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ORIGINAL ARTICLE

Post-vaccination analysis of anti-spike antibody responses in kidney transplant recipients with and without COVID-19 infection in a tertiary care centre, India

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ABSTRACT

Background. To investigate the anti-spike antibody response to vaccination in kidney transplant recipients (KTRs) previously infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as compared with KTRs with no history of coronavirus disease 2019 (COVID-19) from India.

Methods. SARS-CoV-2 spike immunoglobulin (Ig) G antibody response was measured in 105 post-COVID-19 KTRs with PCR-confirmed SARS-CoV-2 infection who received either no vaccination (cohort 1), a single dose (cohort 2) or two doses (cohort 3) of vaccine and compared with 103 two-dose vaccinated COVID-19-naïve KTRs with no history of COVID-19 (cohort 4).

Results. Out of 103 COVID-19-naïve two-dose vaccinated KTRs, <50% became seropositive with anti-spike antibody titres >50 arbitrary unit/mL subsequent to complete vaccination, the seroconversion rate being comparable in subjects receiving Covishield™ versus Covaxin™ vaccines. However, the seropositive KTRs vaccinated with Covishield™ had higher anti-spike antibody titres as compared with those who received Covaxin™. We observed higher anti-SARS-CoV-2 spike antibody levels in post-COVID-19 KTRs after one dose of vaccine as compared with COVID-19-naïve two-dose vaccinated KTRs. Importantly, the second dose in post-COVID-19 KTRs did not significantly increase anti-spike antibody levels compared with the single-dose recipients.

Conclusions. Our data present that in KTRs with previous SARS-CoV-2 infection, a single dose of vaccine (Covishield™) may be effective in mounting an optimal immune response. In contrast, COVID-19-naïve two-dose vaccinated KTRs respond poorly (<50%) to the current recommendation of a two-dose regimen in India.

Keywords: anti-spike antibody, COVID-19, kidney transplant recipients, previously infected, SARS-CoV-2

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INTRODUCTION

Kidney transplant recipients (KTRs) are at an elevated risk of developing severe coronavirus disease 2019 (COVID-19) [1]. Studies have demonstrated increased morbidity and mortality in transplant patients [1–17]. In the absence of a definitive cure for COVID-19, vaccines are perhaps the most promising option available to control the pandemic. There are several severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines currently available whose immunogenicity and safety have been assessed in various clinical trials [18]. However, no vaccine trial included transplant recipients. Recent investigations demonstrate that even though mRNA vaccines induce robust immune response in non-transplant individuals protecting against severe COVID-19, KTRs develop significantly lower antibody response post-vaccination [19–30]. In contrast, studies evaluating the serologic response of transplant recipients to COVID-19 infection provide conflicting results reporting normal levels of anti-SARS-CoV-2 antibodies in KTRs subsequent to past COVID-19 infection [31–33]. However, the majority of these studies explored the immune response to mRNA vaccines, currently not available in India; similar data following immunization with vaccines approved in India are not available. Importantly, the dynamics of vaccination after natural infection in transplant recipients remain unexplored. In this study, we investigated the spectrum of antibody responses to SARS-CoV-2 in a cohort of KTRs with different vaccination status.

MATERIALS AND METHODS

Study design and population

SARS-CoV-2 anti-spike IgG antibody titres were assessed in 208 KTRs, treated at a tertiary care hospital in New Delhi, India between 1 April 2020 and 30 November 2021. Out of the 208 KTRs, 105 KTRs were previously infected with COVID-19 (confirmed with SARS-CoV-2 real-time reverse transcription polymerase chain reaction) and had not received convalescent plasma during treatment. The 105 KTRs were either not vaccinated (referred to as 'post-COVID-19 non-vaccinated') or received a single dose (referred to as 'post-COVID-19 single-dose vaccinated') or both doses (referred to as 'post-COVID-19 two-dose vaccinated') of the approved vaccines, Covishield™ (ChAdOx1-nCOV or AZD1222, Oxford-AstraZeneca, manufactured by Serum Institute of India, Pune, India) and Covaxin™ [BBV-152, manufactured by Bharat Biotech, Hyderabad, in collaboration with Indian Council of Medical Research (ICMR), India] subsequent to their recovery from COVID-19. The remaining 103 KTRs with no history of COVID-19 were fully vaccinated with two doses of either of the approved vaccines (referred to as 'COVID-19-naïve two-dose vaccinated'). The distribution of study cohorts is summarized in Figure 1. Necessary institutional approvals were secured for carrying out the data analysis and manuscript development.

Data collection

Data were collected retrospectively from the medical records of the hospitals' or patients' follow-up submissions. Clinical data collected included demographics (age, height, weight, sex, duration) from transplant to COVID-19, comorbidities, baseline immunosuppression regimen and details of vaccination.

Outcomes

The primary objective of this study was to quantitatively evaluate the SARS-CoV-2 anti-spike IgG antibody response in previously infected KTRs with respect to their vaccination status, comparing with fully vaccinated uninfected KTRs. The secondary outcomes included evaluating the association and correlation of anti-spike antibody levels with comorbidities and other baseline transplant characteristics.

Anti-spike IgG antibody evaluation

Anti-spike IgG antibodies to SARS-CoV-2 were assayed with the AdviseDx SARS-CoV-2 IgG II assay (Abbott Diagnostics, Chicago, IL, USA) using a chemiluminescent microparticle immunoassay intended for the qualitative and semi-quantitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma on the Alinity i system (Abbott Diagnostics, Chicago, IL, USA). The analytical measurement interval is stated as 22–40 000 arbitrary unit (AU)/mL, and the positivity cut-off is ≥50 AU/mL (manufacturer defined). According to the manufacturer, the observed limit of quantification on the Alinity i system was 7.2 AU/mL, representing the lowest concentration at which a maximum allowable precision was met. The observed limit of detection (LoD) on the Alinity i system was 4.8 AU/mL and represents the lowest

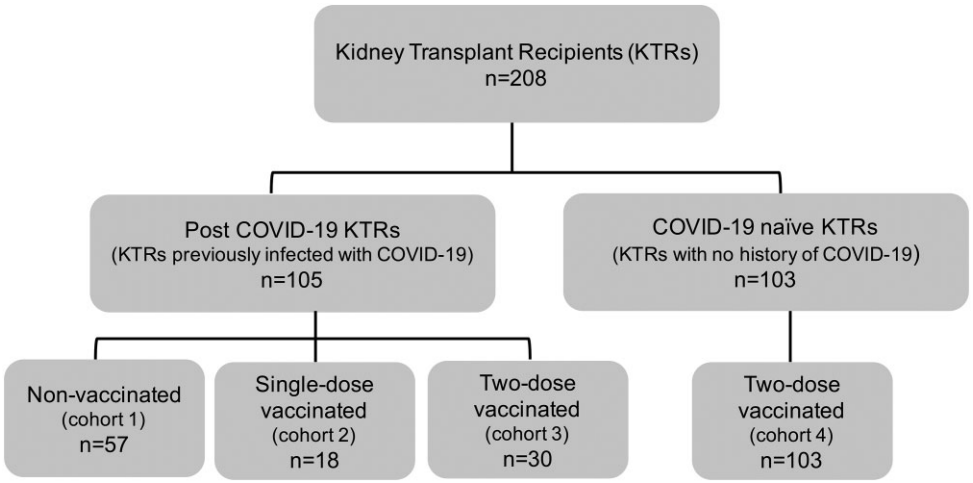

FIGURE 1: Details of the four study cohorts of KTRs based on COVID-19 infection and vaccinations.

concentration at which the analytes can be detected [34]. However, in real-world reports generated in the laboratory, low values are reported as undetectable or numeric values <7.2 AU/mL. Undetectable reports are considered zero (0.0) for calculation purposes.

These tests were conducted 10–45 weeks post onset of COVID-19 infection or 10–120 days since the last dose of vaccination. Samples were collected as either serum or plasma using EDTA vials from each participant and analysed at Dr Lal's Path Lab, New Delhi, India.

Statistical analysis

Data were tabulated using Microsoft Excel, imported to SPSS statistical software version 16.0 (SPSS Inc., Chicago, IL, USA) for analysis, and R-software version 3.6.1 was applied for determining the median difference 95% confidence interval. The continuous variables were summarized as mean ± standard deviation (SD) and median [inter-quartile range (IQR)]. The qualitative variables were reported with number and percentage.

To compare normally distributed continuous variables among the cohorts, a one-way ANOVA followed by a Tukey's test was performed. Skewed distributed variables were tested using the non-parametric Kurskal–Wallis followed by the Mann–Whintney *U*-test, and P-values were adjusted as per the Bonferroni correction. For comparing qualitative variables among the cohorts, the chi-squared test was applied. The unpaired Student's *t*-test, the Mann–Whitney *U*-test and the simple logistic regression were performed to find the association between responders and non-responders with regard to demographic and other clinical variables. We applied Spearman's correlation to find the strength of association between anti-spike antibody titres and other continuous variables. The Bonferroni correction was applied, keeping the small sample size in consideration and multiple variable testing. P-value <0.05 was considered as significant.

RESULTS

Demographics, comorbidities and baseline transplant characteristics of study cohorts

The study subjects were categorized into four cohorts based on their COVID-19 infection and vaccination status (Figure 1). A total of 208 KTRs were included in the study, out of which 105 KTRs were infected in the past with COVID-19 and 103 KTRs remained uninfected. Amongst the previously infected 105 KTRs, 57 patients were non-vaccinated (cohort 1: post-COVID-19 non-vaccinated), whereas 18 patients received only one dose (cohort 2: post-COVID-19 single-dose vaccinated) and 30 KTRs received both vaccination doses (cohort 3: post-COVID-19 two-dose vaccinated) of either of the approved vaccines. The 103 uninfected KTRs were fully vaccinated with the recommended two-dose regimen of the approved vaccines in India (cohort 4: COVID-19-naïve two-dose vaccinated). Table 1 summarizes the demographics, baseline characteristics, comorbidities and vaccination details of the four study cohorts. No significant difference was observed between the cohorts with respect to mean weight, height, gender and median time interval from transplant to COVID-19 and laboratory investigations. There was a significant difference observed in the average age of the KTRs between the four cohorts. The average age of the post-COVID-19 two-dose vaccinated KTRs (54.70 ± 11.35 years) was significantly higher than the post-COVID-19 non-vaccinated (44.11 ± 12.63 years; P = 0.001) and COVID-19-naïve two-dose vaccinated KTRs (45.91 ± 12.21 years; P = 0.004).

Nearly all the individuals in the study documented the presence of pre-existing comorbidities. Comorbidities such as diabetes mellitus (DM), hypertension (HTN), chronic liver disease (CLD) and chronic allograft dysfunction were comparable between the cohorts. Interestingly, significantly fewer COVID-19-naïve two-dose vaccinated KTRs reported a history of chronic obstructive airway disease (COAD) (1.9% P = 0.001) and vascular disease (1%, P < 0.001).

Treatment with mycophenolate mofetil/mycophenolic acid (MMF/MPA) was significantly higher in the post-COVID-19 non-vaccinated cohort (100%) as compared with the COVID-19-naïve two-dose vaccinated cohort (85.4%, P = 0.018), whereas treatment with steroids and calcineurin inhibitors (CNIs) was comparable.

Vaccination details of the study cohorts

Details about vaccination are summarized in Table 1. Amongst the 18 post-COVID-19 single-dose vaccinated KTRs, 17 received Covishield™ and only 1 received Covaxin™, whereas out of the 30 post-COVID-19 two-dose vaccinated KTRs, 20 individuals received Covishield™ and 10 received Covaxin™. Amongst the COVID-19-naïve two-dose vaccinated cohort, 75 KTRs were vaccinated with Covishield™ and 25 with Covaxin™; 3 KTRs were vaccinated with other anti-SARS-CoV-2 vaccines approved in India.

To assess the immune response elicited upon vaccination against SARS-CoV-2, anti–SARS-CoV-2 spike protein IgG ('anti-spike antibody') levels were measured. Individuals with antibody titres >50 AUs/mL were considered seropositive. Despite being fully vaccinated, only 50 out the 103 COVID-19-naïve two-dose vaccinated KTRs became seropositive (Figure 2A); more than half of the cohort (53/103; 51.5%) had anti-spike antibody titres < 50 AUs/mL (P < 0.001). Amongst KTRs with past COVID-19 infection, 96.7% of non-vaccinated patients, 100% of vaccines receiving single-dose vaccination and 94.7% of two-dose vaccinated KTRs were seropositive (Figure 2A). Out of the four KTRs that were non-responsive, three KTRs were non-vaccinated and one subject, despite receiving both doses, did not express antibody >60 AUs/mL.

The anti-spike antibody levels were significantly different between the cohorts (P < 0.001). Notably, the median antibody titres of the COVID-19 two-dose vaccinated KTRs, inclusive of seropositive and seronegative individuals, [17.1 (IQR 1.6–2125) AU/mL] were significantly lower than KTRs with past COVID-19 infection, irrespective of their vaccination status (P < 0.001) (Table 1 and Figure 2B).

Amongst the KTRs with past COVID-19 infection, non-vaccinated patients had lower median antibody titres [745 (IQR 239–3022) AU/mL] as compared with post-COVID-19 single-dose vaccinees [3436 (IQR 661–10 450) AU/mL; P = 0.066] or post-COVID-19 two-dose vaccinated KTRs [3706(IQR 867–10 700) AU/mL; P = 0.006]. Interestingly, median antibody titres of post-COVID-19 KTRs vaccinated with a single dose were comparable to those who received two doses (P = 1.00, Bonferroni adjusted) (Table 1 and Figure 2B).

Amongst the vaccinated cohort, the median time interval for assessment of the serological response past vaccination was comparable. Anti-spike antibody tests were conducted for post-COVID-19 single-dose vaccinated cohort at median 47 days (IQR 28–84.8), post-COVID-19 two-dose vaccinated cohort at median

Table 1. Demographics and baseline characteristics of COVID-19-naïve and post-COVID-19 KTRs based on their vaccination status

	Post-COVID-19 KTRs			COVID-19-naïve		
	Non-vaccinated N = 57	Single-dose vaccinated n = 18	Two-dose vaccinated n = 30	Two-dose vaccinated N = 103	P-value (F-test/chi-squared test)	Multiple group comparison (Tukey's test)/Bonferroni adjustment
Demographics						
Age (years), mean (SD)	44.11 (12.63)	47.83 (14.57)	54.70 (11.35)	45.91 (12.21)	0.002[a]	• Post-COVID-19 two-dose vaccinated versus post-COVID-19 non-vaccinated: P = 0.001 • Post-COVID-19 two-dose vaccinated versus COVID-19-naïve two-dose vaccinated: P = 0.004
Height (m), mean (SD)	1.68 (0.10)	1.67 (0.09)	1.68 (0.09)	1.66 (0.09)	0.511[a]	NA
Weight (kg), mean (SD)	66.51 (13.7)	74.6 (16.11)	30 (70.1)	65.86 (12.82)	0.056[a]	NA
Gender, *n* (%)						
Male	40 (70.2)	13 (72.2)	22 (73.3)	70 (68.0)	0.941[b]	NA
Comorbidities, n (%)						
Any	51 (89.5)	18 (100.0)	29 (96.7)	91 (88.3)	0.276	NA
DM	30 (52.6)	9 (50.0)	16 (53.3)	45 (43.7)	0.663[b]	NA
HTN	48 (84.2)	17 (94.4)	28 (93.3)	86 (83.5)	0.376[b]	NA
CLD	5 (8.8)	0 (0.0)	2 (6.7)	6 (5.8)	0.647[b]	NA
COAD	2 (3.5)	1 (5.6)	6 (20.0)	1 (1.0)	0.001[b]	Post-COVID-19 two-dose vaccinated versus COVID-19-naïve two-dose vaccinated: P = 0.006
Vascular disease (CAD/PVD)	5 (8.8)	4 (22.2)	10 (33.3)	2 (1.9)	<0.001[b]	• Post-COVID-19 two-dose vaccinated versus COVID-19-naïve two-dose vaccinated: P < 0.001 • Post-COVID-19 single-dose vaccinated versus COVID-19-naïve two-dose vaccinated: P = 0.012
Chronic allograft dysfunction	11 (19.3)	5 (27.8)	6 (20.0)	35 (34.0)	0.182[b]	NA
Baseline transplant characteristics, n (%)						
Duration from transplant to COVID-19 onset (weeks), median (IQR)	301 (116.5–477)	243 (112–411)	199 (112–329)	NA	0.451[c]	NA
Baseline immunosuppression						
Steroid	57 (100.0)	18 (100.0)	30 (100.0)	103 (100)	[e]	[e]
CNI	56 (98.2)	18 (100.0)	30 (100.0)	101 (98.1)	0.560[b]	NA
MMF/MPA	57 (100.0)	15 (83.3)	29 (96.7)	88 (85.4)	<0.008[b]	Post-COVID-19 non-vaccinated versus COVID-19-naïve two-dose vaccinated P = 0.018
Vaccination details						
Type of vaccine						
Covishield	NA	17 (94.4)	20 (66.7)	75 (72.8)[d]	0.096	NA
Covaxin	NA	1 (5.6)	10 (33.3)	25 (24.3)[d]		
Anti-spike antibody (AU/mL), median (IQR)	745 (239–3022)	3436 (661–10 450)	3706 (867–10 660)	17.1 (1.6–2125)	P < 0.001[c]	• COVID-19-naïve two-dose vaccinated versus post-COVID-19 non-vaccinated, single-dose and two-dose vaccinated groups: P < 0.001[c] • Post-COVID-19 non-vaccinated versus post-COVID-19 two-dose vaccinated: P = 0.066, •Post-COVID-19 non-vaccinated versus post-COVID-19 two-dose vaccinated: P = 0.006
Seropositivity						
Anti-spike antibody titre >50 AU/mL	54 (94.7)	18 (100.0)	29 (96.7)	50 (48.5)	P < 0.001	COVID-19-naïve two-dose vaccinated versus post-COVID-19 non-vaccinated, single-dose and two-dose vaccinated groups: P < 0.001

Table 1. Continued.

	Post-COVID-19 KTRs			COVID-19-naïve		
	Non-vaccinated $N = 57$	Single-dose vaccinated $n = 18$	Two-dose vaccinated $n = 30$	Two-dose vaccinated $N = 103$	P-value (F-test/chi-squared test)	Multiple group comparison (Tukey's test)/Bonferroni adjustment
Duration from COVID-19 onset to anti-spike antibody test (weeks)	12.0 (10.0–31.5)	18.0 (10.8–44.3)	35.0 (25.8–43.0)	NA	P < 0.001[c]	Post-COVID-19 non- vaccinated versus post-COVID-19 two-dose vaccinated: P < 0.001
Duration from last vaccine dose to anti-spike antibody test (days)	NA	47.0 (28.0–84.8)	65.5 (24.0–95.5)	54.0 (29.0–120.0)	0.584[c]	NA

CAD/PVD, coronary artery disease/peripheral vascular disease; TLC, total leucocyte count; and Hb, haemoglobin. NA, not applicable because not significant in overall comparison (F-test/chi-squared test).
[a]One-way ANOVA followed by Tukey's test (The Tukey's/Bonferroni is applicable only when the overall effect was significant).
[b]Chi-squared/exact chi-squared test.
[c]Mann–Whitney U-test with Bonferroni corrected P-values.
[d]In group 'COVID-19-naïve two-dose vaccinated', three patients received vaccine other than Covishied and Covaxin.
[e]Data/P-value could not be computed.

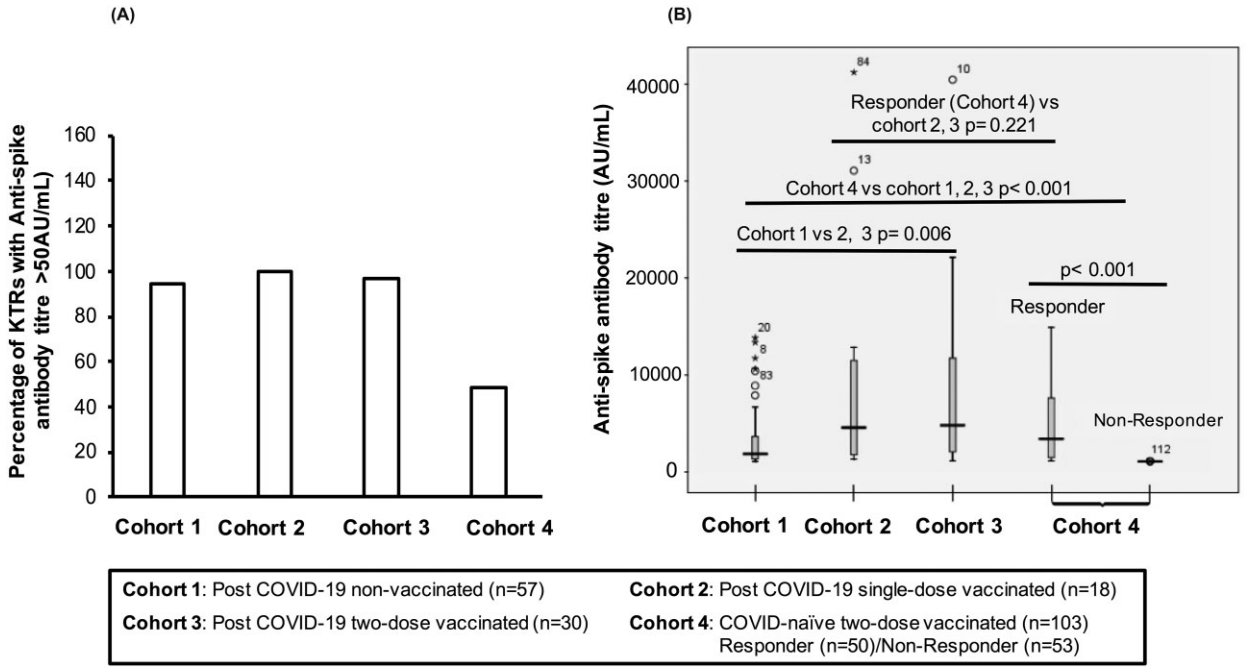

FIGURE 2: (A) Percentage of seropositive KTRs (anti-spike antibody titre >50 AU/mL) in each patient cohort. (B) Box plot for anti spike SARS-CoV-2 antibodies for different cohorts. Anti-spike antibody levels (AU/mL) were measured for cohort 1 (post-COVID-19 non-vaccinated), cohort 2 (post-COVID-19 single-dose vaccinated), cohort 3 (post-COVID-19 two-dose vaccinated) and cohort 4 (COVID-19-naïve two-dose vaccinated). For cohort 4, seropositive responders (anti-spike antibody titre > 50 AU/mL) and non-responders (anti-spike antibody titre <50 AU/mL) were analysed separately. *P-value < 0.05 is significant.

65.5 days (IQR 24.0–95.5) and COVID-19-naïve two-dose vaccinated cohort at median 54 days (IQR 29–120) past last vaccine dose. For post-COVID-19 non-vaccinated cohort, the anti-spike antibody was assessed at median 12 weeks (IQR 10–31.5) from onset of COVID-19.

Demographics, comorbidities and baseline transplant characteristics of responders versus non-responders in fully vaccinated uninfected KTRs

Out of the 103 COVID-19-naïve two-dose vaccinated subjects, 50 seropositive individuals with anti-spike antibody titre >50 AU/mL were considered as 'responders' and the remaining subjects with anti-spike antibody titre <50 AU/mL were identified as 'non-responders'. The demographics, baseline transplant characteristics, comorbidities and laboratory investigations, along with vaccination details are documented in Table 2. The average age (48.28 ± 12.34 years) of non-responder was significantly higher, whereas average weight (63.22 ± 10.63 kg) was lower than the responders (age: 43.40 ± 11.67 years, P = 0.042; weight: 68.55 ± 14.41 kg; P = 0.038). No significant difference was observed regards to height, gender, comorbidities and immunosuppressive treatment. Median anti-spike antibody titre for non-responders was 1.9 (IQR 0.33–5.45) AU/mL and that of responders were 2313.0 (IQR 389.1–6518.0) AU/mL (P < 0.001) (Table 2 and Figure 2B).

Table 2. Comparison between responder and non-responders in COVID-19-naïve two-dose vaccinated KTRs (no history of COVID-19)

Parameters	Total ($n = 103$)	Responders (anti-spike antibody titre >50 AU/mL) ($n = 50$)	Non-responders (anti-spike antibody titre <50 AU/mL) ($n = 53$)[a]	Mean or median difference/odds ratio (95% CI)	P-value
Demographics					
Age (years), mean (SD)	45.91 (12.21)	43.40 (11.67)	48.28 (12.34)	4.88 (0.18 to 9.59)	0.042
Height (m), mean (SD)	1.66 (0.09)	1.67 (0.10)	1.65 (0.09)	–0.017 (–0.05 to 0.019)	0.350
Weight (kg), mean (SD)	65.86 (12.82)	68.55 (14.41)	63.22 (10.63)	–5.23 (–10.16 to –0.30)	0.038
Gender, *n* (%)					
Male	70 (68.0)	37 (74.0)	33 (62.3)	1.73 (0.74–4.0)	0.202
Comorbidities, n (%)					
DM	45 (43.7)	25 (50.0)	20 (37.7)	0.61 (0.28–1.33)	0.210
HTN	86 (83.5)	42 (84.0)	44 (83.0)	0.93 (0.33–2.64)	1.00
CLD	6 (5.8)	1 (2.0)	5 (9.4)	5.10 (0.58–45.32)	0.206
COAD	1 (1.0)	1 (2.0)	0 (0.0)	[b]	0.485
Vascular disease (CAD/PVD)	2 (1.9)	2 (4.0)	0 (0.0)	[b]	0.233
Chronic allograft dysfunction	35 (34.0)	18 (36.0)	17 (32.1)	0.84 [0.37–1.90]	0.684
Diabetic neuropathy	25 (24.3)	14 (28.0)	11 (20.8)	0.67 [0.27–1.67]	0.391
Baseline immunosuppressant, n (%)					
MMF	88 (85.4)	40 (80.0)	48 (90.6)	2.40 (0.76–7.60)	0.129
CNI	101 (98.1)	49 (98.0)	52 (98.1)	1.06 (0.07–17.44)	1.00
Vaccination details					
Vaccine type					
Covishield	75 (72.8)	36 (72.0)	39 (78.0)		P = 0.488 (responders versus non-responders)
Covaxin	25 (24.2)	14 (28.0)	11 (22.0)		
Anti-spike antibody (AU/mL), median (IQR)	17.1 (1.6–212.5)	2313.0 (389.1–6518.0)	1.9 (0.33–5.45)	2173 (1012.8–3447.6)	<0.001
Covishield		2943 (965–7055)			0.042
Covaxin		378.05 (161.5–4272)			
Duration from last vaccine dose (days), median (IQR)	54.0 (29.0–120.0)	41.50 (25.0–90.50)	74.0 (34.0–137.0)	–20.0 (–42.0 to –1.0)	0.036
Duration of transplant to vaccination (weeks), median (IQR)	281 (132 to 378)	233.0 (142 to 423)	295 (123 to 360)	–3.0 (–96 to 63.0)	0.911

[a]Three patients received vaccine other than Covishied and Covaxin.
[b]Cannot be computed due to zero count.

Out of 103 COVID-19-naïve two-dose vaccinated KTRs, 75 subjects received Covishield™ and 25 were vaccinated by Covaxin™ (Table 1). The seroconversion rate in KTRs receiving Covishield™ (36 out of 75, 48%) versus Covaxin™ (14 out of 25, 56%) was comparable (P = 0.488) (Table 2). The distribution of subjects receiving Covishield™ and Covaxin™ between the responders (Covishield™: 36/50 and Covaxin™: 14/50) and non-responders (Covishield™: 39/50 and Covaxin™: 11/50) was also comparable (P = 0.488). However, amongst the responders, subjects receiving Covishield™ had a significantly higher anti-spike antibody titre [median (IQR): 378.05 (161.5–4272); P = 0.042]. Interestingly, the median time interval for anti-spike antibody assessment past vaccination was higher for non-responders [74 days (IQR 34–137)] as compared with responders [41.5 days (IQR 25–90.5); P = 0.036] (Table 2).

Association and correlation of anti-spike antibody levels with demographics, comorbidities and other baseline characteristics of the KTRs

No significant association of anti-spike antibody levels assessed in KTRs from all cohorts with demographics, comorbidities, vaccination and anti-spike antibody assessment details was observed (Table 3). Similar results were obtained when we studied the association of anti-spike antibody titres of only seropositive KTRs (anti-spike antibody levels >50 AU/mL) with the baseline characteristics (Supplementary data, Table S1). Further, the correlation between anti-spike antibody levels in post-COVID-19 (non-vaccinated, single-dose and two-dose vaccinated) and COVID-19-naïve two-dose vaccinated KTRs with clinical variables such as age, transplant duration up to vaccination, duration from onset of COVID-19 to vaccination and days from last dose of vaccine to serological assessment was studied (Table 4). No significant correlation was observed except in cohort 3, where anti-spike antibody levels from previously infected KTRs who received both doses of vaccine showed a negative correlation between age and anti-spike antibody levels (Spearman's correlation coefficient: –0.380; P = 0.038).

DISCUSSION

The current study, to the best of our knowledge, is the first to investigate the longitudinal serological response to SARS-CoV-2

Table 3. Association of anti-spike antibody levels with baseline characteristics and comorbidities in post-COVID-19 non-vaccinated, vaccinated (both single and two-dose vaccinated) and COVID-19-naïve two-dose vaccinated KTRs. The data shown corresponds to anti-spike antibody titres (AU/mL)

	Post-COVID-19 KTRs					
Characteristics	Non-vaccinated $n = 57$	P-value	Vaccinated (single-dose and two-dose vaccinated) $n = 48$	P-value	COVID-19-naïve two-dose vaccinated $n = 103$	P-value
Demographics						
Age						
<60 years	768 (250–2228) $n = 47$	0.973	3697 (716–10 450) $n = 37$	0.873	57.90 (2.23–2551) $n = 92$	0.184
>60 years	499 (153–6348) $n = 10$		3540 (371–10 626) $n = 11$		3.90 (0.80–220.0) $n = 11$	
Gender						
Male	768 (250–1941) $n = 39$	0.993	3697 (974–10 360) $n = 35$	0.719	87.2 (1.35–2756) $n = 70$	0.522
Female	694 (184.8–4294) $n = 17$		2298 (426–12 220) $n = 13$		6.80 (2.0–1339) $n = 33$	
Transplant duration						
≤1 year	1710 (523–10 760) $n = 5$	0.284	Three cases	0.841	NA	NA
>1 year	745 (249–2228) $n = 51$		3540 (716–10 450) $n = 45$		NA	
Vaccination details						
Anti-spike antibody levels (AU/mL) from onset of COVID (weeks)						
<12 weeks	768 (205–3168) $n = 31$	0.921	3114 (633–6188) $n = 10$	0.339	NA	NA
>12–24 weeks	1132 (249–1941) $n = 11$		750 (519–4835) $n = 7$		NA	
>24 weeks	750 (382–9774) $n = 15$		5883 (1233–10 780) $n = 31$		NA	
Anti-spike antibody levels from last vaccine dose (days)						
<21 days	NA	NA	3619 (510–7960) $n = 10$	0.910	31.1 (0.08–1191) $n = 10$	0.280
>21 days	NA		3741 (733–10 560) $n = 38$		17.1 (1.9–2534) $n = 93$	
Comorbidities						
Any						
Present	76 (250–2390) $n = 50$	0.969	3697 (682–10 550) $n = 47$	NA	17.10 (1.90–1801) $N = 91$	0.930
Absent	1228 (66.8–4508) $n = 6$		One-case only		390.9 (0.70–3416) $n = 12$	
DM						
Present	7680 (238–1772) $n = 29$	0.825	3481 (532–5403) $n = 25$	0.197	119 (4.0–4710) $n = 45$	0.022
Absent	745 (250–4150) $n = 29$		7022 (1233–12 120) $n = 23$		8.0 (0.40–839.5) $n = 58$	
HTN						
Present	754 (249–2228) $n = 47$	0.713	3697 (614–10 580) $n = 45$	0.873	23.5 (1.80–2219) $n = 86$	0.657
Absent	1710 (181–4294) $n = 9$		3436 $n = 3$[a]		4.40 (1.0–2214) $n = 17$	
CLD						
Present	1196 (645–4680) $n = 5$	0.339	Only two cases	0.255	5.0 (0.8–52.10) $n = 6$	0.084
Absent	745 (228–2228) $n = 51$		3706 (733–10 560) $n = 46$		56.10 (2.05–2534) $n = 97$	
COAD						
Present	Two cases	0.026	4234 (371–10 620) $n = 7$	0909	One case	0.719
Absent	877 (273–2950) $n = 54$		3540 (862–10 450) $n = 41$		17.0 (1.6–2219) $n = 102$	
Vascular disease (CAD/PVD)						
Present	164 (128– 5321) $n = 5$	0.449	2997 (480–6472) $n = 14$	0.297	Two cases	0.038
Absent	768 [280–2877] $n = 51$		3628 (918–11 110) $n = 34$		16.90 (1.6–1759) $n = 101$	
Chronic allograft dysfunction						
Present	1196 (515–6791) $n = 11$	0.348	4000 (2700–10 780) $n = 11$	0.244	100.5 (0.40–978.9) $n = 35$	0.473
Absent	754 (216–2552) $n = 45$		3481 (583–9172) $n = 37$		16.45 (2.0–2595) $n = 68$	

[a]IQR could not be calculated due to insufficient n values.

natural infection and subsequent vaccination in KTRs in India. We have assessed the anti-spike antibody levels in 105 COVID-19-infected KTRs who have not been vaccinated (cohort 1) or vaccinated with either a single (cohort 2) or two doses (cohort 3) with 103 COVID-19-naïve two-dose vaccinated KTRs (cohort 4).

Recent studies have demonstrated that KTRs elicit an impaired immune response to the SARS-CoV-2 vaccine, with only 4–48% of KTRs showing detectable anti-spike IgG after complete vaccination [19–24, 30]. However, all these investigations were done in response to mRNA vaccines, which are currently unavailable in India. In our study cohorts, the majority of the subjects were vaccinated by Covishield™, an adenovirus-vectored vaccine expressing the SARS-CoV-2 spike protein (ChAdOx1-nCOV or AZD1222, acquired from Oxford University and AstraZeneca, manufactured by Serum Institute of India, Pune, India) and rest with inactivated whole virus–based vaccine Covaxin™ [BBV-152, manufactured by Bharat Biotech, Hyderabad, in collaboration with the Indian Council of Medical Research (ICMR), India]. The data available on the serological response to Covishield™ and Covaxin™ is based on immune responses from immune-competent individuals [35–37], and similar information from KTRs is scarce. Recently, Prendecki *et al.* [38] reported immunological responses to two-dose vaccination with ChAdOx1 (Oxford University–AstraZeneca) in KTRs; only

Table 4. Correlation of clinical variables with anti-spike antibody levels in post-COVID-19 (non-vaccinated and single-dose and two-dose vaccinated) and COVID-19-naïve two-dose vaccinated KTRs

	Post-COVID-19 KTRs							
	Non-vaccinated		Single-dose vaccinated		Two-dose vaccinated		COVID-19-naïve two-dose vaccinated	
Variables	Spearman's correlation	P-value	Spearman's correlation	P-value	Spearman's correlation	P-value	Spearman's correlation	P-value
Age (years)	0.037	.788	0.445	0.064	–0.380	**0.038**	–0.107	0.281
Transplant duration up to vaccination date (weeks)	NA	NA	*0.303*	*0.222*	*–0.072*	*0.706*	*0.158*	*0.11*
Duration from onset of COVID-19 to vaccination date (weeks)	NA	NA	*0.395*	*0.104*	*0.015*	*0.938*	NA	*NA*
Days from last dose of vaccine	NA	NA	*0.061*	*0.810*	*–0.068*	*0.720*	*–0.160*	*0.107*

Bold value represent the statistically significant value. The italic has no significance.

44% of infection-naïve KTRs receiving ChAdOx1 seroconverted. In agreement with the available literature, we also observed that only 48.5% KTRs (50/103) with no history of COVID-19 (COVID-19-naïve two-dose vaccinated cohort) responded positively (anti-spike antibody titre of >50 AU/mL) despite receiving a complete two doses of the vaccination regimen. This is lower in comparison with a recent report from India by Kute *et al.* [39], where 19 out of 31 uninfected KTRs (61.2%) seroconverted, probably because they considered a lower cut-off of ≥15 AU/mL (as opposed to 50 AU/mL in our study) as an indication of an antibody response.

In our study, proportions of responders and non-responders receiving Covishield™ versus Covaxin™ were comparable. No significant difference was observed in the seroconversion rate of Covishield™ and Covaxin™. However, the serological response to vaccination was significantly lower in responders who received Covaxin™ as compared with those who were administered Covishield™. Similar observations have been reported by two independent studies, including one on rheumatology patients [36, 40]. Interestingly, the non-responders were significantly older than the responders, with older age being associated with poorer vaccination responses [20].

Notably, amongst KTRs who were previously infected with COVID-19, only four subjects reported anti-spike antibody <50 AU/mL, out of which three were non-vaccinated and one subject had received both vaccine doses. This is in agreement with a recent study, where only 5% of previously infected KTRs were seronegative after vaccination [38]. Similarly, in a study in an immunocompetent population, investigators reported that 100% of healthcare workers with a history of COVID-19 became seropositive after the vaccination [36].

Interestingly, the SARS-CoV-2 anti-spike IgG antibody response [with a median antibody titre of 768 (249.0–3022)] in post-COVID-19 non-vaccinated KTRs was significantly higher than the COVID-19-naïve two-dose vaccinated KTRs. This observation is supported by studies that have investigated the development of SARS-CoV-2 antibodies in transplant recipients, including KTRs following natural COVID-19 infection [31–33]. It is to be noted that the low antibody levels in vaccinated uninfected KTRs are likely attributable to non-responders in the cohort. Further analysis of the median anti-spike antibody titres of the responders from the COVID-19-naïve two-dose vaccinated cohort revealed that the immune response elicited by vaccination in uninfected KTRs was comparable to KTRs with COVID-19 history ($P = 0.221$).

The antibody responses to Covishield™ and Covaxin™ vaccines in KTRs who have been previously infected with SARS-CoV-2 are largely unknown. In our study, we observed that previously infected KTRs showed a significant 4-fold increase in anti-spike antibody response to a single dose of vaccine. However, the median antibody titres between KTRs who received only one dose as compared with those who received both doses were comparable. This is in agreement to multiple studies conducted in non-transplant individuals [35–37, 41, 42] and a study by Benotmane *et al.* [43] in KTRs, where one dose of vaccine yielded significantly higher anti-spike antibody titre in COVID-19 recovered subjects. The robust post-vaccination immune response in individuals with past COVID-19 infection could be explained by immune memory that may persist for months [44–46], possibly resulting in a quicker and sustained response to COVID-19 vaccines.

We also analysed association of anti-spike antibody levels with demographics, vaccination details and comorbidities, and no significant association was observed. Similar results were reported by Singh *et al.* [36], with no significant difference in seropositivity rate with regard to age, sex, BMI, blood group, and any comorbidities, including its duration and treatment. However, when we calculated the correlation of anti-spike antibody with clinical variables, we observed a negative correlation of antibody levels with age in post-COVID-19 two-dose vaccinated KTRs; older age has been associated with a poorer immune response to vaccination.

There are several limitations to this study, including the relatively small sample size, especially in KTRs vaccinated with Covaxin. We also acknowledge the variation in anti-spike antibody levels of individuals, which could be due to variation in the interval between transplantation, COVID-19 diagnosis and vaccination days. It has been reported that patients who contracted COVID-19 within the first year of transplant may have a poorer immune response due to immunosuppression therapy [20]. Another important consideration is the variation in timing of antibody testing past infection or vaccination within our study cohorts. It is possible that anti-SARS-CoV-2 antibody levels have started to decline over time in some individuals, especially in KTRs who experience mild COVID-19 symptoms or with compromised immune response [46]. This could be applicable

in our study, where we observed that the median time interval for assessment of anti-spike antibody after the last vaccine dose in non-responders of the COVID-19-naïve two-dose vaccinated cohort was longer [74 days (IQR 34–137)] as compared with responders [41.5 days (IQR 25–90.5)]. This could be one of the reasons for low antibody levels in some of the non-responders.

Our findings provide evidence that KTRs infected with COVID-19 develop anti-spike antibody following natural infection, albeit lower than the KTRs that received vaccination subsequent to their recovery from COVID-19. The antibody response significantly increases after the administration of a single dose of vaccine (Covishield™), suggesting that a previous infection with SARS-CoV-2 primed the immune system of the KTRs against COVID-19. Although no increase in the antibody level was observed following the second dose of vaccination, it is possible that the second dose could improve the longevity and durability of the response. However, due to inadequate number, the inference could not be extrapolated to patients receiving Covaxin™. Further studies with larger sample sizes, sequential anti-spike antibody monitoring over time and comparing COVID-19-infected KTRs with COVID-19-naïve KTRs are warranted.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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AUTHORS' CONTRIBUTIONS

All authors contributed equally in research design and execution, data collection, analysis and interpretation of data and writing of the manuscript. All authors provided intellectual content of critical importance to the work described, approved the version for publication and agreed to be accountable for all aspects of the work.

CONFLICT OF INTEREST STATEMENT

V.J. has research grants from Baxter, GSK and NephroPlus, and reports honoraria from speaking engagements (lectures, presentations, speakers' bureaus, manuscript writing or educational events) from AstraZeneca, Boehringer Ingelheim, Baxter and Zydus Cadila, and participation in the Advisory Board of Zydus Cadila and GSK, outside the published work. All the other authors reported no conflict. The results presented in this paper have not been published previously in whole or part, except in abstract format.

REFERENCES

1. Kronbichler A, Gauckler P, Windpessl M *et al*. COVID-19: implications for immunosuppression in kidney disease and transplantation. *Nat Rev Nephrol* 2020; 16: 365–367
2. Banerjee D, Popoola J, Shah S *et al*. COVID-19 infection in kidney transplant recipients. *Kidney Int* 2020; 97: 1076–1082
3. Jha PK, Yadav DK, Siddini V *et al*. A retrospective multi-center experience of renal transplants from India during COVID-19 pandemic. *Clin Transplant* 2021; 35: e14423
4. Kute VB, Bhalla AK, Guleria S *et al*. Clinical profile and outcome of COVID-19 in 250 kidney transplant recipients: a multicenter cohort study from India. *Transplantation* 2021; 105: 851–860
5. Elias M, Pievani D, Randoux C *et al*. COVID-19 infection in kidney transplant recipients: disease incidence and clinical outcomes. *J Am Soc Nephrol* 2020; 31: 2413–2423
6. Requião-Moura LR, de Sandes-Freitas TV, Viana LA *et al*. High mortality among kidney transplant recipients diagnosed with coronavirus disease 2019: results from the Brazilian multicenter cohort study. *PLoS One* 2021; 16: e0254822
7. Jasuja S, Sagar G, Bahl A *et al*. COVID-19 infection clinical profile, management, outcome, and antibody response in kidney transplant recipients: a single centre experience. *Int J Nephrol* 2021; 2021: 1
8. Aubert O, Yoo D, Zielinski D *et al*. COVID-19 pandemic and worldwide organ transplantation: a population-based study. *Lancet Public Health* 2021; 6: e709–e719
9. Azzi Y, Bartash R, Scalea J *et al*. COVID-19 and solid organ transplantation: a review article. *Transplantation* 2021; 105: 37–55
10. Elec FI, Bolboacă SD, Muntean A *et al*. Comparing the first and second wave of COVID-19 in kidney transplant recipients: an East-European perspective. *Eur Surg Res* 2022; 63: 25–32
11. Kremer D, Pieters TT, Verhaar MC *et al*. A systematic review and meta-analysis of COVID-19 in kidney transplant recipients: lessons to be learned. *Am J Transplant* 2021; 21: 3936–3945
12. Kute VB, Meshram HS, Navadiya VV *et al*. Consequences of the first and second COVID-19 wave on kidney transplant recipients at a large Indian transplant centre. *Nephrology* 2022; 27: 195–207
13. Elhadedy MA, Marie Y, Halawa A. COVID-19 in renal transplant recipients: case series and a brief review of current evidence. *Nephron* 2021; 145: 192–198
14. Miarons M, Larrosa-García M, García-García S *et al*. COVID-19 in solid organ transplantation: a matched retrospective cohort study and evaluation of immunosuppression management. *Transplantation* 2021; 105: 138–150
15. Kakkanattu TJ, Sankarasubbaiyan S, Yadav AK *et al*. Outcome and determinants of outcome of COVID-19 infection among hemodialysis patients: findings from a national dialysis network program in India. *Kidney Int Rep* 2021; 6: 1429–1432
16. Tau N, Yahav D, Schneider S *et al*. Severe consequences of COVID-19 infection among vaccinated kidney transplant recipients. *Am J Transplant* 2021; 21: 2910–2912
17. Yadav AK, Sankarasubbaiyan S, Gowda BGM *et al*. The high mortality and impact of vaccination on COVID-19 in hemodialysis population in India during the second wave. *Kidney Int Rep* 2021; 6: 2731
18. Heinz FX, Stiasny K. Distinguishing features of current COVID-19 vaccines: knowns and unknowns of antigen presentation and modes of action. *npj Vaccines* 2021; 6: 1–13

19. Ebinger JE, Fert-Bober J, Printsev I *et al*. Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2. *Nat Med* 2021; 27: 981–984
20. Caillard S, Thaunat O. COVID-19 vaccination in kidney transplant recipients. *Nat Rev Nephrol* 2021; 17: 785–787
21. Naaber P, Tserel L, Kangro K *et al*. Dynamics of antibody response to BNT162b2 vaccine after six months: a longitudinal prospective study. *Lancet Regional Health Eur* 2021; 10: 100208
22. Rincon-Arevalo H, Choi M, Stefanski A-L *et al*. Impaired humoral immunity to SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients and dialysis patients. *Sci Immunol* 2021; 6: eabj1031
23. Benotmane I, Gautier-Vargas G, Cognard N *et al*. Low immunization rates among kidney transplant recipients who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine. *Kidney Int* 2021; 99: 1498–1500
24. Benotmane I, Gautier-Vargas G, Cognard N *et al*. Weak anti–SARS-CoV-2 antibody response after the first injection of an mRNA COVID-19 vaccine in kidney transplant recipients. *Kidney Int* 2021; 99: 1487–1489
25. Cucchiari D, Egri N, Bodro M *et al*. Cellular and humoral response after MRNA-1273 SARS-CoV-2 vaccine in kidney transplant recipients. *Am J Transplant* 2021; 21: 2727–2739
26. Korth J, Jahn M, Dorsch O *et al*. Impaired humoral response in renal transplant recipients to SARS-CoV-2 vaccination with BNT162b2 (Pfizer-BioNTech). *Viruses* 2021; 13: 756
27. Grupper A, Rabinowich L, Schwartz D *et al*. Reduced humoral response to mRNA SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients without prior exposure to the virus. *Am J Transplant* 2021; 21: 2719–2726
28. Boyarsky BJ, Werbel WA, Avery RK *et al*. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA* 2021; 325: 2204–2206
29. Rozen-Zvi B, Yahav D, Agur T *et al*. Antibody response to SARS-CoV-2 mRNA vaccine among kidney transplant recipients: a prospective cohort study. *Clin Microbiol Infect* 2021; 27: 1173.e1–1173.e4
30. Seija M, Rammauro F, Santiago J *et al*. Comparison of antibody response to SARS-CoV-2 after two doses of inactivated virus and BNT162b2 mRNA vaccines in kidney transplant. *Clin Kidney J* 2021; 15: 527–533
31. Fung M, Chiu CY, DeVoe C *et al*. Clinical outcomes and serologic response in solid organ transplant recipients with COVID-19: a case series from the United States. *Am J Transplant* 2020; 20: 3225–3233
32. Benotmane I, Gautier Vargas G, Wendling M *et al*. In-depth virological assessment of kidney transplant recipients with COVID-19. *Am J Transplant* 2020; 20; 3162–3172
33. Prendecki M, Clarke C, Gleeson S *et al*. Detection of SARS-CoV-2 antibodies in kidney transplant recipients. *J Am Soc Nephrol* 2020; 31: 2753–2756
34. English E, Cook LE, Piec I *et al*. Performance of the Abbott SARS-CoV-2 IgG II quantitative antibody assay including the new variants of concern, VOC 202012/V1 (United Kingdom) and VOC 202012/V2 (South Africa), and first steps towards global harmonization of COVID-19 antibody methods. *J Clin Microbiol* 2021; 59: e0028821
35. Havervall S, Marking U, Greilert-Norin N *et al*. Antibody responses after a single dose of ChAdOx1 nCoV-19 vaccine in healthcare workers previously infected with SARS-CoV-2. *EBioMedicine* 2021; 70: 103523
36. Singh AK, Phatak SR, Singh R *et al*. Antibody response after first and second-dose of ChAdOx1-nCOV (CovishieldTM®) and BBV-152 (CovaxinTM®) among health care workers in India: the final results of Cross-Sectional Coronavirus Vaccine-Induced Antibody Titre (COVAT) study. *Vaccine* 2021; 39: 6492–6509
37. Jeewandara C, Kamaladasa A, Pushpakumara PD *et al*. Immune responses to a single dose of the AZD1222/Covishield vaccine in health care workers. *Nat Commun* 2021; 12: 4617
38. Prendecki M, Thomson T, Clarke CL *et al*. Immunological responses to SARS-CoV-2 vaccines in kidney transplant recipients. *Lancet North Am Ed* 2021; 398: 1482–1484
39. Kute VB, Shah N, Meshram HS *et al*. Safety and efficacy of Oxford vaccine in kidney transplant recipients: a single-center prospective analysis from India. *Nephrology (Carlton)* 2022; 27: 292–293
40. Shenoy P, Ahmed S, Paul A *et al*. Inactivated vaccines may not provide adequate protection in immunosuppressed patients with rheumatic diseases. *Ann Rheum Dis* 2022; 81: 295–296
41. Lombardi A, Consonni D, Oggioni M *et al*. SARS-CoV-2 anti-spike antibody titres after vaccination with BNT162b2 in naïve and previously infected individuals. *J Infect Public Health* 2021; 14: 1120–1122
42. Anderson M, Stec M, Rewane A *et al*. SARS-CoV-2 antibody responses in infection-naive or previously infected individuals after 1 and 2 doses of the BNT162b2 vaccine. *JAMA Netw Open* 2021; 4: e2119741
43. Benotmane I, Gautier -Vargas G, Gallais F *et al*. Strong antibody response after a first dose of a SARS-CoV-2 mRNA-based vaccine in kidney transplant recipients with a previous history of COVID-19. *Am J Transplant* 2021; 21: 3808–3810
44. Chavarot N, Leruez-Ville M, Scemla A *et al*. Decline and loss of anti–SARS-CoV-2 antibodies in kidney transplant recipients in the 6 months following SARS-CoV-2 infection. *Kidney Int* 2021; 99: 486–488
45. Bajpai D, Shah D, Bose S *et al*. Development and longevity of antibodies against SARS-CoV-2 in kidney transplant recipients after symptomatic COVID-19. *Transpl Infect Dis* 2021; 23: e13646
46. Pradenas E, Trinité B, Urrea V *et al*. Stable neutralizing antibody levels 6 months after mild and severe COVID-19 episodes. *Med (N Y)* 2021; 2: 313–320.e4