A TWO YEAR OBSERVATION ON TREND OF PRIMARY GLOMERULONEPHRITIS IN A TERTIARY CARE HOSPITAL OF BANGLADESH

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Abstract

Aim: *Glomerulonephritis 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 glomerulonephritis is inadequately described. We performed a study, aiming to determine pattern of primary glomerulonephritis in a tertiary care hospital of our country.*

Material & Methods: *It was a cross-sectional hospital based prospective study conducted at BIRDEM general hospital starting from from July 2013 to June 2015. It included all patients with primary glomerulonephritis and who underwent native kidney biopsy.*

Result: *Total 67 biopsy were performed and among them primary glomerulonephritis was 42. Female and male ratio was 1.3:1 and mean age was 42.73±14 (14-75) years. Indications of biopsy were proteinuria (>1gm/day) and unexplained acute kidney injury. The commonest histopathological pattern in primary glomerulonephritis was membranoproliferative glomerulonephritis 33.33% (14/42) followed by mesangial proliferative glomerulonephritis 30.95% (13/42). Only three (7%) patient required blood transfusion for post biopsy bleeding. No one required nephrectomy.*

Conclusion: *In conclusion, mesangial proliferative and membranoproliferative glomerulonephritis are the two most common causes of primary glomerulonephritis. 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: *Glomerulonephritis, Histopathology, DM*

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Introduction

Glomerular disease is a common cause of end stage kidney disease (ESKD) 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 has also been changing over the last few decades.[1] IgA nephropathy is the common primary glomerular disease from East Asia, as well as in white Europeans and American.[2-5] In contrast, focal segmental glomerulosclerosis (FSGS) is the most common glomerular disease among African-Americans, South Americans and 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 primary glomerular disease in a tertiary care hospital in Bangladesh.

Material and Methods

This was a cross- sectional hospital based observational study. It included all patients with primary GN and who underwent native kidney biopsy that were performed in "Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine

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and Metabolic Disorders" (BIRDEM) General Hospital over a period of two years starting from July 2013, were analyzed. Total 67 biopsy were performed and among them primary GN was 42.

Variables

We recorded the demographics of cases, co - morbidities, fundoscopic examination findings, 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 were biopsied if they had unexplained proteinuria, proteinuria 6 gm or more in 24 hours or any features suggestive of glomerulonephritis.

Biopsy technique

Kidney biopsy was performed for all selected patients using 16 G automated biopsy needle. Atleast two cores of tissue were taken from each patient for light microscopy and direct immunoflurescence (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. Immunofluroscence 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

Minimal change disease (MCD),focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), mesangialproliferative 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), pauciimmune GN were included in PGN.[8]

Cases were again classified into a) proliferative GN which included MesPGN, MPGN, IgM nephropathy,Ig A nephropathy, FSPGN, DPGN, CresGN, PSGN, pauci-immune GN b) non- proliferative GN which include MCD,MN,FSGS.

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

Primary GN was found in total 62.68% (42/67) cases. Female and male ratio was 1.3:1 and mean age was 42.73±14 (14-75) years. 50% of the study population had diabetes mellitus.

Indications of biopsy were nephrotic range proteinuria (17/42, 40.47%) including diabetic patients irrespective of the status of retinopathy if 24 hour urinary protein excretion is 6 gm or more, non-nephrotic range proteinuria with /without hematuria (14/42,33.33%) including diabetic patients but with normal fundus and unexplained AKI (11/42,26%).

The commonest histopathological pattern in PGN was MPGN 33.33% (14/42) followed by MesPGN 30.95% (13/42) (Fig 1). These cases were also classied as proliferative (35) and non proliferative GN (7) (Table I).No distinct pathological pattern were found in any age group (Table II) though most of the MPGN and MesPGN were in between 31-60 age range.

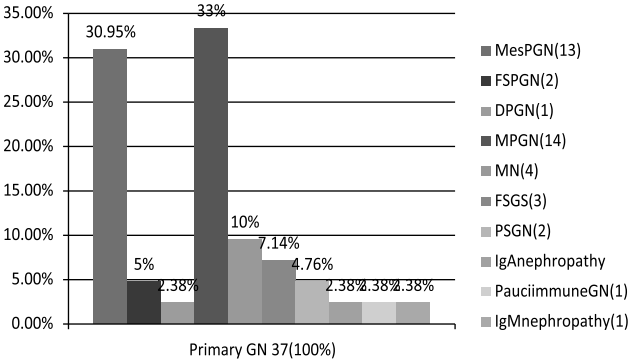

Fig 1: *Histological pattern of primary glomerulonephritis*

(MPGN= Membranoproliferative GN, MesPGN= Mesangioproliferative GN, DPGN & FSPGN=Diffuse & focal segmental proliferative GN, MN=Membranous nephropathy, FSGS=Focal segmental nephropathy, PSGN=PoststreptococcalGN)

Table I

Proliferative and non proliferative classification of GN

	Proliferative GN (n=35)	Non- proliferative GN (n=7)
Primary GN	MesPGN (13) FSPGN(2) DiffusePGN(1) MPGN(14) IgM nephropathy(1) IgA nephropathy(1) PauciimmuneGN(1) PSGN(2)	.MN(4) FSGS(3)

(MesPGN:Mesangial proliferative GN,MPGN: MembranoproliferativeGN, FSPGN:Focal segmental proliferative GN,DPGN: Diffuse proliferative GN, MN:Membranousnephropathy,FSGS:Focal segmental GN,PSGN:Post streptococcalGN)

Table II

Pathological pattern of PGN in different age group (n=42)

Diagnosis (no of cases)	10-20 years (n=4)	21-30 years (n=4)	31-40 years (n=13)	41-50 years (n=8)	51-60 years (n=8)	61-70 years (n=3)	71-80 years (n=2)
MesPGN(13)	2	0	3	3	2	1	2
MPGN(14)	0	2	3	3	5	1	0
FSPGN(2)	1	0	0	0	0	1	0
DPGN(1)	0	0	1	0	0	0	0
MN(4)	0	1	3	0	0	0	0
FSGS(3)	0	1	1	1	0	0	0
IgMnephropathy(1)	0	0	1	0	0	0	0
PauciimmuneGN(1)	0	0	0	1	0	0	0
PSGN(2)IgMnephropathy(1)	10	00	01	00	10	00	00

(MesPGN:Mesangial proliferative GN,MPGN: MembranoproliferativeGN, FSPGN:Focal segmental proliferative GN,DPGN: Diffuse proliferative GN, MN:Membranousnephropathy,FSGS:Focal segmental GN,PSGN:Post streptococcalGN)

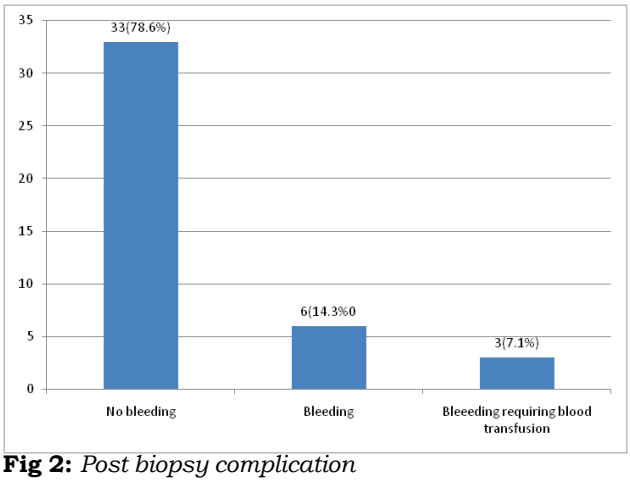

Fig 2: *Post biopsy complication*

The commonest cause of proteinuria (9/42,21%) and unexplained acute kidney injury (5/42,12%) was MPGN .Only three (7%) patient required blood transfusion for post biopsy bleeding(Table-III). No one required nephrectomy.

Discussion

The age range of our cases was 14-75 years with a slight female predominance (1.3:1). Habib M A from Bangladesh also found female predominance although most of the studies depict male predominance.[9,10-12]

There was no distinct pathological pattern observed in any age group in our study. Mundi I et al found most of the cases were in 21-40 age range and distinct pattern of PGN was found in different age ranges.[13]

Proliferative glomerular disease is the most prominent renal disease in our study as well as in all recent studies.[2,14-22]

In the current study MPGN is the commonest primary GN seen. It is the second most common GN reported by Ahmed et al(11.50%) and third most common cause (13%) of primary GN in Saudi Arabia .[10,23] MesPGN is the second common GN found in current study but in other studies from Bangladesh MesPGN was found to be the commonest primary and proliferative GN.[9,15,24].

A study on global evolutionary trend of GN done in Singapore for three decades stated that in the 1st decade most Asians countries had MPGN and MesPGN as the most common form of primary GN and still it is prevalent in some Asians 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 China, Indonesia , Malaysia,Thailand and Singapore which have a high prevalence of MesPGN.[24,26-29] In some countries like Malaysia and Singapore the prevalence of MesPGN is already decreasing in keeping the urbanization and better housing and other amenities

in these countries.[24,28] Bangladesh is a rising country in context of urbanization and other field of developments, i.e, this hypothesis can explain the majority of MPGN as well as MesPGN in our study. Chugh KS also found high prevalence of MesPGN in India but Golay V etal found lower incidence (0.6%) in a recent study which does not match our findings and we could not explain that.[30,31]

Post infectious GN due to streptococcus used to be prevalent in India and this could account for the high incidence of MPGN as MPGN could also result from post infectious GN.[32] In our study PSGN rate is low (4.76%) 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)(10%) and focal segmental glomerulosclerosis (FSGS) (7.14%) slightly differs with Rahman et al showing MN (7.34%) and FSGS (2.8%) and with Habib MA which showed MN 7.37 % but FSGS was 11.58%.[9,33]Mundi I etal and Mannan R et al demonstrated FSGS, MN and minimal change disease(MCD) being the commonest form of PGN in India.[12,13]Data from Singapore and other countries also showed that the prevalence of FSGS and MN have become increased in recent time[1] 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 predilection.[13]Meckenzie etel, have suggested that genetic variation may play a role in sporadic FSGS in adult.,[34] These hypothesis also fits with our findings of FSGS but the reason of low incidence of MN could not be explained by us.

Other findings with low incidence of IgM nephropathy and pauciimmune GN matches with other studies like in Pakistan where the incidence of IgM nephropathy was 2.47%.[12,13,35]Most of the studies did not mention IgM nephropathy as a distinct category.[12]

Incidence of IgA nephropathy in our study is only 2.3% (1/42. 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 America but the incidence of IgA nephropathy in our country is much lower (4.67%-7%)in comparison with other Asian countries. [9,12,35,36,39] It was also uncommon in studies from this region of world like in India and Pakistan.[32,35]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.[18]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.

We found that nephrotic range proteinuria is the most frequent clinical presentation,accounting for 40.47% of all cases. This is similar to that reported in many studies around the world, including India , Pakistan and also Bangladesh.[9,17,19,22,32] The underlying eitiology of nephrotic syndrome is variable across the world .In our study the commonest cause of nephrotic range proteinuria is MPGN (26%), and than MesPGN (17%). Huq N also reported MesPGN (36.48%) and MPGN (20.27%) as the common cause of nephrotic syndrome.[38]In Korea and other northeast countries like Japan, the most common cause of NS was MCD, followed by MN and IgA nephropathy.[14]Membranous nephropathy (10.81%) was not much common in Bangladesh as we reported. We did not get any minimal change disease.[38]Several studies have shown a decline in the relative frequency of MCD.[32]China also reported a very low incidence of MCD.[22]

The overall frequency of important complications after renal biopsy varied from 5% to 13% in previous reports which mainly included hematuria.[36,37] One death was also been reported from renal biopsy.[37]In our study only three patient required post biopsy blood transfusion for bleeding. This may be minimized in future by performing biopsy under USG guidance.

Limitation

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 PGN is different all over the world due to various factors. PGN related to infection i.e MesPGN and MPGN, is more common in our country whereas IgA nephropathy, FSGS is not very prevalent. Nephrotic syndrome is most commonly encountered indication for biopsy and the study depect 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.

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