Clinicopathilogical Correlation of Nephrotic Syndrome in a Tertiary Care Hospital

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Abstract

Background: Nephrotic Syndrome (NS) in adult is diagnosed by renal biopsy. 50% of causes are secondary. Clinical features may or may not correlate with the histopathological features. For this, renal histopathology is important. The aim of our study is to find out the clinical features and its correlation with histopathological types of nephrotic syndrome in our context.

Materials and methods: Study was conducted among 50 patients of nephrotic syndrome admitted in the Department of Nephrology CMCH. Data was collected in a structured case record form, renal biopsy was done . Investigations was done in the Department of pathology of CMCH. Data was analyzed by SPSS-20.

Results: Among 50 cases, male to female ratio was 1.2:1. Regarding renal biopsy findings Membranous Nephropathy (MN) Focal Segmental Glomerulosclerosis (FSGS) Membranoproliferative Glomerulonephritis (MPGN) Focal Segmental Glomerulonephritis (FSGN) Diffuse Proliferative Glomerulonephritis (DPGN) and Lupus Nephritis (LN) was found in 10,2,22,12,2,2 cases respectively. Generalised oedema, pleural effusion, ascites, hypertension (Blood pressure >140/90) were present in 46,35,43,18 cases respectively. Microscopically, hematuria, proteinuria (>8gm/day), severe hypercholesterolaemia (>400mg/day), severe hypoalbuminaemia (<2.5mg/day) renal failure were found in 16,10,16,44,22 caese respectively.

Conclusion: The study partially gave a snap shot of clinical features of patients correlating with corresponding histopathological features. Knowledge deducting from NS correlation will help us to initiate treatment and later on referral to tertiary center when patient is found with clinical features of NS in a remote place where renal biopsy is not available.

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Introduction

Nephrotic syndrome includes massive proteinuria (3.5 gm/24hr), hypoalbumiinemia (Serum albumin< 2.5gm/dl), generalized edema and hyperlipidemia (S. Cholesterol >250 mg/dl).[1] Kidney biopsy is mandatory for adult nephrotic syndrome diagnosis. It defines the morphologic patterns of GN. Sufficient tissue is needed to perform not only an examination by light microscopy, but also immunohistochemical staining to detect immune reactants and electron microscopy to define precisely the location, extent and, potentially, the specific characteristics of the immune deposits.[2] The relative frequencies of the several causes of the nephrotic syndrome vary according to age and geography. In children younger than 17 years in North America, for example, the nephrotic syndrome is almost always caused by a lesion primary to the kidney; whereas among adults, it may often be associated with a systemic disease. Systemic cause of the nephrotic syndrome are diabetes, amyloidosis, and SLE. The most important of the primary glomerular lesions are minimal change disease, membranous glomerulopathy, and focal segmental glomerulosclerosis. The first is most common in children in North America, the second is most common in older adults, but focal segmental glomerulosclerosis occurs at all ages. Other primary causes, the various proliferative glomerulonephritis, frequently present as a mixed syndrome with nephrotic and nephritic features.[3] Presentation of nephrotic syndrome varies with age. Its histological type also influence the clinical presentation. The aim of our study is to find out the clinical features and its correlation with histopathological types of nephrotic syndrome in our context.

Materials and methods

This was a cross sectional descriptive study done in the Medicine and Nephrology Department of Chittagong Medical College Hospital (CMCH)

during a period of 6 months from 15/11/2014 to 15/5/2015. Ethical clearance was obtained from ethical committee, CMCH. Those patients who was admitted Medicine and Nephrology Departments, CMCH and are suffering from NS were the study patients and sampling technique was purposive. A total of 50 consecutive cases of adult NS were enrolled in this study and severe comorbid disease like heart failure, jaundice and DM and chronic infection, subject who are contraindicated for renal biopsy were excluded. From all eligible subjects after getting consent, clinical history was taken and clinical examination was done. All clinical data was taken. Blood pressure was recorded at sitting position with mercury manometer. Weight was recorded by the machine. For other test like dipstick test and blood sugar .3 cc of blood sample was collected at morning. For 24 hour UTP, urine was collected for 24 hours from 8 am to next day 8 am in a plastic jar. First morning urine was discarded at starting 8 am and on next day urine of 8 am was included in the jar. For dipstick test commercially available kit was collected and presence of protein was evaluated as per assay procedure and color combination. With all aseptic precaution renal biopsy was done by a nephrologist. One sample was put in formalin jar for histopathology and another sample was put in normal saline for immune histo chemical staining and then sent to Dhaka for reporting. All sample were sent in same institute. After histopathology, Crescentic glomerulonephritis cases excluded. Blood were collected by researcher herself. All relevant data was noted in the pre tested data sheet. All investigations except histopathology was done in the Clinical Pathology Department of CMCH. Data was processed and analyzed by using computer bases software SPSS (Statistical Package for Social Science). Qualitative variables like sex, occupation, different clinical features and outcome were analyzed by percent and proportion and quantitative variables like age, creatinine levels were analyzed by mean and standard deviation. Different statistical method like t- test and Chi squared test was applied for data analysis. p value was considered as statistically significant when it is less than 0.05. Informed written consent was taken from the patients or eligible attendants.

Results

Table I Different basic clinical parameters

	n	Minimum	Maximum	Mean	Std. Deviation
Age		14	75	28.98	13.766
Pulse		70	92	83.70	5.389
Systolic blood pressure		100	180	126.60	20.353
Diastolic blood pressure		70	100	78.04	10.262
Ht (cm)		140.2	182.0	162.373	18.58
Wt (Kg)		48	82	65.98	8.085
HCT level	50	8	16	11.06	1.302
Hb level		10	18.0	12.19	4.785
WBC count		5500	14000	8693.62	2369.682
Nutrophil (%)		47	90	66.19	7.996
S. creatinine (mg/dl)		0.4	5.8	1.275	0.8524
B. Urea (mg/dl)		15	76	27.77	13.813
B. Sugar (mg/dl)		72	130	98.70	10.919
S.Cholesterol (mg/dl)		200	793	365.83	141.187
S. Albumin (g/dl)		0.8	3.3	1.941	0.5483
24 hrs UTP (gm/day)		4	17	5.96	2.731

Table I showing different basic clinical parameters.

Table II Renal biopsy findings

	Frequency	Percent
MN	10	20.0
FSGS	2	4.0
MPGN	22	44
FSGN	12	24.0
DPGN	2	4.0
LN	2	4.0
Total	50	100.0

Table II showing renal biopsy findings where most cases where Mesengioproliferative Glomerulonephritis (MPGN) 22(44%) next to which was focal segmental glomerulonephritis 12(24%).

Table III Clinical features in different renal biopsy findings

		Renal Biopsy						
		MN	FSGS	MPGN	FSGN	DPGN	LN	Total
Types of edema	Moderate	1(10)	0	0	2(16.7)	0	1(50)	4(8)
	Generalized	9(90)	2(100)	22(100)	10(83.3)	2(100)	1(50)	46(92)
Pleural effusion	Present	7(70)	2(100)	15(68.18)	9(75)	1(50)	1(50)	35(70)
	Absent	3(30)	0	7(31.81)	3(25)	1(50)	1(50)	15(30)
Ascites	Present	8(80)	2(100)	19(83.36)	10(83.3)	2(100)	2(100)	43(86.0)
	Absent	2(20)	0	3 (13.63)	2(16.7)	0	0	7(14.0)
Hypertension (>14 0/90	Present	6(60)	2(100)	6(27.27)	4(25)	0	0	18(36)
	Absent	4(40)	0	16(72.72)	8(75)	2(100)	2(100)	32(64)
		100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Table III showing Clinical features in different renal biopsy findings.

Table IV Relation of urine RME with renal biopsy

		Renal Biopsy						
		MN	FSGS	MPGN	FSGN	DPGN	LN	Total
Pyuria	Present	1(10)	1(50)	8(36.36)	2(16.7)	0	1(50)	13(8)
	Absent	9(90)	1(50)	14(63.63))	10(83.3)	2(100)	1(50)	46(92)
Hematuria	Present	8(80)	2(100)	2(9.09)	4(33.3))	0	0	16(32)
	Absent	2(20)	0	20(90.91)	8(66.6))	2(100)	2(100)	34(68)
Cast in urine	Present	1(10)	0	9(40.91)	3(25.0)	0	1(50)	14(28)
	Absent	9(90)	2(100)	13(59.09)	9(75.0)	2(100)	1(50)	36(72)
Heat coagulation								
test ++	proteinuria	1(10)	0	3(13.63)	0	0	0	4(8)
>++	proteinuria	9(90)	2(100)	19(86.36))	12(100)	2(100)	2(100)	46(92)
24 h UTP	<8gm/d	4(40)	0	20(90.91)	12(100)	2(100)	2(100)	40(80)
	>8 gm/d	6(60)	2(100)	2(9.09)	0	o	0	10(20)
		100 %	100%	100%	100 %	100%	100%	100%

Table IV showing different urine routine examination findings with different types of renal biopsy findings.

Table V Metabolic profile with renal biopsy findings

		Renal Biopsy						
		MN	FSGS	MPGN	FSGN	DPGN	LN	Total
Serum	<400 mg/dl	6(60)	1(50)	16(72.7)	7(58.3)	2(100)	2(100)	34(68)
cholesterol	>400 mg/dl	4(40)	1(50)	6(27.3)	5(41.7)	0	0	16(32)
Serum	<2.5 gm/l	10(100)	2(100)	18(81.8)	11(91.7)	2(100)	1(50)	44(88)
albumin	>2.5 gm/l	0	0	4(18.2)	1(8.3)	0	1(50)	6(12)
Serum	>1.5mg/dl	6(60)	2(100)	6(27.3)	5(41.6)	1(50)	2(100)	22(44)
creatitine	<1.5mg/dl	4(40)	0	16(69.6)	7(58.4)	1(50)	0	28(56)

Table V showing serum cholesterol, serum albumin and serum creatinine in relation with renal biopsy.

Discussion

In the present study male was 27(54%) and female was 23(46%). Male to female ratio was 1.2: 1. In one similar study done by Hoque et al there were 64.9% males and 35.1% were female patients.[4] Average age was (33.14±11.70) years. Thorough clinical assessment 46(92%) patient revealed generalized edema, 38(76%) had oliguria and 1(2%) had anuria, 6(12%) had joint pain, 3(6%) had leuconychia, 35(70%) had clinical evidence of pleural effusion, 1(2%) had basal crepitation and 43(86%) had clinical evidence of ascites. It is concluded in a study that regarding clinical findings progressive lower extremity edema, weight gain, and fatigue are typical presenting symptoms of nephrotic syndrome. In advanced disease, patients may develop periorbital or genital edema, ascites, or pleural or pericardial effusion.[5] In a study done in Pakistan found at the time of presentation in 100% patients of nephrotic syndrome had oedema, among these, generalized oedema was present in 57.20% cases, 31.30% presented with peri-orbital oedema and only 11.50% had scrotal oedema.[4-6] Renal biopsy findings revealed most cases where Mesengioproliferative Glomerulonephritis (MPGN) 22(44%) next to which was focal segmental 12(24%). Most cases of nephrotic syndrome appear to be caused by primary kidney disease.[7] In a study it was found that FSGS(54%) was found to be most predominant renal biopsy finding followed by MCD(28%). 88% had primary glomerular disease and 12% had secondary glomerular disease.[8] In another study it was found that membranous nephropathy and Focal Segmental Glomerulosclerosis (FSGS) each account for about one third of cases of primary nephrotic syndrome. Minimal change disease and (Less commonly) Immunoglobulin A (IgA) nephropathy cause approximately 25 percent of cases of idiopathic nephrotic syndrome. Other conditions, such as membranoproliferative glomerulonephritis, are less common. FSGS accounts for approximately 3.3 percent of new cases of end-stage renal disease.[9] In a study of saudi arab, the most frequent primary GN is Membranous GN (MN) constituting 25.7%, followed by FSGS at 21.3%. Less frequent GN are Immunoglobulins A Nephropathy (IgAN) representing 17.6%, membranoproliferative GN (MPGN) 11.5%, Immunoglobulin M Nephropathy (IgMN) 7.8%, Minimal Change Disease (MCD) 5.4%.[10] In a study of Bangladesh focal and segmental mesangial proliferative glomerulonephritis was the most common histological lesion (29.47%). Diffuse mesangial proliferative Glomerulonephritis (GN) was the second most common lesion (15.79%), followed by focal segmental GN (11.58%), minimal change disease (10.53%), membranous GN (7.37%), IgA nephropathy (6.85%), chronic sclerosing GN (2.11%) and crescentic GN (2.11%). Lupus nephritis was the most prevalent among secondary GN.[4] In a study of Thailand, the prevalence of IgAN, FSGS, and MN were 31.0%, 24.9% and 13.1%, respectively.[11] Study on india, MPGN was the predominant pathology (20.2%), followed by idiopathic FSGS (17%), MCD (11.6%), MN (9.8%), IgA nephropathy (8.6%).[12]

In our study, 46 patient was presented with generalized edema, of them 22 are MPGN. There were 35(70%) patient who had clinical evidence of pleural effusion, 15 patient were MPGN, 9/35 patient were FSGN. Clinical evidence of ascites were present in 43 patient, 13 of 19(83.4%) cases were MPGN and 10 of 12 (83.3%) were FSGN, 2 cases (100%) were FSGS, DPGN, LN, 8 of 10 (80%) cases were MN.

Hypertension (Blood pressure >140/90) were present in 18 cases (36%) of our study. Of them 2 cases (100%) were FSGS, 6 of the 10 cases(60%) were MN, 6 of the 22 cases (27.3%) were MPGN, 4 of the 12 cases (25%) were FSGN. Three of the 11 cases of MCNS, seven of the 23 cases of FSGS and four of the 16 cases of MN had hypertension in another study[13].

In our study, 16 patient (32%) had microscopic hematuria, 2 cases (100%) were FSGS, 8 of the 10 cases (80%) were MN, 4 of the 12 cases (33.3%) were FSGN, 2 of the 22 cases (9.1%) were MPGN. Hyaline cast mostly found in MPGN. 2+ heat coagulation test was found in only 4 patient. Of them 3 were MPGN and 1 was MN. 10 patients (20%) had proteinuria >8gm/day, 2 cases (100%) were FSGS, 6 of the 10 cases (60%) were MN, 2 of the 22 cases were (9.1%) MPGN. Renal Failure (s. creatinine >1.5mg/dl) was found in 22 (44%) patient. 2 cases (100%) were FSGS, 2 cases (100%) were LN, 6 of the 10 cases (60%) were MN,1 of the 2 cases (50%) were DPGN, 5 of the 12 cases were (41.6%) were FSGN, 6 of the 22 cases (27.3%) were MPGN. In another study, 6 of 50 (12%) patients had renal impairment, all had FSGS.[12] Several schemes have been proposed whereby the histology could be reasonably predicted so that steroids are started without a renal biopsy.[14-16] These include various demographic, clinical and laboratory parameters of adult Nephrotic Syndrome (NS) patients, such as age, renal function, hypertension and urinary sediment with the histological type so that empirical steroid therapy can be offered to a selected group of adult NS patients before renal biopsy. There was a substantial clinicomorphological correlation (60%) in our study. Considering the ease of renal biopsy in adults, the unpredictability of steroid therapy in the designated patients and its toxicity, a model for histological prediction does not appear to be viable.Renal biopsy is often recommended in persons with nephrotic syndrome to establish the pathologic subtype of the disease, to assess disease activity, or to confirm the diagnosis of disease. There are, however, no clear guidelines on when renal biopsy is indicated or whether it is needed in all persons with nephrotic syndrome. For example, in diabetic nephropathy, renal biopsy may not be necessary if the patient has enlarged kidneys, a bland urinary sediment without cellular casts, or other evidence of microvascular disease, such as proliferative retinopathy or peripheral neuropathy. No recent studies have elucidated the true benefit of renal biopsy in guiding management, the best available evidence is from a prospective study in which the results of renal biopsy changed management in 24 of 28 persons with nephrotic syndrome, primarily through the addition of corticosteroid treatment, although the actual patient benefit is unknown.[17]

Limitation

Present study has its limitations, first sample size was small. Second, only single center was selected. Third, it was a cross sectional study.

Conclusion

The findings of the study suggest that clinical and biochemical features would not give clue to the more precise diagnosis of nephrotic syndrome. Histological diagnosis of renal biopsy, therefore, required for correct diagnosis and deciding treatment strategy. Nevertheless clinical and biochemical features has some value where biopsy is not feasible because of financial constraint and non-availability of facilities for biopsy. In these circumstances, at least we can predict the type of GN from these findings and started treatment.

Recommendation

To draw any significant conclusion from this type of study large sample size and multi center study should be carried out.

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Contribution of authors

MM-Conception, acquisition of data, drafting & final approval.

PB-Data analysis, interpretation of data, drafting & final approval.

EKS-Acquisition of data, data analysis, critical revision & final approval.
PKD-Design, interpretation of data, critical revision & final approval.

Disclosure
All the authors declared no competing interests.

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