Original Research Paper

Volume-8 | Issue-12 | December-2018 | PRINT ISSN No 2249-555X

Nephrology

A STUDY ON THE PATTERN OF BIOPSY-PROVEN RENAL DISEASE FROM A TIER -2 CITY IN SOUTH INDIA

Dr. S. Balamurugan	M.D.,D.M, Associate Professor, Dept Of Nephrology, Govt KAPV Medical College, Trichy
Dr. Chandrasekar*	M.D.,D.M *Corresponding Author
Dr. S. Kandasamy	M.D.,D.M
Dr. P. Kumaresh	M.D,

ABSTRACT

BACKGROUND:. Percutaneous renal biopsy is the mainstay of diagnosis of renal parenchymal disease. This study was done to evaluate the histo-pathological spectrum of (Glomerular Disease)GDs at our Renal centre in two hospitals in Madurai,South Tamilnadu and analyze its clinico-pathological correlation.

METHODS: All renal biopsies performed for suspected glomerular diseases at the Two hospitals over a period 5 years from 2012 to 2017 were analyzed (n= 114). Biopsies were performed under ultrasound guidance and processed for light microscopy and immunofluorescence.

RESULTS: Among the total biopsies 114 done, 111 (97.3%)) had biopsy proven GD . The average age of male patients were 37.3 ± 17.62 years and that of females were34.9 +18 years.Male: Female ratio was0.62 :1. 1. The most common clinical syndrome was nephrotic syndrome (41%). Primary Glomerular disease(PGDs) were more common than secondary Glomerular disesase(SGDs) The most common GD presenting as NS was Membranous Nephropathy(MN) (17.5%) followed by Minimal Change disease(MCD),Focal segmental Glomerulosclerosis(FSGS) and MPGN. Lupus nephritis (LN) (16.6%) was the commonest SGD, followed by Diabetic Nephropathy/Nondiabetic renal disease(DN/ NDRD) . Crescentic GN was seen in4.4% cases majority presenting as RPGN. IgAN comprised 7% GNs. Amyloidosis was diagnosed in 0.87% 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:

There are various presentation of glomerular diseases and renal biopsy is an important tool in its assessment because histopathological diagnosis is an essential part of evidence-based practice of nephrology. It can guide in deciding therapeutic options and can be of prognostic value. Pattern of biopsy proven renal disease (BPRD) varies with time and geographical region[1]. A review of the renal biopsy data can give idea about the spectrum of renal diseases and its epidemiology data in our community. We conducted the present study to report the spectrum of BPRD from a two hospitals in Madurai,southern Tamilnadu and comparing it with previous other studies to see the changing trend.

AIM:

To study the spectrum of BPRD in our centre and analyzing its trend with studies from other areas in India.

MATERIALS AND METHODS:

This was an observational, retrospective study conducted at division of renal clinic in Nephrology department of two private hospitals, Madurai. Institute's ethics committee approval was obtained for this study. The records of all the patients who underwent renal biopsy in the two private hospitals in Madurai during the period 2012 to 2017 were retrospectively reviewed. The patient's detail and laboratory investigation reports were obtained. Inadequate biopsy were excluded. All the biopsies were performed under ultrasound guidance using Bard® Max-Core® disposable core biopsy instrument [3]. All the biopsies were analyzed by light microscopy using hematoxylin and eosin, periodic acid–Schiff, Jone's silver methenamine & Gomori ' stri chromestains , and immunofluorescence studies were performed using antihuman IgG, IgA, IgM, C3, C1q, and kappa and lambda light chains. The diagnosis of BPRD was made as per standard diagnostic criteria for each disease.

Indications for renal biopsy

1. Nephrotic syndrome(NS) defined as proteinuria > 3.5 gram/24hours ,serum albumin < 2.5 gram/dl2.
2. Acute Nephritic Syndrome(ANS) where a diagnosis of PIGN/ IRGN couldnot be ascertained
3. Acute kidney injury(AKI) -Biopsy done when the cause of renal failure is not clear or non recovery or suspected systemic cause
4. Rapidly progressing renal failure(RPRF) defined as deterioration in GFR with azotemia, over a period of few days, with radiologically normal sized kidneys.
5. Post transplant graft dysfunction or Proteinuria
6. Diabetic patients in whom we suspect Non Diabetic renal disease (NDRD) .

Histological categories

1. Primary Glomerular disease (PGD)- Minimal change disease (MCD), Membranous nephropathy(MN), Membrano proliferative glomerulonephritis (MPGN), Infection related glomerulonephritis (IRGN)/PIGN, Crescentic Glomerulonephritis (CresGN), Focal and segmental glomerulosclerosis (FSGS), chronic glomerulo nephritis(CGN), IgA nephropathy (IgAN)
2. Secondary Glomerular diseases (SGD)- Diabetic nephropathy (DN), lupus nephritis(LN),Amyloidosis,Collapsing Glomerulopathy & Hypertensive Nephrosclerosis[6]

Others

Acute Tubular necrosis(ATN),Acute Interstitial nephritis(AIN)

Statistics

Simple descriptive statistics such as median and mean±SD was used for variables such as age, clinical and laboratory features. The percentages were used for categorical data

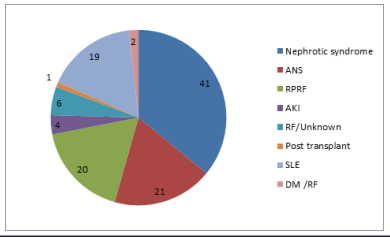
KIDNEY BIOPSY:

RESULTS

There were 114 cases

Male	Female	Total
44(38.5%)	70(61.5%)	114

The average age of male patients were 37.3 ± 17.62 years and that of females were34.9 +18 years.Male: Female ratio was0.62 :1. The contribution of the various glomerular syndromes to the performance of kidney biopsy is presented in Figure 1.



The Biopsy reports of 114 patients is given in table 1

Table 1.

	Total	Male	Female	Percentage of Total
Primary Glomerular Disease (PGD)				
1.Membranous nephropathy	20	10	10	17.5%
Minimal change disease	16	7	9	14%
Focal segmental Glomerulosclerosis	15	10	5	13.1%
Immunoglobulin A(lgA N)	8	6	2	7%
IRGN	16	5	11	14%
MPGN	6	3	3	5.26%
Crescentic GN	5	-	5	4.38%
Secondary Glomerular Disease(SGD)				
SLE/LN	19	0	19	16.6%
Amyloidosis	1	1	-	0.87%
Hypertensive Nephrosclerosis	1	1	0	0.87%
Collapsing Glomerulopathy	1	1	-	0.87%
Diabetic Nephropathy	1	0	1	0.87%
Others Disease(OD)				
ATN	4	3	2	4.38%
AIN	1	1		0.87%

Table2:Gender Distribution Of Glomerular Diseases

Biopsy Diagnosis	Gender		Total (n=114)
	Male (n=44)	Female (n=70)	
Membranous Nephropathy	10(8.7%)	10(8.7%)	20(17.51%)
Minimal change Disease	07(6.1%)	09(7.8%)	16(12.2%)
Focal segmental glomerulosclerosis(FSGS)	06(5.5%)	09(9.09%)	15(13.6%)
Immunoglobulin a (lga)nephropathy	06(5.5%)	02(1.8%)	08(7.5%)
Lupus nephritis	-	19(17.3%)	19(17.3%)
IRGN	05(4.5%)	11(10%)	16(14.5%)
MPGN (Membranoproliferative Glomerulonephritis	03(2.7%)	03(2.7%)	06(5.5%)
Crescentic GN	-	05(3.6%)	05(3.6%)
ATN	03(1.8%)	02(0.9%)	03(2.7%)
Amyloidosis	01(1.8%)	01(0.9%)	03(2.7%)

MEMBRANOUS NEPHROPATHY:

Total	Male	Female
20	10	10

19 cases appear to be primary.1 secondary to SLE. Anti PLA2R staining of kidney biopsy specimens was done in 6 cases found to be negative .Search for secondary causes of MN was done in all cases & was not found.,.

Minimal change disease(MCD):

Total	Male	Female
16	7	9

All of them presented as nephrotic syndrome.However 2 cases had renal failure with serum creatinine (3.9/2.1 mg) presented with oliguria. Biopsy showed associated ATN in those cases.It is likely that this type of presentation could be secondary to NSAIDS over the counter administration.

FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS)

FEMALE	MALE	TOTAL
9	6	15

Around 14 cases (13 with native kidney and 1 with post renal transplant).All the cases had significant edema and hypertension on presentation.Renal failure was present 4/14 cases with serum creatinine around 1.4-3.2.FSGS-NOS is the most common subtype.All the cases were treated with steroids for a period 0f 16-24 weeks.However complete remission was achieved only in 7/14(50%). Partial or no response in others. One patient responded to Tacrolimus therapy. One Post transplant patient had Proteinuria and Graft dysfunction with biopsy showing FSGS. He was treated with Plasmapheresis.

IMMUNOGLOBULIN-A(IgA)Nephropathy

FEMAL	MALE	TOTAL
2	6	8

There is a definite male preponderance.These patients presented either as accelerated hypertension with renal failure, macrohematuria or severe renal failure or acute nephritic syndrome. Biopsy showed advanced IgA in those with severe renal failure(3/8). One patient had HCV infection with proteinuria /hypertension. Biopsy showed IgAN (Likely secondary IgA nephropathy).He was treated with Direct acting Antivirals for HCV(DAA).Most of the cases are progressive. One case of IgA nephropathy presented as RPGN showed C ANCA positivity.

IRGN (Infection Related Glomerulonephritis)

FEMALE	MALE	TOTAL
11	5	16

Most of them presented as either acute nephritic syndrome or RPGN. 8/16(50%) cases needed HD due to volume overload.One patient had anuria for 1 month from which she recovered completely and having normal renal function for past 3 years.In majority of cases site of primary infection could not be made out.

MPGN(Membranoproliferative GN)

FEMAL	MALE	TOTAL
3	3	6

Their mode of presentation is either nephrotic syndrome or RPGN.Two female patients had associated connective tissue disorder like Rheumatoid arthritis.One patient needed RRT.

CRESCENTIC GN

FEMAL	MALE	TOTAL
5	-	5

All are females.Two cases of vasculitis(necrotising pauci immune Glomerulonephritis microscopic polyangitis), 2 cases of Immune-complex GN,one case of Anti GBM positivity (Goodpasture Disease)was diagnosed found. Immunosuppression treatment was started in all & plasmapheresis was given in vasculitis and Anti GBM positivity.

Lupus Nephritis

FEMALE	MALE	TOTAL
19	-	19

19 cases of SLE were found.All are females in the age group around 16-53 years. Majority of them had significant proteinuria with microhematuria.3/19 patients had severe renal failure.1/19 needed HD Biopsy showed DPGN with crescents.

Diabetic nephropathy:

Total	Male	Female
1		1

One patient had been diagnosed as nephrotic syndrome with recently diagnosed diabetes.However biopsy showed Diabetic nephropathy RPS class2 b.

NDRD in Diabetic:

One patient had DM with HT and renal failure.Biopsy showed non-diabetic renal disease(NDRD)- MGN with severe arteriosclerosis and ATN.Another 53/f known diabetic with skin lesions, Arthralgia with Nephrotic Proteinuria (No e/o retinopathy) showed Lupus nephritis . One patient with diabetes and renal failure had severe arteriosclerosis on biopsy.

Amyloidosis:

A 46 year old male named presented with HT/renal failure with proteinuria.Biopsy showed AL amyloidosis.subsequent investigations like bone marrow showed light chain myeloma.

Hypertension Nephrosclerosis:

Total	Male	Female
1	-	1

12.Collapsing glomerulopathy:

A 33/M presented with severe renal failure & subnephrotic

proteinuria.Biopsy showed collapsing glomerulopathy(HIV negative).Pictures attached

ATN(Acute Tubular Necrosis) -3

Table3:Distribution Of Glomerular Diseases According To Age

Biopsy Diagnosis	Age Group(in yrs)				Total (n=114)
	<20 (n=16)	21-40 (n=58)	41-60 (n=33)	61-70 (n=07)	
Membranous Nephropathy	-	10 (8.7%)	07 (8.7%)	03 (2.7%)	20 (17.5%)
Minimal change Disease	07 (8.7%)	05 (4.4%)	03 (2.7%)	01 (0.9%)	16 (14.5%)
Focal segmental glomerulosclerosis(FSGS)	01 (0.87%)	09 (9.09%)	05 (4.5%)	-	15 (13.6%)
Immunoglobulin a (lga)nephropathy	02 (1.8%)	04 (3.6%)	02 (1.8%)	-	08 (7.3%)
Lupus nephritis	02 (1.8%)	11 (10%)	02 (1.8%)	-	19 (17.3%)
IRGN	01 (0.9%)	06 (5.5%)	07 (6.4%)	02 (1.8)	16 (14.5)
MPGN (Membranoproliferative Glomerulonephritis	02 (1.8%)	02 (1.8%)	02 (1.8%)	-	06 (5.5%)
Crescentic GN	01-	02 (1.7%)	02 (1.7%)	-	05 (4.3.%)
ATN	-	03 (2.7%)	2-	1-	06 (2.7%)
Amyloidosis	-	1 (0.87%)			01
Diabetic Nephropathy			1		
others	0	5	1		

DISCUSSION OF RESULTS :

In our study of 114 patients with BPRD were retrospectively analyzed Primary glomerular diseases constituted to about 78% and secondary glomerular diseases were about 22%.Primary glomerular disease is the most common cause of BPRD correlating with majority of studies done worldwide[5]. The most common indication for renal biopsy was NS accounting for 41%, which is similar to most of the studies done worldwide and also in india[6],. Female predominance is seen in our study, in contrast to other studies done. In our study Membranous Nephropathy(MN) is the most common followed by MCD,IRGN & FSGS [8,5]. MN, being quoted as most common cause of NS in adults in is found to be similar in our study. Even in SLE (secondary GN) MN (Class 5 LN) is the commonest lesion observed either alone or on combination with class 3 or 4 glomerular disease in our study (14.5%). MN incidence peak during third and fourth decade (26.7%).Its also the most common cause of Nephrotic syndrome in the elderly(>60 years). However PLA2 R Antibody was not found positive in the tested cases. Regarding MCD is the second most common cause of PGD in our study.It also affects a younger population(<20 years) and in significant proportion presented with renal failure due associated ATN. Compared with the study by Das *et al*., that showed MCD was the most common PGD irrespective of the age of presentation we had MCD is the second most common PGD. Regarding FSGS we may be underestimating FSGS because of its predilection to juxtamedullary glomeruli & focal distribution (Unsampled FSGS).There is a worldwide increase in incidence of FSGS in recent times. It is the third cause of Primary glomerular disease in our study with incidence peaking at 3rd -4th decade (19.4%)[6]. Even though IgA nephropathy is considered most common cause of glomerular disease worldwide, it is the 4th common of Primary glomerular disease in our study (3.2%) which is similar to other Indian studies.However we may be underestimating true incidence in the general population as many of them are asymptomatic and only be having microscopic haemuturia & hypertension. 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. Unless there is a community based screening with emphasis with Government or NGO support on preventive nephrology we may not be able to identify the true burden of IgA Nephropathy in our country. In adults or elderly with IRGN the classical presentation of PIGN in children(Hypertesion,Cola colured urine,Edema)is rare. Many a time there is atypical presentation in the form of RPGN,Renal failure with sub-Nephrotic Proteinuria or sometimes Anuric renal failure .The site of infection may not be obvious in many cases in adults & elderly. In the remaining patients skin infection (cellulitis,furuncle, herpes zoster) ,blood borne organisms(blood culture grew Staphylococcus)& in some urinary tract UTI(E.Coli,Klebisiella in urine culture) could be the site of infection acts & acting as triggering factor .Steroids were used in those who presented as RPGN. In a significant proportion of adults & elderly there is a risk of progression to Chronic kidney disease which is similar to studies published[9,10]. In our study 2/16(12.%) progressed to ESRD over a period of 1 year. In our study we didn't have have any IgA dominant IRGN probably related to small sample size. In Our study the incidence of MPGN was 4.38% which is much lower when compared to other studies. More often they are associated with Connective tissue disorders. In patients with crescentic GN Pauci-immune Vasculitis(Microscopic Polyangitis) was present in 2 patients followed by Immune-complex glomerulonephritis of which IRGN & SLE were the main etiological agents. All were treated with immunosuppression as per protocol.Among the secondary glomerular diseases, LN is the most common cause (9.7%) which is followed by DN/NDRD. Lupus nephritis class 5 was most common either alone or in combination with class3 or 4 .Class 3 alone seen in 2 cases. Majority of cases responded well to NIH protocol/MMF. Since most of DN cases are diagnosed by ophthalmic evaluation and without renal biopsy, it has a lesser representation in the study.However we had cases of NDRD in the form of Membranous Nephropathy or Lupus Nephritis or Severe arteiosclerosis in Diabetic patients, We had only one case of Amyloidosis which incidence was lower when compared to other studies.It turned out be a primary Amyloid.

CONCLUSION

Our epidemiological data represents that of two Kidney care centres in Madurai, South India. 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. MN was the most frequent primary GD reported. The most common SGD was Lupus nephritis. And our observations are in concurrence with that of other studies done in south India,.. Large demographic variation of histopathological patterns of BPRD are seen across the world and within various parts of India. So, in order to have an accurate data, it is imperative to maintain a local renal biopsy registry.

Limitations

1. Electron Microscopy study of biopsy specimens were not done
2. Some cases of IRGN with C3 deposition could well represent C3 Glomerulopathies

REFERENCES:

1. 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.
2. 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.
3. Prasad N, Kumar S, Manjunath R, et al. Realtime ultrasound-guided percutaneous renabiopsy with needle guide by nephrologists decreases post-biopsy complications. Clin Kidney J 2015;8:151-6.
4. Chang JH, Kim DK, Kim HW, Park SY, Yoo TH, Kim BS, et al. Changing prevalence of glomerular diseases in Korean adults: A review of 20 years of experience. Nephrol Dial Transplant. 2009;24:2406–10.
5. 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.
6. 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.
7. Balakrishnan N, John GT, Korula A. Spectrum of biopsy proven renal disease and changing trends at a tropical tertiary care centre1990-2001. Indian J Nephrol 2003;13:29-35.
8 Chang JH, Kim DK, Kim W. Changing prevalence of glomerular diseases in Korean adults: A review of 20 years of experience. Nephrol Dial Transplant 2009;24:2406-10.
9. Nasr SH, Fidler ME, Valeri AM et al. Postinfectious glomerulonephritis in the elderly. J Am Soc Nephrol 2011; 22: 187–195.
10. Nadasdy T, Hebert LA. Infection-related glomerulonephritis: understanding mechanisms. Sem Nephrol 2011; 31: 369–375.