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Research Article

INTERPRETATION OF RENAL BIOPSY AND CORRELATION OF BIOCHEMICAL PARAMETERS IN PATIENTS OF MINIMAL CHANGE DISEASE & MEMBRANOUS GLOMERULOPATHY

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Abstract: The main objective of the present study is to Study the relevance of biochemical parameters in classifying nephrotic syndrome and Comparison of the importance of histopathologic study with biochemical parameters. For this study patients clinically diagnosed with nephrotic syndrome & admitted to Nephrology department of KIMS, BBSR during the study period (Sept, 2011 to Sept, 2013), found to have Minimal change disease (MCD) & Membranous glomerulopathy (MGN) on renal biopsy have been enrolled. Biochemical investigations like serum albumin, 24 hour urine protein, serum cholesterol, serum creatinine and blood urea was carried out. Renal biopsy was done after taking consent. Statistical analysis was done using graph pad prism 6. A total of 50 cases were included in the study. After renal biopsy and H/P diagnosis, two groups of patients of MCD and MGN were created which included 28 cases of MCD and 22 cases of MGN. Most of the patients had Proteinuria in the range of 3.5-7.4gm/24 hrs (76%). 70% had serum albumin ≤2.5gm/dl. Mean value was 2.13±0.68 gm/dl. Mean value of serum cholesterol was 368±119 mg/dl and maximum patients had cholesterol in the range of 200-400 mg/dl. Mean serum creatinine & cholesterol values was higher in MGN as compared to MCD. Statistically correlating biochemical parameters were 24 hour urine protein, serum albumin, cholesterol and creatinine whereas in differentiating between MGN & MCD no biochemical parameters were statistically significant. This study gives a statistical evidence of the fact that biochemical parameters are not helpful in classifying nephrotic syndrome & in differentiating between MCD & MGN, which is the sole responsibility of renal biopsy and H/P study.

Keywords: MCD, MGN, Nephrotic syndrome.

INTRODUCTION

Nephrotic syndrome is one of the best known presentations of adult or pediatric kidney diseases. The disease has an incidence of 3 new cases per 1,00,000 each year in adults[1]. NS can be caused by either primary (idiopathic) or secondary causes. Diagnostic criteria for Nephrotic syndrome.[1]

1. Proteinuria greater than 3.0-3.5 gm/24 hours or spot urine protein : creatinine ratio>300-350mg/mmol
2. Hypoalbuminemia<25g/l
3. Clinical evidence of peripheral edema
4. Hypercholesterolemia

This rigid criterion as used conventionally has been discarded by many authors and association of hematuria, azotemia and hypertension has now been also taken into consideration for diagnosis of Nephrotic syndrome.[1] Renal biopsy study has now become indispensable not only for diagnosis of specific renal lesions but also for the adequate therapeutic management and prognosis of the cases. Keeping these facts in mind, an attempt has been made to study the importance of clinical and biochemical parameters as compared to histopathology by renal biopsy in finding the specific cause of Nephrotic syndrome in this part of the country.

MATERIALS AND METHODS

Ethical clearance was taken from the Institutional Ethics Committee for this study. Patients admitted to the Nephrology department of KIMS, BBSR, with a clinical diagnosis of nephrotic syndrome were subjected to renal biopsy after taking proper consent. A provisional diagnosis was given with the help of light microscopic and Immunoflourescence study. Patients with Minimal change disease and membranous glomerulopathy on renal biopsy were included in this study. Total of 50 cases were included (MCD=28 cases, MGN=22 cases). Special stains like PAS (Periodic acid Schiff) and JMS (Jones methenamine silver) was done to arrive at a final histologic diagnosis. Biochemical investigations done on these patients included 24 hour urine protein estimation, serum albumin, serum cholesterol, serum creatinine and blood urea. These biochemical parameters were then analysed in a correlation matrix to find out the correlating and statistically significant parameters in nephrotic syndrome as a whole. Subsequently an attempt was made to find the significance of these parameters in differentiating between the groups of MCD and MGN, which were already been segregated on the basis of renal biopsy, so as to compare the usefulness of renal biopsy and H/P study with that of important biochemical parameters.

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RESULTS

Age range affected was 4-73 years with most of the cases in the age group of 21-40 years (42%). The mean age was 31.74 years. Males are affected more than females with a male to female ratio of 2.3: 1. 28 cases were of MCD (56%) and 22 cases were of MGN (44%). [Table No.1]

Table No.1

AGE	MCD			MGN		
	M	F	T	M	F	T
0-20	12	3	15	0	0	0
21-40	4	5	9	8	4	12
41-60	3	1	4	5	2	7
61-80	0	0	0	3	0	3
TOTAL	19	9	28	16	6	22
M:F	2.1:1			2.6:1		

Immunoflourescence was done in 42 cases out of 50(23 cases of MCD & 19 cases of MGN). In all the cases of MCD, the renal biopsy was normal light microscopically (Figure 1) and Immunoflourescence did not reveal any immune deposits, whereas in MGN cases light microscopically, the glomeruli were normocellular with uniform thickening of the GBM as was evident on H/E & PAS stain (Figure 2) & presence of spike and dome pattern was demonstrated by JMS stain. On Immunofluorescence, 19 cases showed granular GBM deposits for IgG (Figure 3) & C3, 3 cases were showed IgM deposits, 2 cases showed weak positivity for IgA & 3 cases had weak immunofluoresecnce for C1q.

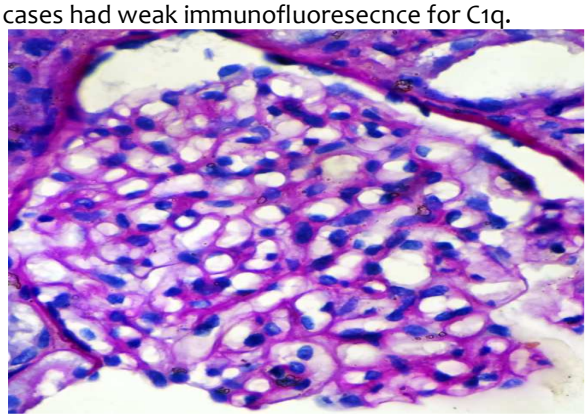

Figure.1: Normal appearing glomeruli of MCD (PAS stain-400X)

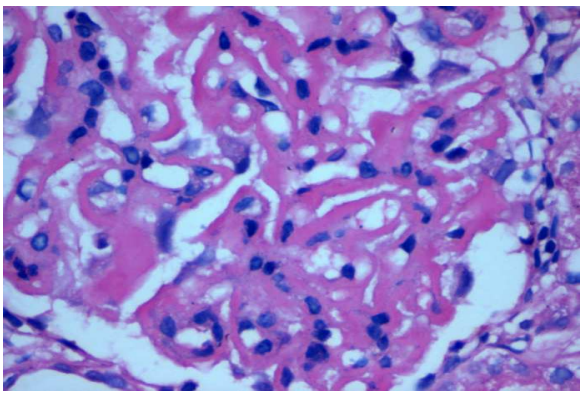

Figure.2: Uniform GBM thickening (H/E-400X)

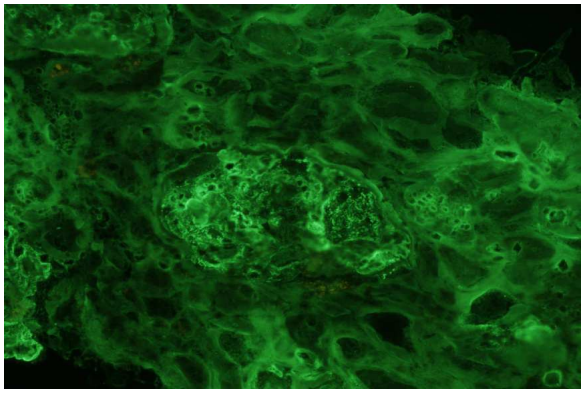

Figure. 3: Immunoflourescence for IgG

All cases presented with Proteinuria, with a mean value of 6.17 gm/24 hr. Maximum cases (76%) had Proteinuria in the range of 3.5-7.4 gm/24 hr [Figure 4]. Variable amount of serum albumin was observed, range being 0.8-3.3gm/dl and the mean value was 2.13gm/dl [Figure 5]. Most patients (70%) had serum albumin ≤ 2.5gm/dl.

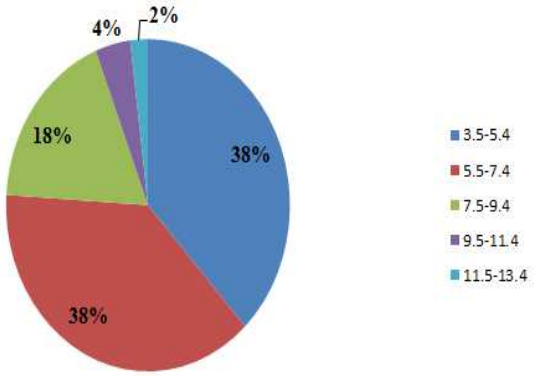

Figure.4: 24 hour urine protein estimation (gm/day)

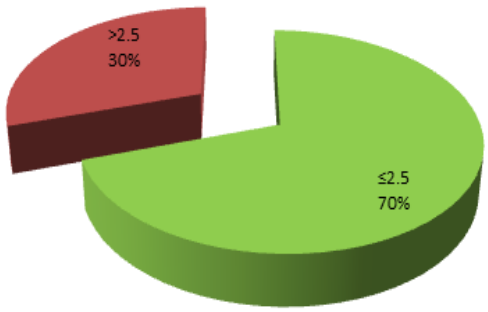

Figure.5: Serum albumin distribution (gm/dl)

Serum cholesterol was in normal range only in one patient and rest of the cases had hypercholesterolemia of varying portions. Most of the cases (60%) were clustered in the serum cholesterol range of 200-400mg/dl (Figure 6). Blood urea and serum creatinine was found in normal range in 16% and 10% cases respectively.

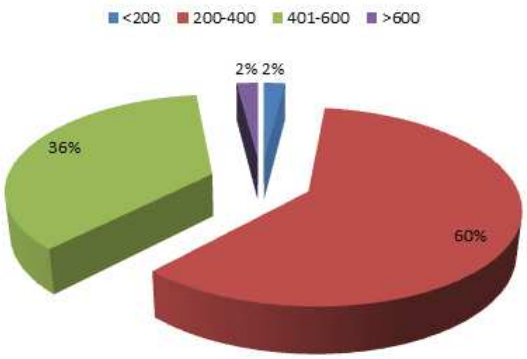

Figure.6: Serum cholesterol distribution (mg/dl)

Table.2:

H/P Type	No. Of Cases	24 Hour Urine Protein		Serum Albumin		Serum Cholesterol		Serum Creatinine		Blood Urea	
		Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
MCD	28	3.6-11.9	5.9 ± 2.4	0.8-3.3	2.3 ± 0.8	162-552	326.7 ± 116.3	1-3.5	1.96 ± 0.80	23-73	50.6 ± 13.7
MGN	22	4.6-10.4	6.4 ± 1.2	1.4-2.6	1.9 ± 0.33	250-620	422.5 ± 101.7	1.3-4.6	2.84 ± 0.95	46-88	67 ± 12.4

Correlation studies done in the two groups of MCD & MGN, showed strong negative correlation in between 24 hr urine protein & serum albumin; serum cholesterol and serum albumin; serum creatinine & serum albumin. Strong positive correlation was found between serum cholesterol and serum creatinine and in between serum creatinine and urea (Table no.3 & 4).

Table.3: Correlation matrix in minimal change disease

	Age	Sys BP	Dias BP	24 HR PR	Hb	Ser alb	Ser Chol	Ser Cr	Bld urea
Age									
Sys BP	0.06								
Dias BP	0.079	0.84							
24 HR PR	-0.002	0.002	0.132						
Hb	-0.145	0.229	0.343	-0.308					
Ser alb	0.05	0.032	-0.082	-0.948	0.347				
Ser chol	-0.156	-0.026	0.158	0.786	-0.044	-0.833			
Ser Cr	0.026	0.021	0.171	0.884	-0.238	-0.891	0.867		
Bld urea	-0.157	-0.144	-0.049	0.682	-0.157	-0.707	0.776	0.818	

r= 0.6-0.8 (moderate correlation), r >0.8 (strong correlation)

Table.4: Correlation matrix in membranous glomerulopathy

	Age	Sys BP	Dias BP	24 HR PR	Hb	Ser alb	Ser chol	Ser Cr	Bld urea
Age									
Sys BP	0.673								
Dias BP	0.431	0.862							
24 HR PR	0.123	-0.223	-0.268						
Hb	-0.268	-0.026	0.178	0.051					
Ser alb	0.337	0.616	0.586	-0.722	-0.227				
Ser chol	-0.177	-0.46	-0.437	0.77	0.099	-0.662			
Ser Cr	-0.208	-0.498	-0.468	0.688	0.091	-0.646	0.919		
Bld urea	-0.243	-0.471	-0.478	0.632	0.103	-0.683	0.855	0.953	

r= 0.6-0.8 (moderate correlation), r >0.8 (strong correlation)

An attempt was made to see the importance of these above parameters in distinguishing among the groups of MCD & MGN but none were found to be statistically significant in classifying NS and finding the specific cause for the same (Table no.5).

Table.5:

Value	24 hr Ur pr	Ser albumin	Ser chol	Ser Creat	Blood urea
t value	0.45	0.04	0.003	4.38	3.53
p value	0.65	0.97	0.99	<0.0001*	0.0009*

*P value: <0.05 (significant)

In this study serum creatinine & blood urea showed significant levels, as because most of the cases in our study presented in renal failure. These parameters are not the defining features of nephrotic syndrome but they predict the progression of renal failure.

DISCUSSION

Histopathological diagnosis after the use of renal biopsy changed the mode of clinical management of NS cases. Apart from histopathological evaluation, the modern sophisticated methods in immunology like Immunoflourescence, Immunoperoxidase and over all Electron microscopy have added precision to the etiology and pathogenesis of NS. However in words of Forland (1969)[2] "This increasing sophistication doesn't necessarily indicate a better concept of etiology or pathogenesis. It often provides important guidelines in regards to therapy and prognosis."

In this study almost all patients (except one) had hypercholesterolemia. Hypercholesterolemia was seen maximum in the range of 200-400 gm/dl. The degree of Proteinuria in NS patients depends on the underlying cause, the stage and duration of the disease process and the amount of activities of the patients. The mean Proteinuria levels were higher in MGN group. These datas were similar with other studies[3,4]. The serum albumin levels in most of the patients were less than 2.5gm/dl. Similar results have been observed in other studies on nephrotic syndrome.[5] However the serum creatinine levels of patients in our study was higher than other similar studies[4]. The higher mean value may be due to the fact that it was conducted in a tertiary care hospital where the patients usually present at a later stage. Our patients showed a strong positive correlation between degree of Proteinuria and the serum cholesterol values. Serum albumin levels also were found to be negatively strongly correlating with serum cholesterol and 24 hour urine protein. A similar finding was also obtained by some western workers[5-8] and in one Indian study.[9] But when tried to differentiate between MCD and MGN by applying the unpaired 't' test, these parameters were found to be of no value. Despite wide acceptance of these clinical impressions, their validity has not been critically assessed. Several studies have suggested that predictions of glomerular histology from clinical and laboratory characteristics may be less accurate than generally held. Similar results have been obtained in our study, which shows that no clinical or biochemical parameters are statistically significant in predicting the glomerular histology. Our observations support the view that renal biopsy is mandatory in patients of NS.

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