International Journal of Research in Medical Sciences
Lingaraju U et al. Int J Res Med Sci. 2015 Aug;3(8):2004-2013
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20150317

Research Article

Spectrum of glomerular diseases – clinico-pathologic observations from a state run tertiary care centre

Umesha Lingaraju*, Shyam S. Varma, Satishkumar M.M., Leelavathi V., Shreedhar C.G.

Department of Nephrology, Institute of Nephro-Urology, Bangalore, Karnataka, India

Received: 09 June 2015
Accepted: 09 July 2015

***Correspondence:**
Dr. Umesha Lingaraju,
E-mail: shyamvarmas@yahoo.co.in

ABSTRACT

Background: Renal biopsy is an accurate tool for the diagnosis of glomerular disorders. This study was done to evaluate the histo-pathological spectrum of GDs at our centre and analyze its clinico-pathological correlation.
Methods: All renal biopsies performed for suspected glomerular diseases at our institute over a period of 2 years from Jan 2013 to Jan 2015 were analyzed (n= 597). Biopsies were performed under ultrasound guidance and processed for light microscopy and immunofluorescence.
Results: Among the total biopsies done**,** 597 (69.49%) had biopsy proven GD .The mean age of the patients included was 37.96 ± 15.58 years. M:F ratio was 2.3 : 1. The most common clinical syndrome was nephrotic syndrome (44.38%). PGDs were more common than SGDs The most common GD presenting as NS was FSGS (29.8%). Among patients with nephrotic syndrome, FSGS, MCD, and MGN predominated. DN was the commonest SGD, followed by Lupus nephritis. NDRD was reported in 33 patients (5.52%).Crescentic GN was seen in 11.89% cases majority presenting as RPGN. IgAN comprised 40.42% of the immune complex crescentic GNs. Amyloidosis was diagnosed in 1.84% of biopsies.
Conclusion: Histo-pathological examination with LM and IF techniques and correlation with clinical, biochemical and serological markers as done in this study, have proved useful for the accurate diagnosis of glomerular diseases. It also provides important epidemiological information towards setting up a renal biopsy registry.

Keywords: Glomerular disorders, Renal biopsy, Spectrum, Histopathology

INTRODUCTION

Chronic kidney disease is a worldwide public health problem with increasing incidence and prevalence, largely due to the demographic changes and lack of recognition in early stages, and also result in increasing number of patients ending up in Renal Replacement Therapy.[1] According to 2010 Global Burden of Disease Study, chronic kidney disease was ranked 27th in the list of causes of total number of global deaths in 1990(age standardised annual death rate of 15.7 per 100000), but rose to 18th in 2010(annual death rate of 16.3per 100000).[2] The insidious and asymptomatic course of certain glomerular diseases (GDs) is the factor which determines diagnostic delay, contributing to a poorer kidney and patient's clinical survival.[3]

Renal biopsy is an accurate tool for the diagnosis of glomerular disorders and Immunofluoroscence (IF) studies provide additional information for histopathologic confirmation. However, the spectrum of GDs varies greatly with factors such as age, gender, race, geographical location, and the nature of biopsy indications.[4] Also, literature shows evidence of change in the spectrum of renal diseases with time in many parts of the world during the recent past.[5] Therefore, regional epidemiological studies of GDs are important over a particular period of time as they contribute to a better understanding of the

incidence of different histopathologies and helps in adopting different strategies for prevention and treatment. Many developed countries have established national renal biopsy registries to document such variations and changing trends in the disease spectrum.[4] However, developing countries including India have few such registries and there is paucity of data regarding renal diseases. Single or multicenter renal biopsy registries helps avoid such situations.

The aim of this study was to detect the prevalence of GDs at this state run tertiary referral centre in Southern India and to determine the histo-pathological spectrum of biopsy proven GDs at our centre. This study was done also to analyze its clinic opathological correlation and has thus to contribute valuable epidemiological data from our part of the world.

METHODS

We analyzed all renal biopsies on natïve kidneys that were performed for suspected glomerular diseases at our institute over a period of 2 years from Jan 2013 to Jan 2015. Patients with clinically suspected CKD were biopsied only if they had active urinary sediments with normal sized kidneys on ultrasonography. Diabetic patients were biopsied if there was clinical suspicion of non diabetic renal disease (NDRD).Biopsies done on transplanted kidneys and on those with tubulointerstitial disorders were excluded from the study.

All the baseline clinical details including age, gender, clinical presentation, presence of hypertension, hematuria (microscopic as well as macroscopic) were recorded. Baseline laboratory investigations included serum creatinine, serum albumin, haemoglobin, urine microscopy, and 24 hour urine protein levels. Patients were also evaluated for dyslipidemia, complement dysregulation (C3, C4 levels) and antinuclear antibodies (ANA) positivity depending on their histological diagnosis. Majority of the patients were worked up for secondary etiologies depending on the glomerular histology.

All biopsies were performed under realtime USG guidance using the Bard®MaxCore®DisposableCore BiopsyInstrument (Bard Biopsy Systems, USA). A 18G × 16 cm size instrument was used for all patients. At least two cores were obtained and samples were sent for light microscopy (LM) and immunofluorescence (IF) microscopy in all cases. LM was carried out using H and E, Periodic acid–Schiff, and Jones silver stains. Additional special stains were used whenever indicated. IF staining was performed on 3µm cryostat sections. This used polyclonal fluorescein isothiocyanateconjugated (FITC) antibodies to IgG, IgM, IgA, C3, C1q, and kappa and lambda light chains. The intensity of IF staining was graded on a scale of 0to 4+.All renal biopsies were reported by the same pathologist. If a biopsy sample was inadequate for diagnosis, a second biopsy was performed, if the patients were willing. The procedures followed were in accordance with the ethical standards set up by the responsible committee of the institution.

Standard definitions were used for classifying the clinical syndromes.[6] Patients were classified into five categories accordingly: Nephrotic Syndrome (NS), Acute Nephriticsyndrome (ANeS), AKI/Rapidly Progressing Renal Failure (RPRF)/ Rapidly progressive glomerulonephritis (RPGN), Macroscopic Hematuria (MH)/ asymptomatic urinaryabnormalities (AUA), and CKD.

Hypertension was defined according to Eighth Joint National Committee (JNC8) guidelines.[7] Hematuria was defined as presence of 3 or more RBCs per high power field of centrifuged urine.[8]Serum albumin level less than3.5g/dl was considered as hypoalbuminemia.[9] Nephrotic range of proteinuria was defined as 24 hour urinary protein excretion >3.5g/1.73 m^2/24 hrurine and subnephrotic proteinuria as protein excretion >0.2 g and <3.5 g/d.[10].The normal reference range of C3 and C4 level was taken as 90-180 mg/dl and 10-40 mg/dl respectively.

Glomerular pathologies were classified into the following:

(a) Primary glomerular diseases (PGD) which included IgAN, FSGS, MN, MCD, MPGN, MesPGN, Crescenticglomerulonephritis, and less common lesions suchas idiopathicNodularglomerulosclerosis, and C1q nephropathy.

(b) Secondary glomerular diseases (SGD) which includedlupus nephritis (LN), Postinfectious glomerulonephritis (PIGN), glomerulonephritis related tohepatitis B or C, systemic vasculitides, Henoch–Schönleinpurpura, diabetic nephropathy (DN), vascular diseases including benign and malignantnephrosclerosis and thrombotic microangiopathies (TMA); and amyloidosis

Statistical Analysis

Descriptive statistical analysis was used and results were expressedas frequencies, percentages, and mean ± SD.Statisticalanalysis was carried out using Windows ver.16 (SPSS,).

RESULTS

A total of 859 biopsies were done in our centre during the period of study, of which 597(69.49%) were biopsy proven GD cases. LM and IF were performed in all biopsies. The average glomerular yield was 13.16 +/- 6.73 glomeruli. The average age of the patients included was 37.96 ± 15.58 years. Male: Female ratio was 2.3: 1 (419 males: 178 females) [Table 1 and 2].

Cases were divided into five clinical syndromes according to their clinical presentation [Figure 1]. The most common clinical syndrome was nephrotic

syndrome/NS (44.38%; 265 cases), followed by RPRF/Unexplained renal failure/AKI, CKD and ANeS which contributed 32.49% (194), 12.22% (73) and 9.71% (58) respectively. The least common syndrome studied was AUA/MH (1.17%; 7 cases) [Table 3].

The most common GD presenting as NS was FSGS (29.8%) followed by other causes including MGN (16.9%), MCD (16.22%), DN (12.45%), MPGN (7.5%), IgAN (6.03%), amyloidosis (3.77%) and LN (3.01%). Other relatively rare causes include PIGN, C1qNephropathy, C3 glomerulopathy, and IgMNephropathy [Table 4, Figure 2]. Among patients with FSGS presenting as NS, the most common was FSGS-NOS variant (88.6%). Five had collapsing variant, three had tip variant and one cellular FSGS were documented.

Table 1: Demographics and baseline characteristics of patients included in each group.

	ANeS (n=58)	RPRF/URF/ AKI (n=194)	NS (n=265)	AUA/MH (n=7)	CKD (n=73)
Age	35.32(7-75)	38.91(10-92)	37.06(1-72)	31.14(20-48)	41.25(18-81)
Gender (Males)%	74.13	63.40	70.94	57.14	83.56
Hypertension%	89.65	75.77	53.96	14.28	93.15
Hematuria%	91.37	73.71	29.81	57.14	32.87
Creatinine (g/dl)	3.578	6.52	2.45	1.14	7.738
Albumin (g/dl)	3.12	3.13	2.63	3.61	3.11
Hemoglobin(g/dl)	8.89	9.02	10.5	11.67	8.35
Dyslipidemia%	22.41	21.13	42.64	28.57	41.09
24 hr protein(g)	2.319	2.54	5.02	1.51	2.407

ANeS – Acute Nephritic Syndrome, RPRF- Rapidly progressing Renal Failure, URF-Unexplained renal failure, AKI- Acute Kidney Injury, AUA- Asymptomatic Urinary Abnormalities, MH- Macroscopic Hematuria, NS- Nephrotic Syndrome, CKD- Chronic Kidney Disease.

Table 2: Age specific distribution of common glomerular disorders.

	<18 Years	18-60 years	>60 Years
MCD	8	33	5
FSGS	6	89	7
IgAN	5	74	1
MGN	1	39	6
MPGN	8	20	4
DN	0	71	18
LN	5	36	1
AMYLOIDOSIS	0	7	4
PIGN	8	23	3

MCD-Minimal Change Disease, FSGS-Focal Segmental Glomerulosclerosis, IgAN- IgA Nephropathy, MGN - Membraneous glomerulonephritis, MPGN- Membranoproliferative glomerulonephritis, DN-Diabetic Nephropathy, LN- Lupus Nephritis, PIGN- Post infectious GN

Clinical diagnosis of CKD was made in 73 cases and were biopsied for etiological diagnosis if they had sonologically normal sized kidneys. Secondary causes were detected to be more common among this study group (84.93).Majority of cases were DN (36.98%) and C/cGS (35.61%). Mean serum creatinine was 7.738 (2.3-23.6). Sixty nine (94.52%) cases had serum creatinine>3mg/dl, among which 24 (32.87%) had biopsies showing features of c/c glomerulosclerosis. Others included mainly IgAN and FSGS.

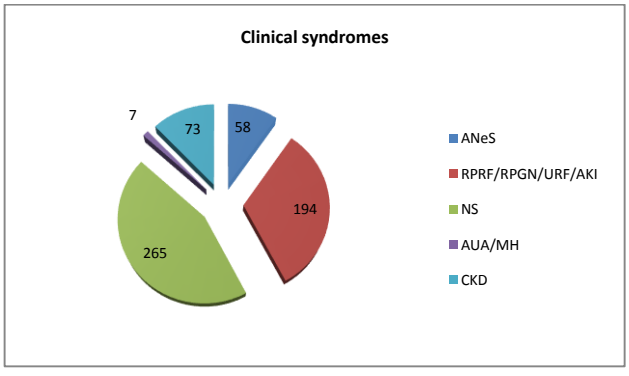


Figure 1: Spectrum of various clinical syndromes.

[#]Crescentin GN, [$]IgM Nephropathy, *Mesangioproliferative GN, [##]C1q Nephropathy, [a]Chronic glomerulosclerosis, [b]Thrombotic micro angiopathy, [c]Hypertensive Nephrosclerosis, [d]C3 glomerulopathy,

[e]Nodular sclerosis, [f]Combined features of IgAN and Anti GBM disease, [g]Diffuse proliferative GN

Table 3: Spectrum of glomerular histopathologies presenting as each clinical syndrome.

	ANeS	RPRF/ URF/ AKI	NS	AUA/ MH	CKD
MCD(n=44)	1	1	42	0	0
FSGS(n=102)	0	13	79	0	10
MGN(n=46)	0	1	44	0	1
MPGN(n=32)	4	8	20	0	0
CRESC GN(n=71)[#]	8	59	3	0	1
IgMN (n=1)[$]	0	0	1	0	0
IgAN(n=80)	13	37	19	5	6
LN(n=42)	4	30	7	1	0
MesPGN(n=3)*	0	1	2	0	0
DN(n=89)	1	26	33	0	29
AMYLOIDOSIS (n=11)	0	0	10	0	1
C1qN(n=3)[##]	0	1	1	1	0
PIGN(n=34)	28	3	3	0	0
CGS(n=25)[a]	0	4	1	0	20
HIVAN(n=1)	1	0	0	0	0
TMA(n=4)[b]	0	3	0	0	1
ANTI GBM DS(n=11)	0	10	1	0	0
HNS(n=13)[c]	0	7	3	0	3
C3 GLOM(n=1)[d]	0	0	1	0	0
NOD SCL (n=4)[e]	0	2	1	0	0
Pauci immune (n=14)	1	10	0	0	3
Double positive (n=4)[f]	0	4	0	0	0
DPGN(n=7)[g]	6	1	0	0	0
(n=2)					
Anti GBM (n=1)	0	1	0		
Secondary GDs					
DN(n=33)	0	28	5		
LN(n=7)	1	6	0		
Amyloidosis (n=10)	0	7	3		
PIGN(n=3)	0	3	0		
Nod Scl (n=1)	0	1	0		
HNS (n= 3)	0	3	0		

MCD-Minimal Change Disease, FSGS-Focal Segmental Glomerulosclerosis, IgAN- IgA Nephropathy, IgMN-IgM Nephropathy, C1qN- C1qNephropathy, MGN - Membraneous glomerulonephritis, MPGN- Membranoproliferative glomerulonephritis, MesPGN- Mesangioproliferative GN, DN-Diabetic Nephropathy, LN- Lupus Nephritis, PIGN- Post infectious GN, Nod Scl- Nodular sclerosis, HNS- Hypertensive Nephrosclerosis

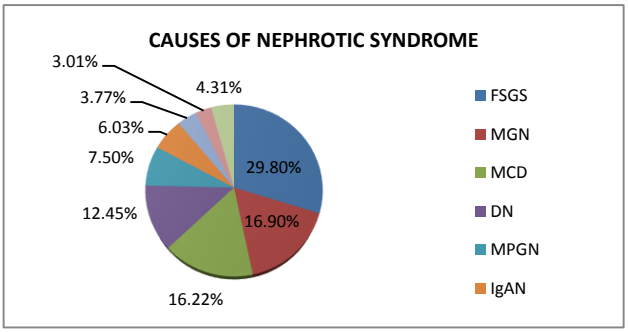


Figure 2: Causes of nephrotic syndrome.

Seven patients were classified in the AUA/MH. Serum creatinine was elevated only in one case (IgAN). Histopathology included 6 IgANand one LNclass II.PIGN was the most common GD causing ANeS (50%), followed by IgAN (18.96%), LN and DPGN (10.34%), MPGN (6.89%) and MesPGN (5.17%).

Table 4: Age specific distribution of GDs presenting as NS.

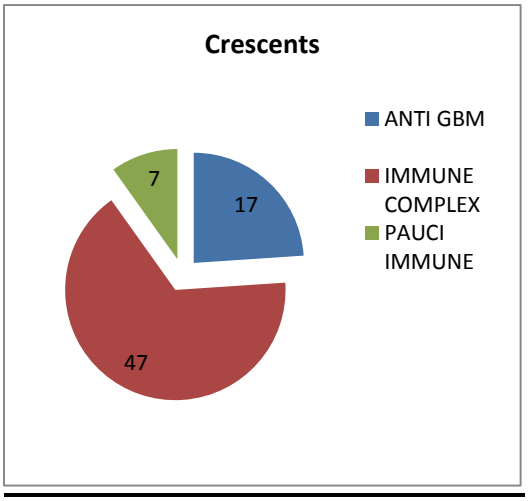
Primary GDs	<18 yrs (n=22)	18-60 yrs (n=224)	>60 yrs (n=19)
MCD(n=42)	6	34	2
FSGS (n=79)	6	71	2
IgAN(n=19)	2	16	1
MGN(n=44)	1	39	4
MPGN(n=20)	5	13	2
C3 glom(n=1)	0	1	0
IgM N(n=1)	0	1	0
C1qN(n=1)	1	0	0
MesPGN	0	2	0

Among the 194 cases included in RPGN/RPRF/AKI group, 142 presented like RPGN, 35 like RPRF, 5 AKI, and 12 URF. Mean creatinine was 6.52mg/dl(ranging 1.2-24.2) Among them, 159 had serum creatinine above 3 mg/dl. Nephrotic range of proteinuria was seen in 61 patients, while 132 cases hadproteinuria in sub-nephrotic range. Primary GD was diagnosed histopathologically in 90 cases. The most common cause detected was IgAN (17.01%), followed by LN (14.94%), DN (12.37%), antiGBM disease (6.18%), FSGS (6.18%-12 cases out of which three were collapsing FSGS), C/c GS (5.67%) and HNS (4.12%). Other causes include MPGN, TMA, PIGN, DPGN, MCD, MGN, C1q N, and idiopathic NOD SCL. Anti-dsDna was found positive in 27 patients. ANCA positivity was found in three with one positivecANCA and two positive pANCA.

Crescents were identified in 71 biopsy specimens, of which most presented like the RPGN/RPRF/URF, followed by ANeS, NS and CKD. M:F ratio of Crescentic GN was 2.55:1. Hypertension was documented in 42, while 63 had associated hematuria. Mean creatinine of the group was 7.24mg/dl (range 1.2-24.2). Serum

Creatinine>3mg/dl in was seen in 66cases.Mean albumin, haemoglobin and 24 hr protein excretion were 3.10g/d, 6.32g/dl, and 2.52g/d respectively.

Primary GD was the cause for crescent formation in 53(74.64%) patients. Most common cause of crescentic GN was Anti-GBM disease. Among immune mediated type of RPGN, the most common was IgAN, and others include PIGN, MPGN, and LN. Pauci immune CresGN was found in seven biopsies.



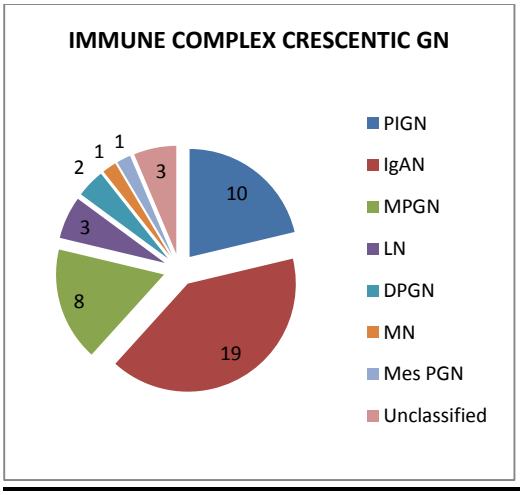


Figure 3: GDs causing crescentic GN and spectrum of renal pathologies causing Immune complex crescentic GN.

Table 5: FSGS variants.

	No.of cases (n=102)	Percentage
FSGS NOS	78	76.47 %
Collapsing	8	7.84 %
Tip	7	6.86 %
Cellular	5	4.90 %
Perihilar	4	3.92 %

Table 6: Frequency of primary and secondary disorders in each clinical syndrome.

	Total	Primary (%)	Secondary (%)
ANes	58	18	40
RPRF/RPGN/URF	194	97	97
NS	265	207	58
AUA/MH	7	6	1(14.28)
CKD	73	15	58

ANeS – Acute Nephritic Syndrome, RPRF- Rapidly progressing Renal Failure, URF-Unexplained renal failure, AKI- Acute Kidney Injury, AUA- Asymptomatic Urinary Abnormalities, MH- Macroscopic Hematuria, NS-Nephrotic Syndrome, CKD- Chronic Kidney Disease.

Primary GDs were diagnosed in 343 patients, majority presenting with NS (60.34%). [Table 6 and 7; Figure 4] The most common primary glomerular disorder in the study population was FSGS (n=102). The commonest presentation was nephrotic syndrome (77.45%) followed by AKI/RPRF/URF (12.74%) and CKD (9.8%). Dyslipidemia was reported in 80 patients. The most common class of FSGS lesions described were FSGS NOS(78), followed by Collapsing variant (8), tip variant (7), cellular (5) and perihilar (4) [Table 5].

Table 7: Primary and secondary GDs- Demographic characteristics.

	Age mean	Gender (% males)	Serum creatinine	Albumin	Hb	24 hr protein
FSGS	36.04	76.53	3.5	2.72	9.98	3.81
MCD	33.0	61.36	1.4	2.33	11.62	5.29
MN	40.06	63.04	2.23	2.61	10.61	6.14
IgAN	32.57	73.52	4.95	3.14	9.62	2.67
MPGN	35.12	78.12	3.16	2.81	10.11	3.24
LN	29.0	11.90	3.12	2.99	8.86	3.16
DN	50.48	83.14	5.69	3.10	9.01	3.91
AMYLOIDOSIS	47.36	81.81	3.47	2.23	9.32	3.98
PIGN	32.85	75.67	3.63	3.20	9.63	3.01

MCD-Minimal Change Disease, FSGS-Focal Segmental Glomerulosclerosis, IgAN- IgA Nephropathy, IgMN-IgM Nephropathy ,C1qN- C1qNephropathy, MGN - Membraneous glomerulonephritis, MPGN- Membranoproliferative glomerulonephritis, MesPGN-Mesangioproliferative GN, DN-Diabetic Nephropathy, LN- Lupus Nephritis, PIGN- Post infectious GN,Nod Scl- Nodular sclerosis, HNS- Hypertensive Nephrosclerosis

Table 8: Shows comparison of our study with similar studies from India, and other countries.

	Present (INU, bangalore)	Golay et al Kolkata[11]	Balakrishnan et al NIMS[16]	Narasimhan et al CMC[27]	Mubarak M Pakistan[28]	Alwahaibi NY et al Oman[29]	Ferraz Fabio et al Brazil[3]
Duration	2013-2015	2010-2012	1990-2008	1990-2001	1995-2008	1999-2010	2005-2009
No.of biopsies	597	666	1615	3773	1536	424	113
Mean age in years	37.96 ± 15.58	28+/-14.62	32.27	>15 yrs	32.9+/-12.8	0-60yrs	34.9+/-16.3
PGD %	57.45	79.13	79.23	-	86.9	69.1	46
SGD %	42.54	20.87	20.77	-	13.1	30.9	33.3
MCD %	7.37	20.12	17.28	11.8	6.77	17.0	9.7
FSGS %	17.08	18.02	12.07	18.28	24.74	21.2	12.3
MN %	7.70	12.01	7.99	10.37	20.05	12.3	6.19
MPGN %	5.36	5.25	4.52	3.21	1.3	1.4	-
IgAN %	13.40	8.1	5.02	9.13	1.76	8.3	11.5
LN%	7.03	15.32	16.72	7.53	5.66	30.4	16.8
PIGN %	5.69	4.95	5.33	14.66	4.56	4.5	-
CGS %	4.18	3	7.68	4.62	13.54	-	-
Amyloidosis %	1.84	1.2	1.67	1.16	5.4	2.3	-
DN %	14.90	0.15	1.36	2.99	1.04	-	-
MesPGN %	0.50	0.6	5.94	1.11	2.21	1.9	-
Cresc GN %	11.89	7.51	5.14	2.78	6.44	1.5	-
NGS %	0.67	0.45	-	-	-	-	-
C1qN %	0.50	0.15	-	-	-	-	-
IgMN %	0.16	-	0.43	-	2.47	-	-
DPGN %	1.17	-	-	-	-	-	11.5
Pauci %	2.34	-	-	-	-	-	2.6
HNS %	2.17	-	-	-	-	-	2.6
TMA %	0.67	-	-	-	-	1.5	-

PGD- Primary Glomerular disorders, SGD- Secondary Glomerular Disorders, MCD-Minimal Change Disease, FSGS-Focal Segmental Glomerulosclerosis, IgAN- IgA Nephropathy, IgMN-IgM Nephropathy ,C1qN- C1qNephropathy,MGN - Membraneous glomerulonephritis, MPGN- Membranoproliferative glomerulonephritis, MesPGN-Mesangioproliferative GN, DN-Diabetic Nephropathy, LN- Lupus Nephritis, PIGN- Post infectious GN, NGSl- Nodular Glomerulosclerosis, HNS- Hypertensive Nephrosclerosis,DPGN- Diffuse Proliferative GN,Pauci- Pauciimmune GN, TMA- Thrombotic Microangiopathy

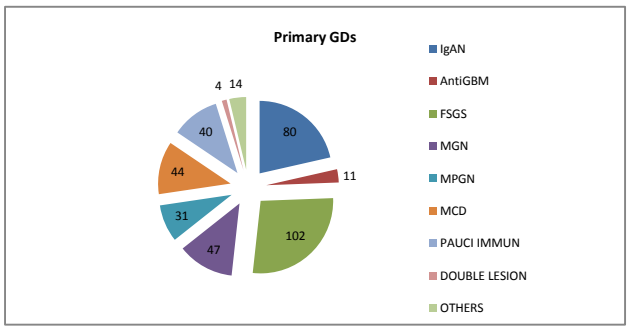


Figure 5: Spectrum of Primary GDs.

IgAN was seen in 80 patients with age of presentation ranging from 13-60 years (mean 32.51) M:F ratio was 2.77:1. Majority of them presented as RPGN(40%). Forty six biopsies showed features diagnostic of MN, among which 44 (95.65%) presented as NS. Mean age was 40.06 years(16-70).M:F ratio was 1.70:1.

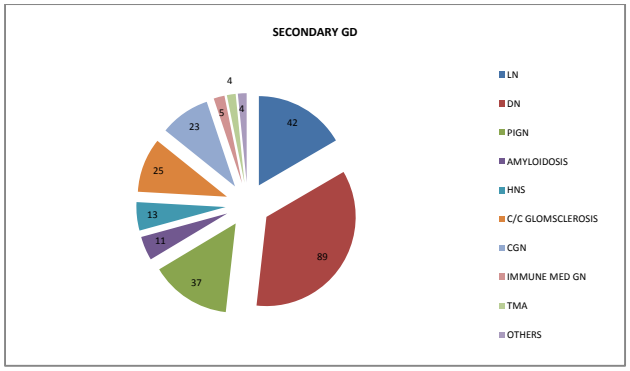


Figure 6: Spectrum of Secondary GDs.

Minimal change disease (MCD) was reported in 44 patients with a mean age of 33.0yrs. Male to female ratio was 1.58:1.Nephrotic syndrome was the presenting feature in 42 patients. All the patients had dyslipidemia. Hypertension was detected in two (4.7%), hematuria in 11(26.19%) of them.

Histological features of MPGN was present in 32cases,the most common clinical syndrome of presentation being NS(20), followed by RPRF/RPGN (8) and ANeS (4). Mean age of patients included was 35.12(8-75 years). M:F ratio was 25:7.

DN was the most common secondary GD described in our study population. [Table 6,7; Fig. 5] Among 103 patients having glomerular disease had history of Diabetes Mellitus, 89 (86.4%) had features of DN, of which 70 (67.96%) had isolated DN, while the rest had other renal (glomerular and non-glomerular) pathologies super imposed with DN. Among the 89 patients with DN, 32 (35.95%/) presented with NS, 27(30.33%) had CKD, 24 (26.96%) in RPRF/RPGN/URF and one with ANeS. Mean age was 50.74yrs (21-81 yrs). M:F ratio was 2.96:1. Fourteen patients diabetes (13.59%) had non diabetic glomerular causes for renal dysfunction. IgAN (21.21%) was the most common NDRD noted.

The second commonest of secondary GDs was LN, diagnosed in 42 cases. The mean age of presentation was 29yrs(11-67yrs). LN showed a female preponderance of 37(M:F ratio 0.13:1). Majority presented with clinical syndrome of RPGN/RPRF (31), followed by NS(8), and ANeS (6) The most common class of LN was LN IV(29 biopsies). IF showed full house pattern in 40 biopsies with IgG,M,C3 as predominant deposits. Forty cases were detected to have both low C3 and C4. One patient had positive APLA and dsDNA was positive in 36 patients.

Patients detected to have PIGN presented with clinical picture of ANeS (82.35%), NS(11.76%) and RPRF/URF. (11.76%). Among the 11 cases of Amyloidosis, 10 presented with NS and one presented with advanced renal failure. Mean age was 47.36yrs (24-67yrs). There were 9 males and 2 females affected. Three cases of primary amyloidosis and eight secondary amyloidosis were reported.

DISCUSSION

This study is a single tertiary care centre experience from southern India and presents the data over a period of two years. The data represents all classes of society and includes age group from 1-92years.

Nearly all forms of acute glomerulonephritis have a tendency to progress to chronic glomerulonephritis. In most types of chronic GN, patients have slowly progressive renal impairment. If no clinical detection is made early in the course of the disease, patients may present late with established hypertension, proteinuria, and renal impairment. Renal biopsy at this stage, when kidneys shrink due to longstanding GN, is hazardous and is less likely to provide diagnostic material. In our study patients who presented with CKD or long standing renal disease were biopsied for etiological diagnosis only if renal ultrasound showed normal sized kidneys. Light microscopy at this stage of disease often shows non-specific features of end-stage renal disease (ESRD), consisting of focal or global glomerulosclerosis and dense tubulo-interstitial fibrosis, and it may not be possible to define the glomerular disease which was the initiating renal injury. Immunofluorescence may be helpful in such circumstances for e.g c/c IgA nephropathy.

Biopsy proven GDs contributed to 69.49% of total biopsies, which indicates a relatively high prevalence of GDs in our study population. The most common indication for renal biopsy for GD was Nephrotic syndrome (44.38%) comparable to other studies where contribution of NS to total biopsies ranged from 34-60%.[3,11]

Biopsies done for asymptomatic urinary abnormalities were the least common indication amongst the clinical syndromes in this study (1.17%), similar to many of the studies from the Indian subcontinent. This incidence is quite low compared to the data from biopsy registries of some centres in Europe and the far-east. Urinary abnormalities represent the second clinical indication to perform a biopsy after nephrotic syndrome, possibly due to the nationwide accepted kidney disease screening programmes in those countries.[12]

Primary GDs were found to predominate as compared to secondary GDs, as mentioned in several other studies.[3,11] FSGS was the most common primary GD in the study group(17.08% of total biopsy proven GDs;29.73% of all primary GDs). Most of the studies from Indian subcontinent and neighbouring countries show similar rising trends in the incidence of FSGS.[3,11]

The most common FSGS variant was NOS (76.49%) followed by collapsing in 7.8%,tip in 6.8%, cellular in 4.9% and perihilar in 3.92%. Similarly, Golay et al reported 119 FSGS patients. Here NOS variant was predominant 80% followed by tip (10.83%)and perihilar (5.83%) lesion[11] and another reported on 210 biopsies of FSGS , where the NOS variant was seen in 72.5%, and

tip lesion, cellular, perihilar, and collapsing variants were seen in 13.5%, 8%, 4%, and 2%, respectively.[13] Most studies have noted that tip lesion and collapsing FSGS are likely to present with nephrotic syndrome, with the collapsing variant much more frequently associated with a reduced GFR. Also, collapsing subgroup tend to have an older age of disease onset (median age 16.5 years) compared to NOS and tip lesions. Our study showed a higher incidence of collapsing variant probably due to racial variations and since the study population comprised of older subjects (mean age 37.96yrs).[14]

Meanwhile, IgAN is seen most frequently, being the most common form of GD in studies from East Asia, Europe and America.[11,12,15] IgAN constituted only 13.40% of total GDs in our study. This could be explained by racial factors and differences in biopsy indications especially in the western countries, where they have adopted a screening policy to detect minor urinary abnormalities as the presenting feature of IgAN.

Our study showed that FSGS was the most common PGD in adults (18 - 60years) and MN was the most common PGD in elderly patients (≥60 years), similar to most studies from south and Eastern India.[11,16]. In patients <18years, FSGS and MCD showed an equal incidence. Another study by Das *et al*., from India showed that MCD was the most common PGD irrespective of the age of presentation.[17]

Hypertension is very common in GN; it is almost universal as long standing and chronic GN progresses toward ESRD and is the key modifiable factor in the preservation of renal function.[18] In our study, hypertension was detected in 68.84% patients.

As evident from the literature, the incidence of MesPGN is quite low in the recent glomerular studies compared to the older.[11] We also found a low incidence of 0.5% Of MesPGN among our study group. Mesangial proliferative GN is described as increased mesangial cell number (more than three mesangial cells per mesangial region in at least 80% of all glomeruli) in LM. This can be seen in several types of GN such as IgA nephropathy, in the resolution phase of post infectious GN and in GN associated with SLE, which can be further differentiated with immunoflurescence techniques.[19] The lower incidence in recent studies can be explained by these improved techniques of IF, and better interpretation of biopsy specimens.

MCD was diagnosed in 7.37% patients in the present study. But a higher incidence of MCD is seen in other studies from India.[11] The study groups defined in these comprised of a higher proportion of children and young adults(<18yrs) ,around 31.15% of total subjects.The younger group(<18yrs) included in our study was only 6.87% of the total subjects.This could have accounted for the lower incidence of MCD reported.

DN was the most common SGD in this study, on contrary to other studies where LN was reported as the most prevalent SGD[3,11,20,21]. DN was seen in 14.90% of total subjects (35.03% of all SGDs),with mean age of 50.48yrs, and mean creatinine of 5.69mg/dl. These patients were biopsied for suspected NDRD; however in 70 patients (67.96%) no associated primary renal pathologies were detected in biopsy.

DN has shown a rising trend in recent past ,accounting for over 40% of new cases of end-stage renal disease (ESRD) annually, and is considered the leading cause of ESRD in the USA as well as Europe and Japan.[22]Among the 103 patients with history of Diabetes Mellitus, 89 (86.4%) had features of DN, of which 70 (67.96%) had isolated DN ,while the rest had other renal (glomerular and non-glomerular) pathologies super imposed with DN.14 out of 103 patients with diabetes (13.59%) had non diabetic glomerular causes for renal dysfunction. In a similar study by Ghani et al, 54.8% cases were found to have isolated diabetic glomerulosclerosis whereas 45.2% subjects had NDRD superimposed on diabetic glomerulosclerosis[22]. IgAN(21.21%), FSGS (18.18%) and PIGN(18.18%) were the most frequent NDRDs as per our study. Pham TT et al reported FSGS as the most common lesion found in patients with NDRD (21.0%), followed by minimal-change disease (15.3%). IgA nephropathy (15.6%) and membranous glomerulonephritis (13.3%).[23] The commonest NDRD were MCD (12.5%), tubuloin terstitial nephritis (10.4%) and LN (6.3%) in a study conducted by Das et al.[24]

LN was the second commonest SGD in the study (7.03%). As reported in other studies, LN is the only GD shown to have female predominance.[11,12] Amyloidosis was present in 11 cases (1.84%) ,among which two had AL subtype, one AHL and 8 cases had secondary amyloidosis. This is comparable to that reported by recent studies;[11,25] but much lower compared to older Indian studies(8.4%), of which the major subclass was secondary (59.1%).[26] This could be attributed to lowered prevalence of tuberculosis and other chronic infections in the present era. We also noted a high incidence of PIGN (5.69% of all biopsies) which evolve to rapidly progressive RF (10.71% of all PIGNs), comparable to other studies from developing countries.[11,16,27]

This study was done to provide a comprehensive information about the spectrum of biopsy-proven GDs in our institute over a period of 24 months. Also, the results of our study are compared here with other similar studies from different centres in India as well as other countries. The clinical features of the different forms of glomerulonephritis do not differ much across the different countries. Table 8 shows comparison of present study with similar studies in India and other countries.

Electron microscopy was not carried out on the biopsy specimens which might have led to the under-diagnosis of certain pathologies, such as thin basement membrane

disease, Alport's syndrome etc. Despite this limitation, this study aims at providing relevant data for establishing renal biopsy registry for GDs in India. Such registries provide valuable data, for correct epidemiological description and clinical correlations, development of protocols for prevention and treatment and also evaluate the long-term outcome of patients when combined with data from renal replacement therapy and CKD registries.[12]

CONCLUSION

Histo-pathological examination with LM and IF techniques and correlation with clinical, biochemical and serological markers have proved useful for the accurate diagnosis of glomerular diseases. The most common indication for renal biopsy here was Nephrotic Syndrome. FSGS was the most frequent primary GD reported. The most common SGD was DN, followed by Lupus nephritis. Our study provides important epidemiological information regarding clinical and laboratory profile of patients with glomerular diseases who underwent renal biopsy at our institute, and also aims at contributing data for setting up a renal biopsy registry in our country.

ACKNOWLEDGEMENT

We thank all the residents and paramedical staff who have helped in conducting the study. We also thank the Professors and staff, Department of Pathology, for contributing data to this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Chávez Valencia V, et al: *Epidemiology* of *glomerular disease* in adults: A database review; Gacetamedica de mexico 2014;150,403-8.
2. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2013;380**:**2095–128.
3. Ferraz, Fabio HumbertoRibeiroPaes et al. Profile of glomerular diseases in a public hospital of Federal District, Brazil. J Bras Nefrol. 2010;32(3):249-56.
4. Gesualdo L, DiPalma AM, Morrone LF, Strippoli GF, Schena FP. Italian Immunopathology Group, Italian Society of Nephrology. The Italian experience of the national registry of renal biopsies. Kidney Int. 2004;66:890-4.
5. Hanko JB, Mullan RN, O'Rourke DM, McNamee PT, Maxwell AP, Courtney AE. The changing pattern of adult primary glomerular disease. Nephrol Dial Transplant. 2009;24:3050.
6. Floege J, Feehally J. Introduction to glomerular disease: Clinical presentations. In: Floege J, Johnson RJ, Feehally J. editors. Comprehensive Clinical Nephrology. 4th ed. St. Louis, Missouri: Saunders; 2010; 193.
7. PA James; 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507-20.
8. Sharp VJ, Barnes KT, Erickson BA. Assessment of asymptomatic microscopic hematuria in adults. Am Fam Physician. 2013;88:747–54.
9. Gupta K, Iskandar SS, Daeihagh P, et al. Distribution of pathologic findings in individuals with nephrotic proteinuria according to serum albumin. Nephrol Dial Transplant. 2008;23(5):1595-9.
10. Lafayette RA, Perrone RD, Levey AS. Laboratory evaluation of renal function, in Schrier RW (ed): Diseases of the Kidney and Urinary Tract. Philadelphia, Lippincott, Williams and Wilkins, 2001, ed 7, pp 333-369.
11. V. Golay, M. Trivedi, A. Abraham, A. Roychowdhary, R. Pandey. The spectrum of glomerular diseases in a single center: A clinic pathological correlation. Indian J Nephrol. 2013;23(3):168–75.
12. Pecse et al; Worldwide distribution of glomerular diseases: the role of renal biopsy registries. Nephrol Dial Transplant. 2010;25(2):334-6.
13. Chugh KS, Sakhuja V. Glomerular diseases in the tropics. Am J Nephrol. 1990;10:437–50.
14. Kristin Meliambro, Monica Schwartzman, Paolo Cravedi, and Kirk N. Campbell, "The Impact of Histologic Variants on FSGS Outcomes," International Scholarly Research Notices, vol. 2014, Article ID 913690, 7 pages, 2014. doi:10.1155/2014/913690.
15. Swaminathan S, Leung N, Lager DJ, Melton LJ, 3rd, Bergstralh EJ, Rohlinger A, et al. Changing incidence of glomerular disease in Olmsted County, Minnesota: A 30-year renal biopsy study. Clin J Am Soc Nephrol. 2006;1:483–7.
16. Balakrishnan N, John GT, Korula A. Spectrum of biopsy proven renal disease and changing trends at a tropical tertiary care centre 1990-2001. Indian J Nephrol. 2003;13:29–35.
17. Das U, Dakshinamurty KV, Prayaga A. Pattern of biopsy-proven renal disease in a single center of south India: 19 years experience. Indian J Nephrol. 2011;21:250–7.
18. Floege J, Feehally J. Introduction to glomerular disease: Clinical presentations. In: Floege J, Johnson RJ, Feehally J. editors. Comprehensive Clinical Nephrology. 4th ed. St. Louis, Missouri: Saunders; 2010. p. 194.
19. Churg J, Bernstein J, Glassock R. Renal disease: classification and atlas of glomerular diseases. New York, Tokyo: Igaku-Shoin 1995.

20. Arias LF, Paulo S. Glomerular diseases in a Hispanic population: review of a regional renal biopsy database Enfermedadesglomerulares en unapoblaciónhispánica: resultados de un registro regional de biopsiasrenales. Med J. 2009;127(3):140-4.
21. RiyamI DA. The Spectrum of Glomerular Diseases on Renal Biopsy: Data From A Single Tertiary Center In Oman. Oman Med J. 2013;28(3):213–5.
22. Ghani AA, Al Waheeb S, Al Sahow A, Hussain N. Renal biopsy in patients with type 2 diabetes mellitus: indications and nature of the lesions. Annals of Saudi Medicine. 2009;29(6):450-3.
23. Pham TT, Sim JJ, Kujubu DA, et al. Prevalence of non-diabetic renal disease in diabetic patients. Am J Nephrol. 2007;27:322-8.
24. Das U, Dakshinamurty KV, Prayaga A, Uppin MS. Nondiabetic kidney disease in type 2 diabetic patients: A single center experience. Indian J Nephrol. 2012;22:358–62.
25. Abdalah E, Waked E. Incidence and clinical outcome of renal amyloidosis: a retrospective study. Saudi J Kidney Dis Transpl. 2013;24(5):950–8.
26. Chugh KS, Datta BN, Singhal PC, Jain SK, Sakhuja V, Dash SC. Pattern of renal amyloidosis in Indian patients. Postgrad Med J. 1981;57:31–5.
27. Narasimhan B, Chacko B, John GT, Korula A, Kirubakaran MG, Jacob CK. Characterization of kidney lesions in Indian adults: Towards a renal biopsy registry. J Nephrol. 2006;19:205–10.
28. Mubarak M; Pattern of renal diseases observed in native renal biopsies in adults in a single centre in Pakistan. Nephrology. 2011;16:87-92.
29. Alwahaibi NY, Alhabsi TA, Alrawahi SA. Pattern of glomerular diseases in Oman; A study based on light microscopy and immunoflurescence. Saudi J Kidney Dis Transpl. 2013;24:387-91.

Cite this article as: Lingaraju U, Varma SS, Satishkumar MM, Leelavathi V, Shreedhar CG. Spectrum of glomerular diseases – clinico-pathologic observations from a state run tertiary care centre. Int J Res Med Sci 2015;3(8):2004-13.