Time-to-onset of glomerular diseases following COVID-19 vaccination: a case series analysis

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Background
Glomerular diseases (GD) following COVID-19 vaccination have been reported post-marketing, but causality has not been confirmed to date. Examining time-to-onset (TTO) patterns for different GDs may support clinical assessment of a signal beyond routine disproportionality analysis. IgA nephropathy (IgAN) has been suggested to be associated with rapid immune mechanisms, while the pathophysiology of minimal change disease (MCD) may involve cell-mediated immunity.

Objectives
To compare the TTO distribution of GDs following COVID-19 vaccination reported in VigiBase, the WHO global database of reported potential side effects of medicinal products.

Methods
Reports concerning the MedDRA Preferred Terms (PTs) IgAN, MCD, glomerulonephritis membranous (GM), and focal segmental glomerulosclerosis (FSGS), and which also listed COVID-19 vaccines as suspected, were identified and de-duplicated for analysis. Distributions of TTO were summarised for each PT and compared using the Kruskal-Wallis test, overall and per vaccine dose.

Results
By 3 April, 2023, VigiBase contained 4,962,301 reports for COVID-19 vaccines as suspected, including 42,333 (0.85%) reporting renal and urinary disorders, and 1,972 (4.7%) with glomerulonephritis and nephrotic syndrome. After de-duplication, there were 336 (expected 146) reports of IgAN, 177 (expected 85) of MCD, 101 (expected 112) of GM, and 81 (expected 125) of FSGS. TTO information was available in 71–79% of the reports. Median TTO (the interquartile range, IQR) two days (1–7) for IgAN, nine days (4–21) for MCD, 13 days (3–36.5) for FSGS, and 19.5 days (2–60) for GM (p<0.001), (see figure below). A similar pattern of results was observed when restricting analyses to 1st and 2nd vaccine dose reports (p=0.006 and <0.001 respectively).

Conclusions
TTO distribution following COVID-19 vaccination varies for different GDs, which is consistent with proposed pathophysiological mechanisms. These results underscore the value of TTO analysis as a complement to disproportionality analysis in signal management. For assessing causality, further in-depth analysis including narrative information is necessary.

References

TTO for different glomerular diseases in VigiBase*