

Histopathological Spectrum of Native Kidney Biopsy from Eastern India: A Single-Center Observational Study

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ABSTRACT

Objective: Kidney biopsy is a valuable tool for the diagnosis and management of kidney diseases. In India, there is no central registry for kidney biopsy, and data from eastern part of India is very sparse.

Methods: This is a retrospective observational study of 1312 native kidney biopsies done between 2013 and 2019. In all cases, light microscopy and immunofluorescence studies were done. Electron microscopy was performed on need basis.

Results: Eight hundred two patients (61.1%) were male. Nephrotic syndrome was the commonest indication for kidney biopsy (63.6%). Primary glomerular disease was the most common lesion accounting for 84.76% of cases. The most common diagnosis among primary glomerulonephritis was focal segmental glomerulosclerosis (23.02%) followed by minimal change disease (13.34%) and membranous nephropathy (13.26%). Secondary glomerulonephritis accounted for only 8.08% of total cases. Lupus nephritis accounted for only 4.88%. Lupus nephritis was seen more commonly in females (female: male = 9:1). Interstitial diseases accounted for 4.57% of total cases while vascular diseases were seen in 2.29% of cases. In patients with serum creatinine between 1.2 and 2.49 mg/dL, focal segmental glomerulosclerosis was the most common lesion, followed by diffuse proliferative glomerulonephritis and IgA nephropathy. In subjects with serum creatinine \geq 2.50 mg/dL, IgA nephropathy was the most common histopathology reported, followed by diffuse proliferative glomerulonephritis.

Conclusion: Focal segmental glomerulosclerosis was the commonest histopathological diagnosis followed by minimal change disease and membranous nephropathy. Lupus nephritis was the commonest lesion among secondary glomerulonephritis and was mostly seen in female patients. Kidney dysfunction was more common in IgA nephropathy, diffuse proliferative glomerulonephritis, and focal segmental glomerulosclerosis.

Keywords: Focal segmental glomerulosclerosis, IgA nephropathy, kidney biopsy, membranous glomerulopathy, minimal change disease

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INTRODUCTION

Real-time ultrasonography-guided percutaneous kidney biopsy is an indispensable tool for nephrologists. Besides providing the histopathological diagnosis of kidney parenchymal disease, it also helps in therapeutic decision-making and in prognostication of individual cases. Despite recent attempts to develop noninvasive alternatives, biopsy remains the “gold standard” for the diagnosis of various kidney parenchymal lesions.^{1,2} The prevalence of biopsy-proven kidney diseases varies with

age, gender, ethnicity, geographic location, and socioeconomic condition. In India, there is no central registry for kidney biopsies, and there is also a disparity in access to nephrological services.³ We present the data of 1312 consecutive native kidney biopsies performed at our institute between January 1, 2013, and December 31, 2019.

METHODS

This retrospective observational study was done in the Department of Nephrology at a Tertiary Care Teaching



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Institute in Eastern India. Approval from the Institutional Ethics Committee was obtained (1905/IEC/2020). All native kidney biopsies performed at our institution between January 1, 2013, and December 31, 2019, were reviewed.

For all patients, demographic, clinicopathological data, and relevant laboratory investigations were noted, and age and gender-appropriate workup for secondary etiology were also recorded. Indications for biopsy included nephrotic syndrome (NS) in patients over 12 years, steroid-dependent and steroid-resistant NS in children, rapidly progressive kidney failure (RPKF), unexplained kidney failure, and suspected nondiabetic kidney disease in diabetic patients.

Kidney biopsy was done in real-time ultrasonography guidance using automated single-use 18 G BARD® Max-Core® biopsy gun. At least 2 tissue cores were obtained and were sent for light microscopy and immunofluorescent (IF) microscopy. Additionally, tissue samples for electron microscopy were also sent for evaluation as needed. The kidney biopsies were analyzed by the same kidney histopathologist. Patients were observed for at least 24 hours postprocedure, and complications of kidney biopsy, if any, were also noted. Inadequate biopsy and/or incomplete data were excluded.

We used the version 20.0 (IBM SPSS Corp.; Armonk, NY, USA). In order to store and analyze the data. The quantitative variables were expressed as mean with SD, while qualitative variables were expressed as numbers and percentages.

RESULTS

Total of 1380 kidney biopsies were performed between January 1, 2013, and December 31, 2019. In 68 cases, tissue samples were inadequate and hence excluded. The remaining 1312 biopsy reports were analyzed. Analysis for electron microscopy was available for 651 cases. The patient characteristics at the time of biopsy are shown in Table 1.

MAIN POINTS

- Kidney biopsy is the gold standard for the diagnosis of kidney diseases.
- In India, like most third-world countries, there is no central registry for kidney biopsy; hence there is a paucity of data about the prevalence of various biopsy-proven kidney diseases.
- The study provides data about biopsy-proven kidney disease in one of the most resource-limited states of India.
- Focal segmental glomerulosclerosis was the most common biopsy-proven condition across all age groups and gender, contrary to the Western data.
- Membranous nephropathy and MCD were the second and third most common lesions, respectively, in our study.

In our study, NS was the commonest indication for kidney biopsy. Eight hundred thirty-four (63.6%) biopsies were performed for this indication alone followed by 236 (18%) for rapidly progressive renal failure (RPRF), 154 (11.7%) for unexplained kidney failure, 40 (3%) for steroid-resistant nephrotic syndrome in children, 38 (2.9%) in suspected non-diabetic kidney disease (NDKD) in diabetics, and 10 (0.8%) in nonrecovery of acute kidney injury.

In this study, 802 patients (61.1%) were male. Eighteen patients (1.4%) were found to be positive for hepatitis B surface antigen (HBsAg) on screening. None of the patients had hepatitis C or HIV infection at the time of biopsy.

Our study showed that primary glomerular disease was the most common lesion accounting for 1112 (84.76%) cases. The most common diagnosis among primary glomerulonephritis (GN) was focal segmental glomerulosclerosis (FSGS) which accounted for 23.02% of all cases and 27.16% of cases of primary glomerulonephritis. Minimal change disease (MCD) and membranous nephropathy (MN) were second and third most common lesions among primary GN, accounting for 13.34% and 13.26% of total cases, respectively (Table 2).

Secondary glomerulonephritis accounted for only 8.08% (106) of total cases. Though lupus nephritis (LN) accounted for over 60.37% of cases of secondary GN, it was only 4.88% of total cases. Amyloidosis (1.75% of total cases) and diabetic nephropathy (DN) (0.99%) were other common causes of secondary GN.

Interstitial diseases accounted for 4.57% of total cases, while vascular diseases were seen in 2.29% of cases. Acute tubular necrosis (ATN) was the commonest lesion (2.44%), followed by chronic interstitial nephritis (CIN) (1.06%) and acute interstitial nephritis (AIN) (0.76%).

Table 1. Patient’s Characteristics at the Time of Biopsy	
Variable	Median (IQR)
Age (years)	30 (21-42)
Duration of illness (months)	4 (2-6)
Systolic BP (mmHg)	140 (120-150)
Diastolic BP (mmHg)	88 (80-90)
Hemoglobin (g/dL)	11.6 (10-12.6)
Serum creatinine (mg/dL)	1.5 (1-3.2)
Serum protein (g/dL)	5.1 (4.4-6)
Serum albumin (g/dL)	2.5 (2.1-3)
Serum total cholesterol (mg/dL)	276 (200-356)
Serum triglyceride (mg/dL)	135 (110-180)
24-Hour urinary protein (g/24 h)	4.68 (3-6.2)
BP, blood pressure; IQR, interquartile range.	

Table 2. Histopathological Distribution of Kidney Diseases

Major Category	Kidney Disease	Number of Cases (%)	Gender	Age (Years)		
			Male:female ratio	Age < 18	Age 18-59	Age > 60
Primary GN	MCD	175 (13.34)	1.58:1	37	128	10
	FSGS	302 (23.02)	2.47:1	50	236	16
	MN	174 (13.26)	3.05:1	17	147	10
	MPGN	90 (6.86)	1.05:1	13	67	10
	MesPGN	24 (1.83)	1.18:1	8	15	1
	Crescentic GN	30 (2.29)	0.58:1	10	19	1
	IgAN	153 (11.66)	3.14:1	17	132	4
	DPGN	109 (8.31)	0.76:1	8	91	10
	CSGN	23 (1.75)	1.86:1	0	22	1
	Other GN	32 (2.44)	1:1.13	7	25	0
Secondary GN	Lupus nephritis	64 (4.88)	0.07:1	12	52	0
	Amyloidosis	23 (1.75)	2.83:1	0	15	8
	DN	13 (0.99)	3.33:1	0	6	7
	LCDD	6 (0.45)	5:1	0	4	2
Interstitial disease	ATN	32 (2.44)	1.67:1	2	23	7
	ACN	4 (0.31)	0:4	1	3	0
	AIN	10 (0.76)	3:2	0	6	4
	CIN	14 (1.06)	3.76:1	0	11	3
Vascular disease	Vasculitis	19 (1.49)	0.73:1	1	13	5
	TMA	11 (0.84)	0.57:1	1	12	0
Miscellaneous		4	0.33:1	0	4	0
Total		1312 (100)	1.87:1	184	1029	99

ACN, acute cortical necrosis; AIN, acute interstitial nephritis; ATN, acute tubular necrosis; C1qN, C1q nephropathy; CIN, chronic interstitial nephritis; CSGN, chronic sclerosing glomerulonephritis; DN, diabetic nephropathy; DPGN, diffuse proliferative glomerulonephritis; FNGN, focal necrotizing glomerulonephritis; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; IgAN, IgA nephropathy; IgMN, IgM nephropathy; LCDD, light chain deposition disease; MCD, minimal change disease; MesPGN, mesangial proliferative GN; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis; TMA, thrombotic microangiopathy.

In our biopsy series, LN was seen mostly in females (female:male = 9:1). Diffuse proliferative glomerulonephritis (DPGN), crescentic GN, and focal necrotizing glomerulonephritis (FNGN) were seen more commonly in females while MCD, FSGS, MN, IgA, amyloidosis, DN, light chain deposition disease (LCDD), ATN, AIN, and CIN were more common in males.

In subgroup analysis on the basis of age, FSGS was the commonest lesion in all age groups. In pediatric population (age < 18 years), FSGS was followed by MCD, IgAN, and MN. While those in age group 18-59 years, MN and IgAN were the second and third most common histopathology respectively. In elderly (age ≥ 60 years), FSGS was the commonest lesion, followed by MCD, MN, membranoproliferative glomerulonephritis (MPGN), and DPGN occurring in equal frequency. In the pediatric age group, DN, amyloidosis, LCDD, AIN, or CIN were not reported. Similarly, in the elderly, no cases of LN, C1Q nephropathy

(C1qN), FNGN, Alport’s, or acute cortical necrosis (ACN) were noted.

On subgroup analysis, on the basis of serum creatinine, it was found that 538 (41.01%) had creatinine level less than 1.20 mg/dL. Three hundred fifty-three (26.91%) had serum creatinine between 1.20 and 2.49 mg/dL, while 421 (32.09%) had creatinine level of ≥ 2.50 mg/dL. Among those with serum creatinine < 1.2 mg/dL, FSGS was the most common diagnosis, followed by MCD and MN. In patients with serum creatinine between 1.2 and 2.49 mg/dL FSGS was the most common lesion followed by DPGN and IgAN. In subjects with serum creatinine ≥ 2.50 mg/dL, IgAN was the most common histopathology reported followed by DPGN and MPGN (Figure 1).

Almost all patients diagnosed as crescentic GN, CSGN, ATN, ACN, AIN, and CIN presented with serum creatinine (S. Cr) of

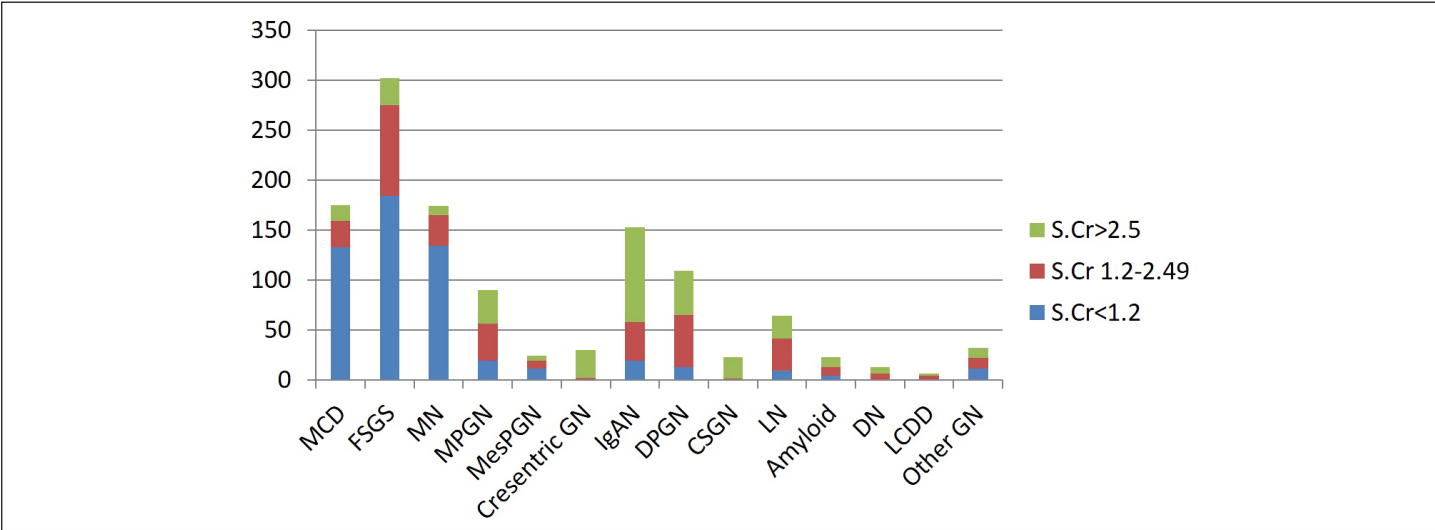


Figure 1. Distribution of glomerular disease as per serum creatinine level.

2.50 mg/dL or more. Biopsy specimens diagnosed as MCD and FSGS having S. Cr > 1.2 mg/dL had evidence of ATN also.

FSGS, MCD, MN, and MPGN presented usually with nephrotic range proteinuria. In our study, 64% of patients with IgAN presented with nephrotic range proteinuria (Figure 2).

DISCUSSION

Overall health infrastructure and health indices are poor in this part of eastern India.⁴ There is lack of data regarding biopsy-proven kidney disease, and this study is an attempt to fulfill this gap in knowledge.

In our study, biopsy was performed more commonly on male subjects. Similar observations have been made in other studies^{5,6} and are probably related to the fact that in developing

countries more male patients seek medical advice than females, which may be a reflection of gender bias in health care access.

The most common indication for kidney biopsy was NS and 63.6% of kidney biopsies were performed for this indication alone. This trend has also been observed in most of the biopsy series worldwide.⁵⁻¹⁰ (Table 3) Our finding of FSGS as the most common diagnosis is consistent with most of the studies from the Indian subcontinent.^{6,7,11,12} Rathi et al¹¹ observed that the incidence of FSGS in their series was 30.6%, while Golay et al¹² reported an incidence of 24.63% in their study. Diverse populations from Africa and South America also have reported FSGS as the commonest lesion identified on kidney biopsy.^{13,14} However, Kim et al⁸ and O’Shaughnessy et al⁹ reported the incidence of FSGS in their study as 7.65% and 6.9%, respectively, and IgAN as the commonest diagnosis. However, the study population in

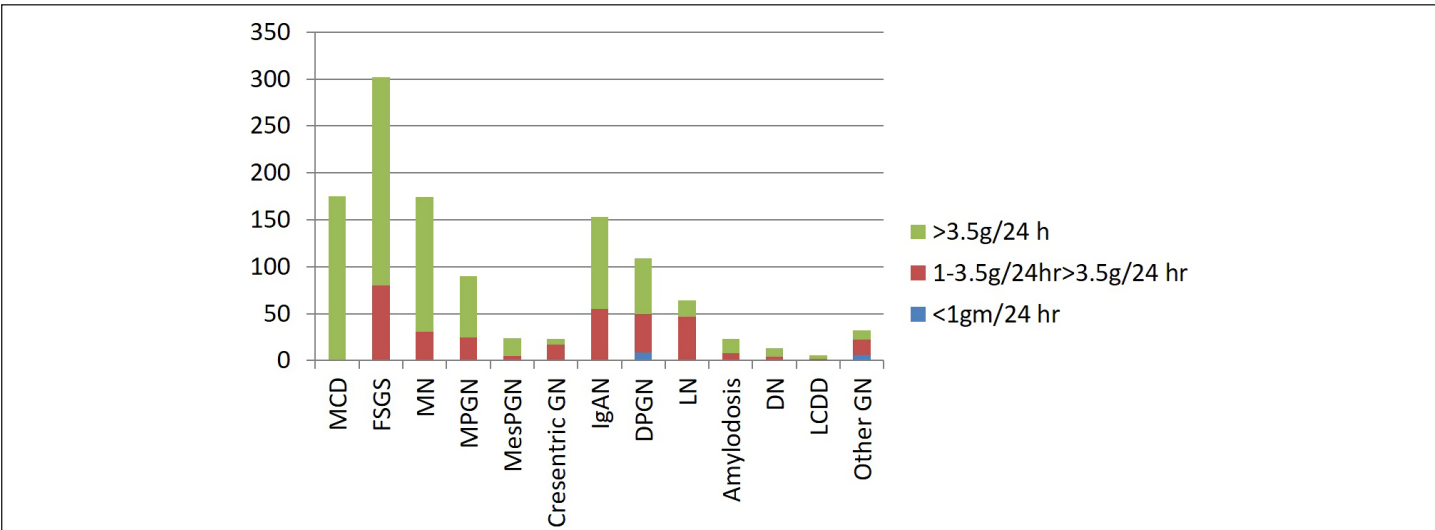


Figure 2. Distribution of glomerular diseases as per level of proteinuria.

Table 3. Comparison of Our Study with Different Studies in Indian Subcontinent and Abroad

Variable	Present Study	Das et al ⁵	Balkrishnan et al ⁷	Mubarak M et al ⁶	Kipyo Kim et al ⁸	O'Shaughnessy et al ^{9*}	Polito et al ¹⁰
Duration	2013-2019	1990-2008	1990-2001	1995-2008	1997-2018	2012-2013	1993-2007
Number of subject	1312	1849	5258	1793	22 203	1609	9062
Center	IGIMS, Patna	NIMS, Hyderabad	CMC, Vellore	Karachi, Pakistan	Korea (18 hospitals)	Japan, Thailand (2 hospitals)	Sao Paulo, Brazil
Male:Female	1.58:1	1.44:1	-	1.6:1	1.17:1	1:1	
Mean age	33.06 ± 14.90	32.27 ± 18.4	-	32.9 ± 12.8	42.1 ± 17.7	42.0	31.93 ± 18.65
MCD	13.34%	15.1%	10.8%	5.8%	9.13%	3.4%	7.47%
FSGS	23.02%	10.5%	16.8%	21.2%	7.65%	6.9%	11.04%
MN	13.26%	7.0%	9.5%	17.2%	9.17%	10.1%	10.56%
MPGN	6.86%	3.9%	2.9%	1.1%	2.63%	1.1%	2.13%
MesPGN	1.83%	5.2%	7.3%	1.9%	1.77%	3.1%	2.64%
Crescentic GN	2.29%	4.5%	3.5	5.2%	1.85%		0.88%
IgAN	11.66%	4.4%	8.4%	1.5%	34.17%	39.5%	10.24%
DPGN	8.31%	4.7%	13.5%	3.9%			2.41%
CSGN	1.75%	6.7%	3.5%	11.6%	1.77%	0.1%	3.3%
Lupus nephritis	4.88%	14.6%	6.9%	4.9%	6.30%	16.8%	-
DN	0.99%	1.2%	2.8%	0.9%	3.99%	10.7%	1.92%
ATN	2.44%	2%	1.2%	6.9%	1.86%	-	0.87%

ATN, acute tubular necrosis; CSGN, chronic sclerosing glomerulonephritis; DN, diabetic nephropathy; DPGN, diffuse proliferative glomerulonephritis; FSGN, focal necrotizing glomerulonephritis; FSGS, focal segmental glomerulosclerosis; GN, glomerulonephritis; IgAN, IgA nephropathy; MCD, minimal change disease; MesPGN, mesangial proliferative GN; MGN, membranous glomerulonephritis; MPGN, membranoproliferative glomerulonephritis.

*Analyzed only glomerular diseases.

these 2 reports was of East Asian ethnicity, which is different from our study.

Minimal change disease was the second most common lesion in our study, with an incidence of 13.34%. This is consistent with other studies from India, which estimated the incidence of MCD between 5.56% and 15.1%.^{3,5,7}

The incidence of MN has been reported variably in Indian studies. In our study, MN was the third most common histological finding (13.26%). Though the incidence of MN is higher than that reported by Das et al⁵ (7.0%) or Balkrishnan et al⁷ (9.5%), it is much lower than that reported by Rathie et al¹⁰ (24.4%) or Golay et al¹² (22.4%). The reason for this difference is not clear.

The incidence of MPGN is decreasing globally, and now it is considered to be a rare entity seen mainly in adolescent age group.⁷⁻¹⁰ We found 6.86% of the patients with MPGN which is much higher than that reported in other studies. It is much more common in patients with serum creatinine level more than 1.2 mg/dL and in the age group of 18-59 years in our series. The higher incidence of MPGN may be explained on the basis of

poor socioeconomic condition, poor access to health care services and immunization. The incidence of IgAN and DPGN was 11.66% and 8.3%, respectively. Studies from Far East Asia have observed IgAN as the commonest lesion in their series (34.17%⁸ and 39.5%⁹). The incidence of both IgAN and DPGN was much higher in this study than that reported by similar studies from the Indian subcontinent.^{5,6} We observed a significant increase in incidence of IgAN in India as compared to studies from the previous 3 decades. This may reflect more and more centers performing IF studies and low threshold for kidney biopsy in younger patients. The mean serum creatinine level of our study population was 2.49 mg/dL, which is much higher than in the other studies. The subgroup analysis revealed IgAN being the GN, most commonly associated with serum creatinine higher than 2.5 mg/dL followed by DPGN.

We found that LN was the most common secondary GN accounting for 4.88% of all cases. The result is similar to the finding of other studies.⁶⁻⁸ In this study also, LN was seen mostly in female patients (9:1). Amyloidosis was the second most common secondary GN, which we came across with an incidence of 1.75%. The incidence of amyloidosis, as reported by other studies, is between 0.88% and 4.6%.⁵⁻¹⁰

Our study has reported the incidence of DN as 0.99%, while most of the studies report a higher incidence between 1.2% and 10.7%.^{5,7-9} This lower incidence may be explained by the fact that most diabetic patients might not have proper healthcare access, particularly in rural areas or were under the care of primary care physicians and being referred to us too late.

The incidence of vasculitis in this study (1.49%) was higher than that reported at other Indian centers.^{5,7} This may be explained by our aggressive policy of performing kidney biopsy at the earliest in those presenting with RPGN.

Limitations

Limitations of an observational retrospective study and hospital-based studies are inherent to this study.

CONCLUSION

Our study is an attempt to generate information about biopsy-proven kidney diseases from eastern India so that health policies and resources could be utilized maximally and appropriately. Nephrotic syndrome was the commonest indication for performing kidney biopsy at our center. Focal segmental glomerulosclerosis remained the commonest lesion across different age groups and gender. Minimal change disease and MN were the second and third most common lesions overall. However, in the age group of less than 18 years, MCD was more common than MN and in older patients, MN was more common than MCD.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Indira Gandhi Institute of Medical Sciences, Patna, (Statutory University, Govt. of Bihar), (Date: December 18, 2020, Number: 1905/IEC/IGIMS/2020).

Informed Consent: Written informed consent was obtained from the patients/patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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