

# Clinicopathological Analysis of Glomerular Disease of Adult Onset Nephrotic Syndrome in an Indian Cohort- A Retrospective Study

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## ABSTRACT

**Introduction:** Primary glomerular disease presenting with adult onset nephrotic syndrome are a major cause of chronic renal failure worldwide. The spectrum of renal disease presenting with nephrotic syndrome has undergone a gradual change globally over the course of time. However, there still exist regional differences in the incidence of primary glomerular diseases causing adult onset nephrotic syndrome.

**Aim:** To observe the spectrum of renal diseases presenting with adult onset nephrotic syndrome with comparative analysis of changing trends over the last five decades with regards to Western and Indian literature.

**Materials and Methods:** Subjects included patients with age of 18-80 years presenting with nephrotic syndrome. Renal biopsies with immunofluorescence studies were performed in all patients. Baseline clinical parameters of serum urea, creatinine, albumin, globulin, cholesterol, 24 hour urine protein and urine microscopy were recorded. Descriptive statistics was used and results were expressed as frequencies, percentages, and mean±standard deviation.

**Results:** A total of 227 patients (72% males) were included for the study. Primary glomerular diseases formed 74.01% of total cases and majority of patients included males in the 4<sup>th</sup> decade. Minimal Change Disease (MCD) (15.8%) including its variants was the most common primary glomerular disease for adult onset of nephrotic syndrome followed by Mesangial proliferative Glomerulonephritis (MSGN) (13.2%). Membranous nephropathy and Type I Membranoproliferative Glomerulonephritis (MPGN) individually accounted for 12.3% of patients. Focal and Segmental Glomerulosclerosis (FSGS) accounted for only 11% of patients. Although, increased incidence of FSGS has been observed worldwide, there exist important regional differences in primary glomerular diseases in Indian population. MCD remains a major glomerular disease for adult onset nephrotic syndrome in different parts of India.

**Conclusion:** Our study over three years represents important data of regional variations of primary glomerular diseases presenting with adult onset nephrotic syndrome.

**Keywords:** Focal segmental glomerulosclerosis, Mesangioproliferative glomerulonephritis, Minimal change disease

## INTRODUCTION

Adult onset nephrotic syndrome is one of the most common presentations of primary glomerular diseases worldwide today. The salient features are proteinuria (> 3.5 gm/24 hours), hypoalbuminemia (< 2.5 gm/dL) hypercholesterolemia, oedema and hypertension [1]. The predominant glomerular diseases giving rise to adult onset nephrotic syndrome have been listed worldwide as Membranous Nephropathy (MN) [1,2], MCD [1], FSGS [1-4], MSGN [1] and MPGN [1]. Lupus nephritis [1-4]. Diabetes Mellitus [1-3] and Amyloidosis [1] are among the common systemic diseases which have been also found to be associated with nephrotic syndrome.

The renal biopsy is an invaluable method in evaluation of patients with renal disease. This procedure helps us to establish an accurate diagnosis, obtain critical information on the evaluation of prognosis of disease process and in developing a rational approach to the treatment of renal disorder [3].

MN has been reported as the most common cause of adult onset nephrotic syndrome in European and North American population [1]. However, recent studies have found the incidence of FSGS to be gradually increasing worldwide [4-7]. Limited Indian studies on spectrum of glomerular disease causing adult onset nephrotic syndrome exist till date. Among the Indian studies, MN [8] and MCD [9] have been found to be predominant primary glomerular disease although an increasing trend of FSGS has been recently observed [10-12]. MCD has been found in a few studies to be the most common overall cause of nephrotic syndrome [11,13].

The present study aimed to analyse the spectrum of glomerular diseases presenting with adult onset nephrotic syndrome in our centre over a period of three years.

## MATERIALS AND METHODS

This retrospective study was carried out at Ruby Hall Clinic, which is a tertiary referral centre in Pune. Adequate renal biopsies of 227 patients were analysed over a period three years from January 2007 to December 2010. Patients included for the study were between 18 to 80 years of age and presented with nephrotic syndrome. Renal biopsies with more than five glomeruli were considered adequate. Nephrotic range proteinuria was defined as proteinuria >3.5 g/1.73 m<sup>2</sup> body surface area/day or >50 mg/kg/day. Patients <18 years of age, inadequate biopsies, allograft biopsies and incomplete immunofluorescence data or clinical parameters were excluded from the study. All baseline clinical parameters of serum urea, serum creatinine, 24 hour urine protein, serum albumin, serum globulin, serum cholesterol and urine microscopy were recorded.

Following local anaesthesia, the renal biopsy was performed under ultrasound guidance using a 14 G Trucut biopsy gun. The biopsy material included a single core which was subjected to histopathological and Immunofluorescence (IF) examination. Three micron sections were cut and stained with Haematoxylin and Eosin, Periodic Schiff reagent, Masson Trichrome and Jones methenamine silver for light microscopy. Additional special stains (Martius scarlet blue for fibrin) were done as and when required. IF examination was done by direct method using fluorescein isothiocyanate conjugated antibodies against immunoglobulins G, A and M and complement C3 (DAKO). IF was graded (0-3+) based on intensity of staining. The renal biopsies were analysed by two pathologists.

Due to lack of financial resources, electron microscopic examination of renal biopsies could not be carried out in this study.

All the procedures were followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional) and with the revised Helsinki Declaration of 2000.

### STATISTICAL ANALYSIS

The data was entered using Microsoft excel sheet. Descriptive statistics was used and results were expressed as frequencies, percentages, and mean±standard deviation.

### RESULTS

A total of 227 adequate renal biopsies were analysed over a period three years from January 2007 to December 2010. Subjects included 164 (72%) males and 63 (28%) females with 63/227 (27.8%) of patients present in the 4<sup>th</sup> decade [Table/Fig-1]. Our study cohort included 36 MCD [Table/Fig-2a-c] including its variants (21 mild mesangial hypercellularity and nine diffuse mesangial hypercellularity), 30 MSGN, two FSGS [Table/Fig-3a-c], 21 IgA nephropathy, 28 MPGN (Type I), 28 MN [Table/Fig-4a-d], 19 lupus nephritis, 22 diabetic glomerulosclerosis [Table/Fig-5a-c], eight amyloidosis and 10 hypertensive nephrosclerosis.

**Morphological spectrum of glomerular lesions with age and sex distribution:** MCD and its variants i.e., mild mesangial hypercellularity and diffuse mesangial hypercellularity, 36/227 (15.9 %) was the commonest cause of adult onset nephrotic syndrome followed by MN, 28/227 (12.3%) and MPGN (Type I) 28/227 [Table/Fig-6].

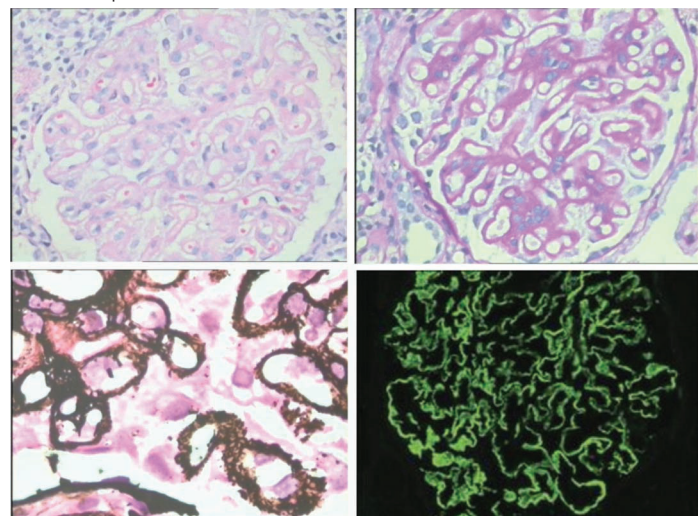
Age group	Number (%)
< 20	18 (7.9)
21-30	58 (25.6)
31-40	63 (27.8)
41-50	46 (20.3)
51-60	28 (12.3)
61-70	11 (4.8)
> 70	3 (1.3)
Total	227

[Table/Fig-1]: Age distribution in study population.

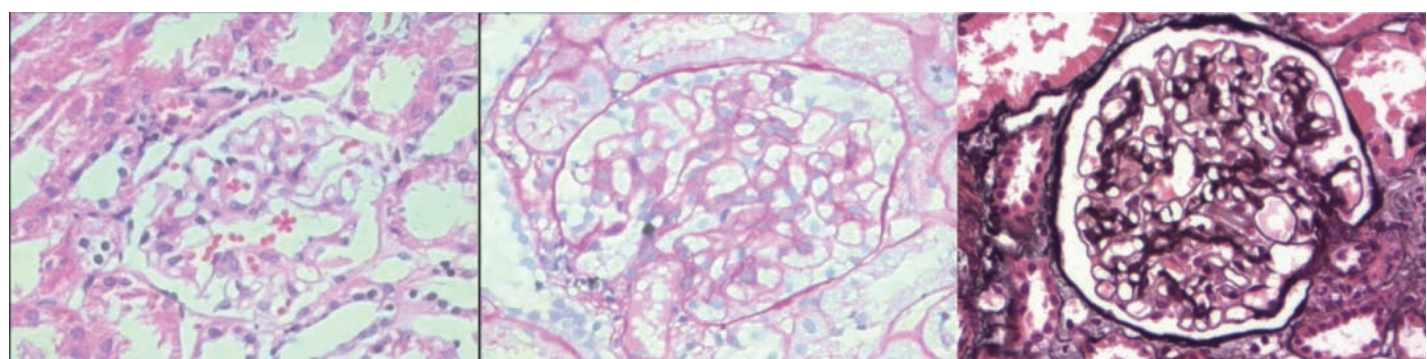
Minimal change disease and its variants were seen most frequently in female subjects 28/36 (77.8%) and in the 4<sup>th</sup> decade, 10/36 (27.8%). Membranous nephropathy was commonly seen in the 4<sup>th</sup> decade, 8/28 (28.6%) whereas, MPGN (Type I) was seen more frequently in 3<sup>rd</sup> decade, 8/28 cases (28.6%).

**Serum Creatinine:** A total of 68/227 (29.86%) patients presented with abnormal creatinine levels among which 7/10 (70%) patients with hypertensive nephrosclerosis showed abnormal creatinine levels more than 1.8 mg% [Table/Fig-7]. A total of 45/227 (i.e., 19.83 %) showed raised blood urea level.

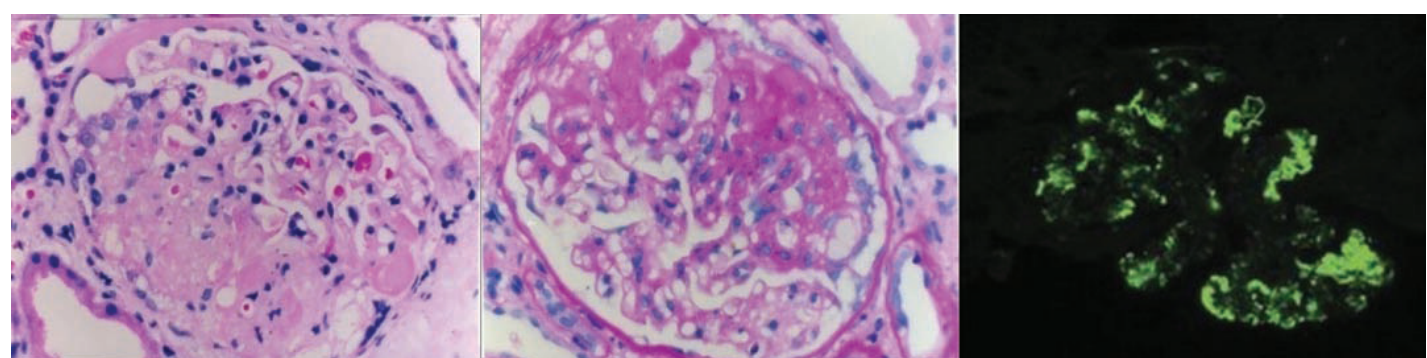
**Serum and urinary protein examination:** A total of 211/227 (92.9%) patients had total protein < 6.0 gm/dl. Only a single case of hypertensive nephrosclerosis had protein levels < 3.0 gm/dl [Table/Fig-8]. 12/28 (42.9%) patients and 6/28 (21.4%) patients with a diagnosis of MN showed proteinuria of 5 gm-8 gm and >8 gm in 24 hours respectively. 20/30 (66.7%) patients with MSGN showed pus cells in urine and 14/30 (46.7%) patients with MSGN presented macroscopic haematuria.



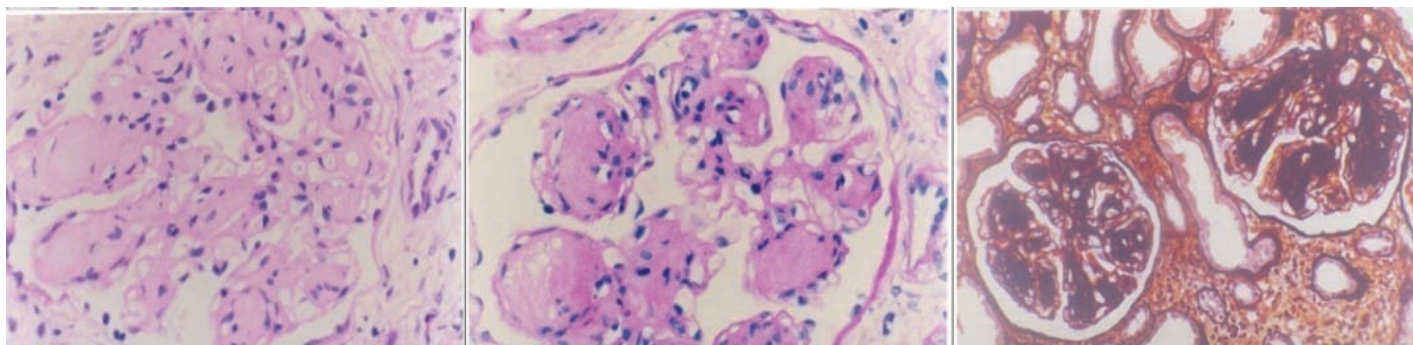
[Table/Fig-4]: Membranous nephropathy- Light microscopy shows thickening of the capillary basement membrane: (a) H&E (20X); (b) PAS (20X); (c) Jones methenamine silver shows presence of epimembranous spikes (20X); (d) Immunofluorescence reveals finely granular contiguous deposits of IgG along capillary walls (20X). (All images left to right)



[Table/Fig-2]: Minimal change disease; glomeruli and tubules showing no lesions on light microscopy (20X): (a) H&E (20X); (b) PAS (20X); (c) Jones methenamine silver. (All images left to right)



[Table/Fig-3]: Focal and segmental glomerulosclerosis: Light microscopy shows segments of sclerosis in glomerular tufts: (a) H&E (20X); (b) PAS (20X); (c) Immunofluorescence shows IgM deposits in sclerotic tufts (20X). (All images left to right)



**[Table/Fig-5]:** Diabetic nephropathy- light microscopy shows nodular diabetic glomerulosclerosis: (a) H&E (20X); (b) PAS (20X); (c) Jones methenamine silver (20X). (All images left to right)

Diagnosis	Age (Yrs) (N) (%)								Sex (N) (%)	
	< 20	21-30	31-40	41-50	51-60	61-70	>70	Total	M	F
1a. Minimal change disease	0	0	2 (33.3)	4 (66.6)	0	0	0	6	2 (33.3)	4 (66.6)
1b. Mild mesangial hypercellularity	7 (33.3)	4 (19.1)	6 (28.6)	3 (14.3)	1 (4.76)	0	0	21	4 (19.1)	17 (80.9)
1c. Diffuse mesangial hypercellularity	1 (11.1)	4 (44.4)	2 (22.2)	1 (11.1)	0	1 (11.1)	0	9	2 (22.2)	7 (77.8)
2. Mesangioproliferative GN	3 (10)	14 (46.7)	9 (30)	1 (3.33)	3 (10)	0	0	30	12 (40)	18 (60)
3. Focal segmental glomerulosclerosis	2 (8)	3 (12)	8 (32)	7 (28)	2 (8)	2 (8)	1 (4)	25	6 (24)	19 (76)
4. IgA nephropathy	0	9 (42.9)	7 (33.3)	5 (23.8)	0	0	0	21	2 (9.5)	19 (90.5)
5. Membranoproliferative GN	3 (10.7)	8 (28.6)	6 (21.4)	7 (25)	2 (7.14)	2 (7.14)	0	28	6 (21.4)	22 (78.6)
6. Membranous nephropathy	0	5 (17.9)	8 (28.6)	7 (25)	6 (21.4)	2 (7.14)	0	28	8 (28.6)	20 (71.4)
7. Lupus nephritis	2 (10.5)	6 (31.6)	7 (36.8)	3 (15.8)	1 (5.26)	0	0	19	14 (73.7)	5 (26.3)
8. Diabetes glomerulosclerosis	0	0	5 (22.7)	5 (22.7)	7 (31.8)	4 (18.2)	1 (4.55)	22	3 (13.6)	19 (86.4)
9. Amyloidosis	0	1 (12.5)	1 (12.5)	1 (12.5)	4 (50)	0	1 (12.5)	8	2 (25)	6 (75)
10. Hypertensive nephrosclerosis	0	4 (40)	2 (20)	2 (20)	2 (20)	0	0	10	2 (20)	8 (80)

**[Table/Fig-6]:** Morphological lesions and their age and sex distribution.

Diagnosis	Serum creatinine					Total
	0.3-0.7	0.8-1.2	1.3-1.7	1.8-2.2	>2.2	
1a. Minimal change disease	0	6 (100%)	0	0	0	6
1b. Mild mesangial hypercellularity	1 (4.8%)	16 (76.2%)	0	2 (9.5%)	2 (9.5%)	21
1c. Diffuse mesangial hypercellularity	0	7 (77.8%)	0	0	2 (22.2%)	9
2. Mesangioproliferative GN	1 (3.3%)	22 (73.3%)	0	0	7 (23.3%)	30
3. Focal segmental glomerulosclerosis	0	15 (60%)	0	2 (8%)	8 (32%)	25
4. IgA nephropathy	0	11 (52.4%)	0	2 (9.5%)	8 (38.1%)	21
5. Membranoproliferative GN	0	21 (75%)	1 (3.6%)	1 (3.6%)	5 (17.9%)	28
6. Membranous nephropathy	0	25 (89.3%)	0	1 (3.6%)	2 (7.1%)	28
7. Lupus nephritis	0	14 (73.7%)	0	1 (5.3%)	4 (21%)	19
8. Diabetes glomerulosclerosis	0	10 (45.5%)	0	5 (22.7%)	7 (31.8%)	22
9. Amyloidosis	0	7 (87.5%)	0	1 (12.5%)	0	8
10. Hypertensive nephrosclerosis	0	3 (30%)	0	2 (20%)	5 (50%)	10

**[Table/Fig-7]:** Blood creatinine levels.

Diagnosis	Total	24 hour urinary protein (mg)(%)			Urine sugar	Urine microscopy (h/p/f)(%)		
		3.5-5	5-8	>8		Pus cells	RBCs	Casts
1a. Minimal change disease	6	2 (33.3)	4 (66.7)	0	0	5 (83.3)	0	0
1b. Mild mesangial hypercellularity	21	9 (42.9)	12 (57.1)	0	0	17 (80.9)	11 (52.4)	0
1c. Diffuse mesangial hypercellularity	9	3 (33.3)	4 (44.4)	2 (22.2)	0	5 (55.55)	6 (66.7)	0
2. Mesangioproliferative GN	30	16 (53.3)	9 (30)	5 (16.7)	0	20 (66.67)	14 (46.7)	0
3. Focal segmental glomerulosclerosis	25	10 (40)	11 (44)	4 (16)	0	15 (60)	5 (20)	0
4. IgA nephropathy	21	10 (47.6)	7 (33.3)	4 (19.05)	0	1 (4.76)	1 (4.76)	4 (19.1)
5. Membranoproliferative GN	28	12 (42.9)	11 (39.3)	5 (17.9)	0	17 (60.7)	26 (92.9)	0
6. Membranous nephropathy	28	10 (35.7)	12 (42.9)	6 (21.4)	0	1 (3.57)	2 (7.14)	0
7. Lupus nephritis	19	10 (52.6)	7 (36.8)	2 (10.5)	0	2 (10.5)	2 (10.5)	4 (21.1)
8. Diabetes glomerulosclerosis	22	12 (54.5)	9 (40.9)	1 (4.55)	19 (86.4)	17 (77.3)	5 (22.7)	6 (27.3)
9. Amyloidosis	8	3 (12)	4 (16)	1 (4)	0	0	0	0
10. Hypertensive nephrosclerosis	10	7 (70)	2 (20)	1 (10)	0	3 (30)	1 (10)	0

**[Table/Fig-8]:** Urinary findings in study population.

**Correlation with serum cholesterol:** Patients with Diabetic glomerulosclerosis, IgA nephropathy, lupus nephritis, hypertensive nephrosclerosis, minimal change disease and diffuse mesangial hypercellularity had raised serum cholesterol levels. A total of 66.7% of patients of MCD and its variant, diffuse mesangial hypercellularity had serum cholesterol 301-400 mg/dl. Among the systemic glomerular diseases, 90.9% of patients of diabetic glomerulosclerosis had 301-400 mg/dl of serum cholesterol [Table/Fig-9].

Diagnosis	Serum cholesterol level (mg/dl) (%)				Total
	101-200	201-300	301-400	401-500	
1a. Minimal change disease	0	0	4 (66.7)	2 (33.3)	6
1b. Mild mesangial hypercellularity	3 (14.3)	8 (38.1)	8 (38.1)	2 (9.5)	21
1c. Diffuse mesangial hypercellularity	1 (11.1)	2 (22.2)	6 (66.7)	0	9
2. Mesangioproliferative GN	26 (86.7)	4 (13.3)	0	0	30
3. Focal segmental glomerulosclerosis	13 (52)	11 (44)	1 (4)	0	25
4. IgA nephropathy	2 (9.5)	19 (90.5)	0	0	21
5. Membranoproliferative GN	20 (71.4)	1 (3.6)	7 (25)	0	28
6. Membranous nephropathy	13 (46.4)	15 (53.6)	0	0	28
7. Lupus nephritis	5 (26.3)	14 (73.7)	0	0	19
8. Diabetes glomerulosclerosis	0	2 (9.1)	20 (90.9)	0	22
9. Amyloidosis	7 (87.5)	1 (12.5)	0	0	8
10. Hypertensive nephrosclerosis	2 (20)	8 (80)	0	0	10

[Table/Fig-9]: Morphological lesions and serum cholesterol level in study group.

Diagnosis	Total	Immunofluorescence (%)			
		IgG	IgA	IgM	C3
1a. Minimal change disease	6	0	0	0	0
1b. Mild mesangial hypercellularity	21	0	0	5 (23.8)	0
1c. Diffuse mesangial hypercellularity	9	1 (11.1)	0	5 (55.55)	1 (11.11)
2. Mesangioproliferative GN	30	2 (6.67)	1 (3.33)	6 (20)	3 (10)
3. Focal segmental glomerulosclerosis	25	1 (4)	0	14 (56)	4 (16)
4. IgA nephropathy	21	6 (28.57)	21 (100)	9 (42.86)	7 (33.33)
5. Membranoproliferative GN	28	20 (71.43)	0	0	28 (100)
6. Membranous nephropathy	28	25 (89.29)	0	0	10 (35.71)
7. Lupus nephritis	19	19 (100)	19 (100)	19 (100)	19 (100)
8. Diabetes glomerulosclerosis	22	7 (31.82)	0	7 (31.82)	9 (40.91)
9. Amyloidosis	8	2 (8)	0	3 (12)	1 (4)
10. Hypertensive nephrosclerosis	10	2 (20)	6 (60)	2 (20)	3 (30)

[Table/Fig-10]: Immunofluorescence categorisation of glomerular diseases.

Authors	Sample size	Place	MPGN (Type I) (%)	Minimal change Disease (%)	Membranous nephropathy (%)	Mesangioproliferative GN (%)	FSGS
Gandra D and Chennamaneni B [7]	50	Telangana	7.3	17	24.4	12.1	17
Date A et al., [8]	1532	Vellore	13.9	35.8	13.6	4.5	18.6
Rathi M et al., [10]	364	Chandigarh	17.9	14.8	24.4	1.8	30.6
Das U et al., [11]	1615	Hyderabad	5.7	21.8	10.1	13.8	15.2
Golay B et al., [12]	410	Kolkata	6.6	27.1	24.6	8.1	27.4
Agarwal SK and Dash SC [13]	2250	Delhi	11.6	37	20	11.2	20
Aggarwal HK et al., [14]	2000	Rohtak	18.2	33.3	16.9	10	17.6
Present study	227	Pune	12.3	15.9	12.3	13.2	(11.01) 25 cases

[Table/Fig-11]: Comparison of glomerular lesions among nephrotic syndrome in adults in different Indian studies [7,8,10-14].

**Immunofluorescence categorisation of glomerular diseases:**

A total of 40 patients with MCD including its variants presented with a negative immunofluorescence (IF). Five cases of mild mesangial hypercellularity and diffuse mesangial hypercellularity respectively showed IgM(1+) [Table/Fig-10].

Among 30 patients of MSGN, 20/30 patients had a negative IF. Five patients had shown IgM (2+) positivity in the mesangium. Two patients had shown C3 (2+) deposits in the mesangium. Patient with lupus nephritis displayed the classical full house pattern of IgG, IgM, IgA and C3 with 2-3+ intensity.

**DISCUSSION**

The present study included adult patients attending the nephrology clinic with nephrotic syndrome as a presenting feature. The renal biopsy was carried out in 227 cases.

Although, nephrotic syndrome has multiple aetiologies, it is mostly due to intrinsic renal diseases [1,4,12]. In the present study, nephrotic syndrome due to primary glomerular diseases formed 74.01% of total cases. Nephrotic syndrome secondary to systemic diseases accounted for 25.99% cases. Among the array of systemic diseases, amyloidosis, lupus nephritis and diabetic glomerulosclerosis were encountered. The majority of patients were males present commonly in the 4<sup>th</sup> decade with nephrotic syndrome.

**Minimal change disease (MCD):** Our study shows MCD to be the predominant cause of adult onset nephrotic syndrome in the study population. It was reported in 36 (15.8%) cases of adult patients biopsied who presented as nephrotic syndrome in our study. Its incidence in literature has been reported to be from 11.2% to 40.1%.

Among Indian studies by Date A et al., from Vellore, Agarwal SK and Dash SC from Delhi and Aggarwal HK et al., from Rohtak had reported the incidence of MCD to be 35.8%, 37% and 33.3% respectively [Table/Fig-11] [8,13,14].

However studies from other parts of India including Andhra Pradesh and PGI Chandigarh have shown MN and FSGS to be the predominating cause of nephrotic syndrome respectively [7,10].

International studies have shown mixed results with MCD displaying incidences of 25% [15], 40.1% [16], 44.1% [17], 15.5% [18] and 31.5% [19] followed by MN [2,20-24] and FSGS [25] to be predominating causes of adult onset nephrotic syndrome [Table/Fig-12].

**Focal and segmental glomerulosclerosis (FSGS):** The incidence of FSGS was reported from as low as 4% to 18% in Western literature [1,15,16]. Over the course of time, the incidence of FSGS and MN has been seen to be increasing in the world. This change has also been observed in the Indian population. Among Indian studies, the incidence of FSGS from Rathi M et al., and Golay V et al., were reported to be 30.6% and 27.4% respectively [10,12]. However, in our study FSGS was found in 25 (11.01%) cases which in comparison to other studies occupied a minor proportion of primary glomerular diseases.

Authors	MPGN (Type I) (%)	Minimal Change Disease (%)	Membranous Nephropathy (%)	Mesangioproliferative GN (%)	FSGS
Hass M et al., 1976-1979 [2]	6	23	36	-	15
Hass M et al., 1995-1997 [2]	2	15	33	-	35
Cameron JS [15]	14	25	21	13	18
Beaufils H [16]	13	40.1	23	8.5	15.6
Chang JH et al., [18]	4	15.5	12.3	28.3	5.6
Tiebosch AT et al., [19]	20.5	31.5	4.5	26.5	9
Null G and Kaffe RK [20]	21.9	10.2	42.3	2.2	8
Zhou F et al., [21]	1.5	25.3	29.5	20	6
Kark RM et al., [22]	12.2	11.2	28.6	6.1	-
U.S. Cooperative Study [23]	1.4	15.7	52.8	11.4	-
Rosenberg HG [24]	26.5	12	28	11.5	4
Kazi JI et al., [25]	4.3	14.8	26.6	2.5	39.9
Present study	12.3	15.9	12.3	13.2	11

**[Table/Fig-12]:** Comparison of glomerular lesions among nephrotic syndrome in adults in International studies [2,15,16,18-25].

**Mesangioproliferative glomerulonephritis (MSGN):** MSGN in our study was the second most common cause of nephrotic in 30 (13.21%) cases. A study from Korea [18] reported IgA presenting with MSGN as the most common cause of adult onset nephrotic syndrome. Similarly another study from China [21] reported the incidence of MSGN to be 20%. Our study showed 20/30 patients displayed a MSGN pattern in light microscopy with negative IF.

The pattern of mesangial proliferative GN in a renal biopsy serves to identify an important set of differential diagnosis. These include a resolving post-infectious GN, IgM nephropathy, SLE Lupus nephritis (WHO Class II), IgA nephropathy and MSGN (Idiopathic). Patients of MSGN (Idiopathic) with negative IF have been classified as some belonging to the Non IgA MSGN [8,26]. When compared to IgA nephropathy, studies have reported idiopathic non IgA MSGN to be a distinct entity [22-24] with few studies displaying a similar [23] and higher [22] progression rate of end stage renal disease when compared to IgA nephropathy. Patients with non IgA MSGN also had lower degree of haematuria, higher creatinine clearance and less glomerular and tubulointerstitial lesions [24]. Waikhom R et al., from Kolkata had 19/23 (82.6%) patients in the study with non IgA [26], whereas our study had fewer 20/30 (66.7%) patients with non IgA MSGN with absent immune deposits presenting with nephrotic syndrome.

In our study, five patients of MSGN had shown IgM (2+) deposits in the mesangium. A possibility of IgM nephropathy could not be concurred without a detailed ultrastructural examination.

Two patients had shown coarsely granular C3 (2+) deposits in the mesangium. The differential diagnosis of C3 glomerulopathy presenting with nephrotic syndrome versus a recovering/partially treated atypical Post Infectious Glomerulonephritis (PIGN) was considered. A definite clinical history of infection could not be elucidated in these two cases and electron microscopy could not be performed due to financial constraints. An ultrastructural examination would have helped in resolving the diagnosis in these two cases. Subepithelial humps and deposits in the mesangial notch region [27] are more supportive of a diagnosis of PIGN. The patients were lost to follow up.

It is important to understand that being a tertiary care referral centre; we receive biopsies of previously treated patients. Partial or inadequate treatment might be the reason for deviation of classical patterns of diseases making it increasingly difficult to arrive at a conclusive aetiological diagnosis. This may account for negative IF studies in patients with MSGN.

**Membranous Nephropathy (MN):** The incidence of MN showed wide variation from 21.0% in a study by Cameron JS [15] to 52.8% in the series by US cooperation study [23].

MN accounted for 12.3% of patients with adult onset nephrotic syndrome. Our study also shows peak incidence in the 4<sup>th</sup> decade (28.6%) and 5<sup>th</sup> decade (25%) which is consistent with the previous studies.

In the present study, 164 patients were females and 63 were males; most of which belonged to 3<sup>rd</sup> and 4<sup>th</sup> decades i.e., 31.6 % and 36.8 % respectively which is in concordance with the previous studies [22,24].

**Membranoproliferative glomerulonephritis (MPGN) (Type I):** It is also one of the commonest type of lesion in our study i.e., 28 cases (28.6%) of adult patients biopsied who presented as nephrotic syndrome. In western literature, its incidence varies from 1.4% to 26.5%. The low incidence i.e., upto 1.4% in the series by US Cooperation study [23] may be because until its recognition as a separate entity, it was reported under the headings of proliferative GN and membranous GN. Significant incidence of MPGN has also been reported from Nepal (21.9%) [20], Rohtak (18.2%) [14] and Chandigarh (17.9%) [10]. In children and adults, Cameron JS [15] observed that MPGN affects both males and females equally. But in our study we had female preponderance i.e., (78.6%) over male (21.4%). MPGN type I reported to be seen in patients of all ages. Majority of cases of MPGN type II (dense deposit disease) are under the age of 20 years. In our study, MPGN type I cases were distributed in all age groups with highest incidence in 3<sup>rd</sup> decade i.e., 8 out of 28 (28.6%). We did not encounter any case of dense deposit disease in our study group.

**Primary versus secondary glomerular disease:** A total of 59/227 (25.99%) patients in our study had secondary systemic causes for adult onset nephrotic syndrome which is in concordance with Western and Indian literature [Table/Fig-13] [8,10-15,22,28,29].

Authors	Total no. of cases	Primary NS		NS due to systemic diseases	
		No.	%	No.	%
Date A et al., [8]	1532	1276	83.3	256	16.67
Rathi M et al., [10]	364	324	89	40	11
Das U et al., [11]	1615	1278	79.1	49	11.9
Golay V et al., [12]	410	361	88.1	49	11.9
Agarwal SK and Dash SC [13]	2250	1316	58.5	934	41.5
Aggarwal HK et al., [14]	404	318	78.7	86	21.3
Cameron JS [15]	62	48	77.4	14	22.6
Kark RM et al., [22]	98	57	58.8	41	41.2
Schreiner GE [28]	111	87	79.4	34	20.6
Blainey JD et al., [29]	25	18	72	7	28
Present Study	227	168	74.01	59	25.99

**[Table/Fig-13]:** Incidence of primary nephrotic syndrome and nephrotic syndrome secondary to systemic diseases [8,10-15,22,28,29].

Among the secondary causes of nephrotic syndrome in our study, the commonest were diabetes mellitus (9.69%) followed by lupus nephritis (8.37%). Similar prevalence of diabetes was also reported from AIIMS, New Delhi [13] concurring with our results.

## LIMITATION

Our study included a small sample size. Hence, the results may not clearly depict the definite spectrum of primary glomerular diseases prevalent in adults presenting with nephrotic syndrome.

Electron microscopy was unavailable due to financial constraints. The use of EM would have provided a detailed histopathological analysis and thereby, may have contributed to a further change in the spectrum of glomerular diseases.

Follow up data was limited which could have provided a confirmatory diagnosis to cases presenting with diagnostic difficulties.

## CONCLUSION

In conclusion, our study represents a comprehensive three year data of patients presenting with adult onset nephrotic syndrome attending the nephrology clinic of our hospital. Even though a recent increase in incidence of FSGS has been noted, minimal change disease from our study emerged as the predominating cause of adult onset nephrotic syndrome which is in concordance with other studies. Our study may help to understand the various aetiologies of nephrotic syndrome in this region although further studies on a larger population and different geographical locations are warranted for categorisation.

## REFERENCES

- [1] Richards NT, Darby S, Howie AJ, Adu D, Michael J. Knowledge of renal histology alters patient management in over 40% of cases. *Nephrol Dial Transplant*. 1994;9(9):1255–59.
- [2] Haas M, Meehan SM, Karrison TG, Spargo BH. Changing etiologies of unexplained adult nephrotic syndrome: a comparison of renal biopsy findings from 1976–1979 and 1995–1997. *Am J Kidney Dis*. 1997;30(5):621–31.
- [3] Kitiyakara C, Kopp JB, Eggers P. Trends in the epidemiology of focal segmental glomerulosclerosis. *Semin Nephrol*. 2003;23(2):172–82.
- [4] Kitiyakara C, Eggers P, Kopp JB. Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. *Am J Kidney Dis*. 2004;44(5):815–25.
- [5] Bahiense-Oliveira R, Saldanha LB, Mota ELA, Penna DO, Barros RT, Romão-Junior JE. Primary glomerular diseases in Brazil (1979–1999): is the frequency of focal and segmental glomerulosclerosis increasing? *Clin Nephrol*. 2004;61(2):90–97.
- [6] Korbet SM, Genchi RM, Borok RZ, Schwartz MM. The racial prevalence of glomerular lesions in nephrotic adults. *Am J Kidney Dis*. 1996;27(5):647–51.
- [7] Gandra D, Chennamaneni V. Clinico pathological study of nephrotic syndrome in adults. *J Evid Based Med Healthc*. 2015;19;2(49):8518–20.
- [8] Date A, Raghavan R, John TJ, Richard J, Kirubakaran MG, Shastry JCM. Renal disease in adult Indians: a clinicopathological study of 2827 patients. *QJM*. 1987;64(3):729–37.
- [9] Balakrishnan N, John GT, Korula A, Visalakshi J, Talaulikar GS, Thomas PP, et al. Spectrum of biopsy proven renal disease and changing trends at a tropical tertiary care centre. *Indian J Nephrol*. 2003;13:29.
- [10] Rathi M, Bhagat RL, Mukhopadhyay P, Kohli HS, Jha V, Gupta KL, et al. Changing histologic spectrum of adult nephrotic syndrome over five decades in north India: A single center experience. *Indian J Nephrol*. 2014;24(2):86–91.
- [11] Das U, Prayaga A, Dakshinamurty K. Pattern of biopsy-proven renal disease in a single center of south India: 19 years experience. *Indian J Nephrol*. 2011;21(4):250.
- [12] Golay V, Trivedi M, Abraham A, Roychowdhary A, Pandey R. The spectrum of glomerular diseases in a single center: A clinicopathological correlation. *Indian J Nephrol*. 2013;23(3):168.
- [13] Agarwal SK, Dash SC. Spectrum of renal diseases in Indian adults. *J Assoc Physicians India*. 2000;48(6):594–600.
- [14] Aggarwal HK, Yashodara BM, Nand N, Sonia, Chakrabarti D, Bharti K. Spectrum of renal disorders in a tertiary care hospital in Haryana. *J Assoc Physicians India*. 2007;55:198–202.
- [15] Cameron JS. The natural history of glomerulonephritis. In: Kincaid-Smith P, d'Apice AJF, Atkins RC, eds. *Progress in Glomerulonephritis*. N Y Wiley. 1979:209.
- [16] Beaufils H, Alphonse JC, Guedon J, Legrain M. Focal glomerulosclerosis: natural history and treatment. A report of 70 cases. *Nephron*. 1978;21(2):75–85.
- [17] Sugiyama H, Yokoyama H, Sato H, Saito T, Kohda Y, Nishi S, et al. Japan renal biopsy registry: the first nationwide, web-based, and prospective registry system of renal biopsies in Japan. *Clin Exp Nephrol*. 2011;15(4):493–503.
- [18] Chang JH, Kim DK, Kim HW, Park SY, Yoo T-H, Kim BS, et al. Changing prevalence of glomerular diseases in Korean adults: a review of 20 years of experience. *Nephrol Dial Transplant*. 2009;24(8):2406–10.
- [19] Tiebosch AT, Wolters J, Frederik PF, van der Wiel TW, Zeppenfeldt E, van Breda Vriesman PJ. Epidemiology of idiopathic glomerular disease: a prospective study. *Kidney Int*. 1987;32(1):112–16.
- [20] Null G, Kafle RK. Histopathological spectrum of glomerular disease in nepal: a seven-year retrospective study. *Nepal Med Coll J NMCJ*. 2008;10(2):126–28.
- [21] Zhou F, Shen H-Y, Chen M, Liu G, Zou W-Z, Zhao M-H, et al. The renal histopathological spectrum of patients with nephrotic syndrome: an analysis of 1523 patients in a single Chinese centre. *Nephrol Dial Transplant*. 2011;26(12):3993–97.
- [22] Kark RM, Muehrcke RC, Pollak VE, Pirani CL, Kiefer JH. Analysis of 500 percutaneous renal biopsies. *AMA Arch Int Med*. 1958;101(2):439–51.
- [23] Brenner BM. *Brenner & Rector's The Kidney*. 2004; 7<sup>th</sup> edition:2227–54.
- [24] Rosenberg HG. Primary glomerular diseases. *Pathol Res Pract*. 1986;181(5):489–523.
- [25] Kazi JI, Mubarak M, Ahmed E, Akhter F, Naqvi SAA, Rizvi SAH. Spectrum of glomerulonephritides in adults with nephrotic syndrome in Pakistan. *Clin Exp Nephrol*. 2009;13(1):38–43.
- [26] Waikhom R, Sarkar D, Patil K, Pandey R, Dasgupta S, Jadhav J, et al. Non-IgA mesangioproliferative glomerulonephritis: a benign entity? *Nephrol Dial Transplant*. 2012;27(6):2322–27.
- [27] Haas M. Incidental healed postinfectious glomerulonephritis: a study of 1012 renal biopsy specimens examined by electron microscopy. *Hum Pathol*. 2003;34(1):3–10.
- [28] Schreiner GE. The nephrotic syndrome. In: Strauss MB, Welt LG (Eds) *Diseases of the kidney* Little, Brown & Company, New York. 1963:345.
- [29] Blainey JD, Brewer DB, Hardwicke J, Soothill JF. The nephrotic syndrome. Diagnosis by renal biopsy and biochemical and immunological analyses related to the response to steroid therapy. *Q J Med*. 1960;29:235–56.

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