



# The Spectrum and Trends of Glomerulonephritis in Bangladesh: A Single Center Study

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## Research Article

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## Abstract

The wide variation of the spectrum of Glomerulonephritis (GN) is noted worldwide. In Bangladesh, the spectrum and trends of GN cannot be determined definitely due to the absence of central kidney biopsy registry. The aim of this study was to see the spectrum and trends of Glomerulonephritis in our population. All the kidney biopsies were done in Shaheed Sheikh Abu Naser Specialized hospital, Khulna, Bangladesh from 2015 to 2020, and reviewed retrospectively. A total of 151 native kidney biopsies were examined by light and immunofluorescence microscopy. The mean age of the study patients was  $31.3 \pm 13.79$  years with a range of 11-66 years, 52% were male and 48 % were female. Primary glomerulonephritis was observed in 91% of cases and secondary glomerulonephritis was in 9% of cases. Mesangialproliferative glomerulonephritis (36.48%) is on the slight decline in Bangladesh, though it still remains the commonest glomerulonephritis in this study. Membranoproliferative glomerulonephritis (27%) was the second observed GN followed by Membranous nephropathy (11.48%). Minimal change disease was observed very low in number e.g. 2.02%. Lupus Nephritis was the commonest secondary GN. Mesangialproliferative and Membranoproliferative glomerulonephritis were found in high incidence in our population. So it is essential to improve our socioeconomic and hygienic conditions for the prevention of these infection-related glomerulonephritis. This study may be helpful to establish a biopsy registry in this part of the world, which would be opened a platform for future research and planning.

**Keywords:** Glomerulonephritis; Mesangialproliferative Glomerulonephritis; Renal Biopsy; Histopathology

**Abbreviation:** GN= Glomerulonephritis; CKD: Chronic Kidney Disease; ESKD: End Stage Kidney Disease; HBsAg: Hepatitis B Surface Antigen; anti-HCV: Hepatitis C Antibody; HIV: Human Immunodeficiency Virus; ANA: Antinuclear Antibody; DIF: Direct Immunofluorescence; PAS: Periodic

Acid Schiff; MCD: Minimal Change Disease; PGN: Primary Glomerulonephritis; MN: Membranous Nephropathy; SGN: Secondary Glomerulonephritis; LN: Lupus Nephritis; MesPGN: Mesangialproliferative Glomerulonephritis; MPGN: Membranoproliferative Glomerulonephritis; HBV: Hepatitis

B virus; IgAN: IgA Nephropathy.

## Introduction

Incidence of Chronic Kidney Disease (CKD) is increasing annually worldwide [1,2]. Glomerulonephritis (GN) is one of the leading causes of CKD and End Stage Kidney Disease (ESKD). Rashid HU stated that 25% to 45% cases of ESKD were caused by GN in developing country like Bangladesh [3-7]. Several studies demonstrated IgA Nephropathy is the most prevalent glomerulonephritis in Asia, Europe and America [4,8-10]. The spectrum of the glomerular disease varies from country to country. This variation is may be due to geographical, socioeconomic, hygienic condition, genetic and racial variation [11-17]. It is known that socioeconomic and hygienic conditions vary between the countries and between the different regions of the same country. The prevalence and distribution of GN also depends on the policy and indication of kidney biopsy. The policy and indication of biopsy also differs among center to center, even in the same country [18-23]. A kidney biopsy is the gold standard tool for the diagnosis of the specific type of GN, the disease activity, and prognosis. It also helps in treatment decision [21-27]

A central kidney biopsy registry is essential for getting a complete picture of glomerular diseases of a country or region. But Bangladesh does not have any central biopsy registry like many other developing countries [28-32]. Due to the lack of biopsy registry, the pattern and definitive trends of GN cannot be determined in our population. There were few studies pertaining to this entity in our country but most of them were from Dhaka, Bangladesh. The representative data including studies from other parts of the country are limited. Therefore, the aim of our study was to see the spectrum of GN in patients undergoing native kidney biopsy in this geographical area [32-34].

## Data Sources and Methods

This was a cross-sectional hospital-based study. All patients with clinically diagnosed GN, who underwent native kidney biopsy performed in the department of nephrology, Shaheed Sheikh Abu Naser Specialized hospital, Khulna, Bangladesh during five years period starting from 2015, was analyzed. A total of 158 kidney biopsies were performed during this period. Out of these, 7 biopsies were inadequate (less than 5 glomeruli) and excluded from final analysis; the remaining 151 adequate biopsies were analyzed. The recorded data for each patient includes name, age, sex, an indication of kidney biopsy, histopathological diagnosis and laboratory investigations such as serum creatinine, 24-hour urinary protein, urine microscopy, virology; hepatitis B surface antigen (HBsAg), hepatitis C antibody (anti-HCV),

Human Immunodeficiency Virus (HIV) and serology; anti-double stranded DNA antibody, antinuclear antibody (ANA), complements levels 3&4 (C3, C4).

All kidney biopsy specimens obtained were prepared according to the standard protocol and examined by the same renal pathologists at a single center. It was ideal for the following trends in glomerulonephritis [26,32]. The clinical summary of the patient was available to the pathologist at the time of reporting. The biopsy policy was not changed during this study period. Informed written consent was taken prior to doing the biopsy. Kidney biopsy was performed under ultrasound guidance for all patients using Tru-cut needles with 16 G automated biopsy guns. At least two cores of tissue were obtained from each patient for light microscopy and direct immunofluorescence (DIF) techniques. For light microscopy, biopsy specimens were fixed in 10% formalin and embedded in paraffin, and sections were stained with hematoxylin and eosin (H&E), periodic acid Schiff (PAS) and silver stain in some cases [32-34]. Tissue sections were cut at 4µm thickness. The other sample was preserved in normal saline for DIF microscopy and immediately frozen. The sections were then stained with fluorescence conjugated anti-sera against human IgM, IgG, IgA, C3, and C1q. The electron microscope was not available in our country for clinical use.

The biopsy indications in diabetic patients were more selective, with biopsies undertaken only in cases of albuminuria with the absence of diabetic retinopathy, presence of hematuria, presence of active urinary sediment, less than 7 years duration of diabetes, rapid deterioration of renal function and clinical features of systemic diseases [35]. The Classification of GN (World Health Organization, Collaborating Centre for the Histological Classification of Renal Diseases) used in this paper [36]. Results were expressed as median or mean  $\pm$  standard deviation for continuous data and as frequencies with percentages for categorical data. All analyses were done using SPSS version 20 (IBM Corp, Chicago, IL, USA). *P* values less than 0.05 indicated statistical significance. The chi-squared test was used to investigate the statistically significant relationships between patients' sex and different histological patterns of glomerulonephritis.

## Procedure or Steps of Data Collection

All the patients of Glomerulonephritis were diagnosed clinically by a nephrologist in outpatient department of shaheed Sheikh Abu Naser Specialized hospital, Khulna. And advise for admission in inpatient department. After admission all patients were evaluated by history taking, clinical examination and proper investigations. Those who

had contraindication to kidney biopsy were excluded. After taking informed written consent, kidney biopsy was done. After getting biopsy report, appropriate treatment was given to all patients. All data and relevant reports were kept in nephrology registry. At the time of study all data were retrieved nephrology registry.

## Results

A total of 151 patients were included in this study. Among

them, 79 were male and 72 were female. The male to female ratio was 1.1:1. There was a slight male preponderance observed in the whole study population. A significant sexual predilection was observed only in two diseases, namely lupus nephritis, and IgA nephropathy. In all other glomerulonephritis, the sex difference was not statistically significant. A very strong female preponderance was observed in LN as shown in Table 1.

Glomerulonephritis	Male	Female	N	p-value
MesPGN	25	29	54	0.586
MPGN	18	12	30	0.273
MN	10	7	17	0.467
IgA	10	3	13	0.052*
FSGS	4	5	9	0.739
IgM	4	4	8	1
MCD	2	1	3	0.564
LN	0	9	9	.003**
Crescentic	3	0	3	0.083
DM	0	1	1	0.317

**Table 1:** Sex Distribution of Glomerulonephritis.

The mean age of patients at the time of biopsy was 31.3 ± 13.79 years with a range of 11-66 years. Minimal change Disease (MCD) and IgM nephropathy was seen in the young

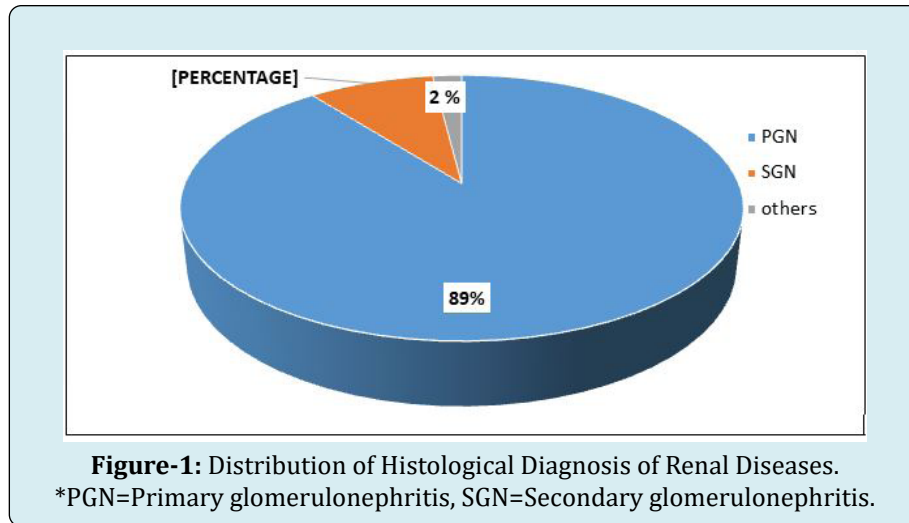
age group. The most common age group being 11-30 years as shown in Table 2.

Glomerulonephritis	Age Ranges					
	20-Nov	21-30	31-40	41-50	51-60	61-70
MesPGN(Mean age-29.5)	18	16	9	6	4	1
MPGN (Mean age-34.5)	7	6	7	6	4	-
MN (Mean age-31.5)	7	1	2	4	3	-
IgA(Mean age-28.8)	4	4	3	2		-
FSGS (Mean age-38.33)	1	3	1	1	3	-
IgM (Mean age-19.3)	5	2	1	-	-	-
MCD(Mean age-19.6)	2	-	1	-	-	-
LN (Mean age-26.5)	2	5	1	1	-	-

**Table 2:** Distribution of GN in Different Age Groups.

There were no HBsAg, anti-HCV, and HIV positive patients in the biopsy cohort. In this study primary Glomerulonephritis (PGN) were the most common renal

disease and accounted for 135 (91%) of the total study population as shown in Figure 1.



Mesangialproliferative glomerulonephritis (MesPGN) was the most common primary glomerulonephritis in 54 (36.48%) cases. Membranoproliferative glomerulonephritis (MPGN) and Membranous nephropathy (MN) came second and third in 30 (20.27%) and 17 (11.48%) cases, respectively.

Secondary glomerulonephritis (SGN) was diagnosed in 13 cases (9%) whereas Lupus Nephritis (LN) was the most common secondary glomerulonephritis seen in 9 cases (6.08%) as Shown in Table 3.

Type of renal disease	Number of cases	Percentage
Primary GN:(n-135)		
MesPGN	54	36.48
MPGN	30	20.27
MN	17	11.48
IgA	13	8.78
FSGS	9	6.08
IgM	8	5.40
MCD	3	2.02
Crescentic GN( Immune)	1	
Secondary GN: (n-13)		
LN	9	6.08
RPGN(Pauciimmne)	2	1.35
DM	1	0.67
Ch. Sclerosing GN	1	0.67
Others(Non GN):n-3		
ATN	2	
Renal cortical necrosis (Large vessel vasculitis)	1	
Total	151	

**Table 3:** Histopathological Pattern of Kidney Biopsies.

There were three cases of crescentic GN; out of which, one case showed immune complex deposition on IF and the rest of the two cases were pauci-immune. Among LN, the most common histological pattern observed was Class

IV (45%) followed by Class II (22%) as Shown in Figure 2. Also a comparison of data of this study with few Bangladeshi studies is shown in Table 4.

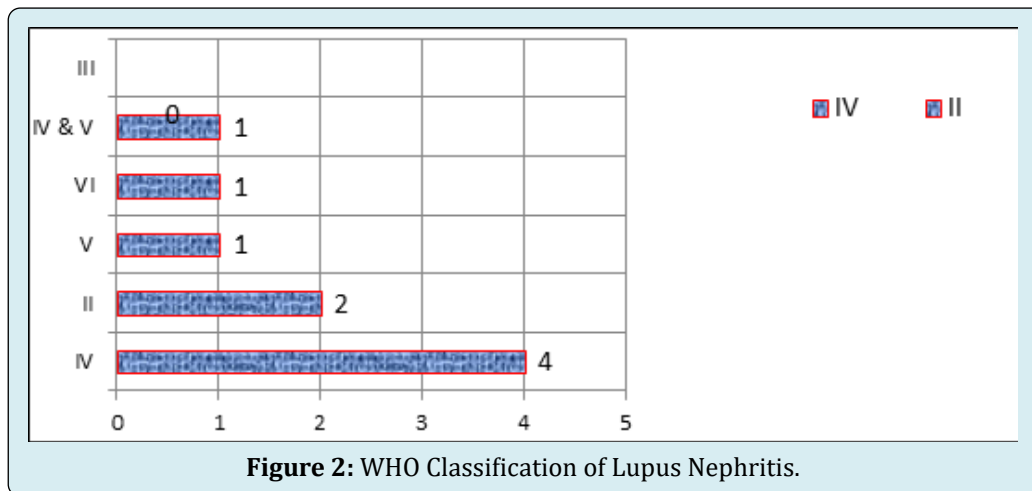


Figure 2: WHO Classification of Lupus Nephritis.

Components	This study	Gupta RD, et al. [42]	Islam SM, et al. [41]	Samad T, et al. [38]	Ahmed PI, et al. [39]	Habib MA, et al. [40]	Das RK, et al. [37]
N	148	206	164	53	128	95	327
Mean age (Years)	31.3	34.5	31.39	42.3	32.92	30.29	-
Sex M:F	1.09:1	01:01.6	01:01.1	1.2:1	1.8:1	01:01.5	1.3:1
MesPGN	36.48%	34.30%	21.34%	40.50%	25%	45%	34.30%
MPGN	20.27%	12%%	18.29%	27%	11.50%	4.20%	20.20%
IgA	8.78%	5.80%	14.63%	-	11.50%	6.80%	3.40%
MN	11.48%	3.90%	10.37%	8%	22.10%	7.30%	10.70%
FSGS	6.08%	11.60%	19.51%	5.40%	7.90%	11.60%	1.80%
LN	6.08%	15%	17.68%	11.20%	-	6.30%	7.90%
MCD	2.02%	5.30%	3.40%	-	10.60%	10.50%	2.10%
IgM	5.40%	2.90%	-	1.88%	-	-	-

Table 4: Comparisons with Few other Studies from Bangladesh.

## Discussion

Our hospital is the only tertiary care center with well-developed nephrology department in this Southwestern region. Kidney biopsy was routinely done as a part of nephrological workup. As such, the pattern of glomerulonephritis observed was relatively representative of prevalent renal diseases in Southwestern Bangladesh. In this study there was a slight male predominance in the overall cases except for lupus nephritis. Some recently published studies from Bangladesh showed a similar sex distribution [37-39]. The mean age of this study population at the time of biopsy was relatively similar to other studies

from Bangladesh with the exception of the study by Samad T, et al. [37-41]. The study by Samad T et al. was conducted in Diabetic hospital so major portion patients were diabetic and the mean age of these population was higher [5-7,28-30,38]. The majority of the patients who underwent kidney biopsy were in the age group of 11-30 years but no specific histological pattern observed in any age group except IgM nephropathy, MCD, and LN. Patients of these entities like MCD, IgM were in younger age group. PGN was the most common pathological lesion in this cohort followed by SGN. This result was concordant with studies from Bangladesh and other countries [38-47].

In this study, Mesangialproliferative glomerulonephritis (MesPGN) was the most common GN. In several studies from Bangladesh also showed similar results that mean MesPGN was the commonest glomerulonephritis in Bangladesh [37-42]. MesPGN was also one of the leading forms of glomerulonephritis in many of the Asian countries namely Singapore, Malaysia, China, Japan, Thailand, and India [11,47-53]. Heaf also found a high prevalence of MesPGN in Denmark [5-7,54-57]. A study from Serbia, it was the second most common type of GN (28.9%) following membranoproliferative glomerulonephritis (MPGN) [15-17,19,20,55-57]. However, in Singapore, Japan, China, Malaysia, and India, the frequency MesPGN has been steadily decreasing as seen in follow up and recent study [11,56-58]. The same trend of decreasing MesPGN was also observed in the studies from Bangladesh but the change was not as remarkable as other Asian countries.

Membranoproliferative glomerulonephritis (MPGN) was the second most common glomerulonephritis found in 27 % of all cases in this study. This result was concordant with the reports from other Bangladeshi studies [17,19,20,37,38,41]. The higher rates of MPGN were also observed in studies from Serbia and Romania [55,59].

A study by Rabbani et al from Pakistan found MPGN to be the most common glomerulonephritis [16,60]. It is proposed in different studies that MesPGN and MPGN are related to infection [11,38,61]. Patients from developing countries with poor housing facilities and sanitation exposed to parasitic, bacterial and other infective agents predisposing to MesPGN consistent with large size immune complex deposited in the mesangium and hence triggering the immune response [11,20,62]. The frequency of MesPGN and MPGN have been decreased in those developed countries might be due to improved sanitation, housing, and urbanization. But In Bangladesh, we are improving our socioeconomic indicators very slowly. For this reason, the frequency of MesPGN has been decreased a little in this current study in comparison with previous studies from Bangladesh.

Membranous Nephropathy was found to be the third or fourth causes of glomerulonephritis in different studies [25,53,63-65]. This study result regarding MN (11.48%) was similar to Das RK et al and Islam SM et al showing MN 10.7% and 10.37% respectively [37,41]. Study from the neighboring country, India also depicted a similar frequency of MN (10%) [44-48]. Ibrahim S. from Egypt showed 10.93% of the GN was Membranous nephropathy [17,19,66]. MN is mostly idiopathic. Phospholipase A2 receptor antibody (Anti PLA2R) is an important marker for idiopathic MN. We did not perform antiPLA2R antibody in this study due to unavailability [46,47,67]. Bangladesh is a country with intermediate endemic hepatitis B virus (HBV) and a chronic

HBV carriage rate of 2-6%.<sup>45</sup> Some studies suggested that MN might be also related to occult Hepatitis B infection along with overt hepatitis B infection [68,69].

IgA nephropathy (IgAN) is the commonest PGN in most of the studies throughout the world [68-72]. The frequency of IgAN in our country ranges from 3.4% -14.6% including this study (8.78%) [37,39-42]. Mubarak M, et al. from Pakistan in showed a very low prevalence of IgAN (2%) whereas a recent study from south India showed 21.3% of IgAN in their cohort [44,73]. Different centers adopted different renal biopsy policies for the patient with kidney diseases especially in asymptomatic urinary abnormalities or isolated microscopic hematuria. That may be the reason for the variability of IgAN in different regions as well as the reason of the low incidence of IgAN in our country.

FSGS was low (6.08% of the GN) in this study which was identical with Samad T, et al. (5.4%) Ahmed P, et al. (7.9%) from Bangladesh [15,38,39]. Whereas other few studies from Bangladesh found FSGS in 11.6% and 19.5% which were slightly higher in comparison with this study [41,42]. An increasing trend of FSGS was also observed in many developed countries like USA, Singapore, Australia, Thailand, and India [11,16,52,74]. European kidney biopsy registry showed that the similar lower prevalence FSGS [31-34,55,56,59, 75-77]. This variation of FSGS may be due to obesity, exposure to allergens, ethnic and racial predilections.

IgM nephropathy (IgMN) is a spectrum of morphological pattern ranging from minimal change to FSGS. IgMN is more common in developing countries [13,14,76-78]. The frequency of IgMN varied widely from 2% - 18.5% in different literature [79,80]. In this study, IgM nephropathy was in 5.4% of the glomerulonephritis. Samad T et al and Gupta RD et al from Dhaka, Bangladesh described IgMN in 1.88 % and 2.9% respectively [38,42].

Minimal change disease (MCD) was rare in this study observed in 2.02% of glomerulonephritis. The mean age of study was 31.3 years. We know MCD is the most common GN in children. This finding was similar to other studies from Bangladesh [41,42]. And other neighboring countries named Pakistan, India, and Singapore [44,56,81].

Lupus Nephritis (LN) was the commonest secondary GN in this study which comprises 6.09 % of total GN. Among the secondary glomerulonephritis, lupus nephritis was in 69.23%. This result was comparable with that reported in many other studies all over the world [4,13,73,82-84]. Usually renal biopsy was done to see the class of LN. Like other studies, class IV LN was the most common lesion in our study [13-15,38,39,85,84]. Indication of kidney biopsy in diabetic kidney disease was mentioned in Methods.



Kidney biopsy was rarely performed in diabetes patients in our center due to the conservative biopsy approach. This might be the reason of the low prevalence of diabetic kidney disease in this study.

### Limitation

One of the limitations of this study that all patients were from a single center. But this center is the only referral hospital for nephrology in this Southwestern region. Therefore this study included patients from both rural and urban areas. Another limitation of our study was the lack of electron microscopic examination of the biopsy. If it was available it can modify the diagnosis of some glomerulonephritis. But would not change the final diagnosis in most of the cases [85-87].

### Conclusion

The mean age of this study population at the time of biopsy was relatively similar to other studies from Bangladesh. Primary glomerulonephritis was observed in 91% of cases and secondary glomerulonephritis was in 9% of cases. Mesangialproliferative glomerulonephritis (36.48%) is on the slight decline in Bangladesh, though it still remains the commonest glomerulonephritis in this study. Membranoproliferative glomerulonephritis (27%) was the second observed GN followed by Membranous nephropathy (11.48%). Minimal change disease was observed very low in number e.g. 2.02%. Lupus Nephritis was the commonest secondary GN. In this study, Mesangialproliferative glomerulonephritis (MesPGN) was the most common GN. In several studies from Bangladesh also showed similar results that mean MesPGN was the commonest glomerulonephritis in Bangladesh so that it could be the pathway for future research in this arena.

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### Data Availability

The datasets generated during and/or analyzed during the current study are available from the first author on reasonable request.

### Code Availability

Not applicable

### Compliance with Ethical Standards

There are no conflicts of interest in this study.

### Ethics Approval

After getting biopsy report, appropriate treatment was given to all patients. All data and relevant reports were kept in nephrology registry. At the time of study all data were retrieved nephrology registry. All the patients of Glomerulonephritis were diagnosed clinically by a nephrologist in outpatient department of shaheed Sheikh Abu Naser Specialized hospital, Khulna, Bangladesh.

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