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Association of COVID-19 Versus COVID-19 Vaccination With Kidney Function and Disease Activity in Primary Glomerular Disease: A Report of the Cure Glomerulonephropathy Study

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Abstract

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Rationale & Objective: Patients with glomerular disease (GN) may be at increased risk of severe COVID-19, yet concerns over vaccines causing disease relapse may lead to vaccine hesitancy. We examined the associations of COVID-19 with longitudinal kidney function and proteinuria and compared these to similar associations with COVID-19 vaccination.

Study Design: Observational cohort study from July 1, 2021 to Jan. 1, 2023.

Setting & Participants: A prospective observational study network of 71 centers from North America and Europe (CureGN) with children and adults with primary minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, or IgA nephropathy.

Exposures: COVID-19 and COVID-19 vaccination.

Outcomes: Repeated measure of estimated glomerular filtration rate (eGFR); recurrent time-to-event outcome of GN disease worsening as defined by doubling of UPCR to at least 1.5g/g or increase in dipstick urine protein by two ordinal levels to 3+ (300mg/dL) or above.

Analytical Approach: Interrupted time series analysis for eGFR. Prognostic matched sequential stratification recurrent event analysis for GN disease worsening.

Results: Among 2,055 participants, 722 (35%) reported COVID-19; of these, 92 (13%) were hospitalized and 3 died (<1%). eGFR slope pre-COVID-19 was −1.40ml/min/1.73m^2 (SD 0.29), and −4.26ml/min/1.73m^2 (SD 3.02) within 6 months post-COVID-19, which were not significantly different (p=0.34). COVID-19 was associated with increased risk of worsening GN disease activity (HR 1.35, 95% CI 1.01-1.80). Vaccination was not associated with change in eGFR (−1.34ml/min/1.73m^2, SD 0.15 vs −2.16ml/min/1.73m^2, SD 1.74; p=0.6) or subsequent GN disease worsening (HR 1.02, 95% CI 0.79–1.33) in this cohort.

Limitations: Infrequent or short follow-up.

Conclusions: Among patients with primary GN, COVID-19 was severe for 1 in 8 cases and was associated with subsequent worsening of GN disease activity, as defined by proteinuria. In contrast, vaccination against COVID-19 was not associated with change in disease activity or kidney function decline. These results support COVID-19 vaccination for patients with GN.

Plain Language Summary

In this cohort study of 2,055 patients with minimal change disease, focal segmental glomerulosclerosis, membranous nephropathy, or IgA nephropathy, COVID-19 resulted in hospitalization or death for 1 in 8 cases and was associated with a 35% increase in risk for worsening proteinuria. In contrast, vaccination did not appear to adversely affect kidney function or proteinuria. Our data support vaccination for COVID-19 in patients with glomerular disease.

Keywords

COVID-19; COVID-19 vaccines; vaccination; glomerulonephritis; glomerular filtration rate; focal segmental glomerulosclerosis; membranous glomerulonephritis; lipoid nephrosis; IgA glomerulonephritis

INTRODUCTION

Individuals with primary glomerular diseases (GN) are at risk for severe illness caused by coronavirus SARS-CoV-2 (COVID-19), including hospitalization, kidney replacement therapy (KRT), and death.[1] Putative risk factors include a higher prevalence of hypertension and diminished kidney function.[2–5] Both GN and COVID-19 result in a hypercoagulable state, and thrombotic events in COVID-19 have high morbidity and mortality.[6] Additionally, immunosuppression exposure, a frequent aspect of GN treatment, has been linked to attenuated response to COVID-19 vaccines and could blunt the effectiveness of vaccines in mitigating COVID-19.[1]

Aside from the potential increased risk of severe COVID-19, there is added concern that COVID-19 may exacerbate GN disease and decline in kidney function. COVID-19 produces dysregulated inflammation and has been associated with *de novo* glomerular disease such as collapsing glomerulopathy and membranous nephropathy as well as disease relapse in patients with pre-existing GN.[1] Acute kidney injury (AKI) from severe COVID-19 is also common among patients with GN and may increase the risk of kidney failure.[7,8] Patients with these rare kidney diseases are thus a particularly vulnerable group in the global COVID-19 pandemic, and information on how the illness affects GN disease activity are urgently needed.

As highly effective COVID-19 vaccines have become available to most individuals in high-resource countries, it has become particularly important to understand vaccine uptake in those with GN. Reports of disease relapse following vaccination have been described, which may result in vaccine hesitancy.[9–11] Prospective information on GN disease activity after COVID-19 vaccination is needed to assist patients and clinicians in reaching the decision to vaccinate.

The National Institutes of Health (NIH)-sponsored Cure Glomerulonephropathy (CureGN) observational study, a network of 71 centers and >2,500 patients across the United States (U.S.), Canada, and Europe, implemented a consortium-wide effort to describe COVID-19 epidemiology and vaccination in patients with GN. The aim of this study was to report the association of COVID-19 versus COVID-19 vaccination with kidney function and GN disease activity.

METHODS

CureGN Study Participants

CureGN is a prospective observational cohort study of children and adults with biopsy-proven primary minimal changes disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), or IgA nephropathy/vasculitis (IgAN). Patients are ineligible if they have kidney failure, history of solid-organ or bone marrow transplant, active HIV infection, hepatitis B or C infection, diabetes mellitus, systemic lupus erythematosus, or active malignancy. Participants are enrolled within five years of a diagnostic kidney biopsy and are followed with a minimum of one in-person visit and biospecimen collection (blood and urine samples) per year plus two additional visits to align with outpatient nephrology clinic visits. Serum creatinine and calculated estimated glomerular filtration rate (eGFR; race free CKD-EPI creatinine equation for those ≥25 years and the U25 equation for those <25)[12,13] as well as urine protein to creatinine ratio (UPCR) are obtained from the medical record at all study visits. Participants are recruited from 65 sites in the U.S., four in Canada, one in Poland, and one in Italy. Details on study design and the cohort have been published and are available on the CureGN website (https://curegn.org).[14] Enrollment began in 2015 and is ongoing. As of January 1, 2023, 2,698 participants have been enrolled, with median follow-up of 4.5 years. The CureGN protocol was approved by the single institutional review board (sIRB) per NIH policy for multi-site research. All participants and/or legal guardians of children provided informed consent, and assent was obtained from minors where age appropriate.

COVID-19 and Vaccination

Beginning on July 1, 2021, approximately 1.5 years after the first patients with COVID-19 were identified in the U.S.,[15] COVID-19 infection and vaccination information were collected by study coordinators on all CureGN participants at each study visit. The data collection instrument prompted research coordinators to ask participants and review medical records for COVID-19 diagnosis (definitely, probably or suspected, no, or unknown), method(s) of diagnosis (symptoms, positive antigen test, positive antibody test, and/or close contact with someone who had COVID-19), date(s) of antigen and antibody tests and results, hospitalizations for COVID-19, mechanical ventilation for COVID-19, and COVID-19 vaccine type and vaccination dates (File S1). Detailed information on hospitalizations, such as admission to the intensive care unit (ICU) and need for renal replacement therapy, as well as information on deaths, cause of death, progression to kidney failure (defined by kidney replacement therapy requirement, kidney transplantation, or two eGFR measurements <15ml/min/1.73m^2) were collected as part of ongoing CureGN study procedures.

COVID-19 Association with eGFR and GN Disease Activity

Exposure—COVID-19 was defined as participants who reported “definitely” or “probably or suspected” COVID-19 or had positive antigen test for COVID-19. Incidence of COVID-19 was reported as cases per person-time and plotted as the number of cases over calendar time overlaid with publicly available US national data from the CDC.[16] The proportion of COVID-19 episodes complicated by hospitalization, ICU admission, intubation and mechanical ventilation, dialysis, and death were described.

Outcome Measures—We examined the association of COVID-19 with 1) eGFR and 2) GN disease activity based on the degree of proteinuria (primary measures). The eGFR estimates and proteinuria data are based on serum and urine samples collected during CureGN study visits, which are aligned with outpatient nephrology clinic visits. Lab values associated with hospitalizations or unscheduled clinical care (e.g. emergency room visits) are not used. Worsening GN disease activity was defined as doubling of UPCR to at least 1.5g/g or increase in dipstick urine protein by two ordinal levels to 3+ (300mg/dL) or above. A secondary outcome measure was the progression to kidney failure among those who developed COVID-19.

Statistical Analyses

Association of COVID-19 with eGFR: Change in eGFR associated with COVID-19 was examined using interrupted time series analysis, with COVID-19 as the “interruption” in the trajectory of eGFR over time. Participants with self-reported COVID-19 and at least two eGFR values before and after COVID-19 were included in this analysis. Estimated mean (standard deviation, SD) eGFR value and mean (SD) change in eGFR slope (ml/min/1.73m^2 per year) before and after COVID were tested for statistically significant differences using a segmented mixed effects linear regression model.[17] Participant-specific random intercepts and slopes were included to account for the correlation among eGFR measurements from the same participant. In this way the post-COVID eGFR slope can be interpreted as the average eGFR trajectory post-initial COVID infection. We also described the proportion of participants who progressed to kidney failure following COVID-19, stratified by vaccination status.

Association of COVID-19 with GN Disease Activity: To examine the association of COVID-19 illness with GN disease activity, a prognostic matched sequential stratification recurrent event analysis[18] was performed to compare the risk of GN disease worsening between those who experienced COVID-19 (index) and those who had not experienced COVID-19 (control) but had similar disease trajectory to the index participant before they became ill. Participants were required to have at least two urine protein measurements (UPCR or urine dipstick results) before and after illness. Index participants were matched with controls in a one-to-many scheme based on calculated probability of worsening of GN disease activity within 0.005 at the time of COVID-19. The probability was calculated using a time-dependent recurrent event prognostic model built using time of diagnostic biopsy as time zero with censoring at the time of COVID-19 or last follow-up visit and adjusted for duration of GN disease, COVID-19 vaccination, sex, histology subtype, age at biopsy, race, ethnicity, UPCR at biopsy, and time dependent eGFR. Participants could serve as controls in multiple strata if they met criteria. Median number of matches per index patient, frequency and percent of index participants matched, and the distribution of difference in probability of worsening of GN disease activity before and after matching were explored.

Within the matched sets, participants who had not yet experienced COVID-19 infection were censored from strata in which they served as controls at the time of their first COVID-19 infection and subsequently began their own stratum as the index patient. While analysis of the matched sets is conditional on the probability of worsening of GN disease activity up to the time of matching, they were not conditional on trajectories of worsening of GN disease activity between the time of COVID-19 infection for the index participant and censoring time for control participants that subsequently experienced COVID-19 infections. Given the common use of immunosuppression in this population and the relationships between treatment and worsening of GN disease activity, it is likely that worsening of disease activity was associated with probability of experiencing COVID-19 infection, resulting in dependent censoring for control participants censored due to COVID-19 infection. To account for this dependent censoring, we used inverse probability of treatment weighting within all matched sets.[19] Weights were developed by modeling the probability of COVID-19 infection using a time-dependent Cox model adjusted for duration of GN disease, sex, diagnosis, age at biopsy, race, ethnicity, UPCR at biopsy, and time dependent eGFR.

Once the weighted matched sets were established, a stratified recurrent event model was fitted with COVID-19 as the primary exposure and adjusted for the distance in probability of worsening of GN disease activity at the time of illness between the index participant and matched controls. Standard errors were estimated using bootstrapping.[19] Results were reported as hazard ratio (HR) with 95% confidence interval (95% CI) for GN relapse following COVID-19.

COVID-19 Vaccination Association with eGFR and GN Disease Activity

Exposure—A participant is considered to have received a COVID-19 vaccine if they answered "Yes" on the data collection form and the date of the vaccine was recorded. The proportion of CureGN participants who reported having received at least one COVID-19 vaccine versus those who had not were plotted over calendar time, stratified by age. We described the type of vaccines received; proportion of fully vaccinated participants (two doses of an mRNA COVID-19 vaccine, two doses of the Novavax COVID-19 vaccine, and a single dose of Johnson & Johnson/Janssen COVID-19 vaccine)[20]; and plotted those who received at least one vaccine *vs*. unvaccinated over calendar time, stratified by age.

Outcome Measures—We examined the association of COVID-19 vaccination with 1) eGFR and 2) GN disease activity based on the degree of proteinuria (primary measures).

Statistical Analyses

<u>Association of COVID-19 Vaccination with eGFR and GN Disease Activity:</u> We examined change in eGFR associated with COVID-19 vaccination in a similar approach as described above, with vaccination as the "interruption" in the interrupted time series analysis. To assess the effect of COVID-19 vaccination on GN disease activity, we again performed a weighted prognostic matched sequential stratification recurrent event analysis. However, in this case index participants were defined by COVID vaccination, not COVID infection. All statistical analyses were completed using SAS 9.4 (Cary, North Carolina).

RESULTS

COVID-19 and COVID-19 vaccination among CureGN Participants

From July 1, 2021 to January 1, 2023, 2,055 CureGN participants had study visits and data collected on COVID-19 and vaccination (Table 1). Median number of completed study visits per person with COVID-19 and vaccination information was 3 (interquartile range [IQR], 2-3). A total of 722 (35%) of participants experienced COVID-19, resulting in an incidence rate of 15.2 per 100 person-years since January 1, 2020. Patterns of first incidence of COVID-19 infection in the CureGN cohort were similar to U.S. trends (Figure 1).[16] Of the 722 participants who experienced COVID-19, 92 (13%) were hospitalized including 5 admitted to the ICU (1%) and 3 deaths (<1%). One participant received acute kidney replacement therapy. Eight patients progressed to kidney failure after COVID-19 with a median time of 322 days (IQR 274-453 days); seven of the eight patients were unvaccinated at the time of their COVID-19 episode.

One thousand four hundred seven (68%) CureGN participants reported receiving at least one COVID-19 vaccine. The proportion of vaccinated individuals remained relatively constant since Summer 2021, with the lowest uptake among the pediatric subgroups (Figure 2). The majority of participants received mRNA based vaccines (94%, Table S1). By January 1, 2023, 65% of the CureGN participants were fully vaccinated against COVID-19.

Association of COVID-19 with eGFR and GN Disease Activity

Among the 722 CureGN participants who developed COVID-19, 232 participants had at least two eGFR measurements before and two after their illness. Median duration of follow-up was 3.67 years (IQR 1.22-5.11) before illness and 0.84 years (IQR 0.57-1.32) after illness. Slope of eGFR pre-COVID-19 was −1.40ml/min/1.73m^2 per year (SD 0.29; *p* <0.001 for non-zero slope), based on a median (IQR) of 13 (7-20) eGFR measurements prior to illness. Slopes post-COVID-19 were calculated with a median (IQR) of 3 (2-4) eGFR measurements following COVID-19. The eGFR slope within 6 months post-COVID-19 was −4.26ml/min/1.73m^2 per year (SD 3.02; p=0.16 for non-zero slope), which was not statistically different from pre-COVID-19 (p=0.3) (Figure 3A). No statistically significant differences in slopes were identified between patients who were vaccinated at the time of their COVID-19 infection (n=110) compared to those who were not (n=122).

Five hundred eight-three participants had at least two urine protein or dipstick measurements before and after their illness. A median of 11 (IQR 6-19) measurements of proteinuria were available for those who developed COVID-19 prior to illness, and 3 (IQR 2-4) measurements were available after the illness to generate modeling of risk for GN disease activity worsening. A median of 16 (IQR 7-35) matched controls were identified as the closest prognostic matches to each participant at time of their COVID infection and all patients had at least one prognostic match. Figure S1 shows the distribution of the prognostic match probabilities used in this analysis. Comparing GN disease activity between those who experienced COVID-19 to matched controls who did not experience it, COVID-19 was significantly associated with subsequent GN disease worsening (HR 1.35, 95% CI 1.01 – 1.80, *p* 0.04).

Association of COVID-19 Vaccination with eGFR and GN Disease Activity

Among the 1,407 CureGN participants who received a COVID-19 vaccination, 705 participants had at least two eGFR measurements before and two after their illness. Median duration of follow-up was 3.59 year (95% CI, 1.80-4.75) before vaccination and 1.33 years (95% CI, 1.02-1.63) after vaccination. COVID-19 vaccination was not associated with decline in eGFR following vaccination (Figure 3B). Pre-vaccine eGFR slope was −1.34ml/min/1.73m^2 per year (SD 0.15), based on a median (95% IQR) of 13 (8-21) eGFR measurements prior to vaccination. There was no significant change in eGFR at time of vaccination (−0.01 ml/min/1.73m^2, SD 0.68; *p* 0.98) or post-vaccine (slope within the first 6 months post vaccine −2.16 ml/min/1.73m^2, SD 1.74; p=0.64 compared to pre-vaccine slope; slope >6 moths post vaccine −1.58 ml/min/1.73m^2, SD 0.66; p=0.78 compared to pre-vaccine slope), based on a median (95% IQR) of 3 (2-5) eGFR measurements after vaccination.

One thousand one hundred twenty-nine participants had at least two urine protein or dipstick measurements before and after their COVID-19 vaccination. A median of 12 (IQR 7-19) measurements of proteinuria were available for those who received the COVID-vaccination prior to their vaccination, and 3 (IQR 2-5) measurements were available after vaccination to generate modeling of risk for GN disease activity worsening. A median of 14 (IQR 6-26) matched controls were identified as the closest prognostic matches to patients at the time of their COVID vaccination (Figure S2) and all patients had at least one prognostic match. Comparing GN disease activity between those who received a COVID-19 vaccine to matched controls who did not, vaccination did not associate with higher risk of subsequent GN disease worsening (HR 1.02, 95% CI 0.79 – 1.33, p 0.87). No significant differences in GN disease worsening were identified when comparing patients who were vaccinated at the time of their COVID-19 infection to those who were not vaccinated at the time of their COVID-19 infection.

DISCUSSION

In this large cohort study of 2,055 adults and children with primary GN from North America and Europe, we demonstrate that COVID-19 was frequently reported, about 1 in 3 patients. Among them, COVID-19 was severe and resulted in hospitalization or deaths for 1 in 8 cases. COVID-19 was also associated with higher risk for increased GN disease activity, defined by at least a two-fold increase in proteinuria. In contrast to COVID-19, vaccination against COVID-19 did not associate with higher risk of GN disease activity, as defined by proteinuria. We did not observe significant changes in kidney function associated with COVID-19 or vaccination over this relatively short follow-up.

The vulnerabilities of patients with GN have been observed in other smaller cohorts. The United Kingdom's ICHNT Renal COVID-19 Group reported systematic SARS-CoV-2 serology screening results in 493 patients with primary GN, vasculitis, and systemic lupus erythematosus prior to December 2020. Nineteen percent of all cases required hospitalization and 7% resulted in death, proportions higher than an Icelandic study of the general population which also used systematic screening in a similar time period.21 An analysis by The International Registry of COVID-19 in GN (IRoc-GN) of 125 patients with GN and 85 controls with COVID-19 from April 2020 to April 2021 found that AKI occurred in nearly half of GN patients. Patients with GN were less likely to recover kidney function compared to controls.22 In a smaller subset of CureGN participants with available eGFR data, we observed a decline in kidney function within the first 6 months post-COVID-19. Though our findings were not statistically significant, together with the earlier observations from IRoc-GN, they do suggest that patients with GN may be at higher risk for AKI and declines in kidney function due to COVID-19 and need closer follow-up. Of note, our study period included cases from the start of the COVID-19 pandemic to January 1, 2023, with the majority of cases occurring after Fall 2022. Advancements in COVID-19 treatment as well as changing virulence of the SARS-CoV2 virus strains may explain differences in patient outcome in our cohort compared to earlier reports.

Our finding that COVID-19 was associated with a 35% increase in risk of GN disease worsening after infection further highlights the risks faced by patients with GN during the COVID-19 pandemic as the infection could potentially exacerbate GN disease activity. Unfortunately, we observed a plateau in percentage of vaccinated individuals over time. In promoting vaccine uptake among patients with kidney disease, it is important to communicate information that is relevant to a patient's health and specific concerns.[11] Our data address a fear within the GN community that COVID-19 vaccination may trigger GN disease relapse, as reported in several case series.[9,10,23] In CureGN, 1,407 patients with primary GN received COVID-19 vaccines, and vaccination was not associated with GN disease worsening or declines in kidney function. A recent population-based study of Hong Kong residents similarly found no evidence of increased risk of glomerular disease relapse after COVID-19 vaccination.[24] Another cohort study of 1,105 adult patients with GN in British Columbia, Canada found no association between first dose COVID-19 vaccine and GN relapse, but there was a small 1-5% increase in absolute risk of relapse with a subsequent vaccine dose.[25] Given the risks patients with GN face from COVID-19, including a significantly increased risk of worsening proteinuria, our results strongly support COVID-19 vaccination for patients with GN. Of note, our cohort consisted of only those with primary minimal change disease, primary focal segmental glomerulosclerosis, primary membranous nephropathy, and primary IgA nephropathy. Extrapolation to those with rarer primary GN conditions or secondary GN conditions such as lupus nephritis may not be appropriate.

This report contains COVID-19 and vaccine data collected both retrospectively and prospectively from a large primary GN cohort of adults and children. Data collection instruments were designed by GN disease experts and administered at each study visit for more than one year, capturing up-to-date information as the pandemic evolved. Limitations of this study include incomplete sampling of CureGN participants (2,055 of 2,698 total participants) due to missed or cancelled research visits during the pandemic.[26] In addition, we relied on participant self-report and review of electronic health records for COVID-19 case identification. Mild or asymptomatic infection may have been missed. Overall, available eGFR and proteinuria measurements are relatively few following COVID-19 or vaccination, which reduced the reliability of our estimates of eGFR trajectory and disease activity. Our analyses required participants to have had serum and urine labs performed, and may be biased towards those with more severe GN who are followed more frequently in nephrology clinics, though the comparison of eGFR trajectory between those who developed COVID-19 with and without vaccines would still be valid. Lastly, for those who experienced COVID-19 or received vaccines recently, the associations with eGFR and GN disease activity are yet unclear due to the relatively short follow-up.

In conclusion, COVID-19 occurred commonly and was often severe in patients with primary GN from the CureGN cohort. COVID-19 also associated with higher risk of increased GN disease activity as defined by proteinuria. In contrast, COVID-19 vaccination was not associated with GN disease activity. Strategies to promote COVID-19 vaccination are critical to prevent COVID-19 and its major sequelae including GN relapse and decline in kidney function.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Appendix

CureGN Study Consortium Members: In addition to authors Wang, Glenn, Smith, Bomback, Canetta, Coppock, Khalid, Tuttle, Bou-Matar, Greenbaum, Robinson, Holzman, Smoyer, Rheault, Gipson and Mariani, the CureGN Consortium members listed below, from within the four Participating Clinical Center networks and Data Coordinating Center, are acknowledged by the authors as Collaborators.

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Data Sharing:

De-identified participant data presented in the current report will be available to investigators who submit and receive approval from the CureGN Data Coordinating Center and execute a data sharing agreement. More information can be found at the CureGN website: curegn-org.webflow.io/for-researchers.

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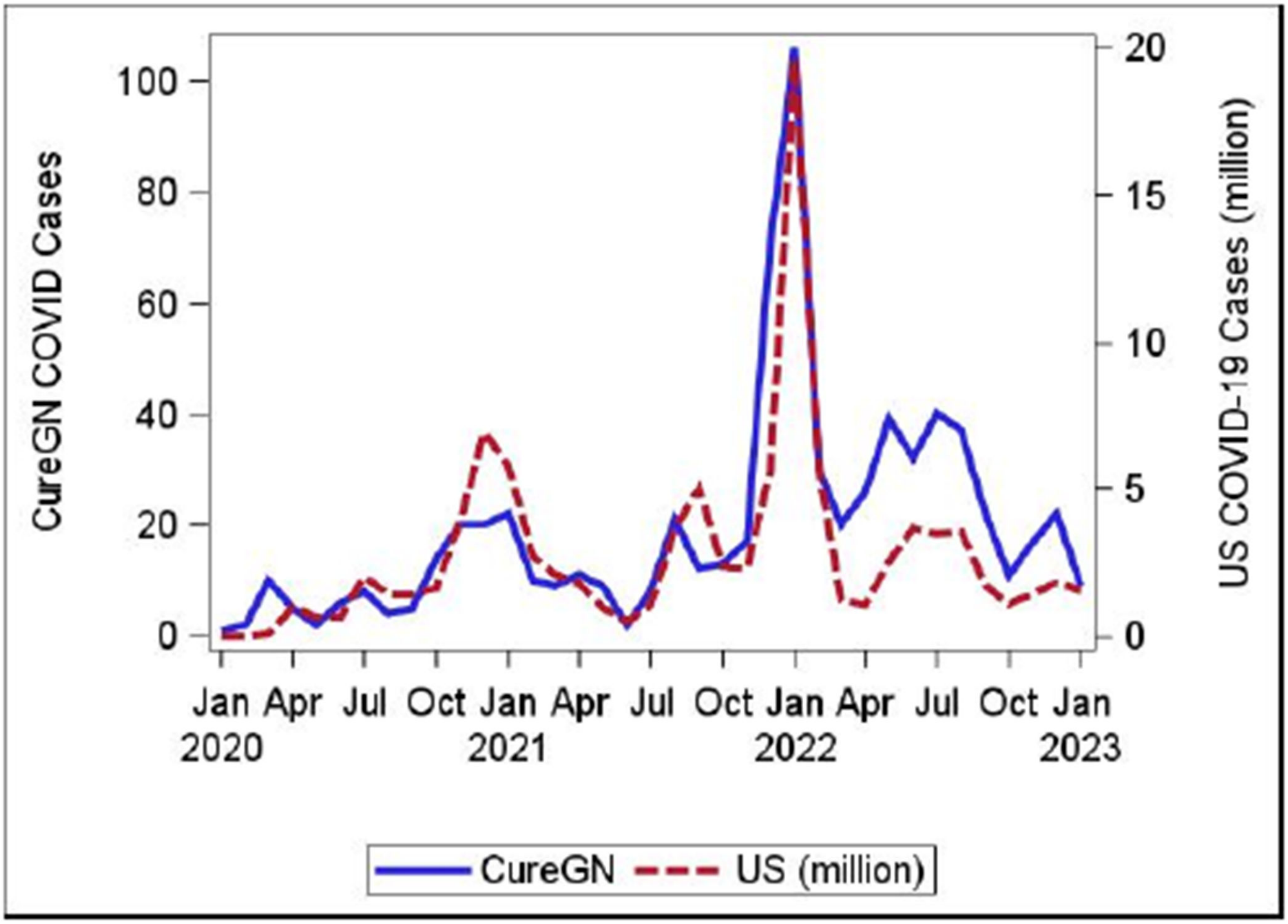
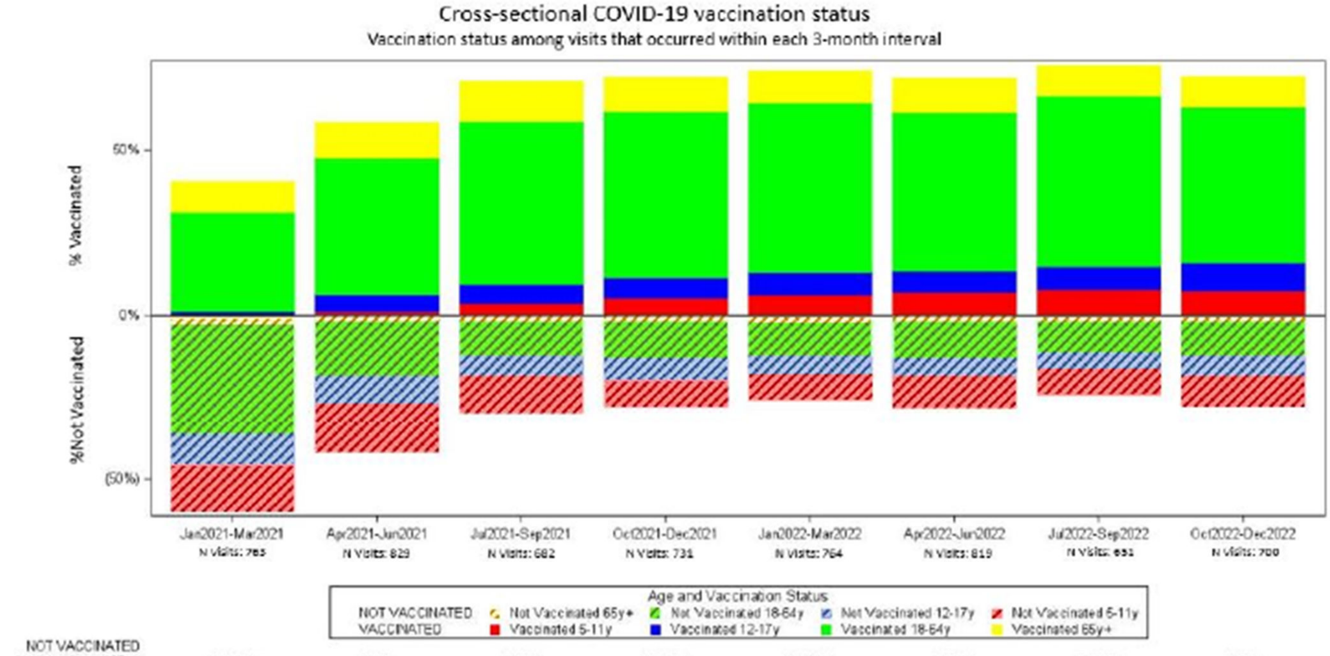


Figure 1. COVID-19 case counts over calendar time among surveyed CureGN study participants with primary glomerular disease, compared to US COVID-19 counts.

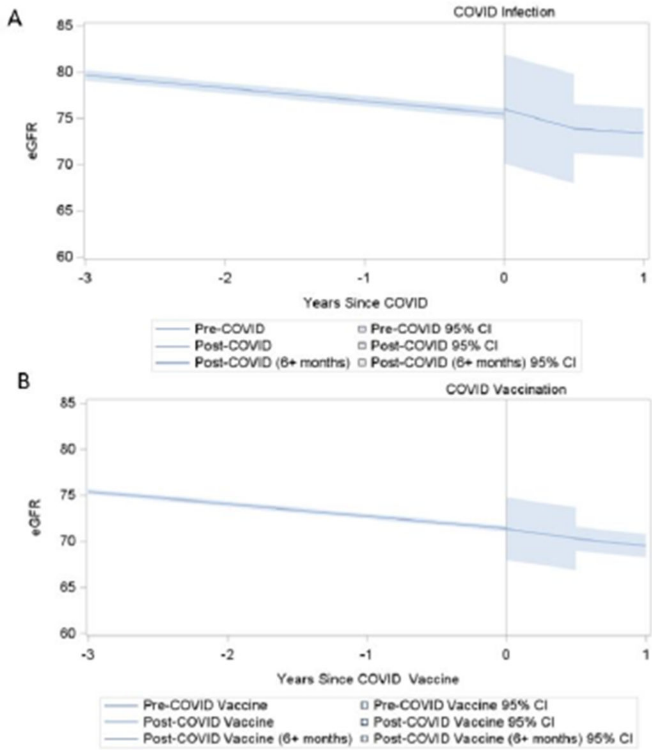
Count of COVID-19 infections per day in CureGN (left y-axis, blue solid line) and the US (right y-axis, in millions of cases, red dashed line).



	Jan2021-Mar2021	Apr2021-Jun2021	Jul2021-Sep2021	Oct2021-Dec2021	Jan2022-Mar2022	Apr2022-Jun2022	Jul2022-Sep2022	Oct2022-Dec2022
NOT VACCINATED								
Not Vaccinated 65y+	23 (25%)	8 (8%)	7 (8%)	13 (14%)	10 (12%)	7 (7%)	8 (12%)	6 (8%)
Not Vaccinated 18-64y	254 (52%)	146 (30%)	78 (19%)	84 (19%)	87 (18%)	103 (21%)	68 (17%)	83 (20%)
Not Vaccinated 12-17y	71 (88%)	70 (62%)	40 (51%)	46 (51%)	39 (43%)	45 (46%)	30 (40%)	42 (41%)
Not Vaccinated 5-11y	106 (100%)	121 (92%)	74 (74%)	58 (59%)	59 (55%)	73 (55%)	50 (49%)	60 (53%)
VACCINATED								
Vaccinated 5-11y	0 (0%)	11 (8%)	26 (26%)	40 (41%)	49 (45%)	59 (45%)	52 (51%)	53 (47%)
Vaccinated 12-17y	10 (12%)	43 (38%)	39 (49%)	45 (49%)	52 (57%)	52 (54%)	45 (60%)	60 (59%)
Vaccinated 18-64y	230 (48%)	342 (70%)	337 (81%)	367 (81%)	392 (82%)	393 (79%)	337 (83%)	329 (80%)
Vaccinated 65y+	69 (75%)	88 (92%)	81 (92%)	78 (86%)	76 (88%)	87 (93%)	61 (88%)	67 (92%)

Figure 2. Cross-sectional COVID-19 vaccination status (one dose) of CureGN study participants since January 2020.

Vaccination status determined by participant self-report and review of medical records at each study visit. Data were assessed in quarterly intervals. Solid bars (up) indicate % reporting at least one COVID-19 vaccination by age group, while hatched bars (down) indicate % not reporting at least one COVID-19 vaccination, by age group. Table at the bottom shows n (%) in each category for each bar.



	Estimate	95% CI	P-value*
Intercept	79.69	(76.14, 83.24)	
eGFR Slope Pre COVID-19 Infection	-1.40	(-1.97, -0.83)	
eGFR Change at COVID-19 Infection	0.54	(-1.66, 2.74)	
eGFR Slope Post COVID-19 Infection (0-6months)	-4.26	(-10.18, 1.66)	0.3
eGFR Slope Post COVID-19 Infection (6+ months)	-0.96	(-3.63, 1.71)	0.4

*Comparing Pre COVID-19 slope to Post COVID-19 slopes

	Estimate	95% CI	P-value*
Intercept	75.41	(73.41, 77.41)	
eGFR Slope Pre COVID-19 Vaccination	-1.34	(-1.63, -1.05)	
eGFR Change at COVID-19 Vaccination	-0.01	(-1.34, 1.32)	
eGFR Slope Post COVID-19 Vaccination (0-6 months)	-2.16	(-5.56, 1.25)	0.6
eGFR Slope Post COVID-19 Vaccination (6+ months)	-1.58	(-2.87, -0.29)	0.8

*Comparing Pre COVID-19 Vaccination slope to Post COVID-19 Vaccination slope

Figure 3. Estimated GFR trajectory among A) CureGN participants who experienced COVID-19, B) CureGN participants who received at least one COVID-19 vaccine.

Results from segmented mixed effects linear regression model, with COVID-19 (A) or COVID-19 vaccination (B) as the “interruption” in the trajectory of eGFR over time, among participants with self-reported COVID-19 (A) or COVID-19 vaccination (B) and at least two eGFR values before and after the interruption event. Models included participant-specific intercepts and slopes. Estimated mean (standard deviation, SD) eGFR value and mean (SD) change in eGFR slope (ml/min/1.73m^2 per year) before and after the interruption are given on the right.

Table 1.

CureGN participants with primary glomerular disease surveyed for COVID-19 and vaccination

Characteristics	Total (n=2,055)	COVID-19 Status			Vaccination Status[a]		
		No COVID-19 (n=1333)	COVID-19 (n=722)	*p*	Vaccinated (n=1407)	Unvaccinated (n=648)	*p*
Age in years at last visit, n (%)				<0.001			<0.0001
<5	7 (<1%)	5 (<1%)	2 (<1%)		0 (0%)	7 (1%)	
5-17	440 (21%)	296 (22%)	144 (20%)		179 (13%)	261 (40%)	
18-44	762 (37%)	472 (35%)	290 (40%)		525 (37%)	237 (37%)	
45-64	538 (26%)	330 (25%)	208 (29%)		440 (31)	98 (15%)	
≥65	308 (15%)	230 (17%)	78 (11%)		263 (19%)	45 (7%)	
Female sex, n (%)	900 (44%)	585 (44%)	315 (44%)	0.9	645 (46%)	255 (39%)	0.006
Race, n (%)				<0.001			0.05
Asian	183 (9%)	117 (9%)	66 (9%)		143 (10%)	40 (6%)	
Black	283 (14%)	198 (15%)	85 (12%)		187 (13%)	96 (15%)	
White	1444 (70%)	933 (70%)	511 (71%)		978 (70%)	466 (72%)	
Other/unknown	145 (7%)	85 (6%)	60 (8%)		99 (7%)	46 (7%)	
Hispanic, n (%)	267 (13%)	152 (11%)	115 (16%)	0.01	189 (13%)	78 (12%)	0.6
Histologic subtype, n (%)				0.4			<0.001
MCD	467 (23%)	305 (23%)	162 (22%)		269 (19%)	198 (31%)	
FSGS	500 (24%)	319 (24%)	181 (25%)		350 (25%)	150 (23%)	
MN	486 (24%)	329 (25%)	157 (22%)		390 (28%)	96 (15%)	
IgAN	602 (29%)	380 (29%)	222 (31%)		398 (28%)	204 (31%)	
Comorbidities ever[b], n (%)							
Hypertension	1056 (52%)	682 (51%)	374 (52%)	0.8	777 (55%)	279 (43%)	<0.001
DM	129 (6%)	88 (7%)	41 (6%)	0.4	100 (7%)	29 (5%)	0.02
CVD	278 (14%)	186 (14)	92 (13%)	0.4	222 (16%)	56 (9%)	<0.001
Asthma/COPD	335 (16%)	208 (16%)	127 (18%)	0.2	240 (17%)	95 (15%)	0.2
Oncologic	189 (9%)	127 (10%)	62 (9%)	0.5	160 (11%)	29 (5%)	<0.001
Obesity	715 (35%)	451 (34%)	264 (37%)	0.2	494 (35%)	221 (34%)	0.7
Any comorbidities, n (%)	1477 (72%)	940 (71%)	537 (74%)	0.06	1061 (6%)	416 (64%)	<0.001

[a]Any type or number of COVID-19 vaccines at time of survey

[b]Self-reported history of all comorbidities except for obesity, which is defined as BMI>=30 for adults or a BMI percentile >=95 for pediatric patients.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; DM, diabetes mellitus; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease; MN, membranous nephropathy