ORIGINAL ARTICLE

Trends in Glomerular Diseases in Northwest India: Has COVID-19 Altered the Diagnostic Landscape?

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Abstract

Background: Glomerular diseases are a major contributor to chronic kidney disease, with regional variability influenced by genetic, environmental, and healthcare factors. In Northwest India, minimal change disease (MCD) was historically the most common primary glomerular disease (PGD). However, evolving diagnostic capabilities and the disruptions caused by the COVID-19 pandemic may have altered the landscape of glomerular disease presentations and biopsy practices.

Objectives: To reassess the clinicopathologic spectrum of glomerular diseases from 2020 to 2024, compare it with data from 2008 to 2013, and evaluate the impact of the COVID-19 pandemic on biopsy activity and disease distribution.

Methodology: We retrospectively analyzed 925 renal biopsies from 2020 to 2024 and compared them with 622 biopsies from 2008 to 2013. All samples underwent light microscopy (LM) and immunofluorescence (IF) staining (IgA, IgG, IgM, C3, and C4). Diagnoses were categorized into PGD, secondary glomerular disease (SGD), and others. Clinical presentations, including nephrotic syndrome (NS) and acute kidney injury (AKI), were recorded. Statistical comparisons were made using Chi-square (χ^2) and *Z*-tests (SPSS v29), with $p < 0.05$ considered significant.

Results: Glomerulonephritis remained predominant (93.9%) with a significant shift in distribution ($\chi^2 = 121.5$, $p < 0.0001$). IgA nephropathy increased from 7.4 to 15.4%, overtaking MCD (which declined from 21.1 to 8.1%) as the leading PGD. Focal segmental glomerulosclerosis (FSGS) rose to 12.4%, while diabetic nephropathy (DN) increased to 3.1%. Nephrotic syndrome was the most common presentation (59.3%). Biopsy volume declined by 60% in 2020 but rebounded by 2022.

Conclusion: These findings highlight evolving diagnostic trends and underscore the need for broader biopsy access, enhanced diagnostic tools, and a national renal biopsy registry in India.

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Introduction

Glomerular diseases remain the leading cause of chronic kidney disease and end-stage renal disease worldwide; [1,2] their prevalence and patterns vary significantly across regions due to differences in genetics and environment.[3–5] They significantly contribute to the global burden of end-stage kidney disease and require region-specific epidemiological insights for optimal management. In 2016, we published a 5-year retrospective study titled "A Clinicopathologic Study of Glomerular Disease: A Single-Center, Five-Year Retrospective Study from Northwest India," which described biopsy-proven glomerular disease patterns at our center from 2008 to 2013. Our study analyzed 622 renal biopsies performed (2008–2013) at Sawai Man Singh Medical College and Hospital in Jaipur, Rajasthan;[6] we provided the first detailed profile of glomerular diseases in this arid and underserved region of India. Glomerulonephritis dominated renal pathology (93.9%), comprising primary glomerular diseases (PGDs, 79.4%) and secondary glomerular diseases (SGDs, 14.5%). Minimal change disease (MCD, 21.1%) was the most frequent PGD, followed by membranous nephropathy (MGN, 15.0%) and focal segmental glomerulosclerosis (FSGS, 10.5%). Lupus nephritis (LN, 7.6%) and amyloidosis (5.9%) predominated among SGDs. Notably, we highlighted significant regional heterogeneity, contrasting the predominance of MCD in Northwest India with immunoglobulin A nephropathy (IgAN) in Western India, and advocated for a national renal biopsy registry to bridge the data gap.

Since that time, the landscape of glomerular disease has been reshaped by significant global and local shifts.[7–9] Advances in diagnostics, evolving epidemiological trends, and the unprecedented disruption caused by the COVID-19 pandemic have all challenged previous understandings. The pandemic, in particular, disrupted healthcare access, delayed renal biopsies, and may have altered both disease presentation at the time of diagnosis and clinician thresholds for initiating biopsy. Moreover, emerging evidence of immune-mediated kidney injury following SARS-CoV-2 infection or vaccination has introduced new clinical and pathological patterns, prompting the need for updated, region-specific data to guide clinical practice.[10]

In response, we analyzed 925 renal biopsies performed between 2020 and 2024 to update the glomerular disease spectrum at our center. This dataset builds on our earlier work and reflects both evolving diagnostic trends and the impact of the COVID-19 pandemic. While some regional data have emerged, postpandemic biopsy trends from Northwest India remain undocumented. This study addresses that gap by examining temporal shifts in disease patterns over the past decade, with a focus on pandemic-related influences.

Methodology

This retrospective study was conducted at the Department of Nephrology, Sawai Man Singh (SMS) Medical College and Hospital, Jaipur, Rajasthan—a major tertiary referral center serving the population of Northwest India. We selected two distinct 5-year cohorts (July 2008–June 2013 and January 2020–December 2024) to allow a decade-long comparison of glomerular disease trends. The earlier cohort was previously published and validated, providing a reliable baseline.[6] This design not only facilitated pre- and postpandemic analysis but also captured broader shifts in diagnostic practices, disease presentation, and clinical decision-making that typically evolve over longer periods. Ethical approval was not required, as the study was retrospective in nature and based solely on anonymized, preexisting clinical and histopathological data.

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For the 2008–2013 cohort, 741 renal biopsies were reviewed. Of these, 209 (28.2%) were excluded—80 (10.8%) due to transplant origin or inadequate sampling, and 129 (17.4%) due to nonglomerular diagnoses—resulting in 532 cases for final analysis. For the 2020–2024 cohort, 1,005 renal biopsies were reviewed, with 925 (92.0%) included after applying the same exclusion criteria; 80 biopsies (8.0%) were excluded due to transplant origin, inadequate sampling, or nonglomerular diagnoses.

Renal biopsies were performed using Tru-Cut 14-gauge needles and Bard® disposable core biopsy instrument (Bard Biopsy Systems®), typically yielding two cores—one fixed in formalin for light microscopy (LM), and the other processed for immunofluorescence (IF). Paraffin-embedded sections were stained with hematoxylin and eosin (H and E), periodic acid–Schiff (PAS), Masson trichrome, Congo red, and Jones methenamine silver stains. IF was performed using antibodies against IgA, IgG, IgM, IgE, C3, and C4. Electron microscopy (EM) was not utilized due to its unavailability.

Diagnoses were classified into three groups: PGDs, SGDs, and other conditions such as tubulointerstitial or vascular pathology. PGDs included MCD, FSGS, MGN, IgAN, membranoproliferative glomerulonephritis (MPGN), diffuse proliferative glomerulonephritis (DPGN), and crescentic glomerulonephritis (Crescentic GN). SGDs included LN, renal amyloidosis, diabetic nephropathy (DN), and Monoclonal Immunoglobulin Deposition Disease(MIDD).[11–13]

Clinical data such as serum creatinine, 24-hour proteinuria, hematuria, and hypertension were retrieved from patient records where available. Annual biopsy volumes (2020–2024) were documented to assess temporal trends. To compare disease distribution between the two cohorts, disease frequencies were calculated for both periods. Statistical comparisons were performed using Chi-square (χ^2) tests for overall pattern shifts and two-sample Z-tests to evaluate changes in specific diagnoses. Statistical analysis was conducted using SPSS software (version 29.0), with a p-value < 0.05 considered statistically significant.

Results

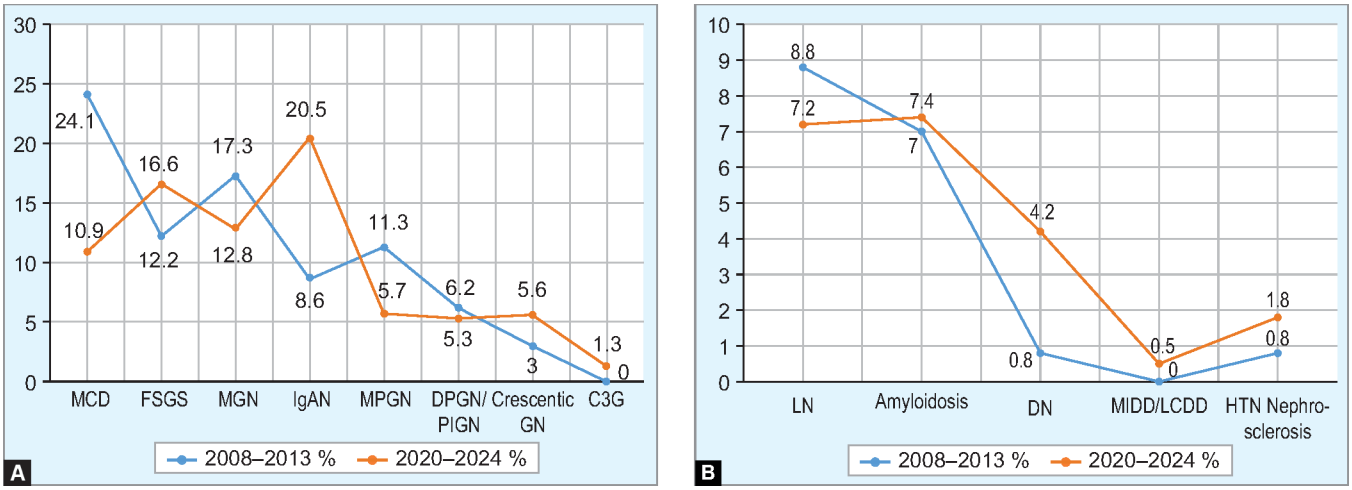
Analysis of 925 renal biopsies performed between 2020 and 2024 revealed significant shifts in the spectrum of glomerular diseases compared to the 2008–2013 cohort. A consolidated summary of these changes is presented in Table 1 and illustrated in Figure 1.

Shifts in Primary Glomerular Diseases

Minimal change disease declined significantly from 128 cases (24.1%) in 2008–2013 to 101 (10.9%) in 2020–2024 (↓13.2%, p < 0.0001). In contrast, IgAN rose markedly

Table 1: Comparative distribution of glomerular diseases in renal biopsies: 2020–2024 vs 2008–2013

Primary /secondary /other	*Diagnosis*	*2008–2013 count (%)*	*2020–2024 count (%)*	*Change (%)*	*p-value*
Primary	MCD	128 (24.1)	101 (10.9)	−13.2	< 0.0001
	FSGS	65 (12.2)	154 (16.6)	4.4	0.174
	MGN	92 (17.3)	118 (12.8)	−4.5	0.0003
	IgAN	46 (8.6)	190 (20.5)	11.9	< 0.0001
	MPGN	60 (11.3)	53 (5.7)	−5.6	< 0.0001
	DPGN	33 (6.2)	49 (5.3)	−0.9	0.192
	Crescentic GN	16 (3.0)	52 (5.6)	2.6	0.08
	C3G	0 (0.0)	12 (1.3)	1.3	0.004
Secondary	LN	47 (8.8)	67 (7.2)	−1.6	0.064
	Amyloidosis	37 (7.0)	68 (7.4)	0.4	0.723
	DN	4 (0.8)	39 (4.2)	3.4	0.0002
	MIDD	0 (0.0)	5 (0.5)	0.5	0.066
	HTN nephrosclerosis	4 (0.8)	17 (1.8)	1	0.123



Figs 1A and B: Comparison of primary and secondary glomerular disease distributions (2008–2013 vs 2020–2024)

from 46 (8.6%) to 190 (20.5%) (↑11.9%, $p <$ 0.0001). MGN also declined from 92 (17.3%) to 118 (12.8%) (↓4.5%, $p = 0.0003$), and MPGN dropped from 60 (11.3%) to 53 (5.7%) (↓5.6%, $p < 0.0001$).

Focal segmental glomerulosclerosis increased from 65 (12.2%) to 154 (16.6%) (↑4.4%) but was not statistically significant ($p = 0.174$). Crescentic GN rose from 16 (3.0%) to 52 (5.6%) (↑2.6%, $p = 0.08$). C3 glomerulopathy (C3G) newly emerged with 12 cases (1.3%) ($p = 0.004$).

Changes in Secondary Glomerular Diseases

Diabetic nephropathy increased significantly from 4 cases (0.8%) to 39 (4.2%) (↑3.4%, $p = 0.0002$). LN declined from 47 (8.8%) to 67 (7.2%) (↓1.6%, $p = 0.064$), approaching significance. Amyloidosis remained stable—37 cases (7.0%) vs 68 (7.4%) (↑0.4%, $p = 0.723$). Hypertensive nephrosclerosis rose from 4 (0.8%) to 17 (1.8%) (↑1.0%, $p = 0.123$). MIDD/LCDD emerged with 5 cases (0.5%) in 2020–2024, though not statistically significant ($p = 0.066$).

Impact of COVID-19 on Biopsy Trends

The trends observed in glomerular disease prevalence from 2020 to 2024 were likely shaped, at least in part, by the impact of the COVID-19 pandemic.[10] With nationwide lockdowns and healthcare services disrupted, access to medical care and timely referrals declined, which may have reduced the number of renal biopsies performed.[11] As a result, milder conditions such as MCD and MPGN may have been underdiagnosed. In contrast, the rise in cases of IgAN and C3G could reflect post-COVID immune responses or a shift toward biopsying only the more severe or atypical presentations during that challenging period.[10,12]

Glomerular Disease Distribution Changes (2008–2013 and 2020–2024)

A Chi-square test of independence was used to assess changes in biopsy-proven glomerular disease distribution. As shown in Figure 2, analysis of ten major diagnoses revealed a significant shift in patterns ($\chi^2 = 121.5$, df =9, $p < 0.0001$). The most marked changes were a decline in MCD (21.1 to 8.1%, ↓13.0%) and a rise in IgAN (7.4 to 15.4%, ↑8.0%). Other notable shifts included declines in MGN (15.0 to 9.5%, ↓5.5%) and MPGN (9.6 to 4.3%, ↓5.3%), and increases in FSGS (10.5 to 12.4%, ↑1.9%) and DN (0.6 to 3.1%, ↑2.5%). These trends may reflect better diagnostics and external factors such as the COVID-19 pandemic.[14]

Key Diagnoses

Z-tests for MCD, IgAN, FSGS, and MGN

Two-sample Z-tests for proportions were performed to assess shifts in four major PGDs—MCD, IgAN, FSGS, and MGN—between 2008–2013 ($n = 622$) and 2020–2024 ($n = 925$), based on χ^2 findings. Significant changes were seen in MCD ($p < 0.0001$), IgAN ($p < 0.0001$), and MGN ($p = 0.0003$), while the increase in FSGS was not significant ($p = 0.174$).

Minimal change disease dropped sharply from 21.1 to 8.1% ($Z = -7.88$), while IgAN rose from 7.4 to 15.4% ($Z = 4.76$), marking the most prominent shifts. MGN declined moderately from 15.0 to 9.5% ($Z = -3.62$), and FSGS showed a slight, nonsignificant rise from 10.5 to 12.4% ($Z = 1.36$). These trends highlight a clear decline in MCD and a notable rise in IgAN as key contributors to the changing glomerular

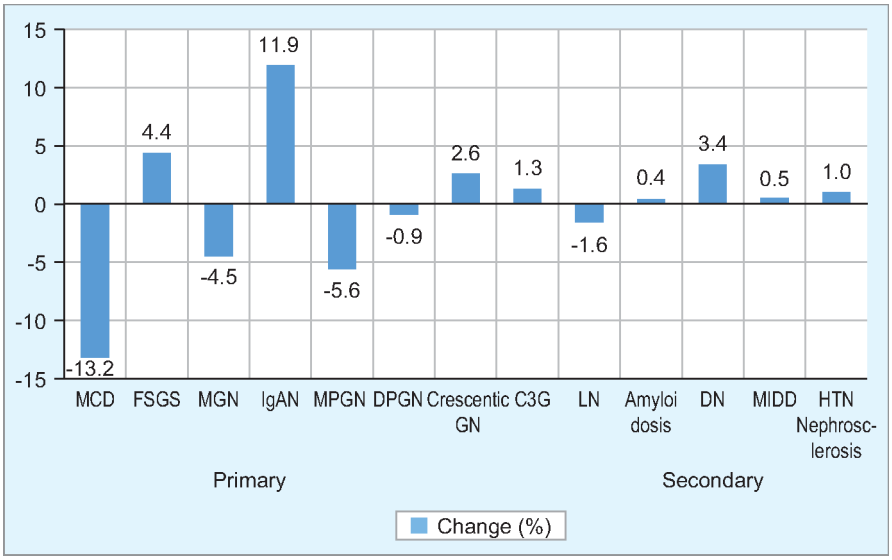


Fig. 2: Percentage change in glomerular disease diagnosed between 2008–2013 and 2020–2024

Table 2: Clinical syndromes and corresponding histological diagnoses in renal biopsies (2020–2024)

Primary/secondary	*Renal disease*	*Number (%)*	*NS (%)*	*AGN (%)*	*RPRF (%)*	*AUA (%)*	*CKD (%)*
Primary	MCD	101 (10.9)	91 (16.6)	7 (5.1)	0 (0.0)	3 (3.4)	0 (0.0)
	FSGS	154 (16.6)	146 (26.6)	8 (5.8)	0 (0.0)	0 (0.0)	0 (0.0)
	MGN	118 (12.8)	107 (19.5)	3 (2.2)	0 (0.0)	7 (8.0)	1 (1.4)
	IgAN	190 (20.5)	32 (5.8)	55 (40.1)	11 (14.3)	64 (72.7)	28 (37.8)
	MPGN	53 (5.7)	35 (6.4)	12 (8.8)	3 (3.9)	3 (3.4)	0 (0.0)
	DPGN	49 (5.3)	24 (4.4)	20 (14.6)	5 (6.5)	0 (0.0)	0 (0.0)
	Crescentic GN	52 (5.6)	13 (2.4)	3 (2.2)	30 (39.0)	0 (0.0)	6 (8.1)
	C3G	12 (1.3)	3 (0.5)	6 (4.4)	1 (1.3)	0 (0.0)	2 (2.7)
Secondary	LN	67 (7.2)	16 (2.9)	20 (14.6)	27 (35.1)	0 (0.0)	4 (5.4)
	Amyloidosis	68 (7.4)	60 (10.9)	0 (0.0)	0 (0.0)	3 (3.4)	5 (6.8)
	DN	39 (4.2)	19 (3.5)	3 (2.2)	0 (0.0)	8 (9.1)	9 (12.2)
	MIDD	5 (0.5)	3 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.7)
	HTN nephrosclerosis	17 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	17 (23.0)
	Totals	925 (100.0)	549 (100.0)	137 (100.0)	77 (100.0)	88 (100.0)	74 (100.0)

disease spectrum, with MGN also playing a significant role.

Clinical Syndromes Associated with Histological Diagnoses (2020–2024)

We analyzed the clinical presentations of biopsy-proven renal diseases from 2020 to 2024 (Table 2). Nephrotic syndrome was the most common indication for biopsy, seen in 549 of 925 cases (59.3%). Among PGDs, FSGS was predominant (146 cases, 26.6%), followed by MGN (107, 19.5%), MCD (91, 16.6%), and IgAN (32, 5.8%).

Immunoglobulin A nephropathy was the most frequent PGD overall (190 cases, 20.5%), leading to acute glomerulonephritis (AGN, 40.1%) and contributing significantly to rapidly progressive renal failure (14.3%) and chronic kidney disease (CKD, 37.8%).

Acute glomerulonephritis was identified in 137 cases (14.8%), predominantly due to IgAN (40.1%), DPGN (14.6%), and MPGN (8.8%). Rapidly progressive renal failure (8.3%) was mainly caused by crescentic GN (39.0%) and LN (35.1%). CKD (8.0%) was frequently associated with hypertensive nephrosclerosis (23.0%) and DN (12.2%). Asymptomatic urinary abnormalities (AUA) were noted in 88 cases (9.5%), mostly due to IgAN (72.7%).

Discussion

This study provides an updated clinicopathologic profile of glomerular diseases based on 925 renal biopsies performed from 2020 to 2024 at our tertiary care center in Northwest India, compared to 622 biopsies from 2008 to 2013. By examining two distinct cohorts separated by a decade, we identified significant temporal shifts reflecting evolving nephrology practices and the impact of the COVID-19 pandemic. A χ^2 analysis confirmed substantial changes in disease distribution ($\chi^2 = 121.5$, df = 9, $p < 0.0001$).

The most notable finding was the sharp decline in MCD from 24.1 to 10.9% ($p < 0.0001$) and the rise of IgAN from 8.6 to 20.5% ($p < 0.0001$). This made it the leading PGD. Other significant changes included a decline in MGN from 17.3 to 12.8% ($p = 0.0003$) and MPGN from 11.3 to 5.7% ($p < 0.0001$). In contrast, FSGS increased from 12.2 to 16.6% ($p = 0.174$), although this change was not statistically significant. Among SGDs, DN increased from 0.8 to 4.2% ($p = 0.0002$). This indicated rising diabetes prevalence in India.[13,14] LN remained stable at 7.2% ($p = 0.064$). Amyloidosis showed only a modest increase from 7.0 to 7.4% ($p = 0.723$).

The evolution of glomerular disease patterns at our center over the past 15 years tells a compelling story—one shaped by improved diagnostics, shifts in clinical decision-making, and the sweeping global impact of the COVID-19 pandemic. Our comparison of renal biopsy data from 2008 to 2013 and 2020 to 2024 reveals both expected trends and new insights that mirror changes in nephrology across India and globally.

Perhaps the most striking shift has been the sharp decline in MCD, from 24.1 to just 10.9%. This is consistent with data from other Indian centers, where similar drops have been observed over time.[15] The decrease likely stems from a more conservative biopsy approach in patients with classic steroid-sensitive NS—especially in children and young adults—who are now often treated empirically with corticosteroids.[16] At the same time, improvements in histopathology and IF have enabled clearer differentiation between MCD, early FSGS, and IgAN, leading to diagnostic reclassification in many cases.[15,16] The COVID-19 pandemic only accelerated this trend, as biopsy activity declined and clinicians prioritized patients with atypical or steroid-resistant features.[17]

In contrast, IgAN emerged as the most common PGD in our recent cohort, rising from 8.6 to 20.5%. This increase likely reflects both a true epidemiological shift and enhanced diagnostic recognition due to greater awareness and improved biopsy practices. At our center, renal biopsies are routinely performed in patients with CKD who present with active urinary sediments and normal-sized kidneys, and a substantial proportion of these cases were diagnosed as IgAN. The Oxford classification has brought greater uniformity and precision to the diagnosis and prognostication of IgAN.[18] IF has become more routinely available, leading to better detection of mesangial IgA deposition. A recent systematic review from India estimates the prevalence of IgAN at 16.5%, higher than in Western populations but lower than in East Asian countries.[13] Interestingly, recent case reports suggest that COVID-19 may also serve as a trigger for new-onset or relapsing IgAN, possibly via immune dysregulation.[19]

We also noted a significant decline in MPGN, from 11.3 to 5.7%, which aligns with recent advances in our understanding of complement-mediated glomerular diseases. Many cases once labeled as MPGN are now being subclassified as C3G, a pathogenic subset within the MPGN pattern, based on dominant C3 staining and complement dysregulation, owing to improved availability of immunohistochemistry and complement pathway analysis.[20] These tools have enhanced diagnostic accuracy and provided a more mechanistic framework for understanding disease progression.[21] However, in many centers such as ours, access to EM remains limited, creating challenges in accurately subtyping these diseases.[22]

A parallel decline was observed in MGN, which fell from 17.3 to 12.8%. This likely reflects a shift in diagnostic strategies. The increased use of antiphospholipase A2 receptor (PLA2R) antibody testing has reduced the reliance on biopsy for typical cases of primary MGN.[23,24] In addition, widespread hepatitis B vaccination and improved antiviral therapy have led to a decrease in secondary MGN, especially in regions such as ours where hepatitis B was once endemic.[25]

Secondary glomerular diseases showed evolving patterns as well. DN increased from 0.8 to 4.2%, in line with India's growing burden of type 2 diabetes.[13,14] LN remained relatively stable at 7.2%, and amyloidosis saw only a modest rise from 7.0 to 7.4%. These numbers highlight how public health trends and improved survival may be influencing biopsy findings.

The COVID-19 pandemic had a clear, though temporary, impact on biopsy activity and disease patterns. In 2020, the number of renal biopsies at our center dropped by 60% (95 cases) compared to the prepandemic average of 234 per year, due to lockdowns and healthcare disruptions. A recovery began in 2021 (185 biopsies), followed by a peak in 2022 (267 biopsies), suggesting a catch-up effect from delayed diagnoses. This period also coincided with increased detection of IgAN and C3G, supporting the hypothesis of postviral immune activation following COVID-19.[19,26] SARS-CoV-2 infection has been linked to a wide range of glomerular pathologies, including MGN, crescentic GN, podocytopathy, and thrombotic microangiopathy largely attributed to direct viral injury and immune dysregulation.[27] In patients with preexisting glomerular diseases, COVID-19 was associated with acute kidney injury (AKI) in approximately 16.9% of cases, with worse outcomes among older patients, males, and those receiving corticosteroids or presenting with hypoalbuminemia.[28]

Focal segmental glomerulosclerosis showed a mild increase in prevalence from 12.2 to 16.6%, although this change was not statistically significant. However, the trend may reflect a growing recognition of FSGS, particularly as more patients with steroid-resistant NS are being biopsied. This observation is consistent with global patterns, notably in East Asia and Europe, where FSGS has been increasingly identified as a major cause of NS.[5,29] Additionally, the COVID-19 pandemic brought attention to collapsing glomerulopathy (COVAN), a distinct variant of

FSGS, especially among patients with high-risk APOL1 genotypes.[26]

As expected, the clinical presentations closely reflected the underlying histological patterns. Nephrotic syndrome was the most common presentation in podocytopathies such as MGN, FSGS, MCD, and amyloidosis, where damage to the glomerular filtration barrier leads to heavy proteinuria.[30] C3 glomerulopathy, driven by dysregulation of the complement pathway, is typically presented as AGN, consistent with its pathophysiological mechanism.[31] Interestingly, only 33.7% of IgAN cases in our cohort presented with AUA, a notable decline from historical figures exceeding 50%. This may reflect pandemic-era biopsy practices, where patients with milder urinary findings were often managed conservatively.[32] Hypertensive nephrosclerosis consistently presented with CKD, reflecting its silent progression. CKD was also the predominant presentation in chronic immune complex-mediated diseases such as MPGN and LN, suggesting delays in diagnosis or evolving referral patterns.

Limitations

This was a single-center, retrospective study, potentially limiting generalizability. EM and complement assays were unavailable, restricting diagnostic precision for certain conditions. Pandemic-related selection bias in biopsy decisions may have influenced disease prevalence data.

Conclusion

The evolving spectrum of glomerular diseases highlights significant shifts in nephrology practice, diagnostics, and public health trends. Our findings emphasize the need to improve renal biopsy access and strengthen advanced diagnostics, including IF, complement assays, and EM. Crucially, our results support earlier recommendations to establish a national renal biopsy registry, such as the Indian TrANslational GlomerulonephrItis BioLogy nEtwork (I-TANGIBLE), currently underway in India.[33] This initiative would allow standardized tracking of disease patterns, validate our observed trends nationally, and guide evidence-based nephrology care.

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