ORIGINAL RESEARCH ARTICLE

Evaluation of the Frequency of Nephrotic Syndrome Subtypes Following COVID-19 Vaccination in Zanjan, Iran

Hanieh Davoodi[1], Nadia Agharafiei[1], Bahareh Hajisalimi[2]

Published: 30 February 2026

Abstract

Background The global outbreak of coronavirus (SARS-CoV-2), first reported in Wuhan, China, in December 2019, rapidly evolved into a worldwide health crisis. Various vaccines were developed to combat COVID-19; however, concerns have emerged regarding potential side effects, particularly renal complications. Nephrotic syndrome has been reported as a post-vaccination adverse effect, potentially triggered by immune system activation through an unknown mechanism. This study aimed to investigate the frequency of different types of nephrotic syndrome following COVID-19 vaccination.

Methods In this cross-sectional study, all new cases of nephrotic syndrome admitted to Vali-Asr Hospital in Zanjan between 2020 and 2023 were reviewed. The study period covered up to three months following COVID 19 vaccination. Collected data included age, gender, type of vaccine, vaccination dose, time interval between vaccination and symptom onset, and kidney biopsy findings. Due to the small sample size, no inferential statistical tests were performed, and data analysis was limited to descriptive statistics.

Results A total of 11 patients met the inclusion criteria. The most common nephrotic syndrome observed was Membranous Nephropathy, reported in all cases following administration of the Sinopharm vaccine, mostly after the first dose. The average time interval to symptom onset after the first dose of vaccine was 26 days. Middle-aged individuals were most affected, and the distribution of nephrotic syndrome subtypes appeared similar across genders; however, the study was not powered to detect statistical associations.

Conclusion Membranous Nephropathy was the most commonly observed subtype of nephrotic syndrome among the studied cases (11 patients) following COVID-19 vaccination, particularly after administration of the Sinopharm vaccine. However, given the limited sample size, a causal relationship between vaccination and the onset of nephrotic syndromes cannot be confirmed. Therefore, larger retrospective studies are recommended to better elucidate this potential association.

Keywords COVID-19, Membranous nephropathy, Nephrotic syndrome, Vaccination

✉ Hanieh Davoodi
hd1376med@yahoo.com

1. Faculty of medicine, Zanjan University of Medical Sciences, Zanjan, Iran
2. Department of Internal Medicine, Vali-Asr Hospital, Zanjan University of Medical Sciences, Zanjan, Iran

Received: 10 October 2025/ Revised: 07 November 2025/ Accepted: 27 December 2025

1 Introduction

The outbreak of the coronavirus (SARS-CoV-2) in December 2019 rapidly evolved into a global crisis. Despite significant progress in the development and distribution of COVID-19 vaccines, numerous reports of adverse effects following immunization have been published. In the initial phases of vaccination campaigns, these adverse effects were predominantly short-term, mild, and self-limiting, often presenting as local symptoms at the injection site, such as pain, swelling, and urticarial rash, or systemic symptoms like fever and headache. However, as mass vaccination programs expanded, reports of more severe adverse effects requiring hospitalization were also reported, including neurological complications, myocarditis, and specific autoimmune diseases.[1]

Meanwhile, the occurrence of renal complications following COVID-19 vaccination has attracted special attention. One of the most significant of these complications is nephrotic syndrome, a condition classically characterized by severe proteinuria (over 3 gr per 24 hours), hypoalbuminemia (less than 3.5 gr/dL), hypertension, edema, hypercholesterolemia, and minimal hematuria. This syndrome often occurs in the context of glomerular diseases, the most important of which include Minimal Change Disease (MCD), Membranous Nephropathy (MN), and Focal Segmental Glomerulosclerosis (FSGS).[2]

Globally, the majority of the published studies on renal complications after COVID-19 vaccination have been presented as case reports, limited case series, or review articles, which have mainly focused on the new onsets [3-7] or relapses of renal diseases following vaccination. [1,8,9] Specifically, multiple case studies have reported the de novo onset of MCD within a few days to two weeks after vaccination with Pfizer, Moderna, AstraZeneca, and Janssen vaccines.[3-6] Analysis of these reports reveals specific patterns in demographic and clinical characteristics of patients, suggesting that the onset or relapse of renal complications has been reported more frequently in certain age groups, in one gender than the other, or in patients with a history of underlying renal disease, autoimmune conditions, or receiving immunosuppressive drugs. However, these data are largely derived from case reports or case series with limited sample sizes. Therefore, given the lake of large population-based studies examining the statistical association between different types of nephrotic syndrome and various vaccines, the existing evidence is insufficient to prove a causal relationship or the independent role of these factors. As a result, these variables are currently considered only as potential and hypothetical factors.[1,8,9]

In contrast, within Iran, research on COVID-19 vaccination has mainly focused on the overall safety of vaccines, general adverse effects, efficacy, and vaccine acceptance rates. Despite the widespread implementation of the national vaccination program utilizing several types of vaccines, including inactivated vaccines (e.g., Sinopharm and COVIran Barekat), mRNA-based vaccines (e.g., Pfizer-BioNTech), and adenoviral vector vaccines (e.g., Sputnik V and Oxford-AstraZeneca),[10] no published study has specifically investigated COVID-19 vaccination-related renal complications in the Iranian population. Data and evidence in this area remain limited. Accordingly, the present study design attempted to minimize the impact of confounding factors by applying strict inclusion and exclusion criteria and focusing solely on the new onsets of nephrotic syndrome following COVID-19 vaccination. For this purpose, all patients with a previous history of nephrotic syndrome or kidney disease (to exclude relapse cases) were excluded from the study. Furthermore, cases with known underlying factors independently associated with nephrotic syndrome were also omitted. Although this rigorous screening led to a reduction in the final sample size, it allowed for a more accurate assessment of the temporal and clinical association of vaccination with the initial onset of nephrotic syndrome and the role of vaccination as a major factor associated with this occurrence. In addition to the lack of population-based studies and systematic evidence in this field, the precise mechanism underlying the onset of nephrotic syndrome following COVID-19 vaccination has not yet been fully elucidated. In this regard, some hypotheses have implicated T-cell dysfunction and the occurrence of abnormal immune responses as potential contributing factors in the pathogenesis of this complication;[1,7] however, the available evidence is still insufficient to reach a definitive conclusion.

Within this context of clinical and mechanistic uncertainties, investigating renal complications associated with COVID-19 vaccines gains particular importance. Identifying the type of renal diseases that develop after vaccination, especially in relation to their possible pathophysiological mechanisms, can help to better understand this phenomenon. Such knowledge would enable more informed vaccine selection for patients with kidney disease or high-risk individuals, potentially reducing the likelihood of unwanted complications. Furthermore, better elucidation of the involved mechanisms could be effective in improving the design and enhancing the safety profile of future vaccines, ultimately leading to a reduction in the therapeutic burden and associated costs.

Within this framework, systematic and targeted studies can serve as a foundation for further exploratory research and pave the way for identifying and preventing these complications. Therefore, the present study was designed

and conducted with the aim of investigating the frequency of various types of nephrotic syndrome following COVID-19 vaccination and analyzing their incidence patterns based on vaccine type and administered dose in a clinical population.

2 Methods

This cross-sectional study was conducted using registry-based data collected between December 2020 and September 2023. The study population included all patients with a new diagnosis of nephrotic syndrome following COVID-19 vaccination who were hospitalized at Valiasr Hospital in Zanjan, Iran.

During the national COVID-19 vaccination program in Iran, several vaccine platforms were used. However, among the patients included in the final analysis, only inactivated (Sinopharm) and adenoviral vector (AstraZeneca) vaccines were identified.

Inclusion criteria were receiving at least one dose of a COVID-19 vaccine and being newly diagnosed with nephrotic syndrome within three months after the last vaccine dose. Exclusion criteria included a history of diabetes, uncontrolled hypertension, chronic kidney, hematologic, or infectious diseases (HCV, HIV, HBV, or confirmed COVID-19 infection prior to vaccination), autoimmune disorders, use of nephrotic syndrome–inducing drugs (such as NSAIDs, D-penicillamine, or captopril), and presence of proteinuria or nephrotic syndrome prior to vaccination.

During the specified period, 169 medical records related to COVID-19 complications were reviewed, among which 91 cases were associated with nephrotic syndrome. After applying inclusion and exclusion criteria, 42 records met the initial eligibility conditions, regardless of the time interval between vaccination and disease onset. Due to incomplete documentation in some patient files, information regarding vaccine type and vaccination date was retrieved from the Zanjan County Health Center. After precise data matching and exclusion of incomplete or time-inconsistent cases (beyond the 3-month criterion), only 11 cases were included in the final analysis.

Demographic data (age, sex), vaccine type, vaccine dose number, time interval from vaccination to symptom onset, and kidney biopsy results were extracted from the patient's medical records and recorded in a predesigned checklist.

Data were analyzed descriptively. Quantitative variables were reported as mean ± standard deviation, and qualitative variables as frequency and percentage. Due to the small sample size, no inferential statistical tests were performed, and data analysis was limited to descriptive statistics.

At the time of admission, all patients at this hospital routinely provided informed consent permitting the use of their medical records for future research. All study procedures were approved by the Ethics Committee of Zanjan University of Medical Sciences and conducted in compliance with confidentiality and ethical standards.

3 Results

In this study, 11 patients with a new diagnosis of nephrotic syndrome following COVID-19 vaccination were included. The mean age of the patients was 46.27 ± 12.07 years. The gender distribution consisted of six males (54.5%) and five females (45.5%). Regarding underlying conditions, four patients (36.4%) had comorbidities such as controlled hypertension, hyperlipidemia, hypothyroidism, or migraine, while seven patients (63.6%) had no prior medical history (Table 1 and Table 2).

Table 1 Demographic characteristics of patients included in the study

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	6	54.5
	Female	5	45.5
Underlying disease	Present	4	36.4
	Absent	7	63.6
		Mean	Standard deviation
Age (years)	-	46.27	12.07

In this study, only Sinopharm and AstraZeneca vaccines were observed among the patients; therefore, the analysis of nephrotic syndrome occurrence was limited to these two vaccines. As shown in Table 3, the highest incidence of nephrotic syndrome occurred following the first vaccine dose, with six cases (54.5%). Among the administered vaccines, Sinopharm was associated with the highest frequency of nephrotic syndrome across all three doses, whereas AstraZeneca was observed in only one case, occurring after the first dose.

According to Table 4, the most common type of nephrotic syndrome observed among the patients was MN, identified in seven cases (63.6%). This was followed by MCD in three patients (27.3%) and FSGS in one patient (9.1%).

Based on the data analysis, the mean interval between vaccination and the onset of nephrotic syndrome symptoms was 41.72 ± 26.38 days. Most patients developed symptoms within the first 60 days after vaccination (Figure 1).

Table 2 Detailed demographic and clinical characteristics of 11 patients with new-onset nephrotic syndrome following COVID-19 vaccination

Case No.	Sex	Age	Underlying disease	Renal biopsy diagnosis	Vaccine name	Dose number at symptom onset	Interval between the last dose and symptom onset
1	F	27	-	MN	Sinopharm	First	14 days
2	M	32	-	MN	Sinopharm	Second	55 days
3	M	34	-	MN	Sinopharm	Second	79 days
4	M	44	-	MCD	AstraZeneca	First	18 days
5	F	45	Controlled HTN	MN	Sinopharm	First	67 days
6	M	45	Controlled HTN HLP	MN	Sinopharm	Second	79 days
7	F	46	-	MCD	Sinopharm	Third	50 days
8	M	52	-	MN	Sinopharm	First	7 days
9	F	59	Controlled HTN HLP	MN	Sinopharm	First	15 days
10	M	62	-	FSGS	Sinopharm	Second	40 days
11	F	63	Controlled HTN HLP, migraine hypothyroidism	MCD	Sinopharm	First	36 days

F: Female, M: Male, HTN: Hypertension, HLP: Hyperlipidemia, MN: Membranous Nephropathy, MCD: Minimal Change Disease, FSGS: Focal Segmental Glomerulosclerosis

Table 3 Frequency of nephrotic syndrome occurrence after COVID-19 vaccination by dose and vaccine type

Vaccine dose	Vaccine type	Frequency (n)	Percentage within dose (%)	Total per dose (n, %)
First dose	Sinopharm	5	83.3	6 (54.5)
	AstraZeneca	1	16.6	
Second dose	Sinopharm	4	100	4 (36.4)
	AstraZeneca	0	0	
Third dose	Sinopharm	1	100	1 (9.1)
	AstraZeneca	0	0	

Table 4 Frequency of different types of nephrotic syndromes following COVID-19 vaccination

Type of nephrotic syndrome	Frequency (n)	Percentage (%)
MN	7	63.6
MCD	3	27.3
FSGS	1	9.1

MN: membranous nephropathy, MCD: minimal change disease, FSGS: focal segmental glomerulosclerosis

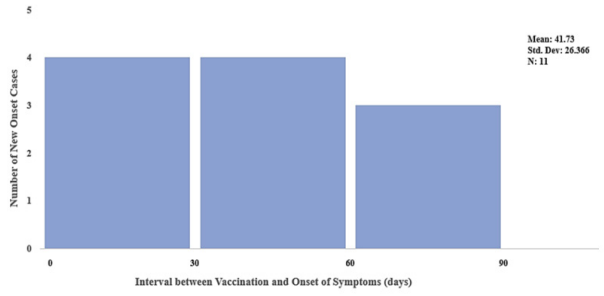

Figure 1 Frequency of nephrotic syndrome occurrence at monthly intervals after vaccination

The analysis showed that the frequency of different types of nephrotic syndrome was similar between patients with and without underlying diseases (Table 5). Similarly, no clear gender-based differences were identified in the distribution of nephrotic syndrome subtypes, although the limited sample size restricted statistical inference (Table 6). However, in both groups, with or without comorbidities, and across both genders, the most frequently observed type of nephrotic syndrome was MN.

Table 5 Frequency of nephrotic syndrome types by presence or absence of underlying disease

Variable	Category	Type of nephrotic syndrome		
		MN n (%)	MCD n (%)	FSGS n (%)
Underlying disease	Present	3 (75.0)	1 (25.0)	0 (0.0)
	Absent	4 (57.1)	2 (28.0)	1 (14.3)

MN: membranous nephropathy, MCD: minimal change disease, FSGS: focal segmental glomerulosclerosis

Table 6 Frequency of nephrotic syndrome types by gender

Gendre	Type of nephrotic syndrome		
	MN n (%)	MCD n (%)	FSGS n (%)
Male	4 (66.7)	1 (16.7)	1 (16.7)
Female	3 (60.0)	2 (40.0)	0 (0.0)

MN: membranous nephropathy, MCD: minimal change disease, FSGS: focal segmental glomerulosclerosis

The data analysis revealed that the highest occurrence of MN was observed after the first and second doses of the Sinopharm vaccine (four cases after the first dose and three cases after the second dose). Additionally, three cases of MCD were identified, one following the first dose of AstraZeneca and two following the first and third doses of Sinopharm. The only case of FSGS occurred after the second dose of Sinopharm. Overall, the highest frequency of nephrotic syndrome types was seen among Sinopharm vaccine recipients, particularly after the first and second doses (Table 7).

Table 7 Frequency of nephrotic syndrome types by vaccine type and dose

Vaccine dose	Vaccine type	Type of nephrotic syndrome		
		MN n (%)	MCD n (%)	FSGS n (%)
First dose	Sinopharm	4 (80.0)	1 (20.0)	0 (0.0)
	AstraZeneca	0 (0.0)	1 (100.0)	0 (0.0)
Second dose	Sinopharm	3 (75.0)	0 (0.0)	1 (25.0)
	AstraZeneca	0 (0.0)	0 (0.0)	0 (0.0)
Third dose	Sinopharm	0 (0.0)	1 (100.0)	0 (0.0)
	AstraZeneca	0 (0.0)	0 (0.0)	0 (0.0)

MN: membranous nephropathy, MCD: minimal change disease, FSGS: focal segmental glomerulosclerosis

4 Discussion

In the present study, MN (seven out of 11 cases) was identified as the most common type of nephrotic syndrome following COVID-19 vaccination. This finding differs from the results of Izzedine et al., where 10 cases of MCD and only one case of MN were reported. [9] Similarly, case reports by Lim et al.[6] Lebedev et al. [3] Thappy et al. [4] and Leclerc et al.[5] have predominantly shown an MCD-dominant pattern in most documented cases. In the systematic review by Zhang et al.[1] both new-onset and relapse cases of nephrotic syndrome following COVID-19 vaccination were evaluated. MCD represented the most frequent histopathological diagnosis (52 of 130), occurring predominantly as new-onset disease (38 of 52), whereas MN (eight of 130) and FSGS (three of 130) were less common and included both de novo and relapse presentations.

One notable finding in the present study is the association between vaccine type and the pattern of nephrotic syndrome. Among the patients, the Sinopharm vaccine was associated with MN in all three administered doses, particularly after the first (four cases) and second doses (three cases). Additionally, two cases of MCD were observed following the first and third doses of Sinopharm. These results contrast with several previous reports that mainly documented MCD. For example, studies by Lebedev et al.[3] Izzedine et al.[9] and Leclerc et al. [5] reported MCD occurrence following Pfizer and AstraZeneca vaccines. However, it is worth noting that in Izzedine's study,[9] only five out of 11 patients represented new-onset disease, while the rest were relapses. In contrast, all cases in the present study were new-onset nephrotic syndromes following vaccination.

In Hummel et al.'s study,[8] which focused on relapse cases, the distribution of relapses across three vaccination doses was examined. More than 80% of the patients had received the Pfizer vaccine, and 18 of 25 relapses occurred after the first dose. In the current study, a similar pattern was observed in terms of the concentration of cases after the first dose. However, all cases were new-onset, mainly associated with Sinopharm and predominantly of the MN type.

Furthermore, Lebedev et al.[3] reported a case of MCD with concurrent acute tubular necrosis (ATN) after the Pfizer vaccine, and Thappy et al.[4] documented MCD accompanied by IgA nephropathy following the Moderna vaccine. In our study, two cases of MCD and one case of FSGS were associated with the Sinopharm vaccine, and one case of MCD occurred after the first dose of AstraZeneca.

In the systematic review by Zhang et al.[1] which analyzed 130 published cases, the most common renal adverse effect was MCD (52 cases, 40.0%), the majority of which were new-onset (38 new-onset (73.1%), 14 relapse (26.9%)). MN was less frequent (eight cases, 6.2%), and FSGS was rare (three cases, 2.3%). The distribution of these pathologies was closely linked to the vaccine platform, dose, and disease onset type. Among MCD cases, which were nearly evenly split between the first (53.8%) and second (46.2%) doses, the Pfizer vaccine was the most frequently implicated (51.9% of MCD cases), followed by Moderna (26.9%). MN cases were predominantly new-onset (five of eight, 62.5%), occurred after the second dose (six of eight, 75%), and were associated with Pfizer (four cases), Moderna (two cases), and CoronaVac (two cases). All three reported FSGS cases (two new-onset, one relapse) occurred after Pfizer vaccination, following either the first (two cases) or second (one case) dose. Overall, mRNA vaccines (Pfizer and Moderna) accounted for 86% of the 128 cases with specified vaccine type, while inactivated vaccines (CoronaVac) comprised only 2.3% of the cases in this systematic review. Despite the similarities and differences

across studies, it is important to recognize that most available reports are based on small samples. Therefore, a definitive conclusion regarding the role of vaccine type in determining the form of nephrotic syndrome cannot yet be made.

In the present study, the mean interval between vaccination and the onset of nephrotic syndrome was 41.72 days, with most cases occurring within the first 60 days post-vaccination. The mean onset time after the first dose was 26 days, which is longer than reported in previous studies. For instance, Lim et al.[6] reported onset around 7 days, Lebedev et al.[3] around 10 days, Leclerc et al.[5] about 13 days, and Thappy et al.[4] approximately 2 weeks after the first dose. Izzedine et al.[9] did not differentiate exact means between new-onset and relapsed cases but reported a range between 3 days and 2 weeks after the first dose. Hummel et al.[8] focusing on relapses, reported a mean relapse time of approximately one month, specifically 17.5 days after the first dose

In the systematic review by Zhang et al.[1] the median time to symptom onset for the most common vaccine-related glomerulopathies, MCD and IgA nephropathy (IgAN), was 7 days and 4 days after the first dose, respectively, with most cases occurring within 2 weeks. Even for conditions with a later median onset, such as anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis or acute interstitial nephritis, the reported median was approximately 14 days after vaccination. For the less common pathologies relevant to our study, namely MN and FSGS, the reported time to onset exhibited wide variability. Among the 8 reported MN cases, presentation ranged from 1 day to 89 days post-vaccination, with several cases occurring around 2 to 4 weeks. Similarly, the three FSGS cases presented between 5 days and 88 days after vaccination. Notably, nearly all these reported MN and FSGS cases were associated with the Pfizer mRNA vaccine. Taken together, while this wide temporal spectrum indicates that delayed presentation is possible across all vaccine platforms, the consistently longer mean interval observed in our study (26 days after the first dose) further supports the notion that the immunogenic properties of the inactivated Sinopharm vaccine may favor a slower and more gradual immunological perturbation. This might explain the different timing pattern seen in our study versus studies focused on mRNA vaccines.

The mean age of patients in this study was 46.27 years, representing a middle-aged group. Previous case reports have shown similar age distributions; for example, Lim et al.[6] Lebedev et al.[3] Thappy,[4] and Leclerc[5] all reported patients between 43 and 51 years, though Leclerc's case involved an older patient aged 71 years. Izzedine [9] reported a higher mean age of 66.2 years for new-onset cases, while Hummel,[8] focusing on relapses, found a lower mean of 39.7 years. The systematic review by Zhang et al.[1] which included both new-onset and relapsed cases, reported a median age of 42 years (range 12–85) among patients with vaccine-associated glomerulopathies, with a median age of 44 years for MCD, the most frequently reported lesion. In this study, age was not stratified by new-onset versus relapsed disease. These findings suggest that post-vaccination nephrotic syndrome tends to occur predominantly in middle-aged adults.

In our study, six patients were male, and five were female, and the gender distribution in the incidence and subtypes of nephrotic syndrome appeared similar, although the small sample size precluded definitive conclusions. Prior reports are partly similar: Lim et al.[6] Lebedev et al.[3] Thappy et al.[4] and Leclerc et al.[5] all reported male patients, while Izzedine et al.[9] described three males and two females among new-onset cases, showing a comparable distribution. Hummel et al.[8] also reported 16 male patients out of 25 total in relapse cases. This gender balance is also seen in the review by Zhang et al.[1] which includes 130 cases (both new-onset and relapsed disease); the overall distribution was nearly equal (53.1% male, 46.9% female). Definitive conclusions about gender are limited by a lack of large studies, but the distribution appears relatively balanced between males and females in the study by Zhang et al.[1]

Among the 11 patients analyzed in this study, four had comorbidities such as controlled hypertension, dyslipidemia, hypothyroidism, and migraine. The incidence and subtype distribution of nephrotic syndrome were generally similar between patients with and without comorbidities, showing no apparent differences; however, the small sample size precluded drawing any meaningful statistical conclusions. Prior case reports have mostly involved patients without significant comorbidities, such as those described by Lim et al.[6] Lebedev et al.[3] Thappy et al.[4] and Leclerc et al.;[5] only Leclerc et al.'s patient had dyslipidemia. Conversely, Izzedine et al.[9] reported that four of five new-onset cases had major underlying conditions such as diabetes, hypertension, thromboembolism, hypothyroidism, and autoimmune hepatitis. The profile of pre-existing conditions varies across different post-vaccination nephrotic syndromes. As detailed in the review by Zhang et al.[1] among 52 patients with MCD, 28.8% had no significant comorbidities, while 19.2% had a prior history of kidney disease or abnormal urinalysis. Hypertension and diabetes/dyslipidemia were reported in 9.6% and 11.5% of MCD cases, respectively. Among the eight reported MN patients, 37.5% had no comorbidities, while dyslipidemia was the most common metabolic condition. Notably, two MN cases were relapses in patients with known MN. All three cases of FSGS were associated with the Pfizer vaccine; two occurred in patients with no prior medical history, and one was a relapse in a patient with known FSGS.These

comparisons suggest that comorbidities may variably influence susceptibility, depending on the underlying disease and individual immune characteristics. Therefore, more extensive research is required.

It is important to note that the current study lacks a control group and therefore cannot determine whether the observed cases represent a true increase in incidence or coincidental occurrences. The background incidence of nephrotic syndrome in the general population of Zanjan is not well documented, and no population-based studies are available for direct comparison. Consequently, the 11 post-vaccination cases identified here may reflect either a genuine vaccine-associated signal or simply the expected sporadic occurrence of nephrotic syndrome in the region. Therefore, any inference regarding a causal relationship between vaccination and nephrotic syndrome should be interpreted with caution.

The exact mechanism of post-vaccination nephrotic syndrome remains unclear. However, studies such as Nakazawa et al.[7] have proposed mechanisms involving overactivation of T cells, cytokine release, and increased glomerular permeability. Although the present study cannot directly confirm these mechanisms, the alignment of its findings with these hypotheses is notable and is further supported by insights from larger systematic reviews by Zhang et al.[1] In this context, available evidence suggests that the pathophysiological mechanisms are not uniform but appear to vary significantly based on both the vaccine platform and the specific glomerular pathology. For instance, for mRNA vaccines (Pfizer-BioNTech, Moderna), the predominant platform in global reports, a robust stimulation of innate immunity is key. The mRNA activates cytosolic and endosomal sensors (e.g., retinoic acid–inducible gene I (RIG-I), Toll-like receptors 7 and 8 (TLR7/8)), triggering a strong type I interferon and pro-inflammatory cytokine response. This environment promotes T-helper cell activation, which is central to the pathogenesis of MCD and may contribute to FSGS via podocyte injury. In contrast, MN following mRNA vaccination is more often attributed to a B-cell driven response, potentially through molecular mimicry where vaccine-induced antibodies cross-react with podocyte antigens like phospholipase A2 receptor (PLA2R). For adenoviral vector vaccines (AstraZeneca, Janssen), the viral DNA activates a distinct innate immune pathway via endosomal Toll-like receptor 9 (TLR9), also leading to type I interferon production but potentially favoring a Th1-polarized response. This pathway has been particularly associated with reports of ANCA-associated vasculitis. For inactivated virus vaccines (Sinopharm, CoronaVac), the main platform in our study, the immunogenic profile may differ, favoring a strong humoral (antibody) immune response. The association observed here between Sinopharm and MN suggests a potential link to polyclonal B-cell activation or alternative molecular mimicry pathways. These platform-specific immune responses (mRNA, adenoviral vector, inactivated) likely interact with individual genetic and immunological host factors to determine the final renal phenotype.

The clinical relevance of investigating Sinopharm-associated complications is amplified by its widespread use. The predominance of the Sinopharm (Covilo) vaccine in our study (n = 9 out of 11) reflects its status as the most widely administered vaccine in Iran, comprising over 80% of all doses. Interestingly, national data show that despite its lower per-dose rate of serious adverse events (3.5 per 10,000 doses), its vast use led to it accounting for the majority (55.8%) of all nationally reported effects.[10] This highlights the importance of studying even low-incidence adverse effects associated with high-use vaccines, as their absolute public health impact can be substantial.

5 Conclusion

This study observed that the occurrence of nephrotic syndrome following COVID-19 vaccination, although rare, can manifest in different pathological forms, including MN, MCD, and FSGS. Unlike many case reports that have identified MCD as the predominant pattern, the present study observed MN to be the most common subtype among the studied cases (7 of 11), occurring mainly after the first dose of the Sinopharm vaccine.

The mean overall interval between vaccination and symptom onset was 41.72 days, with an average of 26.38 days after the first dose. The mean age at disease onset was 46.27 years, corresponding to middle adulthood. Moreover, the observed distribution of nephrotic syndrome types appeared relatively balanced across gender and comorbidity status; however, the small sample size precludes any formal statistical comparisons. To our knowledge, this study represents one of the first clinical investigations describing the pattern of new-onset nephrotic syndrome following COVID-19 vaccination in an Iranian population. Despite its inherent limitations, including a small sample size, single-center design, and lack of a control group, which preclude definitive confirmation of a causal relationship, this study provides valuable insights and data on vaccine-associated nephrotic syndromes, thereby paving the way for future large-scale, multicenter research. Such research is essential to better elucidate the relationship between vaccine platform and nephrotic syndrome phenotype, and to explore the underlying immunopathological mechanisms with greater precision. This deeper understanding is crucial, as it would enable more informed vaccine selection for high-risk patients, potentially reducing the likelihood of complications. Furthermore, elucidating

these mechanisms could guide the design of safer future vaccines, ultimately reducing the associated therapeutic burden and costs.

Declarations

Acknowledgments
The authors sincerely acknowledge the staff of Valiasr Hospital (Zanjan, Iran) for their kind cooperation in providing access to patient data. Special thanks are also extended to the Student Research Committee and the Deputy of Research and Technology of Zanjan University of Medical Sciences for their financial support of this project. The authors also express their gratitude to the Zanjan Country Health Center for granting access to COVID-19 vaccination records. Finally, the authors deeply thank Dr. Ayoub Pezeshki, Professor of Nephrology, for his clinical review and Dr. Farzaneh Ahmadi, statistical advisor, for her invaluable guidance and support throughout the execution of this research project.

Artificial Intelligence Disclosure
This manuscript is based on an original research study conducted by the authors. Artificial intelligence (AI) tools, including ChatGPT (OpenAI, San Francisco, USA), were used solely for language-related purposes, such as refining sentence structure, improving clarity, and translating the original Persian text into English. AI was not used in any part of the research process, including data collection, data analysis, interpretation of results, or preparation of the original thesis report from which this article was derived. The authors take full responsibility for the accuracy, integrity, and originality of all scientific content presented in this paper.

Authors' Contributions
Hanieh Davoodi performed project administration, data collection, investigation, resource provision, original draft writing, review and editing, and submission. Nadia Agharafiei carried out data collection, investigation, and formal analysis. Bahareh Hajisalimi participated in conceptualization, methodology, supervision, and validation. All authors have read and approved the final manuscript.

Availability of Data and Materials
The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request, while maintaining patient confidentiality in accordance with ethical guidelines.

Conflict of Interest
The authors declare that they have no competing interests, financial or otherwise, related to this work.

Consent for Publication
Not applicable.

Ethical Considerations
This study was approved by the Ethics Committee of Zanjan University of Medical Sciences under the Code of Ethics IR.ZUMS.REC.1401.369. All procedures were conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments.

Funding
This research was financially supported by the Deputy of Research and Technology and the Student Research Committee of the Faculty of Medicine at Zanjan University of Medical Sciences. The funding body had no role in study design, data collection, analysis, interpretation, or manuscript preparation.

References

1. Zhang J, Cao J, Ye Q. Renal side effects of COVID-19 vaccination. Vaccines (Basel). 2022;10(11):1783. doi:10.3390/vaccines10111783.
2. Lewis JB, Neilson EG. Glomerular diseases. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 22nd ed. New York: McGraw-Hill Education; 2025. p. 2411-29.
3. Lebedev L, Sapojnikov M, Wechsler A, et al. Minimal change disease following the Pfizer-BioNTech COVID-19 vaccine. Am J Kidney Dis. 2021;78(1):142-5. doi:10.1053/j.ajkd.2021.04.003.
4. Thappy S, Thalappil SR, Abbarh S, Al-Mashdali A, Akhtar M, Alkadi MM. Minimal change disease following the Moderna COVID-19 vaccine: first case report. BMC Nephrol. 2021;22(1):376. doi:10.1186/s12882-021-02578-6.
5. Leclerc S, Monsel G, Vigneau C, et al. Minimal change disease with severe AKI following Oxford-AstraZeneca COVID-19 vaccine: a case report. Kidney Int Rep. 2021;6(8):2287-9. doi:10.1016/j.ekir.2021.06.031.
6. Lim JH, Han MH, Kim YJ, Kim MS, Jung HY, Choi JY, et al. New-onset nephrotic syndrome after Janssen COVID-19 vaccination: a case report and literature review. J Korean Med Sci. 2021;36(30):e218. doi: 10.3346/jkms.2021.36.e218
7. Nakazawa E, Uchimura T, Hirai Y, Togashi H, Oyama Y, Inaba A, et al. New-onset pediatric nephrotic syndrome following Pfizer-BioNTech SARS-CoV-2 vaccination: a case report and literature review. CEN Case Rep. 2022 May;11(2):242-6. doi:10.1007/s13730-021-00656-0
8. Hummel A, Oniszczuk J, Kervella D, Charbit M, Guerrot D, Testa A, et al. Idiopathic nephrotic syndrome relapse following COVID-19 vaccination: a series of 25 cases. Clin Kidney J. 2022 Aug;15(8):1574-82. doi: 10.1093/ckj/sfac134
9. Izzedine H, Bonilla M, Jhaveri KD. Nephrotic syndrome and vasculitis following SARS-CoV-2 vaccine: true association or circumstantial?. Nephrology Dialysis Transplantation. 2021 Sep 1;36(9):1565-9. doi:10.1093/ndt/gfab215
10. Jamaati H, Karimi S, Arshi S, Zahraei SM, Panahi Y, Nouri F, et al. Report on adverse events of COVID-19 vaccines in Iran: a comprehensive national prospective longitudinal analysis. Front