LETTER TO THE EDITOR

Renal outcomes in immunoglobulin A nephropathy following COVID-19 vaccination: a retrospective cohort study

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Cases of relapsed IgA nephropathy (IgAN) following coronavirus disease 2019 (COVID-19) vaccination have been reported [1–3]. The general safety of COVID-19 vaccination in IgAN remains unclear, as COVID-19 vaccine studies generally excluded individuals with kidney disease or those receiving immunosuppression [4], and the previous observational report was limited by small sample size and lacks comparison with baseline changes in proteinuria, kidney function or relapse rates in IgAN prior to COVID-19 vaccination [5]. There is also limited follow-up information on renal outcomes after IgAN flares associated with COVID-19 vaccination. A more recent report of a larger cohort suggests COVID-19 vaccination is safe in patients with IgAN but is largely restricted to the inactivated vaccines [6]. In this observational cohort study, we aim to determine the renal outcomes in IgAN patients, following messenger RNA-based (mRNA) COVID-19 vaccination.

We performed a single-center, retrospective cohort study by identifying all patients (i) with biopsy-proven IgAN on follow-up for at least 1 year before COVID-19 vaccination and (ii) who received at least one dose of mRNA COVID-19 vaccination between 1 January 2021 and 31 October 2021. Individuals were excluded if they were on dialysis or had a kidney transplant prior to COVID-19 vaccination. The outcomes of interest were (i) change in proteinuria and estimated glomerular filtration rate (eGFR) immediately pre- and post-COVID-19 vaccination and (ii) proportion of patients with proteinuria rise ≥0.5 g/day in the 1-year preceding COVID-19 vaccination versus post-COVID-19 vaccination and their status post-vaccination.

There were 154 IgAN patients with at least 1-year of follow-up and who received the mRNA COVID-19 vaccination (BNT162b2 or mRNA-1273), but 38 were excluded as they were on dialysis or received a kidney transplant prior to COVID-19 vaccination. A total of 116 patients were included in the study, of which the mean age ± standard deviation (SD) is 50.6 ± 14.8 years and 41% (n = 48) were male (Table 1). At baseline, the median proteinuria (interquartile range, IQR) is 0.80 (0.26–1.53) g/day and mean eGFR ± SD is 61.2 ± 31.2 mL/min/1.73 m².

In all, 92% (n = 107) received renin-angiotensin inhibitors as the standard of care; 6% (n = 7) were on immunosuppression at time of vaccination, while 38% (n = 44) previously received immunosuppression.

At median (IQR) follow up of 75 (37–109) days post-vaccination, the proteinuria post-COVID-19 vaccination changed from pre-vaccination median (IQR) of 0.8 (0.3–1.5) to 0.7 (0.3–2.1) g/day, P = .03, while the eGFR changed from pre-COVID-19 vaccination mean ± SD of 61.2 ± 31.2 to 59.8 ± 30.8 mL/min/1.73 m² post-vaccination, P = .06 (Fig. 1). Although statistically significant or trending toward significance, the changes in proteinuria and eGFR were both clinically mild.

A total of 24% (n = 28) patients developed a rise in proteinuria ≥0.5 g/day post-COVID-19 vaccination, which was not significantly different from the baseline rate of 18% (n = 21) patients in the 1-year prior to COVID-19 vaccination (P = .26). None of the patients developed visible hematuria. In the 28 patients for whom rise in proteinuria post-COVID-19 vaccination is ≥0.5 g/day, 3 (11%) received an augmentation of renin-angiotensin inhibition, while the remaining 25 were observed with no change in therapy (none required initiation or escalation of immunosuppression). The rise in proteinuria stabilized in 9 (32%) patients and decreased to the previous baseline in 17 (61%) patients.
Table 1. Pre- and post-COVID-19 vaccination characteristics of IgAN patients

|                                | Pre-vaccination | Post-vaccination | P-value |
|--------------------------------|-----------------|------------------|---------|
| Age in years, mean (SD)        | 50.6 (14.8)     | NA               |         |
| Gender                         |                 |                  |         |
| Male                           | 48 (41.4)       | 48 (41.4)        |         |
| Female                         | 68 (58.6)       | 68 (58.6)        |         |
| Race                           |                 |                  |         |
| Chinese                        | 97 (83.6)       | 97 (83.6)        |         |
| Malay                          | 11 (9.5)        | 11 (9.5)         |         |
| Indian                         | 5 (4.3)         | 5 (4.3)          |         |
| Others                         | 3 (2.6)         | 3 (2.6)          |         |
| Medications                    |                 |                  |         |
| RAS inhibition                 | 107 (92.2)      | 107 (92.2)       |         |
| Current immunosuppressant      | 7 (6.0)         | 7 (6.0)          |         |
| Past immunosuppressant         | 44 (37.9)       | 44 (37.9)        |         |
| Interval of COVID vaccination  | 74.5 (36.5–108.5)| 74.5 (36.5–108.5)|         |
| Proteinuria (g/day), median (IQR) | 0.80 (0.26–1.53) | 0.74 (0.30–2.05) | .03a   |
| eGFR, mL/min/1.73 m², mean (SD) | 61.2 (31.2)     | 59.8 (30.8)      | .06b   |
| Albumin, g/L, mean (SD)        | 39.9 (2.8)      | 40.1 (2.7)       | .24b   |
| Increase in proteinuria ≥ 0.5 g/day | 21 (18)        | 28 (24.1)        | .26c   |

All n (%), except where stated; standard deviation, SD; renin-angiotensin system, RAS; interquartile range, IQR; not applicable, NA; aWilcoxon signed-rank test, bpaired t-test, cChi-squared test.

FIGURE 1: (A) Estimated glomerular filtration rate (eGFR) and (B) proteinuria pre- and post-COVID-19 vaccination in IgAN patients.

To our knowledge, this is the first study that examined the renal outcomes in a large cohort of biopsy-proven IgAN patients, following mRNA COVID-19 vaccination. While several cases of IgAN flares temporally following COVID-19 vaccination have been reported to date, our study demonstrates that the overall absolute incidence of change in proteinuria and kidney function remains low. This study further considers the baseline changes in proteinuria and kidney function prior to mRNA COVID-19 vaccination and shows that these changes were not different before and after vaccination. Furthermore, patients with a rise in proteinuria post-vaccination were further followed up and confirmed to have improved or stable renal outcomes. Given the relatively high overall vaccination rate in our local eligible population, individual IgAN patients were not selected for or against COVID-19 vaccination and, hence reducing any possible selection bias. Limitations of this analysis include a single study site, observational in nature and a relatively short follow-up period; hence, these findings require validation in other studies. Nevertheless, we believe that our findings are important, especially in the context of the ongoing vaccination efforts worldwide in our bid to overcome COVID-19.

In summary, COVID-19 mRNA vaccination was generally well tolerated in patients with IgAN, with clinically mild (although significant) changes in post-vaccination proteinuria and eGFR. The proportion of patients with the rise in proteinuria ≥0.5 g/day was not significantly increased post-vaccination, compared with 1-year preceding vaccination. In patients with the rise in proteinuria ≥0.5 g/day, the majority did not require
escalation of existing or the initiation of new treatment and the proteinuria level returned to its baseline in most patients.

CONFLICT OF INTEREST STATEMENT
All authors declare no conflict of interest.

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