# Prospective Observational Cohort Study of Serological Responses to COVID-19 Vaccines in Pediatric Kidney Transplant Recipients at a Single Institution

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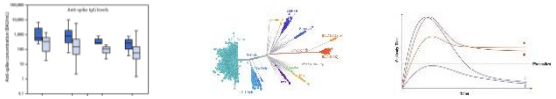
## Introduction

Pediatric kidney transplant recipients (PKTR) are at risk of poor outcomes from COVID-19. Immunosuppression, especially regimens including an antimetabolite such as mycophenolate, can decrease the ability of PKTR to attain robust immunologic response to vaccinations. Data on serologic responses to COVID-19 vaccines in PKTR remain sparse.

## Objectives

We sought to characterize the magnitude, breadth, and longevity of SARS-CoV-2 spike protein binding antibody (Ab) responses in PKTR. We investigated the impact of positive nucleocapsid antibody as a proxy for natural infection on post-vaccination serological responses. We also examined whether patients on Belatacept had decreased vaccine responses, as has been reported in some adult kidney transplant recipients.

Magnitude Breadth Durability



## Methods

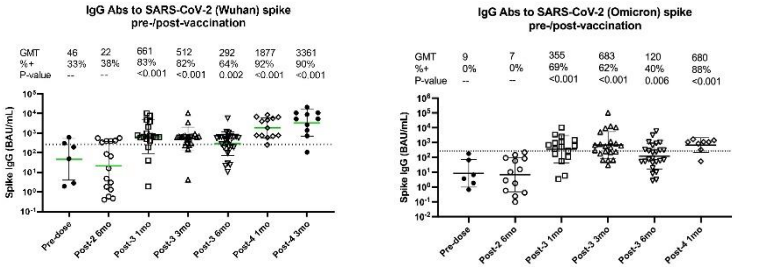
We enrolled PKTR presenting to transplant clinic for routine care who had received or were eligible to receive a COVID-19 vaccine. Demographic data, history of prior COVID-19, and vaccination details were collected. Plasma samples obtained from standard-of-care residual specimens were analyzed for SARS-CoV-2 spike variant IgG using the MesoScale Discovery V-PLEX platform, which quantitatively measures antibodies to SARS-CoV-2 full-length spike wild-type (Wuhan-hu-1), Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2), Gamma (P.1), and Omicron (B.1.1.529; BA.1) variants. Vaccine time points with > 5 samples available were analyzed. Geometric mean titers (GMTs) were calculated and log-transformed titers were compared using one-way ANOVA with Tukey's post-hoc comparisons test.

## Results

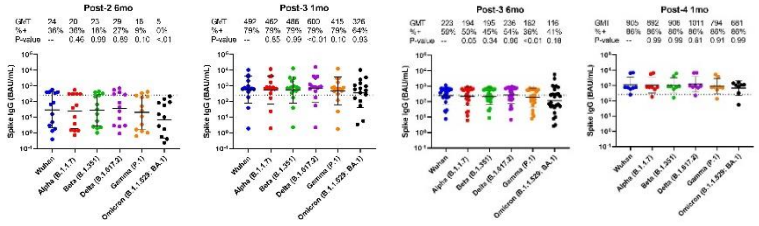
### Characteristics of Study Participants

| | Pediatric Kidney Transplant Recipients (n = 61) |
|---|---|
| Median Age in Years (Range) | 16 (6-20) |
| Female sex – number (%) | 21 (34) |
| Race – number (%) | |
| White | 32 (52) |
| Black or African American | 26 (43) |
| Asian | 2 (3) |
| Native Hawaiian or Pacific Islander | 1 (2) |
| Ethnicity – number (%) | |
| Hispanic/LatinX | 11 (18) |
| ≥3 years from transplant at time of 1st COVID-19 vaccine – number (%) | 32 (52) |
| Vaccine type – number (%) | |
| Pfizer only | 56 (92) |
| COVID-19 vaccines received included at least 1 dose mRNA vaccine | 59 (97) |
| Received at least 1 dose of COVID-19 vaccine in pediatric kidney transplant clinic – number (%) | 47 (77) |
| Immunosuppression includes antimetabolite | 59 (97) |
| Known history of COVID-19 at any time prior to or during vaccination | 23 (38) |
| ≥1 available sample ≥2 weeks after 2-dose primary series | 47 (77) |

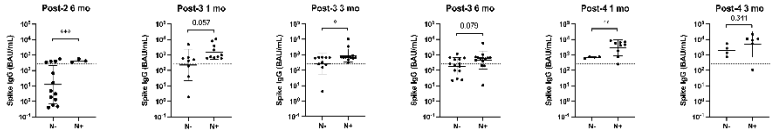
### Magnitude & Durability of Antibody Responses



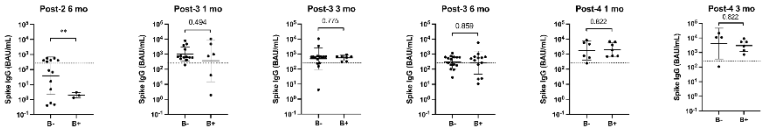

### Breadth of Antibody Responses




### Serological response by Nucleocapsid Ab status




### Serological response by Belatacept status




* P ≤ 0.05, ** P ≤0.01, *** P ≤0.005
N+ Nucleocapsid Ab positive, N- Nucleocapsid Ab negative, B+ On Belatacept, B- Not on Belatacept

## Conclusions

- In this cohort of PKTR, a 3rd (primary) dose of COVID-19 mRNA vaccine significantly boosted broadly cross-reactive binding IgG antibodies to SARS-CoV-2 spike variants, including Omicron. Decreasing titers at 6 months post-dose 3 raise concern for waning protective immunity and support 4th dose (booster) vaccination.
- Nucleocapsid antibody detection was associated with significantly or near-significantly boosted spike titers at all time points.
- Belatacept did not appreciably impact titers, except at 6 months post-dose 2; this was probably skewed due to small sample size (n=3 on Belatacept) at that time point.

## References

1. Biagio P, Rosa C, Nicola SM, Fabrizio S, Amerigo P, Giulia Z, Riccardo S, Riccardo V, Paolo R, Lorenzo S, Ivan G, Federico Ii Covid Team. Serological Response and Clinical Protection of Anti-SARS-CoV-2 Vaccination and the Role of Immunosuppressive Drugs in a Cohort of Kidney Transplant Patients. Viruses. 2022 Sep 2;14(9):1951. doi: 10.3390/v14091951. PMID: 36146758; PMCID: PMC9503455.
2. Mitchell J, Kim J, Alejo J, et al.. Humoral and Cellular Immune Response to a Third Dose of SARS-CoV-2 Vaccine in Kidney Transplant Recipients Taking Belatacept. *Transplantation.* 2022; 106 (5): e264-e265. doi: 10.1097/TP.0000000000004100.