Histomorphological Patterns of Glomerulonephritis in Patients Presenting with Acute Nephritic Syndrome

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The present study was carried out to study in detail the various renal histological lesions in nephritic syndrome and to assess the relationship between degree of proteinuria, biochemical and hematological parameters, and different renal morphological lesions of nephritic syndrome. This was a prospective study done in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period from July 2006 to August 2007. A total of 73 patients with primary and secondary glomerulonephritis who fulfilled the inclusion criteria were selected. The male to female ratio was 1:1.15. Mean age at presentation was 34.97 ± 13.01 years. The common mode of clinical presentation was whole body swelling with anuria, hypertension and renal failure. Out of 73 cases, 65 (89.04%) were primary glomerulonephritis and 08 (10.96%) were secondary glomerulonephritis. Among the primary glomerular diseases mesangiocapillary glomerulonephritis (43.84%) and mesangial proliferative glomerulonephritis (27.39%) were the common histological patterns. All the secondary glomerulonephritis were lupus nephritis. Fifty six patients presented with haematuria and the median values of serum creatinine and blood urea were higher in mesangiocapillary glomerulonephritis and mesangial proliferative glomerulonephritis. All of the cases of the present study had non-nephrotic proteinuria.

[Dinajpur Med Col J 2012 Jan; 5 (1):26-33]

Key words: Nephritic syndrome, immunofluorescence, lupus nephritis.

Introduction

Glomerular diseases are manifested as asymptomatic proteinuria, asymptomatic haematuria, the nephrotic syndrome, the nephritic syndrome, acute/rapidly progressive renal failure, end stage chronic renal failure and hypertension.[1] The nephritic syndrome is a clinical complex characterized by a number of renal and extrarenal features. It frequently manifests as a sudden onset of haematuria, proteinuria, and red cell casts in urine. This clinical picture is often accompanied by hypertension, edema and impaired renal function. Urinary protein excretion varies widely, but the rate is generally less than 3 gram of protein per day.[2] Acute nephritis may occur at any age, but much more common in children than in adults. Most cases occur in patients aged 5-15 years. Only 10% occur in patients older than 40 years.[3] Nephritic syndrome is more common in developing countries than Europe and North America. The reason may be an impaired immune response to various environmental pathogens in association with malnutrition triggering chronic sensitization by antigen (s), which subsequently cause immune complex disease.[4]

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The causal factors that underlie this syndrome can be broadly divided into infectious and non-infectious groups. Pattern of diseases producing nephritic syndrome varies from region to region. Within Asia, post-streptococcal glomerulonephritis is the most common cause of nephritic syndrome in India. In Thailand, the high incidence of IgA nephritis has been reported.[5]

Nephritic syndrome is associated with impairment of renal function as well as complications, such as increased susceptibility to infections, hypertension and nephrotic syndrome. Early recognition of the underlying disease process and initiation of appropriate therapy are essential in preservation of or improvement in renal function.[6]

In Bangladesh there is no consensus of the total number of nephritic cases in both paediatric and adult patients. The present study was carried out to study in detail the various renal histological lesions in nephritic syndrome and to assess the relationship between degree of proteinuria, biochemical and hematological parameters, and different renal morphological lesions of nephritic syndrome.

Methods

This was a prospective study done in the Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period from July 2006 to August 2007. A total of 73 patients with primary and secondary glomerulonephritis who fulfilled the inclusion criteria were selected.

Two samples of renal tissue were obtained from each patient by percutaneous needle biopsy of clinically suspected glomerulonephritis. Biopsy specimens for light microscopic (LM) examination were fixed in 10% formalin and embedded in paraffin. Sections were cut at 4-5 μm thickness from paraffin embedded material and stained routinely with haematoxylin and eosin (H&E). Specimens for direct immunofluorescence (DIF) microscopy were received in normal saline and immediately frozen and embedded in O.C.T (Optimum Cutting Temperature) compound. Cryosectioned at 2-3 μm thickness were done and stained with fluorescence conjugated anti-sera against human IgM, IgG, IgA, C3 and fibrinogen. The clinical data were collected with particular attention to age, sex, clinical presentation, age at onset of nephritic syndrome, duration of symptoms, presence of hypertension, findings on general and systemic examination and results of urine analysis, biochemical and serological parameters.

Histological diagnosis was primarily based on light microscopic features in correlation with clinical and biochemical findings. Immunofluorescence study of the cases was carried out separately by using anti-IgG, IgM, IgA, C3 and fibrin. Both light and immunofluorescence findings were correlated before concluding a definitive histological diagnosis.

Results

Of the 73 biopsies obtained from clinically suspected cases of nephritic syndrome 34 (46.58%) were male and 39 (53.42%) were female with a male to female ratio of 1:1.15. The majority of the patients were in the third and fourth decades, 21 (28.77%) and 20 (27.4%) respectively. The age ranged from 12-65 years with a mean age of 34.97 ± 13.01 years. The distribution of age according to the decades and sex distribution in different renal morphological lesions of nephritic syndrome is shown in Figure 1 and 2 respectively.

Table I: Distribution of various renal histopathological lesions of nephritic syndrome according to age and sex

Histological diagnosis	Total	Male	Female	Age mean ± SD
Primary glomerulonephritis:				
Mesangial proliferative glomerulonephritis	20 (27.39%)	12 (60%)	8 (40%)	34.15 ± 14.23
Mesangiocapillary glomerulonephritis	32 (43.84%)	16 (50%)	16 (50%)	36.75 ± 11.77
Membranous glomerulonephritis	07 (9.59%)	03 (42.8%)	04 (57.1%)	47.29 ± 12.28
IgA nephropathy	04(5.48%)	00	04 (100%)	29.25 ± 10.0
DECPGN	02 (2.74%)	01 (50%)	01(50%)	50
Secondary glomerulonephritis:				
Diffuse proliferative glomerulonephritis, LN, WHO class IV	07 (9.59%)	02(28.57%)	05 (71.43%)	18.57 ± 5.08
Diffuse membranous glomerulonephritis, LN, WHO class V	01 (1.37%)	00	01 (100%)	26S
Total	73	34 (46.58%)	39 (53.42%)	34.97 ± 13.0

DECPGN = diffuse endocapillary proliferative glomerulonephritis; LN = lupus nephritis.

Table II: Renal functional status at the time of biopsy

Features		Distribution of patient	
		Number	%
Urinary total protein gm/24 hrs.	0.5-1.5	17	23.29
	1.6- 2.5	35	47.95
	2.6-3.5	18	28.76
Haematuria	Microscopic	32	43.84
	Macroscopic	24	32.88
	Absent	14	19.18
	Unknown	03	4.1
Serum creatinine	<110 µmol/L	31	42.47
	>110 µmol/L	39	53.42
	Unknown	03	4.1
Blood urea	< 7 mmol/L	54	73.97
	> 7 mmol/L	16	21.92
	Unknown	03	4.1
R.B.C cast	Present	51	69.86
	Absent	14	19.18
	Unknown	08	10.96

Table III: Pattern of glomerular deposits in different morphological lesions of nephritic syndrome cases

Disease	IgG	IgM	IgA	C_3	F
MesPGN (N=20)	2	8	1	6	0
MCGN (N=32)	20	22	5	20	0
MGN (N=07)	5	1	0	2	0
IgAN (N=04)	0	1	4	1	0
DECPGN (N=02)	1	0	0	1	0
DPGN, LN-IV (N=07)	5	6	4	5	1
DPGN, LN-V (N=01)	1	0	1	0	0
Total amount of deposit (%)	34 (46.58)	38(52.05)	15(20.55)	35(47.95)	1(1.37)

MesPGN = Mesangioproliferative GN, MCGN = Mesangiocapillary GN, MGN = Membranous GN, IgAN = IgA Nephropathy, DECPGN = Diffuse endocapillary proliferative GN, DPGN, LN= Diffuse proliferative GN, Lupus Nephritis, F = Fibrinogen

Table IV: Comparative studies of glomerular diseases in nephritic cases by different investigators

Authors	Country	No. of nephritic patients	MesPGN (%)	MCGN (%)	PIGN (%)	LN (%)
Aggarwal et al.2007	Haryana, India	122	24.59	16.39	37.7	1.63
Rychlik et al. 2004	Czech Republic	747	7.2	5.6	14.1	4.6
Schena et al. 1997	Italy	622	-	6.6	16.1	4.8
Present study, 2007	Dhaka, Bangladesh	73	27.39	43.84	2.74	10.96

PIGN = postinfectous glomerulonephritis, LN = lupus nephritis

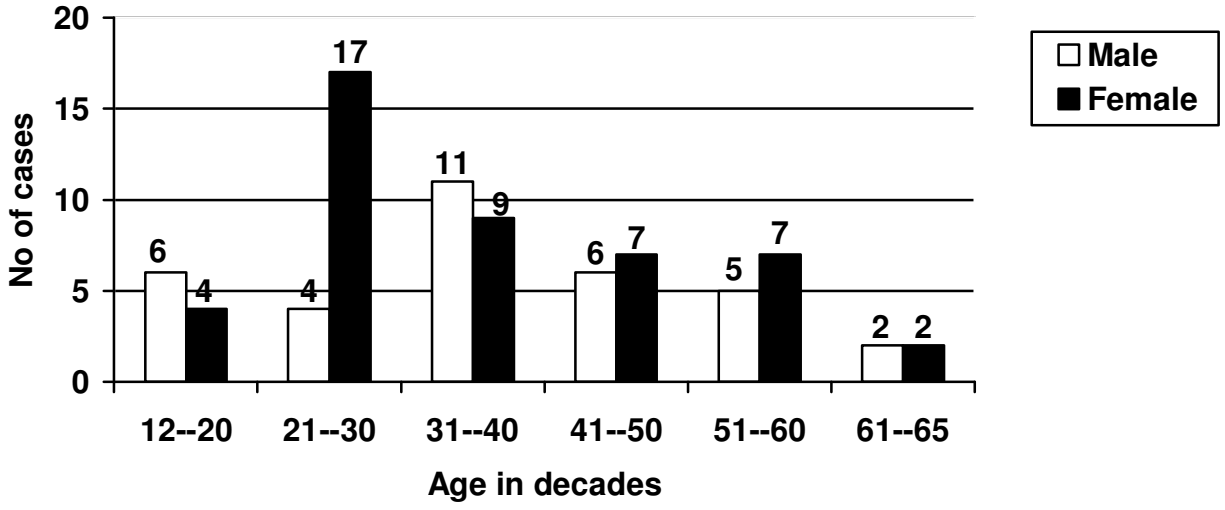

Figure 1. Distribution of age of male and female in each decade

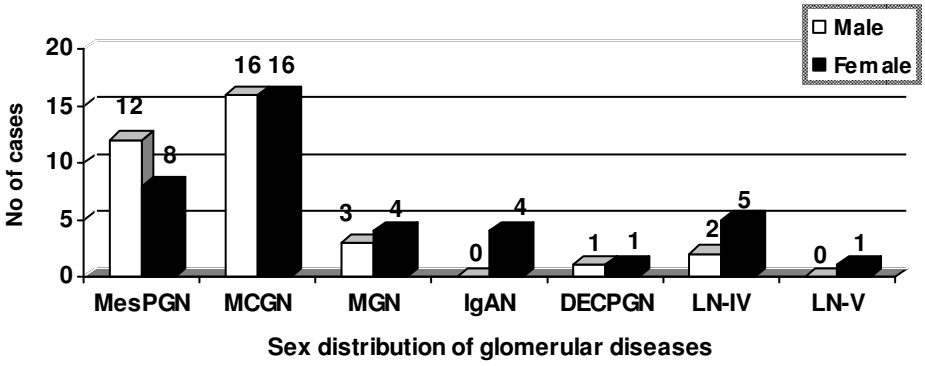

Figure 2. Sex distribution of glomerular diseases

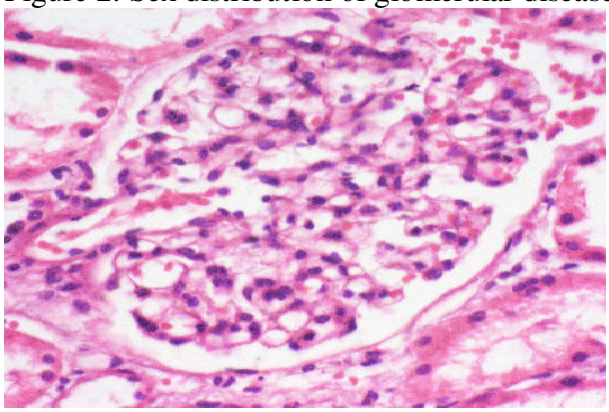

Figure 3. Mesangial proliferative glomerulonephritis showing increase in mesangial cells and matrix (H & E stain x 400).

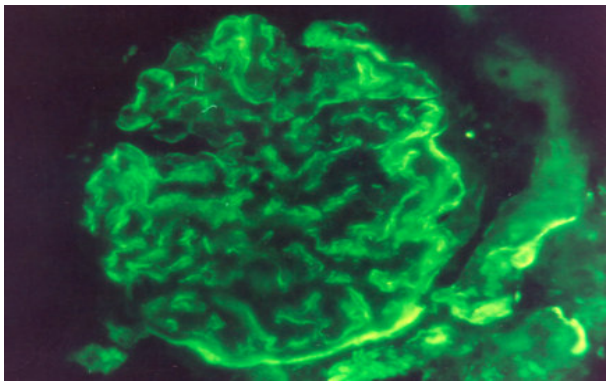

Figure 4. Membranous glomerulonephritis showing granular deposits of C3 along the capillary loops (DIF stain x 400).

Of the total 73 cases 65 had primary GN and 8 secondary GN. Among the primary glomerulonephritis cases 20 (27.39%) were mesangial proliferative glomerulonephritis (MesPGN), 32 (43.84%) were mesangiocapillary glomerulonephritis (MCGN), 7 (9.59%) were membranous glomerulonephritis (MGN), 4 (5.48%) were IgA nephropathy (IgAN), 2 (2.74%) were diffuse endocapillary proliferative glomerulonephritis (DECPGN). All the secondary glomerulonephritis 8 (10.96%) were lupus nephritis, 7 (9.59%) were diffuse proliferative GN (LN IV) and one was diffuse membranous GN, LN V. Distribution of various renal histopathological lesions of nephritic syndrome according to age and sex is shown in Table I.

In this study whole body swelling was the commonest clinical presentation in combination with other clinical features. Whole body swelling with anuria, hypertension and renal failure accounted for 19 (27.12%) cases. The values of different biochemical parameters at the time of renal biopsy among the study group are shown in the Table II. The range of serum creatinine level was 69 µmol/L to 1050 µmol/L in 70 cases with mean of 217.13 ± 171.48. The blood urea level in 73 cases ranged from 0.8 mmol/L to 11.1 mmol/L with a mean of 5.89 ± 1.54 mmol/L. It was observed that median

values of serum creatinine and blood urea were higher in primary GN than in secondary GN.

In 24 hour urinary protein, the range and mean values were 0.5-3.1 gm/24 hrs and 2.03 ± 0.68 respectively. All of the cases had non-nephrotic proteinuria. In majority of the cases (32= 43.84%) patient presented with microscopic haematuria and gross haematuria were in 24 (32.88%) cases. In urine RBC cast and granular cast were seen in 51 and 49 cases respectively. Serum albumin and serum cholesterol were found within normal range. HBsAg was not found positive in any case. Antinuclear antibody (ANA) and anti-ds DNA were positive in all cases of lupus nephritis.

The frequency and distribution of immune deposits in various pattern of nephritic syndrome are shown in Table III. Among the 73 cases, 60 cases showed positive fluorescence findings. In the remaining 13 cases, 10 showed renal medulla and no immunofluorescence findings were found in 3 cases. IgM was the predominant immune deposits (38=52.05% cases) of all types of deposition followed by C_3 (35=47.95% cases) and IgG (34=46.58% cases). In MCGN, IgG deposition was found in 20 (27.39%) cases, IgM in 22 (30.14%) and C3 in 20 (27.39%) cases. Among the 7 cases of DPGN, LN-Class IV, deposition of IgG, IgM, IgA, C_3 were present mostly along the capillary basement membrane and or in the mesangium in all the cases in different combinations.
Hemoglobin estimation, ESR and total count of WBC were done in 70 (95.89%) cases. Among the 73 cases, 20 (27.39%) cases had mild to moderate anaemia and 38 (52.05%) cases ESR were raised.

Discussion

The present study has attempted to assess the variable histomorphological patterns of nephritic syndrome among the admitted patients who had undergone renal biopsy for histological diagnosis. So it is not the representation of nephritic syndrome population in Bangladesh. Since the number of patients assessed is relatively small, all the patterns of nephritic syndrome have not been found in the present series.

In the study of 73 cases MCGN was found to be the most common cause (32=43.84%) of nephritic syndrome. There is a great variation regarding the commonest pattern of glomerulonephritis in different countries. In one report the world wide frequency of MCGN in patients presenting with nephritic syndrome has been calculated to be 16-30%.[7] Aggarwal et al.[8] in their study in India described MCGN in 16.39% cases and was the third commonest cause. In their study, most prevalent was post-infectious glomerulonephritis (37.70%), which is also similar to what has been reported from Italy.[9] But in the present series DECPGN seen in 2 (2.74%) cases. Post-infectious GN cases are not biopsied in our country because most of these resolve with treatment. Also improvement of personal hygiene and health care facilities may have reduced this disease in our society, as well documented in developed countries in later part of the last century. Prevalence of MesPGN was 27.39% in the present study. This finding is similar to what has been reported from India (24.39% and 21.37%). Schena et al.[9] in their study observed that PIGN and IgAN were frequent glomerular lesions in Italy.

Findings of different glomerulonephritis in the present study were compared with those of different investigators in India and other countries (Table IV). A lower incidence of PIGN (2.74% versus 16.1%) and IgAN (5.48% versus 14%) was observed. Naini et al.[10] in their study in Iran observed that IgAN (33%) and MGN (10.5%) were frequent

glomerular lesions. In the present series the frequency of these glomerular diseases were found to be 5.48% and 9.59% respectively. Whether these findings suggest individual variation, differences in environmental influences or different patient selection criteria between the two populations are not very clear.

In the present study, lupus nephritis was found to be the lone secondary cause of nephritic syndrome occurring in 8 patients (10.96%). But Schena et al. found necrotizing vasculitis (6.3%), lupus nephritis (4.8%) and Henoch Schonlein purpura (3.4%) among the secondary causes.[9] In Czech Republic lupus nephritis (14.9%) was the commonest histological pattern in secondary cause of nephritic syndrome. [11]

Age and sex distribution in the present series shows that, there were 34 males and 39 females out of 73 cases. The overall male to female ratio is 1:1.15. The age range was 12-65 years with a mean of 34.97 ± 13.0 which is comparable with studies from Thailand and India. [5, 8] There were 3 (4.11%) patients less than 15 years of age and 9 patients were more than 50 years of age. Nephritic syndrome occurs in all age groups though children were most affected age groups. In this study, the number of pediatric patients (<15years of age) was only three. It might be due to the fact that majority of this group respond well to therapy and so do not undergo renal biopsies. Out of 3 cases less than 15 years of age, one was MesPGN and two were DPGN, LN- IV.

Almost all patients in the present study had nephritic syndrome of variable severity. Twenty (62.5%) cases of MCGN and 4 (20%) cases of MesPGN had whole body swelling with anuria, hypertension and renal failure. Findings suggest that clinical presentation might vary with different patterns of GN in nephritic syndrome.[5]

In the present study hypertension was found in 57 (78.08%) cases; 29 cases in MCGN and 11 cases in MesPGN. In a study carried out in Czech Republic, arterial hypertension was found in 38.7% cases of nephritic syndrome.[11]

Immunofluorescence findings in the present series characteristically showed the presence of single or several immunoglobulin and/ or complement components (Table IV). IgM was the predominant deposit (38=52.05%), which is followed by C_3 in 35 (47.95%) and IgG in 34(46.58%) cases. The findings of the present study were more or less same with different studies done at home and abroad, although their study focused on morphological patterns of glomerulonephritis.[5]

Conclusion

Histomorphological pattern of glomerulonephritis in nephritic syndrome show variation in different studies. In the present study, mesangiocapillary glomerulonephritis (43.84%) and mesangial proliferative glomerulonephritis (27.39%) were found to be the most frequent patterns. Actual incidence of various glomerulonephritis in different parts of the world and variation of patient selection criteria both appear responsible for this.

As this study was done with a small number of patients in whom renal biopsy was done the result may not reflect the correct prevalence. Population based study on a large number of cases may come out with true incidence.

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