamma ELISA, the interpreting results were as follows: negative: <100 mIU/mL, borderline: 100–200 mIU/mL, positive: >200 mIU/mL.

threshold values. Only 40 % of patients on HD presented positive cellular immunity as measured by INFγ compared with the 100 % response rate in controls (Table 2). Factors associated with seropositivity are shown in Supplementary Table 2.

3.8. Adverse events

Among vaccine recipients, mild-to-moderate pain at the injection site was the most commonly reported local reaction, which

Table 5
Factors affecting anti-spike IgG levels (level difference between T2 and T1) by uni-multivariable analysis.

	Crude OR (95 %CI)	P-value	Adjusted OR (95 %CI)	P-value
Type of patient				
Control	2.20 (0.33–14.73)	0.416	2.17 (0.10–45.01)	0.617
CKD	2.80 (0.36–21.73)	0.325	7.86 (0.72–86.49)	0.092
HD	2.84 (0.50–16.2)	0.239	4.74 (0.67–33.66)	0.120
CAPD	NA	NA	NA	NA
Age	1.01 (0.99–1.03)	0.552	1.01 (0.98–1.03)	0.635
Sex: M	1.36 (0.71–2.58)	0.354	1.65 (0.76–3.59)	0.203
BMI	1.04 (0.96–1.12)	0.338	1.08 (0.98–1.19)	0.104
Kidney Diseases	1.07 (0.45–2.58)	0.875	0.60 (0.04–8.93)	0.709
Heart Diseases	1.87 (0.75–4.65)	0.177	1.92 (0.65–5.62)	0.235
Hypertension	0.77 (0.40–1.47)	0.427	0.44 (0.19–1.02)	0.056
Cancer	0.39 (0.04–4.41)	0.448	0.67 (0.04–10.37)	0.773
Blood group				
A	2.80 (0.75–10.48)	0.126	4.10 (0.95–17.78)	0.059
B	2.29 (0.70–7.53)	0.173	2.87 (0.78–10.57)	0.112
O	4.40 (1.34–14.49)	0.015	8.21 (2.12–31.78)	0.002
Vaccine:	6.36 (1.33–30.54)	0.021	9.02 (1.62–50.10)	0.012

Multiple logistics regression.
Significant if p < 0.05.
BMI, body mass index; CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; HD, haemodialysis; KT, kidney transplantation.

Table 6
Comparison of immunogenicity between non-COVID-19 and COVID-19 patients.

	Non-COVID-19 (n = 198)		COVID-19 (n = 14)		P-value
	n	Median (IQR)	n	Median (IQR)	
ChAdOx-1 nCov-19 vaccine					
S1/RBD IgG (BAU/mL)					
T0	155	3.2 (3.2–3.2)	13	3.2 (3.2–3.73)	0.525
T1	145	32 (32–73.6)	6	2673.55 (865–3840)	<0.001
T2	152	130.93 (48.06–274.02)	5	2952.9 (588.28–3619.7)	0.001
ΔT0–T1	142	28.8 (28.8–62.22)	6	2667.11 (861.8–3836.8)	0.003
ΔT1–T2	135	53.2 (0–200.2)	5	−597.4 (−887.1 to 0)	0.051
Neutralizing Abs (%Inhibition)					
T0	162	0 (0–1.89)	13	0 (0–0.16)	0.571
T1	151	0.79 (0–19.76)	6	99.35 (96.12–99.73)	0.001
T2	152	55.4 (23.41–83.21)	5	99.64 (99.63–99.73)	<0.001
ΔT0–T1	149	0.41 (0–15.33)	6	97.73 (95.62–99.73)	0.001
ΔT1–T2	142	38.85 (14.31–65)	5	0.02 (−0.09 to 0.3)	0.001
Interferon gamma (mIU/mL)					
T1	143	521.24 (197.09–1062.24)	4	1890 (1706.46–1890)	0.006
T2	136	602.88 (189.02–1501.61)	4	1573.37 (1175.31–1890)	0.044
ΔT1–T2	124	18.4 (−105.52 to 202.98)	2	0 (0–0)	0.710
Inactivated vaccine					
S1/RBD IgG (BAU/mL)					
T0	7	4.58 (3.2–6.61)	1	3.2 (3.2–3.2)	0.264
T1	19	1496.9 (39–2215.1)	1	3840 (3840–3840)	0.117
T2	11	217.27 (32–776.11)	1	690.5 (690.5–690.5)	0.466
ΔT0–T1	7	28.8 (25.39–36.8)	1	3836.8 (3836.8–3836.8)	0.127
ΔT1–T2	10	0 (−1022.3 to 20)	1	−3149.5 (−3149.5 to 3149.5)	0.111
Neutralizing Abs (%Inhibition)					
T0	8	0 (0–5.12)	1	0 (0–0)	0.490
T1	20	98.18 (9.11–99.5)	1	65.43 (65.43–65.43)	0.740
T2	11	87.88 (35.31–97.7)	1	99.73 (99.73–99.73)	0.111
ΔT0–T1	8	0.28 (−1.9 to 9.8)	1	65.43 (65.43–65.43)	0.120
ΔT1–T2	10	0.3 (−1.75 to 24.54)	1	34.3 (34.3–34.3)	0.343
Interferon gamma (mIU/mL)					
T1	17	1416.24 (675.25–1890)	1	383.47 (383.47–383.47)	0.136
T2	11	957.52 (395.8–1528.06)	1	1890 (1890–1890)	0.189
ΔT1–T2	8	−19.26 (−833.57 to 83.41)	1	1506.53 (1506.53–1506.53)	0.121

T0: Before the first vaccination.
T1: Before the second vaccination.
T2: After T1 for 3 months.
For quantitative determination of anti-SARS-CoV-2 S1 (IgG), samples with a ratio of <25.6 BAU/mL were interpreted as negative. Ratios of 25.6–35.2 BAU/mL was considered borderline, and a ratio ≥35.2 BAU/mL was considered positive.
For the SARS-CoV-2 neutralizing antibody, the interpreting results were as follows: % inhibition (IH) <20: negative, % IH ≥20 to <35: borderline, % IH ≥35: positive.
For the SARS-CoV-2 interferon-gamma ELISA, the interpreting results were as follows: negative: <100 mIU/mL, borderline: 100–200 mIU/mL, positive: >200 mIU/mL.

Table 7
Side effects of the COVID-19 vaccine after the first and second doses.

	No		Yes	
	n	%	n	%
First dose vaccine				
Fever	125	69.44	55	30.56
Numbness	179	100.00	–	
Headache	164	91.11	16	8.89
Other	98	54.44	82	45.56
Second dose vaccine				
Fever	149	93.13	11	6.88
Numbness	158	99.37	1	0.63
Headache	159	100.00	–	
Other	130	81.25	30	18.75

Other: Soreness at the injection site, muscle ache.

resolved within 1–2 days. Fever was the second most common symptom. The local reactions did not increase after the second dose. Fever occurred more frequently in the control group (p = 0.025) and no serious AEs were recorded (Table 7).

4. Discussion

Patients with CKD, especially ESRD undergoing dialysis, are at a very high risk of death following COVID-19 [14,15]. Evidence suggests that patients with CKD may have a less robust antibody response after vaccination than healthy controls [16–20]. Our study consisted of a diverse group of patients with CKD receiving different therapies. Our major finding was that patients with CKD, including those on maintenance HD, developed a substantial humoral response following the two vaccine doses (inactivated and ChAdOx1 nCoV-19 vaccines). Humoral seroconversion responses were maintained for as long as 12 weeks after completing the second dose, and the responses were equivalent to those of healthy individuals. However, patients with KT developed fewer humoral immune responses than those in the other groups. Immunosuppression may induce a weak anti-SARS-CoV-2 antibody response.

The immune response from inactivated whole-virus SARS-CoV-2 vaccine among patients with HD was demonstrated to be satisfactory. However, fewer patients achieved humoral immune responses compared with healthy individuals [21]. In our study, >50 % of all patients except recipients of KT experienced seroconversion after receiving the second dose of inactivated vaccines. Related studies have reported variable responses to COVID-19 vaccines among patients with CKD, with most studies reporting on mRNA vaccines [22–26]. However, the durability of this immune response and the extent to which it translates to protective immunity remain unclear. A systematic review of 18 studies found that the antibody response to full vaccination with two doses of COVID-19 mRNA vaccines among patients undergoing HD, CAPD and KT was lower than that in the healthy population [27]. In phase 3 trials, BNT162b2, mRNA-1273 and ChAdOx1 nCoV-19 prevented COVID-19 in 95, 94.1 and 70.4 % of participants [28–30], respectively, suggesting that the mRNA vaccines might induce protective immunity more reliably than ChAdOx1 nCoV-19. In addition, both mRNA vaccines and viral-vector vaccines induce balanced humoral and T cell immunity [31].

Our study measured cellular immunity to better explore the immunogenicity of these specific populations using IFNγ levels. We found a significant correlation between IFNγ, SARS-CoV-2-specific antibodies and NA.Cytotoxic CD8+ T cells help accelerate the clearance of many respiratory viruses [32] and are essential in reducing the risk of SARS-CoV-2. Here, we demonstrated a good

T cell response among patients with CKD and those on HD, which occurred as early as after the first dose of the ChAdOx1 nCoV-19 vaccine. The level of cellular immunity in this study correlated well with anti-SARS-CoV-2 antibody and NA, as in related studies [33]. Cellular immunity was then extrapolated to a good humoral immune response.

The antibody responses and NA levels in both vaccine groups did not significantly different except in the control group at T1. After the second dose, the level of immunity was similar (Supplementary Tables 3–7). The sample size in the inactivated vaccine group was small, and the protocol for the inactivated vaccine was only 3–4 weeks apart. This implied that antibody levels in the inactivated group declined more rapidly than in the other groups and this vaccine should not be recommended among patients with CKD and those on HD. The inappropriately high level of anti-spike IgG in the control group at T1 after inactivated vaccine might have been caused by natural infection. Since anti-nucleocapsid was performed only before participants recruitment.

The new cases of COVID-19 were detected after the first doses of vaccination; more than one half of these patients were in the HD group (85.71 %). Our study suggested a more rapid vaccination response among patients with CKD and on dialysis. The results also implied that patients on HD should not be considered for a delayed second vaccination dose. To prevent new cases of COVID-19, the second dose should be scheduled early as four to eight weeks after the first dose. Most people with symptomatic SARS-CoV-2 undergo seroconversion to produce a detectable, specific antibody response in the acute phase (Table 6). However, they should be re-vaccinated because the specific IgM rises in the acute phase and the IgG peaks appear later but decline after three to four months [34,35].

Most studies have not reported an association between antibody response and other factors, such as age or sex. Our findings showed significant associations for blood group O, which constitutes a novel finding. Related studies have revealed that blood group O is associated with less viral infection and illness severity [36–38].Blood group A was found to be associated with an increased risk of infection and mortality but a decreased risk of intubation and death [39]. The molecular mechanisms by which ABO polymorphism impacts risks of SARS-CoV2 infection might involve ABO antibodies inhibiting the interaction between angiotensin converting enzyme-2 receptor and the virus, related to the presence of the anti-A antibody [40] or anti-A isohemaglutinin titers [41]. Further studies need to confirm these findings. This study showed the effectiveness of the ChAdOx1 nCoV-19 vaccine over inactivated vaccines among patients with CKD. We found no difference in serious AEs between the two vaccine formulations, except for fever and numbness, which resolved in a few days.

Our study exhibits several strengths, including a comprehensive overview of the immunogenicity of both humoral and cellular

responses to COVID-19 vaccines in a broad sample of patients with CKD. The sizes of the HD and CKD cohorts were sufficiently large for the control group to allow us to identify differences. The results presented here have a long follow-up to three months after vaccination in contrast to only <four weeks in other studies. This may have implications for treatment and policy, because the ChAdOx1 nCoV-19 vaccine remains one of the main COVID-19 vaccine used in many countries. Nevertheless, our findings were limited by the small sample size and unequal distribution of the CKD population The number of patients other than those undergoing HD was insufficient to draw a meaningful conclusion concerning the other subgroups. The loss follow-up rate was also high in the control group.

5. Conclusion

Immunity among patients on HD and those with CKD after completing two vaccinations with candidate vaccines was strong, although the responses among recipients of KT and patients on CAPD were below acceptable levels, reinforcing the idea that this population should be vaccinated as soon as possible and receive a booster dose with the same or a different vaccine platform, such as an mRNA vaccine. A timely second dose of the COVID-19 vaccine seems necessary to ensure protection of patients with kidney disease from SARS-CoV-2. Blood group O and vaccine type were associated with good immune response.

6. Ethics approval

This study protocol was reviewed and approved by the Vajira Institutional Review Board, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, approval number 94/2564.

7. Consent to participate

Written informed consent was obtained from all participants, and the experiment was performed in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice.

Data availability

The data supporting the findings of this study are available from the corresponding author. Data supporting the findings of this study are openly available in "figshare" at http://doi.org/10.6084/m9.figshare.19552222.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Thananda Trakarnvanich reports financial support was provided by Navamindradhiraj University. Thananda Trakarnvanich reports a relationship with Navamindradhiraj University that includes: funding grants and non-financial support. None to be declared.

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Author contributions

Thananda Trakarnvanich: Concept and design, acquisition, analysis, interpretation of data, drafting of the manuscript, supervision, and administrative, technical and material support. Tanun Ngamvitchukorn: Concept and design, acquisition, analysis, or interpretation of data. Uraporn Phumisantiphong: Drafting the manuscript and laboratory analysis. Kittisak Pholtawornkulchai: Concept, design and supervision. Krittima Phochanasomboon: acquisition, analysis and material support. Anan Manomaipiboon: Supervision, and administrative, technical and material support. All authors discussed the results and implications and commented on the manuscript at all stages. All authors read and approved the final manuscript.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.09.067.

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