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Original Article

ORIGINAL ARTICLE

Humoral and cellular immunogenicity of a fourth dose BNT162b2 in children with chronic kidney diseases

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ABSTRACT

Background. Children with chronic kidney disease (CKD) are at risk of severe complications after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and are recommended to receive vaccine boosters. Although coronavirus disease 2019 (COVID-19) boosters are effective in providing immune responses among healthy children, data on the use of a fourth dose among children with CKD are limited.

Methods. We prospectively investigated the immunogenicity and safety of a fourth dose of BNT162b2 in children with CKD. Dosages were 0.1 mL and 0.3 mL for children aged 5–11 years and 11–18 years, respectively. Humoral and cellular immunogenicity was assessed at pre-dose 4, and at 1 and 6 months post-dose 4.

Results. Twenty-one children, with a median age of 14.0 years, were included for evaluation. A fourth dose of BNT162b2 elicited significant increases in humoral spike receptor–binding domain immunoglobulin G levels and T-cell responses. Antibody responses were significantly lower among kidney transplant recipients or children receiving calcineurin inhibitors than other CKD children at 1 month post-dose 4. Breakthrough COVID-19 occurred in three children after the fourth dose, and one was hospitalized. One child developed mild gross hematuria 1 day after the fourth dose, which spontaneously resolved. The overall safety profile was acceptable.

Conclusions. A fourth dose of BNT162b2 was immunogenic and safe in children with CKD.

Keywords: BNT162b2, children, chronic kidney disease, COVID-19, vaccine

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KEY LEARNING POINTS

What was known:

- Children with chronic kidney disease (CKD) are at high risk of severe coronavirus disease 2019 (COVID-19).
- Children with CKD have diminished responses to vaccines compared with healthy individuals.
- A primary vaccination series containing three doses is immunogenic in children with CKD.

This study adds:

- A fourth dose of BNT162b2 can elicit significant antibody and T-cell responses among children with CKD.
- Antibody response was significantly lower in children with transplant history or use of calcineurin inhibitors.

Potential impact:

- A fourth dose of BNT162b2 can be offered to children with CKD to provide adequate protection.
- Children who underwent kidney transplants may be prioritised to receive the fourth dose.

INTRODUCTION

Severe acute kidney injury after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been reported in childhood chronic kidney disease (CKD) and kidney failure, which is associated with poor kidney outcomes and increased mortality [1–4]. Therefore, it is important to protect these children from SARS-CoV-2 infection with an evidence-based vaccination regimen tailored to this group.

Healthy children can achieve adequate antibody and T-cell responses following three doses of the coronavirus disease 2019 (COVID-19) vaccine [5, 6]. While a high level of neutralizing antibody prevents SARS-CoV-2 infection, adequate T-cell responses may lower the risk of developing severe COVID-19 [7]. Data from adult CKD patients showed that COVID-19 vaccines could elicit adequate immune responses, with no additional risk [8, 9]. However, compared with healthy individuals, those with CKD generally had diminished vaccination responses [10]. Vaccine boosters are thus recommended among this vulnerable population. Our previous publications described the immunogenicity and safety of the second and third doses of BNT162b2 among children with CKD [11, 12]. Following three doses of BNT162b2, most children were positive for wild-type (WT) spike receptor-binding domain (S-RBD) immunoglobulin G (IgG) and surrogate virus neutralization test (sVNT). Nonetheless, weaker neutralization responses were noted in children receiving multiple immunosuppressants. In Hong Kong, booster doses are recommended in immunocompromised patients by the Centre for Health Protection (CHP) [13]. However, data on humoral and cellular immunogenicity after a fourth dose of the COVID-19 vaccine among children with CKD are limited.

We initiated a 3-year prospective study to investigate the use of COVID-19 vaccines in children in Hong Kong. In the present interim analysis, we include young children and adolescents between 5 and 18 years old with advanced CKD (stage 3 or above), and those on immunosuppressants, dialysis or post-kidney transplant, to evaluate the immunogenicity and safety of a fourth dose of BNT162b2.

MATERIALS AND METHODS

Study design

COVID-19 Vaccination in Adolescents and Children (COVAC; registered as NCT04800133 at ClinicalTrials.gov on 16 March 2021) is a clinical study investigating the reactogenicity and immunogenicity of BNT162b2 and CoronaVac among healthy children and those with pediatric illnesses, as previously described [6, 11]. The study was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW21-157) and adheres to the Declaration of Helsinki.

Participants

The present analysis included children aged 5–18 years, with advanced CKD (stage 3 or above), who were on immunosuppressive therapy, chronic dialysis or post-kidney transplant.

Procedures

Participants were recruited from the Paediatric Nephrology Centre, Hong Kong Children's Hospital and the Department of Paediatric and Adolescent Medicine, Queen Mary Hospital, Hong Kong. The Paediatric Nephrology Centre of the Hong Kong Children's Hospital served as the territory-wide, designated pediatric referral center for complicated kidney diseases and chronic kidney replacement therapy (KRT), including dialysis and transplant.

Participants aged ≥18 years provided informed consent. For participants <18 years old, informed assent was obtained from the participants and consent from their respective parents or legally acceptable representatives. Demographic information was reported by the participants, and clinical details were extracted from their electronic health records. A dose of 0.1 mL BNT162b2 was offered for those aged 5–11 years, as the original pediatric formulation was unavailable in Hong Kong, and 0.3 mL BNT162b2 was offered for those aged 11–18 years. Additional consent and assent were obtained for dose escalation to 0.3 mL for participants who became 12 years old after initiating the primary series. An accelerated vaccination regimen was adapted with the fourth dose given at least 90 days after the preceding dose. Vaccination was deferred for patients with SARS-CoV-2 infection and was resumed or initiated 28 days later. All participants were observed by a registered nurse or physician for at least 15 min after each dose. Blood sampling and safety data collection were performed pre-dose 4 (on the day of vaccination), 1 month post-dose 4 (13–42 days after dose 4) and 6 months post-dose 4 (126–210 days after dose 4).

Humoral immunogenicity

Humoral immunogenicity was evaluated by measuring WT S-RBD IgG level and performing sVNT. S-RBD IgG is a measurement of the binding antibody level and sVNT is a functional antibody assay that reflects the blocking of S-RBD and human angiotensin-converting enzyme 2 receptor by vaccine sera,

Table 1: Participants' demographic information and clinical characteristics at pre-dose 4.

	All participants	5–11 years old participants	11–18 years old participants
Number of participants	21	8	13
Age, years [median (interquartile range)]	14.0 (10.5–17.0)	10.0 (6.0–11.8)	17.0 (14.5–18.5)
Gender, *n* (%)			
Male	12 (57)	5 (63)	7 (54)
Female	9 (43)	3 (38)	6 (46)
Primary kidney diagnosis, *n* (%)			
CAKUT	2 (10)	0	2 (15)
Glomerular diseases	12 (57)	6 (75)	6 (46)
Hereditary	4 (19)	1 (13)	3 (23)
Miscellaneous	3 (14)	1 (13)	2 (15)
Treatment modality, *n* (%)			
With KRT	11 (52)	3 (38)	8 (62)
Kidney transplant	7 (33)	2 (25)	5 (38)
Dialysis	4 (19)	1 (13)	3 (23)
Without KRT	10 (48)	5 (63)	5 (38)
Concurrent immunosuppressant within 3 months, *n* (%)			
Mycophenolate mofetil	10 (48)	4 (50)	6 (46)
Prednisolone	10 (48)	1 (13)	9 (69)
Tacrolimus/cyclosporine A	11 (52)	3 (38)	8 (62)
Everolimus	2 (10)	2 (25)	0
Number of concurrent immunosuppressant used within 3 months, *n* (%)			
0 immunosuppressant	3 (14)	1 (13)	2 (15)
1 immunosuppressant	6 (29)	5 (63)	1 (8)
2 immunosuppressants	8 (38)	1 (13)	7 (54)
3 immunosuppressants	4 (19)	1 (13)	3 (23)
Kidney function and proteinuria [mean (range)]			
eGFR (mL/min/1.73 m^2)	67.4 (4.0–137.0)	85.8 (72.0–103.0)	59.1 (4.0–137.0)
Urine protein/creatinine ratio (mg/mmol)	56.1 (6.0–239.0)	71.7 (10.0–239.0)	45.7 (6.0–92.0)
Blood count and comorbidities			
Hypertension, *n* (%)	7 (33)	1 (13)	6 (46)
Absolute lymphocyte count ($\times 10^6$/mL) [mean (range)]	2.28 (1.04–5.38)	2.95 (1.04–5.38)	1.84 (1.24–3.46)

eGFR (estimated glomerular filtration rate) was estimated by the modified Schwartz equation.

which correlates with the gold-standard plaque reduction neutralization test [14]. In-house WT S-RBD IgG enzyme-linked immunosorbent assay was carried out as previously published [6, 15]. sVNT was performed according to the manufacturer's instructions (GenScript Inc., Piscataway, NJ, USA) [15].

Cellular immunogenicity

Cellular immunogenicity was evaluated by antiviral cytokine-expressing [interferon (IFN)-γ^+ or interleukin (IL-2$^+$)] helper (CD4$^+$) or cytotoxic (CD8$^+$) T-cell responses against the SARS-CoV-2 S protein. These were assessed by intracellular cytokine staining on flow cytometry after stimulation with SARS-CoV-2 15-mer peptide pools (Miltenyi Biotec, Bergisch Gladbach, Germany) as previously described [6].

Safety and reactogenicity

Participants reported prespecified adverse reactions in an online or paper-based diary for 7 days after vaccination. Unsolicited adverse events (AEs) were captured up to 28 days after vaccination. Severe AEs, including life-threatening complications, unanticipated or prolonged hospitalizations, disabilities, deaths and birth defects of their offspring, or breakthrough COVID-19, would be monitored for 3 years after vaccination. We also monitored graft rejection among kidney transplant recipients and disease flare among those with glomerular disease, if any. AEs reported were reviewed by investigators, who determined the possibility of a causal relationship with the study vaccine.

Statistical analysis

T-cell responses could only be performed for participants with sufficient blood sample volumes. Participants were excluded if they only provided blood in one of the three visits (pre-dose 4, 1 month post-dose 4, 6 months post-dose 4). Samples obtained after SARS-CoV-2 infection were excluded from the analysis.

Negative values, i.e. those below the limit of detection (LOD), limit of quantification (LOQ) or cut-off, were imputed as half of the limit or cut-off and included in the final analyses. Outcome data on humoral immunogenicity were compared longitudinally using the paired *t*-test, while outcome data on cellular immunogenicity were transformed by applying natural logarithm of the values and compared longitudinally using the paired *t*-test. Relationships between immunogenicity and clinical variables were explored by analysis of variance (ANOVA), while the relationship between immunogenicity and the use of immunosuppressants was correlated by multiple linear regression. Tukey's honestly significant difference (HSD) test was performed to interpret the statistical significance of the difference in immunogenicity between groups with different clinical variables after ANOVA. Statistical significance was defined as $P < .05$. Additional details are available in Supplementary Methods.

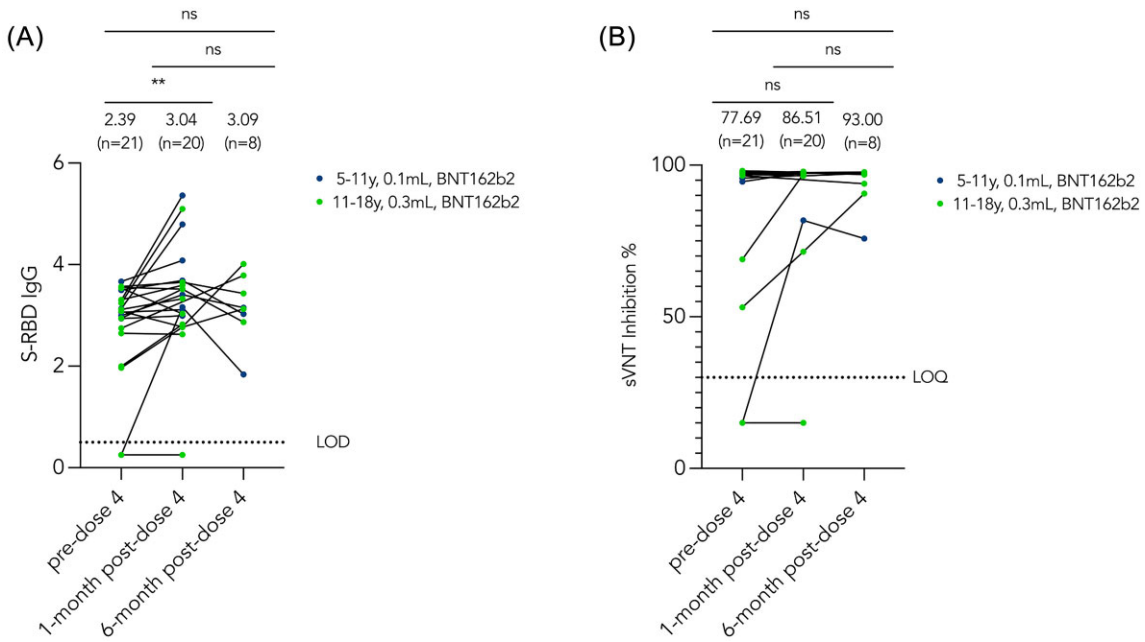

Figure 1: Antibody responses against SARS-CoV-2. Matched timepoints were compared by paired *t*-test with *P*-values denoted by asterisks. (**A**) There was a significant increase of geometric mean S-RBD IgG level after the fourth dose (pre-dose 4 to 1 month post-dose 4; 2.39 to 3.04; $P = .0089$). There was no significant different in geometric mean S-RBD IgG level between 6 months post-dose 4 and pre-dose 4/1 month post-dose 4. (**B**) Although the geometric mean sVNT inhibition level increased from 77.69% to 86.51% after the fourth dose, the difference was not significant. There was no significant different in geometric mean sVNT inhibition level between 6 months post-dose 4 and pre-dose 4/1 month post-dose 4. Geometric means are shown with center lines and stated above each column. LOD (0.5) and LOQ (30%) are drawn as dotted lines. Blue and green dots represent data from children aged 5–11 years and 11–18 years, respectively. $^{**}P < .01$; ns, not significant.

RESULTS

Study participants

A total of 21 children (median age 14.0 years; 57% male) with CKD received a fourth dose of BNT162b2 (Table 1), of which 11 children were on KRT (7 transplant recipients and 4 children on dialysis). Most children (85.7%) were on at least one immunosuppressant. All the children were Chinese. The mean time interval between their third and fourth doses was 149.6 days (minimum: 91 days; maximum: 210 days). Other children in the study were excluded from this analysis due to prior infection or insufficient visits (Supplementary data, Fig. S1).

Humoral immunogenicity

Antibody levels from pre-dose 4 to 6 months post-dose 4 are illustrated in Fig. 1. All children except two were seropositive for S-RBD IgG level at pre-dose 4. There was a significant increase in geometric mean S-RBD IgG level (2.39 to 3.04; $P = .0089$) at 1 month post-dose 4 compared with pre-dose 4. Among the two children who were seronegative at pre-dose 4, one child became seropositive, while the other remained seronegative, after the fourth dose.

The geometric mean sVNT levels rose from 77.7% to 86.5% at pre-dose 4 and 1 month post-dose 4, respectively, albeit this did not reach statistical significance. Three of four children with suboptimal sVNT levels (below 90%) at pre-dose 4 achieved improved neutralization responses at 1 month post-dose 4. sVNT levels of these three children increased from 53.1%, 69.0% and 15.0% at pre-dose 4 to 71.5%, 97.0% and 81.8% at 1 month post-dose 4, respectively. The remaining child with no improvement in neutralization response tested negative on S-RBD IgG level at 1 month post-dose 4 as well. This child was a kidney transplant recipient on triple immunosuppression including prednisolone, tacrolimus and mycophenolate mofetil. The primary diagnosis was congenital anomalies of the kidney and urinary tract (CAKUT).

There was no significant difference in S-RBD IgG or sVNT levels between 6 months post-dose 4 and pre-dose 4 or 1 month post-dose 4. Seropositive rates of different treatment groups were described, and it was found that children with transplant history had generally lower seropositivity compared with children under dialysis or children without KRT (Supplementary data, Table S1).

Cellular immunogenicity

We examined the longitudinal T-cell responses against WT SARS-CoV-2 after the fourth dose (Fig. 2A and D). We observed significant increases in S-specific IFN-γ^+CD4$^+$, IFN-γ^+CD8$^+$ and IL-2$^+$CD4$^+$ responses from pre-dose 4 to 1 month post-dose 4. There was no significant difference between 6 months post-dose 4 and pre-dose 4 or 1 month post-dose 4 in S-specific CD4$^+$ or CD8$^+$ T-cell responses. Post-dose 4 T-cell responses were generally higher among children without KRT compared with children with KRT (Supplementary data, Table S2).

Correlation of immunogenicity with specific diseases and treatments

Children with kidney transplants had significantly lower S-RBD IgG levels at 1 month post-dose 4 ($P = .0258$, mean difference: –1.291; Tukey's HSD test) compared with children without KRT (Fig. 3; Supplementary data, Table S3 and S4). There was no significant difference in immunogenicity between children with

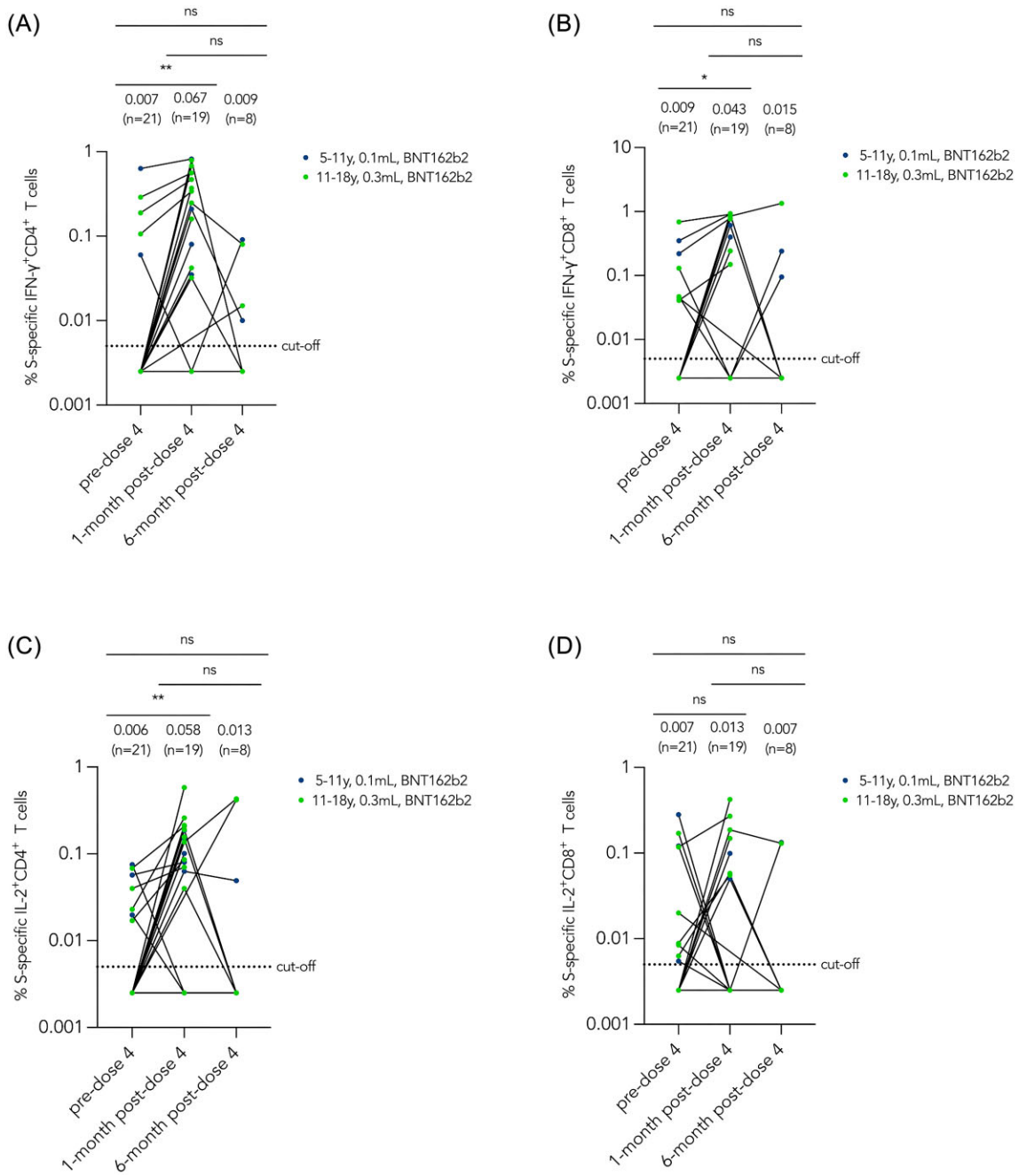

Figure 2: T-cell responses against SARS-CoV-2 proteins. T-cell responses against spike protein were tracked longitudinally. Matched timepoints were compared by paired *t*-test with *P*-values denoted by asterisks. (**A**) There was a significant increase in geometric mean IFN-γ^+CD4$^+$ between pre-dose 4 and 1 month post-dose 4 (0.007 to 0.067; $P = .0011$). (**B**) There was a significant increase in geometric mean IFN-γ^+CD8$^+$ between pre-dose 4 and 1 month post-dose 4 (0.009 to 0.043; $P = .0361$). (**C**) There was a significant increase in geometric mean IL-2$^+$CD4$^+$ between pre-dose 4 and 1 month post-dose 4 (0.007 to 0.067; $P = .0011$). (**D**) There was no significant difference in geometric mean IL-2$^+$CD8$^+$ between any two of the three timepoints (pre-dose 4, 1 month post-dose 4, 6 months post-dose 4). Geometric means are shown with center lines and stated above each column. Cut-offs (0.005) are drawn as dotted lines. Blue and green dots represent data from children aged 5–11 years old and 11–18 years old, respectively. $^*P < .05$; $^{**}P < .01$; ns, not significant.

glomerular diseases and children with non-glomerular diseases (Supplementary data, Fig. S2). While the number of immunosuppressants used did not affect the immunogenicity of the fourth dose (Supplementary data, Table S5), use of calcineurin inhibitors was significantly associated with a lower S-RBD IgG level (estimate –1.815, $P = .0049$) (Supplementary data, Table S6). There was no significant association between sVNT, IFN-γ^+CD4$^+$ and IFN-γ^+CD8$^+$ levels and the type of immunosuppressant used.

Breakthrough COVID-19

Three children (14%) had COVID-19 after receiving the fourth dose, and one child required hospitalization. There was no mortality. Two of these three children were infected within 6 months following dose 4. The sVNT levels were high for these two patients at 6 months post-dose 4 (97.5% and 97.7%).

The child who required hospitalization for SARS-CoV-2 infection was receiving chronic dialysis without any immuno-

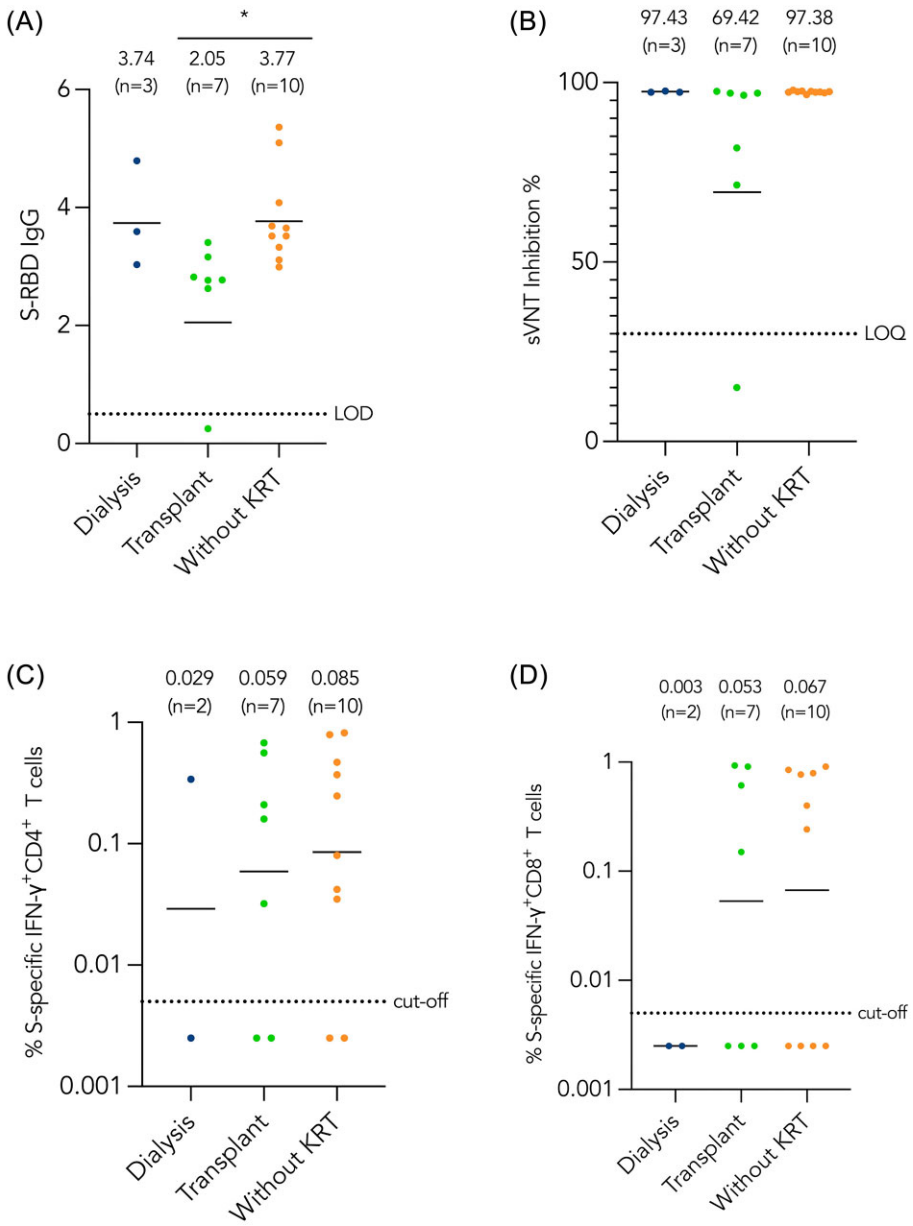

Figure 3: Antibody and T-cell responses at 1 month post-dose 4 by treatment group. Difference in immunogenicity [**(A)** S-RBG IgG, **(B)** sVNT, **(C)** IFN-γ^+CD4$^+$ and **(D)** IFN-γ^+CD8$^+$] between treatment groups were tested by ANOVA first then by Tukey's HSD post-hoc test with P-values denoted by asterisks. There was a significant difference in geometric mean S-RBD IgG level between children with transplant and children without KRT (2.05 vs 3.77; P = .0258). Geometric means are shown with center lines and stated above each column. LOD (0.5), LOQ (30%) and cut-off (0.005) are drawn as dotted lines. $^*P < .05$.

suppressant. He was admitted due to low-grade fever with fatigue. Clinical examination was unremarkable, and his chest X-ray was clear. The child recovered from the acute illness with supportive treatment within 3 days. He remained hospitalized for 1 week for management of dialysis-related issues, which were not related to his COVID-19.

Safety and reactogenicity

During the 7 days that adverse reactions were tracked after the fourth dose, mild and moderate adverse reactions were reported (Fig. 4). Three children reported use of paracetamol after receiving the fourth dose due to headache ($n = 1$) and fever ($n = 2$). During the 28 days that AEs were tracked after the fourth dose, one child with IgA vasculitis–associated nephritis reported mild gross hematuria. The symptom resolved the next day without treatment. None of the kidney transplant recipients had graft rejection after the fourth dose.

DISCUSSION

Our study provided novel data on the immunogenicity and safety of the fourth dose of BNT162b2 among children with CKD. Overall, children with CKD achieved high antibody levels and T-cell responses after the fourth dose. However, antibody

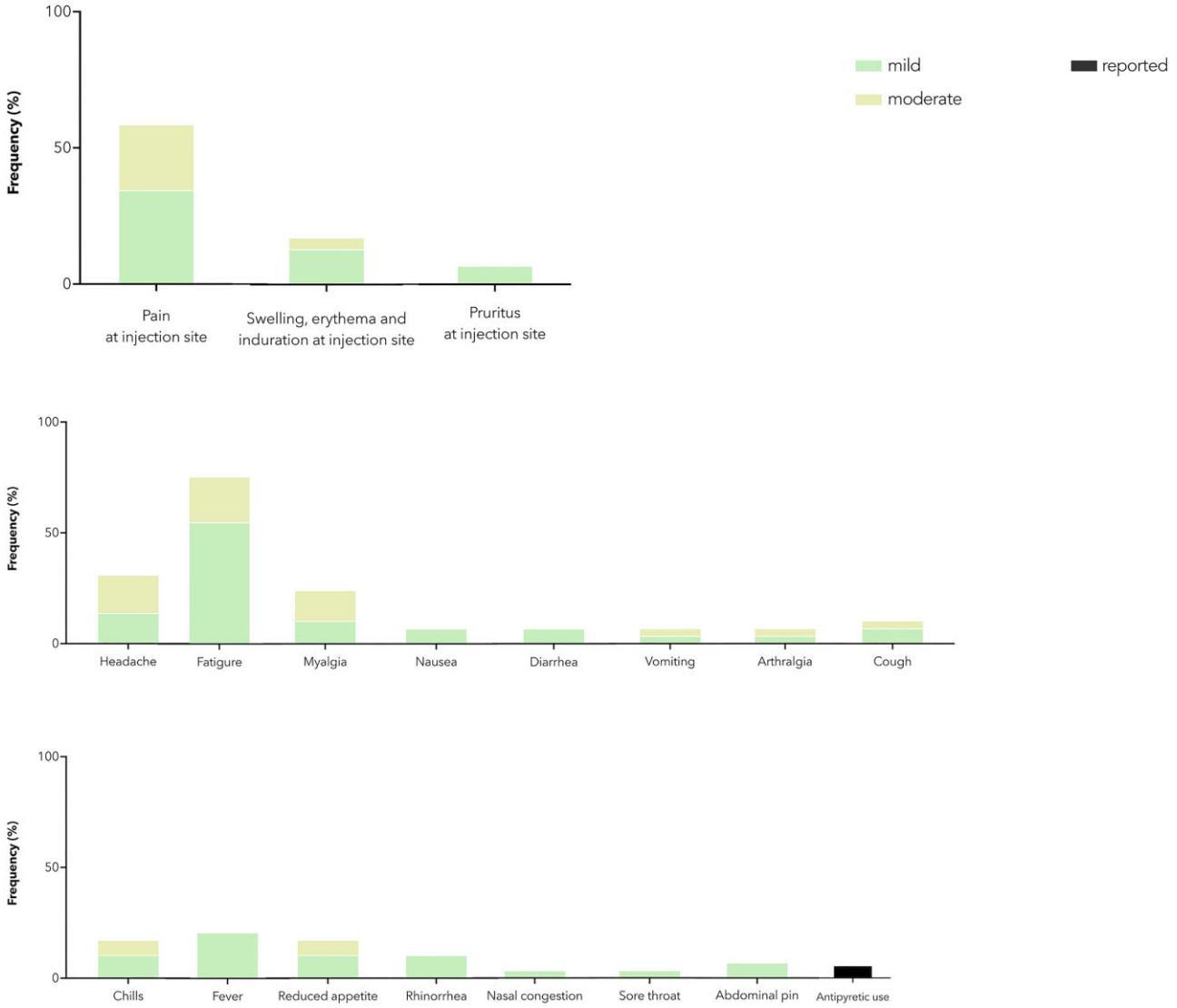

Figure 4: Adverse reactions and antipyretic use reported 7 days after the fourth dose. All adverse reactions were reported as mild or moderate. The five most common adverse reactions were fatigue (75.9%), pain at the injection site (58.6%), headache (31.0%), myalgia (24.1%) and fever (20.7%).

responses were lower in children with transplant history or the use of calcineurin inhibitors compared with other subgroups.

Although it has been over three years since COVID-19 vaccines became available, data on children with CKD receiving the fourth dose remain limited. While antibodies confer protection from developing COVID-19, T-cell immunity is crucial in preventing severe COVID-19 [16]. Our study results showed significant induction of S-RBD IgG and T-cell responses in children with CKD after the fourth dose. In this cohort, four children were seronegative before the fourth dose, among which three children achieved adequate antibody responses after the fourth dose. At 6 months post-dose 4, no significant waning trend was observed. Antibody levels remained high, which should confer protection to children with CKD. Overall, our results suggested a fourth dose of BNT162b2 could confer protection against infection and severe COVID-19 among children with CKD.

In a previous study, adult patients with CKD on KRT were reported to have lower humoral and cellular responses than healthy individuals [17, 18]. In our study, pediatric CKD patients with kidney transplant history had lower humoral responses compared with dialysis patients at both pre-dose and post-dose time points. These patients often receive triple immunosuppression, including corticosteroids, mycophenolate mofetil and calcineurin inhibitors, and are susceptible to reduced immunogenicity and waning of antibody responses [19]. In addition to our previous finding that lower sVNT levels were observed among children receiving mycophenolate mofetil after the second dose, this current study demonstrated that the use of calcineurin inhibitors was associated with lower S-RBD IgG levels after the fourth dose [11].

Safety issues remain acceptable after the fourth dose. It is noteworthy that one child with IgA vasculitis–associated nephritis reported an AE of mild gross hematuria. Gross hematuria after the COVID-19 vaccine among patients with IgA nephropathy has been reported in adults [20, 21]. Nonetheless, these patients remained well and there was spontaneous resolution of gross hematuria without any long-term AE. While breakthrough infection can be common, it was reported that

dialysis patients have a higher risk of being hospitalized [17, 22]. Three children in our study reported breakthrough infections following the fourth dose. None of these children developed severe COVID-19, and one child had prolonged hospitalization mostly due to dialysis-related complications.

Currently, the Centers for Disease Control and Prevention recommend a three-dose COVID-19 vaccine regimen for children who are moderately or severely immunocompromised, including CKD and kidney failure patients [23]. In Hong Kong, CHP recommends individuals with immunocompromised conditions receive an additional booster at least 180 days after previous vaccination or past infection [13]. Our results provided evidence that a fourth dose of the COVID-19 vaccine is safe and immunogenic among pediatric CKD patients. Pediatric CKD patients are advised to receive the fourth dose, especially kidney transplant recipients. This is due to poor immunogenicity and potential waning of humoral responses among kidney transplant recipients.

This study provided prospective data on both antibody and T-cell responses longitudinally in children with CKD after a fourth dose of BNT162b2, which is, to our knowledge, not available in the literature. However, this study was limited by the small sample size of 21 children aged >5 years, and we did not include a control group using the standard vaccination. The majority of patients recruited were aged >12 years, which is a limitation and may interfere with the interpretation of the results. For this study, 0.1 mL BNT162b2 of the adult formulation was utilized for children aged 5–11 years, which could have resulted in differences in reactogenicity and immunogenicity from the actual pediatric formulation, although not likely as the dosages are the same. We were unable to assess the clinical effectiveness of the fourth dose due to the limited study population. Due to the Omicron wave which caused many cases of severe COVID-19 and deaths rapidly in 2022, we have adopted an accelerated vaccination regimen to achieve adequate and timely protection for children with CKD [11]. However, a longer prime-booster interval has been reported to result in better immunogenicity, in general [24].

In conclusion, we demonstrated that a fourth dose of BNT162b2 is safe and immunogenic for children with CKD against COVID-19. Prioritization to pediatric kidney transplant recipients is recommended, owing to their lower immunogenicity compared with other CKD patients.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

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AUTHORS' CONTRIBUTIONS

Y.L.L. conceptualized the study. Y.L.L., M.P., J.S.R.D., W.T. and D.L. designed the study. Y.L.L. led the acquisition of funding. Y.L.L., W.T. and M.P. supervised the project. S.M.C., J.C.H.C., S.M.S.C., D.L., I.Y.S.T., K.Z. and J.H.Y.L. led the study of administrative procedures. A.L.-T.M., Y.L.L., J.S.R.D., E.Y.-H.C., S.C., F.T.-W.H., P.C.T. and M.H.L.L. provided study-related clinical assessments and follow-up. S.M.C., J.H.Y.L., J.C.H.C., D.L., J.S.R.D. and Y.L.L. collected clinical safety data. S.M.S.C., L.C.H.T., T.-C.K. and M.P. developed and performed S-RBD IgG and sVNT assay. H.H.W.W., Y.C.C., M.W., A.M.T.L., W.Y.L. and W.T. developed and performed the T-cell assays. J.C.H.C. and J.H.Y.L. curated, analyzed and visualized the data. J.C.H.C., D.L., S.M.S.C., J.S.R.D., J.H.Y.L., S.M.C. and K.Z. validated the data. J.C.H.C. and E.Y.-H.C. drafted the manuscript and were supervised by A.L.-T.M., J.S.R.D. and Y.L.L., with input from D.L. and S.M.S.C. All authors reviewed and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data can be shared upon reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.

REFERENCES

1. Ortiz A. CKD as a risk factor for severe COVID-19: a critical look back and lessons for the future. *Nephrol Dial Transplant* 2024;**39**:174–6. https://doi.org/10.1093/ndt/gfad216
2. Krishnasamy S, Mantan M, Mishra K *et al*. SARS-CoV-2 infection in children with chronic kidney disease. *Pediatr Nephrol* 2022;**37**:849–57. https://doi.org/10.1007/s00467-021-05218-1
3. Canpolat N, Yıldırım ZY, Yıldız N *et al*. COVID-19 in pediatric patients undergoing chronic dialysis and kidney transplantation. *Eur J Pediatr* 2022;**181**:117–23. https://doi.org/10.1007/s00431-021-04191-z
4. Chan EYH, Yap DYH, Wong WHS *et al*. Demographics and long-term outcomes of children with end-stage kidney disease: a 20-year territory-wide study. *Nephrology* 2022;**27**:171–80. https://doi.org/10.1111/nep.14007
5. Mu X, Cohen CA, Leung D *et al*. Antibody and T cell responses against wild-type and Omicron SARS-CoV-2 after third-dose BNT162b2 in adolescents. *Sig Transduct Target Ther* 2022;**7**:397. https://doi.org/10.1038/s41392-022-01282-7
6. Rosa Duque JS, Wang X, Leung D *et al*. Immunogenicity and reactogenicity of SARS-CoV-2 vaccines BNT162b2 and CoronaVac in healthy adolescents. *Nat Commun* 2022;**13**:3700. https://doi.org/10.1038/s41467-022-31485-z
7. Leung D, Rosa Duque J, Tu W *et al*. Immunogenicity of coronavirus disease 2019 vaccines in children: a review with ChatGPT. *Pediatr Discov* 2023;**1**:e8. https://doi.org/10.1002/pdi3.8
8. Bathish Y, Tuvia N, Eshel E *et al*. Abu-Jabal K. B and T cell responses to the 3rd and 4th dose of the BNT162b2 vaccine in dialysis patients. *Hum Vaccin Immunother* 2024;**20**:2292376. https://doi.org/10.1080/21645515.2023.2292376
9. Choe YJ, Ahn YH, Gwak E *et al*. Safety of BNT162b2 mRNA COVID-19 vaccine in children with chronic kidney disease: a national population study from South Korea. *Pediatr Nephrol* 2024;**39**:625–9. https://doi.org/10.1007/s00467-023-06195-3

10. Babel N, Hugo C, Westhoff TH. Vaccination in patients with kidney failure: lessons from COVID-19. *Nat Rev Nephrol* 2022;**18**:708–23. https://doi.org/10.1038/s41581-022-00617-5
11. Leung D, Chan EY, Mu X *et al*. Humoral and cellular immunogenicity of 3 doses of BNT162b2 in children with kidney diseases. *Kidney Int Rep* 2023;**8**:2356–67. https://doi.org/10.1016/j.ekir.2023.08.014
12. Ma AL-T, Leung D, Chan EY-H *et al*. Antibody responses to 2 doses of mRNA COVID-19 vaccine in pediatric patients with kidney diseases. *Kidney Int* 2022;**101**:1069–72. https://doi.org/10.1016/j.kint.2022.01.035
13. Centre for Health Protection. How Many Doses of COVID-19 Vaccine Are Recommended for Me? 2023. https://www.chp.gov.hk/files/pdf/poster_recommend_dose.pdf (18 July 2024, date last accessed).
14. Perera R, Ko R, Tsang OTY *et al*. Evaluation of a SARS-CoV-2 surrogate virus neutralization test for detection of antibody in human, canine, cat, and hamster sera. *J Clin Microbiol* 2021;**59**. https://doi.org/10.1128/JCM.02504-20
15. Perera RA, Mok CK, Tsang OT *et al*. Serological assays for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), March 2020. *Euro Surveill* 2020;**25**. https://doi.org/10.2807/1560-7917.ES.2020.25.16.2000421
16. Goldblatt D, Alter G, Crotty S *et al*. Correlates of protection against SARS-CoV-2 infection and COVID-19 disease. *Immunol Rev* 2022;**310**:6–26. https://doi.org/10.1111/imr.13091
17. Rouphael N, Bausch-Jurken M. COVID-19 vaccination among patients receiving maintenance renal replacement therapy: immune response, real-world effectiveness, and implications for the future. *J Infect Dis* 2023;**228**:S46–54. https://doi.org/10.1093/infdis/jiad162
18. Vaiciuniene R, Sitkauskiene B, Bumblyte IA *et al*. Immune response after SARS-CoV-2 vaccination in kidney transplant patients. *Medicina (Kaunas)* 2021;**57**:1327. https://doi.org/10.3390/medicina57121327
19. Emmanouilidou-Fotoulaki E, Karava V, Dotis J *et al*. Immunologic response to SARS-CoV-2 vaccination in pediatric kidney transplant recipients: a systematic review and meta-analysis. *Vaccines* 2023;**11**:1080. https://doi.org/10.3390/vaccines11061080
20. Matsuzaki K, Aoki R, Nihei Y *et al*. Gross hematuria after SARS-CoV-2 vaccination: questionnaire survey in Japan. *Clin Exp Nephrol* 2022;**26**:316–22. https://doi.org/10.1007/s10157-021-02157-x
21. Negrea L, Rovin BH. Gross hematuria following vaccination for severe acute respiratory syndrome coronavirus 2 in 2 patients with IgA nephropathy. *Kidney Int* 2021;**99**:1487. https://doi.org/10.1016/j.kint.2021.03.002
22. Artborg A, Caldinelli A, Wijkström J *et al*. Risk factors for COVID-19 hospitalization and mortality in patients with chronic kidney disease: a nationwide cohort study. *Clin Kidney J* 2024;**17**. https://doi.org/10.1093/ckj/sfad283
23. The Centers for Disease Control and Prevention. *COVID-19 Vaccines for People Who Are Moderately or Severely Immunocompromised*. 2024. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html (18 July 2024 , date last accessed).
24. Voysey M, Costa Clemens SA, Madhi SA *et al*. Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials. *Lancet* 2021;**397**:881–91. https://doi.org/10.1016/S0140-6736(21)00432-3

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