

Histopathological Pattern of Glomerulonephritis: Experience from BIRDEM General Hospital, Dhaka, Bangladesh

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Abstract

Background: Glomerulonephritis (GN) remains the most probable underlying cause of end stage renal disease of uncertain aetiology in many developing countries including Bangladesh. The pattern of glomerular disease varies widely from country to country. In Bangladesh, the incidence and histological pattern of GN is inadequately described. We performed a study, aiming to determine the pattern of GN in a diabetic hospital of our country.

Methods: It was a cross-sectional hospital based prospective study conducted at BIRDEM General Hospital starting from July 2013 to December 2014. It included all patients with suspected GN who underwent native kidney biopsy.

Results: Total 57 biopsies were performed and four cases other than primary or secondary GN (renal cortical necrosis 1, tubulointerstitial nephritis 2, chronic GN 1) were excluded i.e total number of PGN was 37 and secondary GN was 16. number of patients with were 53. M:F was 1.2:1. Mean age was 42.35±15(14-72) years. Thirty one (58.49%) of the study subjects had diabetes mellitus (DM).

Mesangialproliferative GN (15/37,40.5%) and diabetic nephropathy (9/16,56%) were the commonest histopathological pattern found among primary and secondary GN respectively. Membranoproliferative GN (10/37,27%), was the second commonly observed pattern followed by focal segmental proliferative GN (8%), membranous nephropathy (8%), focal segmental glomerulosclerosis (5.4%) in primary GN and lupus nephritis (6/16,38%) and Wegeners granulomatosis (1/16) were other varieties in secondary group.

Among 53 cases, 37 had proliferative variety. Nephrotic range proteinuria (41.5%) was the commonest indication of biopsy and 22% had post biopsy bleeding and 3.7% required blood transfusion.

Conclusion: In conclusion, mesangial proliferative and membranoproliferative GN are the two common causes of primary GN. Diabetic nephropathy is the commonest cause of secondary GN. Nephrotic range proteinuria was the main indication of biopsy. Post biopsy complication was negligible. Creation of a national renal registry is essential for obtaining more specific epidemiological data.

Key Words: diabetes mellitus; glomerulonephritis; histopathology

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Introduction

Glomerular disease is a common cause of end stage renal disease (ESRD) in both developing and developed countries. The pattern of glomerulonephritis (GN) varies widely from country to country, reflecting the possible effects of socio-economic, genetic and environmental factors.¹ The disease spectrum is also been changing over the last few decades.¹ IgA nephropathy is the commonest primary glomerular disease from east Asia, as well as in white Europeans and Americans.²⁻⁵ In contrast, focal segmental glomerulosclerosis (FSGS) is the commonest glomerular disease among African-Americans, South Americans and in the Middle East.^{6,7} Currently, we do not have a central biopsy registry in Bangladesh. Statistics on the prevalence of renal disease in Bangladesh are limited. In light of the paucity of published data from our country, this study was done to describe the histopathological pattern of glomerular diseases at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital.

Methods

This was a cross-sectional hospital based observational study. All patients with suspected GN, who underwent native kidney biopsy that were performed in department of nephrology, BIRDEM over a period of one and half years starting from July 2013, were analyzed. Total 57 biopsies were performed and four cases which were not diagnosed as primary or secondary GN [(renal cortical necrosis (1), tubulointerstitial nephritis (2), chronic GN (1)] were excluded i.e total number of patients with were 53.

Variables

We recorded the demographics of cases, co-morbidities, fundoscopic examination findings (if diabetic), indication for renal biopsy, histopathological diagnosis, post biopsy complication and relevant laboratory investigations.

Indication of biopsy

Indications of biopsy were proteinuria > 1gm/day with or without glomerular hematuria and unexplained acute kidney injury. Diabetic patients with only proteinuria were biopsied if there were no other sign of microvascular changes like diabetic retinopathy.

Biopsy technique

Kidney biopsy was performed for all selected patients using 16 G automated biopsy needles. At least two cores of tissue were taken from each patient for light

microscopy and direct immunofluorescence (DIF) techniques.

Histopathology technique

For light microscopy, samples were fixed in 10% formalin solution and sections were stained with hematoxylin and eosin (H&E) and periodic acid Schiff (PAS). The other sample was preserved in normal saline for DIF study. Immunofluorescence microscopy panel included staining for IgA, IgG, IgM, C3 and C1q. Electron microscopy was not available for diagnostic purpose in our country.

Representation of the histopathological reports

Histological categories were classified as follows: I) Primary glomerulonephritis (PGN), II) Secondary glomerulonephritis (SGN).

Minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), mesangial proliferative glomerulonephritis (MesPGN), membranoproliferative/mesangiocapillary glomerulonephritis (MPGN/MCGN), IgM nephropathy, IgA nephropathy, focal segmental proliferative GN (FSPGN), diffuse proliferative GN (DPGN), crescentic GN (Cres GN), poststreptococcal GN (PSGN), pauci-immune GN were included in PGN⁸ lupus nephritis (LN), diabetic nephropathy (DN) and Wegenersgranulomatosis were incorporated in SGN.⁹

Cases were again classified into a) proliferative GN which included MesPGN, MPGN, IgM nephropathy, IgA nephropathy, FSPGN, DPGN, Cres GN, PSGN, pauci-immune GN, LN (class-iv), WG and b) non-proliferative GN which include MCD, MN, FSGS, LN (class v, vi) and DN.

Data handling

All available data were noted into a specially designed questionnaire and were analyzed using Statistical Package for Social Sciences (SPSS) version 20 computer software. Results were expressed as median or mean±standard deviation for continuous data and as frequencies with percentages for categorical data.

Results

Clinical profile

Out of 53 cases twenty nine cases were male (54.71%) and twenty four cases were female (45.28%).M:F was 1.2:1. Mean age was 42.35±15(14-72) years. The majority of study subject who underwent renal biopsy were in the age group of 41-50 years. Thirty one (58.49%) of the study subjects had diabetes mellitus (DM).

Histopathological pattern

The most common histopathological pattern was PGN (70%) (Fig 1). Mes PGN was the commonest form of primary GN followed by MPGN (Fig 2). No distinct pathological pattern were found in any age group in case of primary GN (Table I).

Diabetic nephropathy was maximum in SGN (9/16,56%) cases. All of them except two had associated retinopathy. LN was present in (6/16,38%) cases. There were 3 (50%) class iv, 2 (33%) class v and 1 (17%) class ii LN. ANCA negative Wegenersgranulomatosis(1/16) was found in one case. In secondary GN all cases of LN were in the (21-30) age group. Diabetic nephropathy was common in male patients (Table II).

The cases were also classed as proliferative (37) and non proliferative GN (16) (Table III).

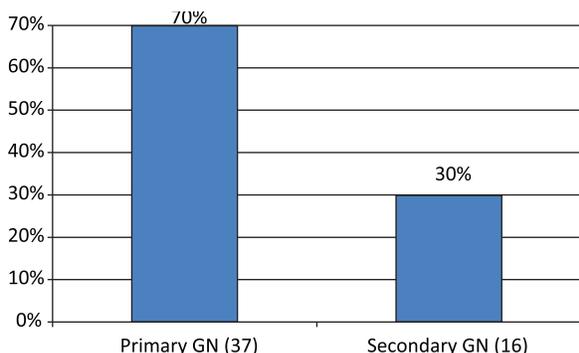


Figure-1: Histopathological pattern of kidney biopsy of study population

There were male predominance in all disease categories, with exception of LN in which five out of six patients (83%) and in MesPGN where ten out of fifteen cases (67%) were female.

Indication of biopsy

The commonest indication of biopsy was nephrotic range proteinuria (22/53,41.5%). Other indications were non- nephrotic range proteinuria with/without hematuria (16/53,30%) and unexplained AKI (15/53, 28%). The commonest cause of nephrotic range proteinuria was

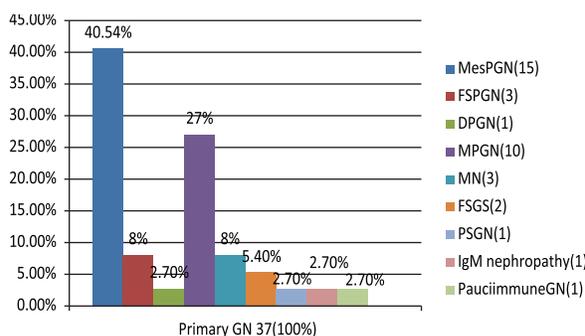


Figure-2: Histological pattern of primary glomerulonephritis

MesPGN: Mesangial proliferative GN,MPGN: Membrano proliferative GN, FSPGN: Focal segmental proliferative GN,DPGN: Diffuse proliferative GN, MN: Membranous nephropathy, FSGS: Focal segmental GN, PSGN: Poststreptococcal GN)

Table I. Pathological pattern of PGN in different age group (n=37)

| Diagnosis (noofcases) | 10-20 years(n=5) | 21-30 years(n=2) | 31-40 years(n=9) | 41-50 years(n=8) | 51-60 years(n=8) | 61-70 years(n=3) | 71-80 years(n=2) |
|-----------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|
| MesPGN(15) | 2 | 0 | 3 | 3 | 4 | 2 | 1 |
| MPGN(10) | 1 | 0 | 3 | 2 | 3 | 0 | 1 |
| FSPGN(3) | 1 | 0 | 0 | 0 | 1 | 1 | 0 |
| DPGN(1) | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| MN(3) | 0 | 1 | 2 | 0 | 0 | 0 | 0 |
| FSGS(2) | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| IgMnephropathy(1) | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| PauciimmuneGN(1) | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| PSGN(1) | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

(MesPGN: Mesangial proliferative GN,MPGN: Membrano proliferative GN, FSPGN: Focal segmental proliferative GN,DPGN: Diffuse proliferative GN, MN: Membranous nephropathy, FSGS: Focal segmental GN, PSGN: Poststreptococcal GN)

Table II. Secondary GN according to age group(16)

| Diagnosis (No of cases) | Sex | | 10-20 years (n=0) | 21-30 years (n=6) | 31-40 years (n=0) | 41-50 years (n=5) | 51-60 years (n=4) (n=1) | 61-70 years (n=0) | 71-80 years |
|----------------------------|-------|--------|-------------------------|-------------------------|-------------------------|-------------------------|----------------------------------|-------------------------|----------------|
| | Male | Female | | | | | | | |
| | LN(6) | 1 | | | | | | | |
| DN(9) | 7 | 2 | - | - | - | 4 | 4 | 1 | - |
| WG(1) | 1 | - | - | - | - | 1 | - | - | - |

(LN:lupus nephritis, DN:Diabetic nephropathy, WG:Wegerensgranulomatosis)

Table-III. Proliferative and non proliferative classification of GN

| | Proliferative GN(n=37) | Non- proliferativeGN(n=16) |
|--------------|---|----------------------------|
| Primary GN | MesPGN (15) FSPGN(3) Diffuse PGN(1) MPGN(10) IgM nephropathy(1) Pauciimmune GN(1) PSGN(1) | .MN(3) FSGS(2) |
| Secondary GN | LN class ii &iv (4) WG(1) | LN classv(2) DN(9) |

MPGN (6/22, 27%) followed by DN(5/22,22.7%) and MesPGN (4/22,18%).

Post biopsy complication

Post biopsy bleeding occurred in (12/53,22%) cases and blood transfusion was required in (2/53,3.7%) cases. No one required nephrectomy

Discussion

Clinical profile

The majority of study subject who underwent renal biopsy were in the age group of 41-50 years but no distinct pathological pattern observed in any age group in PGN. Mundi I et al¹⁰ found most of the cases were in 21-40 age range and distinct pattern of PGN was found in different age ranges. The age range of our cases was 14-72 years with a slight male predominance (1.2:1) except in case of LN and MesPGN. Most of the studies depict male predominance^{11,12,13} with exception of Habib M A¹⁴ from Bangladesh.

Histopathological pattern

Primary glomerular disease (70%) is the most prominent renal disease in our study as well as in all recent studies.^{2,15-23} A study from Jamaica showed SGN were more common probably due to their aggressive biopsy policy in patients with SLE.¹⁰ Like other studies,¹⁶ proliferative GN is more prevalent than non-proliferative GN in our study.

Primary GN

In the current study MesPGN is the commonest primary GN seen. In most studies from Bangladesh MesPGN was found to be the commonest primary²⁴ and proliferative GN¹⁶ though another study from Bangladesh found focal segmental proliferative GN (29.47%) as the commonest entity.¹⁴

A study on global evolutionary trend of GN done in Singapore for three decades stated that in the 1st decade most Asians countries had MesPGN as the most common form of primary GN and still it is prevalent in

some Asian countries like China, Japan and Thailand.¹ Apart from geographical, genetic and socioeconomic factor, one factor which may influence the pattern of glomerulonephritis in various countries could be the hygiene hypothesis.²⁵ The hygiene hypothesis proposes that bacterial and other infections occurring in less developed or developing countries leads to development of some type of human glomerulonephritis, including MPGN and MesPGN. This would be true in Asian countries like China²⁶, Indonesia²⁷, Malaysia²⁸, Thailand²⁹ and Singapore²⁴ which have a high prevalence of MesPGN. In some countries like Malaysia²⁸ and Singapore²⁴ the prevalence of MesPGN is already decreasing in keeping the urbanization and better housing and other amenities in these countries. Bangladesh is a rising country in context of urbanization and other fields of development, i.e, this hypothesis can explain the majority of MesPGN as well as MPGN in our study. Chugh KS also found high prevalence of MesPGN in India³⁰ but Golay V et al found lower incidence (0.6%) in a recent study³¹ which does not match our findings and we could not explain that.

MPGN is the second most common GN found in present study compatible with the report by Ahmed et al¹¹ (11.50%) and third most common cause (13%) of primary GN in Saudi Arabia³² reported. In countries like India³³ and Saudi Arabia³⁴ there is still a relative high prevalence of MPGN possibly due to infection as in case of countries with a high prevalence of MesPGN in Asia mentioned above. Post infectious GN due to streptococcus used to be prevalent in India³⁵ and this could account for the high incidence of MPGN as MPGN could also result from post infectious GN. In our study PSGN rate is low (2.7%) and MPGN is higher which resembles with that of India and the low incidence of PSGN could be the fact that the average age of our study population was higher than that of PSGN age group.

Our study findings regarding membranous GN (MN) (8%) and focal segmental glomerulosclerosis (FSGS) (5.4%) is almost identical with Rahman et al³⁶ showing MN (7.34%) and FSGS (2.8%) and with Habib MA¹⁴ which showed MN (7.37%) and FSGS was (11.58%). Mundi I et al and Mannan R et al^{10,13} demonstrated FSGS, MN and minimal change disease (MCD) being the commonest form of PGN in

India. Data from Singapore and other countries also showed that the prevalence of FSGS and MN have become increased in recent time¹ This may be related to increasing number of patients with obesity, DM and smoking habits, a pattern representing the rising affluence in these countries where FSGS represents the changing life style of fast food and unhealthy diets predisposing to disease like obesity and DM. In our study though many of our cases were diabetic but there average body built and life style do not yet match with that of the affluent society. Apart from this FSGS has been found to have a racial predilection¹⁰. Meckenzie et al,³⁷ have suggested that genetic variation may play a role in sporadic FSGS in adult. These hypothesis also fits with our findings of FSGS but the reason of low incidence of MN could not be explained.

Other findings with low incidence of IgM nephropathy and pauciimmune GN matches with other studies^{10,13} like in Pakistan where the incidence of IgM nephropathy was 2.47%.³⁸ Most of the studies did not mention IgM nephropathy as a distinct category.¹³

We did not get any IgA nephropathy in our study. It is the most common form of primary GN in Asia, accounting for upto 30-40% of all biopsies, for 20% in Europe and for 10% in North America³⁹ but the incidence of IgA nephropathy in our country is much lower (4.67%-7%)^{14,40,41} in comparison with other Asian countries.^{13,41,42,43} It was also uncommon in studies from this region of world like in India and Pakistan.^{35,38} This may be explained by varying approaches to the use of renal biopsy in patient with mild urinary abnormality like asymptomatic microscopic hematuria irrespective of degree of proteinuria.¹⁹ In our center cases with micro/macroscopic hematuria and proteinuria less than 1 gm/L were not indicated for renal biopsy. Thus the paucity of IgA nephropathy is mostly due to the benign presentation of the disease.

Secondary GN

Diabetic nephropathy (DN) is maximum (56%) among secondary GN in our study. Most of the studies showed that LN was the commonest cause.^{14,33,34} The most likely reason of getting more DN is, BIRDEM is a specialized hospital of diabetes and endocrine diseases and also because other centers usually did not biopsy diabetic patients¹⁶ or did if the diagnosis was doubtful.

^{10,31}LN is the second common form of secondary GN in our study. Class iv LN is the commonest followed by class v LN which correlates with the finding of Habib MA¹⁴ from Bangladesh.

Indication of biopsy

We found that nephrotic range proteinuria is the most frequent clinical presentation, accounting for 41.5% of all cases. This is similar to that reported in many studies around the world, including India, Pakistan and also Bangladesh.^{14,18,20,23,33,35} The underlying etiology of nephrotic syndrome is variable across the world. In our study the commonest cause of nephrotic range proteinuria is MPGN (27%), DN (22.7%) and than MesPGN (18%). Huq N⁴³ also reported MesPGN (36.48%) and MPGN (20.27%) as the common cause of nephrotic syndrome. In Korea and other northeast countries like Japan, the most common cause of NS was MCD, followed by MN and IgA nephropathy.¹⁵ Membranous nephropathy (10.81%) was not much common in Bangladesh⁴³ as we reported. We did not get any minimal change disease. Several studies have shown a decline in the relative frequency of MCD.^{35,45} China²³ also reported a very low incidence of MCD.

Post biopsy complication

The overall frequency of important complications after renal biopsy varied from 5% to 13% in previous reports^{44,45} which mainly included hematuria as in our study. One death was also been reported from renal biopsy⁴⁵ but there was no death or even nephrectomy was observed in our study. These complications may be minimized in future by performing biopsy under USG/CT guidance.

Limitation of the study

A large number of study subjects from multi-centre and availability of electron microscope could make our study more representative.

Conclusion

To conclude, from the study and data analyzed, the prevalence of GN is different all over the world due to various factors. PGN related to infection i.e Mes PGN and MPGN, is more common in our country whereas IgA nephropathy, FSGS is not very prevalent. Among SGN, DN is the commonest cause of GN. Nephrotic syndrome is most commonly encountered indication for biopsy and the study depict renal biopsy as a relatively

safe procedure in expert hand. It has also been realized that it is essential and necessary to maintain a central biopsy registry with an increased participation of many more nephrology center of Bangladesh to obtain accurate knowledge about incidence, spectrum and distribution of glomerulonephritis in our country.

Conflict of interest: None

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