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Histological Spectrum of Adult Onset Nephrotic Syndrome in a Tertiary Care Referral Center

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Abstract
Introduction: *Nephrotic syndrome is one of the most common indication f renal biopsy all over the world. There are very few studies on histopathological spectrum of adult onset nephrotic syndrome in Eastern India. In this present study, we have found increase in incidence of minimal change disease (MCD) in younger adults in Eastern India.*
Objectives: *The aim of the present study is to find out the histopathological spectrum of adult onset nephrotic syndrome in our institute which is the largest tertiary care referral center in Eastern India.*
Materials and method: *After obtaining ethical clearance and written consent from the patient adult patient > 18 years attended in the department of nephrology with proteinuria and fulfilling the criteria for nephrotic syndrome underwent renal biopsy over a period of 18 months. Histopathological finding was correlated with immunofluorescence (IF)finding and clinicopathological correlation done.*
.***Result:*** *Total 47 cases were tested in the study, of which MCD was the most common histologicalpattern and most common on 18-29 years of age group. Other common patterns were IgA nephropathy (IgAN), membranous glomerulonephritis (MGN) and focal segmental glomerulosclerosis (FSGS).Lupus nephritis (LN) was found to be the most common cause of secondaryglomerulonephritis (GN).*
Conclusion: *In present study, MCD was found to be the most common cause in Eastern regionespecially in younger age group. Membranous GN was found to be associated with highest range of proteinuria. Renal biopsy was found to be an essential tool in early diagnosis and interpretation of renal diseases.*

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I. Introduction

Nephrotic syndrome is one of the most common indication of renal biopsy all over the world. Nephrotic syndrome was defined as proteinuria > 3.5 gm /day, hypoalbuminemia, hyperlipidemia and edema. The histopathological spectrum of adult onset nephrotic syndrome (AONS) and their correlation with age and sex was studied. Evolution of biopsy needle and improved radiological technique ensure good biopsy material and lesser complication related to the procedure in recent days. Worldwide as well as in India the incidence of focal segmental Glomerulosclerosis (FSGS) has increased and the incidence of MCD has decreased. [1,2,3,4] There are very few studies on histopathological spectrum of adult onset nephrotic syndrome in Eastern India. In present study, we have found increase in incidence of MCD in younger adults.

II. Objectives

The aim of the present study was to find out the histopathological spectrum of adult onset nephrotic syndrome in our institution which is a tertiary care referral center and the largest one in eastern region.

III. Materials and method

After obtaining ethical clearance and written consent from the patient the study was conducted in the department of Pathology in collaboration with department of Nephrology of our institution. The study population included all the adult patient (> 18 years) attended in the department of nephrology and with proteinuria and underwent renal biopsy from January 2017 to June 2018. Proteinuria was defined as urinary

protein excretion > 3.5 g/dl/1.73m2 body surface area per day. All the patients were tested for blood sugar, lipid profile, coagulation profile, serum C3 and C4, HIV, HCV, HBV, cANCA, pANCA, ANA and AntidsDNA, serum albumin, urinary 24 hour protein, serum urea and creatinine , urine analysis for routine examination etc.
Renal biopsy was performed in the department of Nephrology. Biopsy was collected using automatic spring loaded gun under local anesthesia and under Ultrasonic guidance. Two cores were collected, one was fixed in formalin solution and sections were stained with Hematoxylin and Eosin, Periodic acid schiff, Methanamine silver and Masson Trichrome in the department of Pathology. The other core was transported with Michel media and stained with fluorescein isothiocyanate (FITC) conjugated antibodies against IgG, IgM, IgA, C3,C1q and kappa and lambda light chains and direct immunofluorescence study was done.
Two experienced Pathologists examined all the slides. Histopathological finding was correlated with IF finding and clinicopathological correlation was done.

Statistical analysis: For statistical analysis Graph pad prism5 was used. The Kruscal-Wallis test was performed for comparisons between multiple groups. The X2 test was analyzed for categorical evaluation. Correlations were evaluated using Spearman's rank correlation. $p<0.05$ was considered as significant.

IV. Result

Total 47 cases were tested in the study, of which MCD was the most common histological pattern (18 out of 47 cases) constituting 38.29 %, IgA nephropathy was found IN 21.29% of cases, Membranous GN in 14.89% of cases and FSGS in 8.53% of cases. Lupus nephritis (LN) was found to be the most common cause of secondary GN. LN was found in 5out of 47case (10.63%). Diabetic nephropathy affected only two patients in present study. LN showed female preponderance (M: F 4:1). DGGS affected in 2.21% of cases. In present study on AONS, 24 cases were female and 23 cases were male. Primary GN (PGN) was found to the most common cause of AONS. 40 cases belonged to PGN and 7 cases were SGN (85.12% vs 14.88% respectively). [Shown in Table 1]

Table 1: Histopathological spectrum of AONS

Primary GN		Secondary GN	
HP PATTERN(n=40)	No. of cases(%)	HP PATTERN(n=7)	No. of cases(%)
Minimal change disease (n=18)	38.29	Lupus Nephritis(n=5)	10.63
IgA Nephropathy(n=10)	21.27	Diabetic Nephropathy(n=2)	4.25
Membranous(n+=7)	14.89		
Focal segmentaGN(n=4)	8.53		
Diffuse global glomerulosclerosis(n=1)	2.21		

Mean age of all the cases was 34±18.91 years [Table 2]. Twelve out of 18 cases of MCD were in age group of 18-29 years, 4 in 30 to less than 60 years and only 2 were ≥60 years of age group. All the LN cases were in 18-29 years of age group. Four out of five cases of FSGS were in 18-29 years of age group. Single case belonged to≥60 years of age group. Six IgA nephropathy cases were in 18-29 years of age group, three in 30 to < 60 years of age group and none belonged to ≥ 60 years. Out of seven MGN cases, one belonged to 18-29 years of age, three cases belonged to 30 to less than 60 years of age group and three in ≥ 60 years of age group. Two diabetic nephropathy (DN) cases were >60years of age, both were male.

Table2: Age wise distribution of GN

Type of GN	0-29 YEARS	30 < 60YEARS	≥60 YEARS
MCD	12	4	2
IgA	6	3	
MGN	1	3	3
FSGS	3		1
DGGS	1		
MESANGIOPROLIFERATIVE GN		1	
LN	5		
DN			2

In comparing the different patterns in renal biopsies, we have found that membranous glomerulopathy has the highest proteinuria (7.285±4.892 g/dl), although no statistically significant correlation noted (p value <0.40) amongst the histologic pattern and the level of proteinuria.[Table 3]

Table 3: Level of proteinuria in different histological patterns

IgA NEPHROPATHY	FOCAL SEGMENTAL GN	MEMBRANOUS GN	DIABETIC NEPHROPATHY	LN	MINIMAL CHANGE DISEASE	DIFFUSE GLOBAL GLOMERULOSCLEROSIS
6.63	5.05	7.285	5.4	4.66	4.69	3.7
3.067	1.489	4.892	2.46	1.718	1.718	1
10	4	1	2	5	18	1
0.9700	0.7444	1.849	1.800	0.7685	0.3333	0.000
4.436	2.681	2.781	-17.471	2.527	3.991	3.700
8.824	7.419	11.811	28.271	6.793	5.398	3.700
2.600	3.700	3.600	3.600	3.600	3.600	3.700
5.900	4.800	4.700	5.400	3.900	3.900	3.700
12.100	6.900	17.400	7.200	7.700	7.800	3.700
0.2136		0.2728		0.3830	0.2994	
>0.10	Too few values	>0.10	Too few values	0.0157	0.0002	Too few values
Yes		Yes		No	No	

V. Discussion

In this study on 47 cases of AONS, mean age of presentation was 34±18.91 years ranging from 18 years to 79 years. PGN was the most common among all causes of GN which is corroborated with all other studies worldwide. Almost equal sex distribution in present study differs from other studies. Balakrishnan et al found male preponderance except in SLE and cortical necrosis in renal biopsy. [1] Garade CB et al found no sex predilection in their study. In our present study most common histological pattern encountered was MCD (38.29%). Golay et al found the incidence of MCD in 23.5% of cases in a previous study conducted in this institute. Most of the cases of MCD (66.66%) belonged to 18-29 years of cases which is corroborated with Golay study.[5] Zhou F.D. et al found higher incidence of MCD in younger age group. Only 11.1% of MCD belonged to more than 60 years of age group indicating decrease in incidence of MCD with increase in age, probably due to more severe renal involvement with increasing age.[6] Increased incidence in MCD found in present study could be due to increased incidence of MCD in Asian population. However, Kazi et al found lesser number of MCD cases in their study in Pakistan. Next common HP pattern was IgAN (21.29 %). Golay et al found 7.32% in their study in this institution. [5] This lower trend of IgAN was reported in various studies in Indian subcontinent.[7,8,9] Membranous GN (MGN) wasfound in 14.89% and FSGS in 8.53% cases. Romanian data showed incidence of FSGS in 12.1% of cases. The variation in finding may be due to sampling problem in our study. Renal involvement is an important and dreaded complication of SLE. In our study 10.63% of cases of AONS were found to be of LN. Female preponderance in LN was corroborated with other many studies from all over the world. [10,11] All the LN showed full house positivity in IF. This findings were corroborated with a study conducted on SLE patients in our institution.[12] Although no statistically significant correlation was found in HP pattern and range of proteinuria membranous GN was found to be associated with highest range of proteinuria.

VI. Conclusion

In present study, MCD was found to be the most common cause of non-neoplastic renal diseases in Eastern India. MCD was the most commonly occurred histologic pattern in younger age group. Other common histologic patterns found in this study were IgA nephropathy, membranous glomerulonephritis and Focal segmental glomerulonephritis. MGN was found to be associated with highest range of proteinuria. Renal biopsy is an essential tool in interpretation of renal diseases as diagnosis cannot be made solely based on clinical parameters and early diagnosis may prevent progress of many renal diseases.

Limitation of present study

limitation of our present study was we could not use electron microscope and our sample size was limited.

Conflict of interest: There was no conflict of interest.

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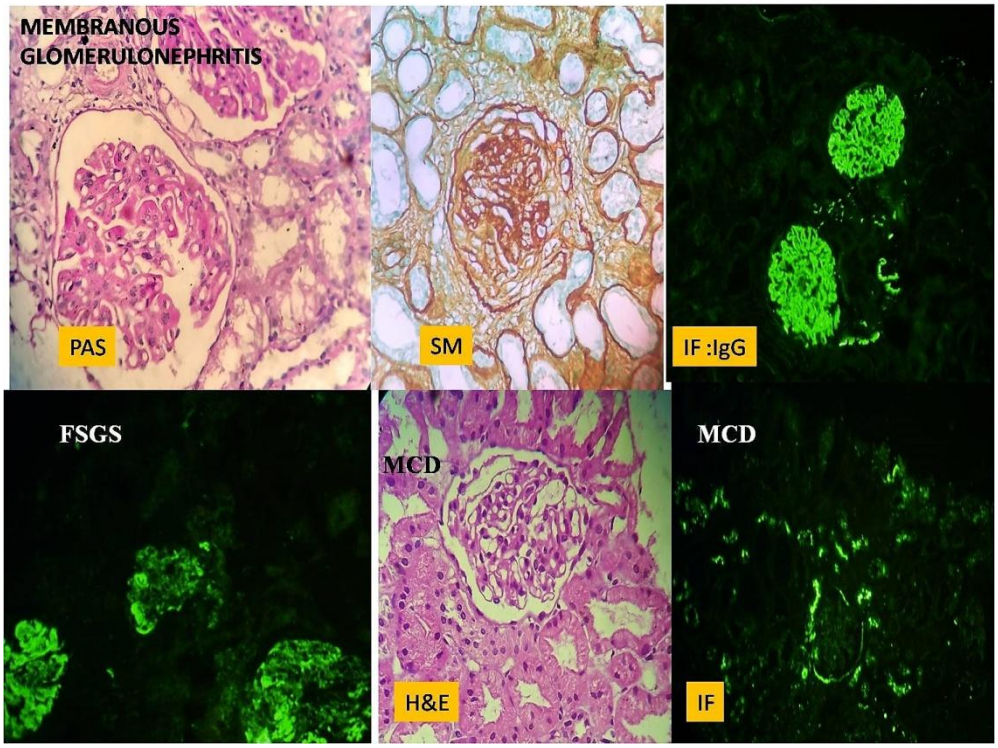

Figure 1:
Upper left: Membranous glomerulopathy in H&E (×400)
Upper middle: Membranous glomerulopathy in SM (×400)
Upper right: Membranous glomerulopathy in IF for IgG (×100)
Lower left: Focal segmental glomerulosclerosis in IF for Ig M (×100)
Lower middle: Minimal change disease in H&E (×400)
Lower right: Minimal change disease in IF for Ig G (×100)

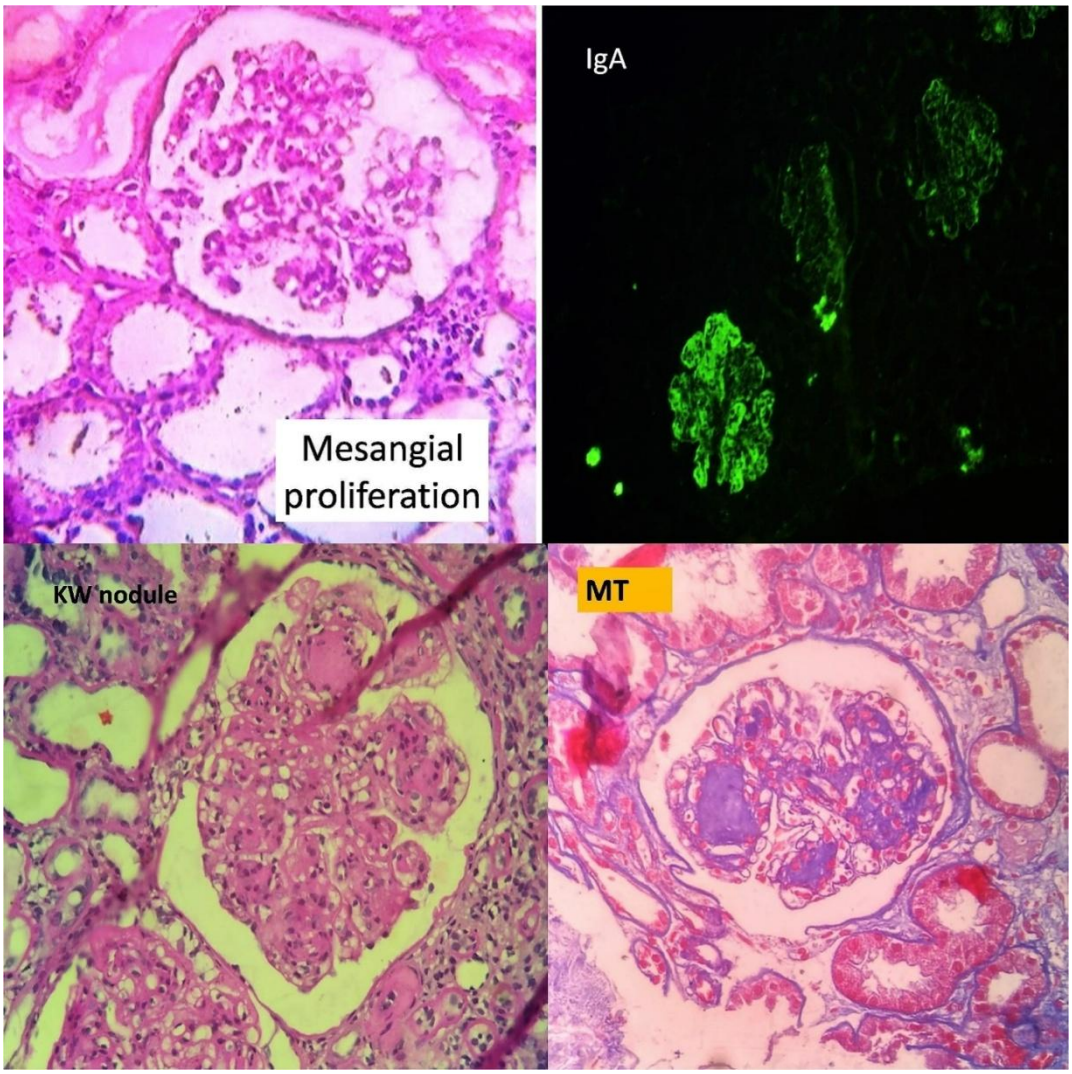

Figure 2:
Upper left: IgA nephropathy in H&E (×400)
Upper right: IgA nephropathy in IF for IgA (×100)
Lower left: Diabetic nephropathy, K W nodules in PAS (×400)
Lower right: Diabetic nephropathy, K W nodules in MT (×400)

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