

Spectrum of Glomerular Disease on Kidney Biopsy: An Observational Study

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ABSTRACT

Introduction: Glomerular diseases are the leading causes of chronic kidney disease and end-stage kidney disease worldwide. Their distribution varies across regions, and data from Nepal are limited. Kidney biopsy is essential for accurate diagnosis, prognosis, and definitive therapy. This study aims to establish the histopathological spectrum of glomerular diseases in patients undergoing native kidney biopsy at specialized transplant hospital of Nepal.

Methods: A retrospective observational study was conducted among 351 patients who underwent renal biopsy at Shahid Dharmabhakta National Transplant Center between January 2016 and December 2019. Demographic, clinical, and laboratory data were compiled from hospital records. Biopsies were performed under ultrasound guidance and examined using light microscopy and immunofluorescence. Data was analyzed descriptively.

Results: Out of 351 patients, the median age of patients was 36 years (IQR 27–48), and 192 (54.70%) were male. Kidney biopsies were performed for nephrotic syndrome in 86 (24.50%) patients, Nephritic Syndrome in 77 (21.94%). IgA Nephropathy was seen in 108 (31.67%) patients. Focal Segmental Glomerulosclerosis in 76 (22.28%) and Non-proliferative Glomerulopathy in 41 (12.02%). Among 35 (10%) of lupus nephritis cases, Class IV (42.85%) was prevalent. The Oxford classification of IgA nephropathy revealed Segmental glomerulosclerosis (S1) in 10 (96.30%) patients, Tubular atrophy/Interstitial fibrosis (T1) in 62 (57.41%).

Conclusions: Primary glomerular disease is common in the biopsy group in Nepal, and histologic evaluation is crucial for guiding diagnosis, prognosis, and prompt treatment of glomerular disorders. The findings also show the value of kidney biopsy in clinical practice and provide significant input into the epidemiology of glomerular disorders in Nepal.



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INTRODUCTION

Glomerular diseases are one of the main causes of end-stage kidney disease (ESKD) and include a wide range of renal disorders that mostly damage the glomeruli.^{1,2} Between 1990 and 2021, the age-standardized prevalence of glomerulonephritis rose by 10.81%.³ The pattern of glomerular disorders differs around the world, with IgA nephropathy being the predominant cause in Asia.⁴

In Nepal, studies show contradictory results regarding predominant histopathological lesions. A study done at

Tribhuvan University Teaching Hospital (TUTH), Institute of Medicine (IOM) showed IgA nephropathy and Lupus Nephritis (LN) as the most common histological lesion whereas study from Shree Birendra Hospital revealed membranous nephropathy to be the most prevalent followed by FSGS.^{5,6} Although glomerular disease has been identified as the most prevalent cause of end-stage kidney disease in Nepal, the actual incidence and prevalence are unknown.⁷ Therefore, this study aims to determine the frequency of biopsy-proven glomerular diseases among native kidney biopsies.

METHOD

A retrospective observational study was conducted among patients who underwent native kidney biopsy between January 2016 and December 2019 at Shahid Dharmabhakta National Transplant Center in Bhaktapur, Nepal. Ethical clearance was granted from the Nepal Health Research Council before commencing the project (Ref No: 1244/2024), and formal hospital approval, including waiver of informed consent, was obtained from the hospital administration. The consents were waived from hospital. Since this was a retrospective review of pre-existing medical information, the hospital administration granted permission to retrieve and use the records and waived the requirement for individual informed consent as stated in the NHRC approved research proposal. The study included patients with glomerular disease who underwent native kidney biopsy during the study period. All consecutive eligible native kidney biopsies during January 2016–December 2019 were included; therefore, no formal sample size calculation was required. Seven patients with inadequate biopsy sample records and kidney transplant recipients were excluded. A total of 358 patients were screened and a total of 351 patients who met the inclusion criteria were included in the study.

All patients who underwent native kidney biopsy at SDNTC between January 2016 and December 2019 were included. This period was selected for its sufficiently large and well-documented dataset. During the COVID-19 pandemic, biopsy procedures declined markedly, with only 20–25 biopsies performed and several records having incomplete clinical and pathological documentation. Post-2022 records were also inconsistently reported and were not comparable with the pre-pandemic data. Therefore, the study period was restricted to 2016–2019 to minimise selection and information bias and ensure data quality and comparability. A total of 351 patients met the inclusion criteria.

A standardized pro forma was designed specifically for the study and used to gather relevant data from histopathology reports and hospital records. Demographic information, including age, gender, and ethnicity, and a history of illness, was compiled. Laboratory reports (Random blood sugar, Serum urea, Serum creatinine, Serum albumin, Urinary protein, Urinary RBC and RBC casts, 24-hour urine protein test, Antinuclear antibodies) were collected.

Syndromic diagnosis was established based on clinical presentation/history of illness and laboratory parameters. Nephrotic syndrome is defined as proteinuria exceeding 3.5 g/day in association with hypoalbuminemia <3.5 g/dl and edema. Sub nephrotic proteinuria is defined as proteinuria >0.2 g and <3.5 g/day with normal renal parameters. Nephritic Syndrome is defined as proteinuria <3 g/day associated with oliguria, hematuria, and RBC casts, edema, and variable degrees of hypertension. Rapidly progressive renal failure is defined as proteinuria <3 g/day associated with renal failure over days/weeks, hematuria, and RBC casts. All patients with a syndromic diagnosis of

Diabetes with suspicion of other renal disease, Nephritic syndrome, Nephrotic syndrome, Sub-nephrotic proteinuria with persistent proteinuria >1 g/day, rapidly progressive renal failure, SLE with renal involvement, and Unexplained renal impairment underwent a renal biopsy procedure. Under aseptic precautions and local anesthesia, nephrologists performed the kidney biopsy procedure. The patient was laid prone, and a pillow was placed under the abdomen at the level of the umbilicus to straighten the lumbar spine and to splint the kidneys. Ultrasound was used to localize the lower pole of the kidney where the biopsy was performed. The skin was sterilized, and a local anesthetic was infiltrated. An 18-gauge disposable automated biopsy needle was passed under continuous (real-time) ultrasound guidance to the kidney. Two kidney biopsy core specimens were obtained, and each sample was stored in a solution of formalin and normal saline. After being labeled, all preserved samples were sent to Lal Path, India for histopathological analysis. Renal biopsy samples were analyzed by light microscopy and immunofluorescence.

The research data were entered in Microsoft Excel and subsequently analyzed using SPSS (version 21). Descriptive statistics were employed to calculate the frequencies and percentages of various glomerular disease patterns. We did not perform inferential statistics as the primary objective was only to determine frequency of biopsy proven glomerular disease. The results were presented in tables and charts for clarity.

RESULTS

The median age of patients was 36 years, with an IQR ranging from 27 to 48 years with male 192 (54.70%) and female 159 (45.29%). There were 179 (49.86%) of the patients in the 19 to 39 years age group while 143 (40.74%) belonged to the Janjati ethnic group. Kidney biopsies were performed for nephrotic syndrome in 86 (24.50%) patients, nephritic syndrome in 77 (21.94%), and unexplained renal impairment in 73 (20.80%) (Table 1). Among the biopsied cases, glomerular diseases were identified in 341 (97.15%), while non-glomerular lesions, including acute pyelonephritis, cortical necrosis, interstitial nephritis, and glomerulosclerosis, were found in 10 (2.84%). Among 341 patients who had glomerular disease, IgA Nephropathy was seen in 108 (31.67%) patients. Focal Segmental Glomerulosclerosis in 76 (22.28%) and Non-proliferative Glomerulopathy in 41 (12.02%). Among patients who had IgA Nephropathy, based on the Oxford MEST-C classification, Segmental glomerulosclerosis (S1) was present in 104 (96.3%) patients (Table 2).

Among patients with glomerular lesion ($n=341$), the 19–39-year age group included 170 (49.85%) patients. Lupus Nephritis were seen among children under 18 years. IgA Nephropathy was seen in 72 (42.35%) inpatients aged 19 to 39 years. Among patients aged 40 years and above FSGS was observed in 5 (25.2%) patients (Table 3).

Among patients diagnosed with Lupus Nephritis ($n=35$), Class IV Lupus nephritis was seen in 15 (42.85%) patients, and combined Class IV and V in 10 (28.57%) patients (Fig 1).

Table 1. Socio-demographic characteristics of patients (n=351).

Variables	n(%)
Age	
Under 18 years	33(9.40)
Young adulthood (19 to 39)	175(49.86)
Middle adulthood (40 to 64)	127(36.18)
Old adulthood (65 and above)	16(4.56)
Median (IQR)	36 (27–48)
Gender	
Male	192(54.70)
Female	159(45.30)
Ethnicity	
Dalit	17(4.84)
Janjati	143(40.74)
Madhesi	46(13.11)
Muslim	4(1.14)
Brahmin/Chhetri	137(39.03)
Others	4(1.14)
Indications for kidney biopsy	
Diabetes with suspicion of other renal disease	21(5.98)
Nephritic syndrome	77(21.94)
Nephrotic syndrome	86(24.50)
Sub-nephrotic proteinuria	45(12.82)
Rapidly progressive renal failure	14(3.99)
SLE with renal involvement	35(9.97)
Unexplained renal impairment	73(20.80)
IQR: interquartile range; SLE: systemic lupus erythematosus; Others: Malla and Thakuri.	

Table 2. Frequency of various renal pathological lesions (N= 351).

Renal pathological lesions	n(%)
IgA Nephropathy	108(30.77)
Focal Segmental Glomerulosclerosis	76(21.65)
Non-proliferative Glomerulopathy	41(11.68)
Lupus Nephritis	35(9.97)
Membranous Glomerulopathy	24(6.84)
Diabetic Nephropathy	14(3.99)
Membranoproliferative Glomerulopathy	11(3.13)
Post-Infectious Glomerulonephritis	9(2.56)
Crescentic Glomerulonephritis	7(1.99)
Hypertensive Nephropathy	6(1.71)
C1q Nephropathy	5(1.42)
Interstitial Nephritis	4(1.14)
C3 Glomerulopathy	3(0.85)
Glomerulosclerosis	3(0.85)
Cortical Necrosis	2(0.57)
Acute Pyelonephritis	1(0.28)
Monoclonal Immunoglobulin Deposition Diseases/Light chain deposition disease	1(0.28)
Renal Amyloidosis	1(0.28)
IgAN: IgA nephropathy; FSGS: focal segmental glomerulosclerosis; NP-GN: non-proliferative glomerulopathy; LN: lupus nephritis; MGN: membranous glomerulopathy; DN: diabetic nephropathy; MPGN: membranoproliferative glomerulonephritis; PIGN: post-infectious glomerulonephritis; Cres. GN: crescentic glomerulonephritis; HN: hypertensive nephropathy; C1qN: C1q nephropathy; C3G: C3 glomerulopathy; MIDD/LCDD: monoclonal immunoglobulin deposition disease/light chain deposition disease.	

Table 3. Distribution of glomerular disease according to age (n=351).

Var- i-ables	C1qN	C3G	Cres. GN	DN	PIGN	FSGS	IgAN	LN	HN	MPGN	MGN	MI/ LC	NP- GN	RA	Total %
Under 18 years	-	-	2 (6.25)	--	1 (3.13)	7 (21.88)	6 (18.75)	9 (28.13)	1 (3.13)	-	-	-	6 (18.75)	-	32 (9.38)
19-39 years	4 (2.35)	2 (1.18)	-	4 (2.35)	6 (3.53)	33 (19.41)	72 (42.35)	20 (11.76)	3 (1.76)	3 (1.76)	12 (7.06)	-	11 (6.47)	-	170 (49.85)
40-64 years	1 (0.81)	1 (0.81)	4 (3.25)	9 (7.32)	2 (1.63)	31 (25.20)	28 (22.76)	6 (4.88)	2 (1.63)	6 (4.88)	12 (9.76)	-	20 (16.26)	1 (0.81)	123 (36.07)
>65 years	-	-	1 (6.25)	1 (6.25)	-	5 (31.25)	2 (12.50)	-	-	2 (12.50)	-	1 (6.25)	4 (25)	-	16 (4.69)
Total	5 (1.47)	3 (0.88)	7 (2.05)	14 (4.11)	9 (2.64)	76 (22.29)	108 (31.67)	35 (10.26)	6 (1.76)	11 (3.23)	24 (7.04)	1 (0.29)	41 (12.02)	1 (0.29)	341 (100)
C1qN: C1q Nephropathy; C3G: C3 Glomerulopathy; Cres. GN: Crescentic Glomerulonephritis; DN: Diabetic Nephropathy; PIGN: Post-Infectious Glomerulonephritis; FSGS: Focal Segmental Glomerulosclerosis; IgAN: Immunoglobulin A Nephropathy; LN: Lupus Nephritis; HN: Hypertensive Nephropathy; MPGN: Membranoproliferative Glomerulopathy; MGN: Membranous Glomerulopathy; MI/LC: Monoclonal Immunoglobulin Deposition Diseases/Light Chain Deposition Disease; NP-GN: Nonproliferative Glomerulopathy; RA: Renal Amyloidosis.															

DISCUSSION

Kidney biopsy has remained the gold standard for identifying the causes of proteinuria, hematuria, and idiopathic renal failure. It is crucial for determining the best course of treatment and prognosis.⁸ We conducted a descriptive retrospective study among 351 patients who underwent

renal biopsy at Shahid Dharmabhakta National Transplant Center.

Nephrotic syndrome was the most frequent indication for kidney biopsy in this study (24.5%), followed by nephritic syndrome (21.9%) and unexplained renal impairment (20.8%). Moreover, nephrotic syndrome is the predominant indication

for renal biopsy, as reported in several Nepalese adults ($\approx 26\text{--}63\%$)^{6,9–11} and stated in several South Asian studies.^{12,13}

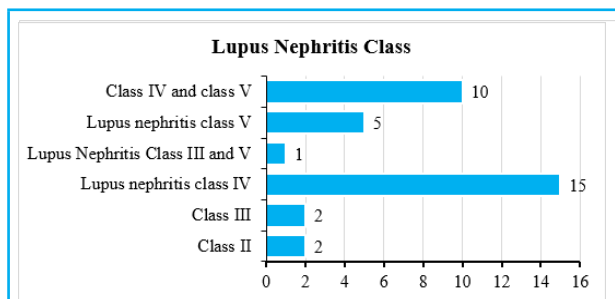


Figure 1. Classification of Lupus Nephritis diagnosed in a kidney biopsy (n=341).

A systematic meta-analysis of 40 studies elucidated that the incidence of idiopathic nephrotic syndrome in children varies between ~ 1.2 and 17 cases per 100,000 annually (pooled estimates $\approx 2\text{--}7$ cases per 100,000 annually).¹⁴ Numerous large-scale biopsy studies from Asia and other regions similarly mentioned nephrotic syndrome as the major indication; however, the percentage varies with each center (from about 23% to over 50%).^{15,16} In contrast, a number of Western registries frequently report a higher percentage of biopsies performed for diabetic glomerulosclerosis or unexplained renal impairment, reflecting variations in biopsy thresholds and regional disease burden.¹⁷

Globally, IgAN is a prevalent glomerular disease, with a higher frequency in some Asian nations than in Western ones.^{18–21} The predominant glomerular disease in our study was IgA nephropathy (IgAN) (30.8%), followed by focal segmental glomerulosclerosis (FSGS, 21.7%), non-proliferative glomerulopathy (11.7%), and lupus nephritis (10.0%). These findings are consistent with the study conducted in Nepal by Mainali et al. (2024), which showed that the leading cause of chronic glomerulonephritis was IgA Nephropathy (38.10%).²² Similarly, a study by Pandey et al. 2017 showed IgA Nephropathy was identified among 35.8% of the patients.²³ A study conducted in TUTH, IOM has illustrated IgA Nephropathy (25.1%) as the commonest histological finding in renal biopsy, followed by LN (21.1%), FSGS (8.1%), MCD (7.2%).⁵ Timely detection of kidney disease is crucial in preventing the worst outcome. In Nepal, kidney disease is a relatively understudied area of interest. These findings show that primary glomerular disease is more common in the biopsy group in Nepal, and histologic detection remains crucial in Nepalese clinical settings.²²

In contrast to our result, some studies have reported different histopathological patterns as the predominant findings. FSGS (15.45%) was the frequent histological pattern in a study performed by Maskey et al., followed by MN (14.85%), MCD (8%), & LN (7.42%).⁹ Furthermore, a study conducted in Shree Birendra Army Hospital has concluded that MN (22%) was the predominant histopathological finding, followed by FSGS (20%), MPGN (20%), and MCD (13%). (6) Similarly, MPGN was the prevalent finding in a study conducted by Ghimire et al, followed by MCD (21.3%), MN (14.7%), and

LN (13.3%).²⁴ IgA Nephropathy was the least frequently diagnosed biopsy finding in a study done by Manandhar et al.²⁵ A variety of etiological, genetic, and socioeconomic variables explain the variation in prevalence of glomerular disease.⁵ The discrepancies in the results might be due to changes in the study sample, its characteristics, sample size, diagnostic techniques, and geographical variations.

The 2016 edition of the Oxford Classification (MEST-C) offers crucial prognostic and treatment recommendations for IgA Nephropathy.^{25,26} S1 (96.3%), T1/T2 (63.9%), M1 (55.5%), E1 (38.8%), and C1/C2 (27.8%) were the most prevalent lesions in our study. This suggests that both persistent scarring and active inflammatory alterations are more common. Similar to this result, Moriyama et al.²⁷ reported a high prevalence of segmental Glomerulosclerosis (S1). These results demonstrate the chronic nature of IgA nephropathy and may reflect delayed diagnosis and presentation, leading to more advanced histological alterations at the time of biopsy. To prevent irreversible damage and enhance patient outcomes, early kidney biopsy for precise prognostication and prompt treatment shouldn't be missed.

We analyzed the prevalent Lupus Nephritis Class in this study, in which 35 of the renal biopsies showed Lupus Nephritis. Among them, the most prevalent was Lupus Nephritis Class IV (n=15), followed by mixed Class IV and Class V (n=10). Similar conclusions have been reported in multiple studies. In a study by Bartaula et al. in Nepal, Class IV was the most frequent subtype (35% of biopsies with LN).²⁸ Similarly, a study conducted in Patan Hospital observed Class IV lupus nephritis as the commonest, followed by mixed class (IV+V).²⁹ Class IV is the predominant histologic pattern, accounting for 35–65% of LN biopsies according to various studies from India and other Asian nations. Class V (membranous) and mixed lesions comprise a smaller but clinically significant portion of the total.^{30,31} The kidney biopsy provides predictive data on activity and chronicity in addition to confirming the diagnosis of LN. Proliferative forms (Class III/IV, either by themselves or in conjunction with V) are the most aggressive, are frequently linked to widespread inflammation, and have the potential for swift progression to irreversible injury.³² Therefore, prompt therapy and early biopsy are essential because delay in treatments has been associated with much worse renal outcomes, including a dramatically higher incidence of ESKD.^{33–35}

In this study, the median age was 36 years (IQR 27–48 years). Moreover, almost half of the patients in our study were aged 19–40 (49.9%). Similar results were observed in studies conducted in Nepal by Manandhar et al.²⁵ and Subedi et al.³⁶ where the average age of biopsy patients was 31 years and 35.37 years, respectively. These results indicate that kidney disorders are a prevalent issue among young people, especially in the productive age group.^{25,36} In contrast, Western countries such as the United States and Europe have biopsy registries that frequently report a higher mean age at biopsy, typically in the fifth or sixth decade. This might be primarily because older populations are more likely to have secondary glomerular diseases, diabetic

nephropathy, and hypertensive nephrosclerosis.¹⁷

Males constituted the majority of our sample (54.7%), with a male-to-female ratio of 1.21:1, which was consistent with other studies conducted in Nepal, India, and China.^{3,5,11,37} However, some literature has shown a female predominance in their studies. According to studies by Maskey et al., Ghimire et al., Kafle et al., and Tuladhar et al., the majority of biopsy samples were from females (52%, 56%, 51.5%, and 56%, respectively).^{9,24,38,39} These discrepancies can result from changes in study population, disease patterns, referral procedures, and population demographics, as well as from sex-specific biological factors that cause kidney disorders, which require further investigation.⁵

We analyzed the prevalence of glomerular disease by age, and results varied across age groups. Lupus Nephritis (28.1%) was the most common glomerular disease among children (14 to 18 years), followed by FSGS (21.9%). Corresponding results were observed in a study done at Kanti Children's Hospital, where LN and FSGS were the frequent findings (27.58%).⁴⁰ Among Asian children, Minimal Change Disease (MCD) is thought to be the leading cause of primary glomerular disease.⁴¹ As MCD typically occurs normally on light microscopy and confirmation of MCD necessitates electron microscopy, which was unavailable in our study setting, some individuals with characteristics suggestive of MCD were classified as non-proliferative glomerulopathy.

In this study, IgA Nephropathy is the most prevalent cause of glomerular disease among adult patients aged 19-64 years (65.2% of the study population). The findings correlate with the 15-year (2006 to 2020 AD) scientific analysis of renal biopsy data from Hungary, which also found that IgA Nephropathy was the predominant glomerular disease among adults.⁴² FSGS is still a major issue in the elderly, although it is less prevalent as individuals' age.⁴³ FSGS is the most prevalent histological finding in patients above 65 years of age in this study (31.3%). In a study of 1368 renal biopsies taken from individuals older than 60, 5.4% of those with nephrotic syndrome had FSGS.⁴³

This study is one of the few that use a substantial amount of data from a national center in Nepal to assess the histological spectrum of glomerular disorders in Nepal. SDNTC receives Referrals from all corners of the nation are received by Shahid Dharma Bhakta National Transplant Center (SDNTC), which offers a broad and varied patient population. Consistency and dependability in diagnosis are ensured by standardized biopsy procedures and histological analysis. Additionally, because the analysis spans a pre-pandemic period, it avoids the confounding effects of COVID-19 disruptions on biopsy trends and patient access to care.

Limitations: The results of this retrospective, single-center investigation might not be generalized to the whole Nepalese population. Information bias may be introduced by incomplete records and missing data inherent to retrospective designs. The results may not accurately represent the current spectrum of glomerular disorders because the study was limited to the pre-COVID-19 time frame (2016–2019). Kidney biopsy services

were significantly disrupted by the COVID-19 pandemic, and after 2022 records were not routinely or completely documented to enable a reliable comparison with the research cohort. Histopathological results and clinical outcomes cannot be correlated due to the absence of long-term follow-up data. All the biopsy specimens could not be examined by electron microscopy, which could have affected the precision of the diagnosis in some circumstances. Furthermore, differences in biopsy indications and referral patterns could affect the distribution of detected glomerular disease types.

CONCLUSION

To conclude, this study has shown that IgA nephropathy is the most prevalent histopathological diagnosis, followed by Focal segmental glomerulosclerosis, non-proliferative glomerulopathy, and Lupus nephritis. Nephrotic Syndrome was the predominant indication for renal biopsy. IgA nephropathy and FSGS were common in younger patients, but FSGS was common in older patients. Oxford S1/T1 lesions in IgA nephropathy and diffuse proliferative lupus nephritis (Class IV) were prevalent in this study. These findings demonstrate that primary glomerular disease was common among the biopsies group in SDNTC, and histologic evaluation remains crucial for guiding diagnosis, prognosis, and prompt treatment of glomerular disorders.

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Data availability: The data are available from the corresponding author upon reasonable request.

Ethical consideration: Ethical issues (including plagiarism, data fabrication, and double publication) have been completely

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