Original Article

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Clinicopathological Study of Renal Biopsies in Glomerular Diseases: One Year Retrosopective and Two Years Prospective Study

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Abstract

Background and Objectives: The technique of percutaneous renal biopsies is the cornerstone for our understanding of diseases of the kidney. Studies done on percutaneous gun biopsies performed under real-time ultrasound guidance have given higher diagnostic yield with fewer complications. The present study aims the spectrum of glomerular diseases which require renal biopsy and to correlate the pathological findings of glomerular diseases with clinical and laboratory parameters. *Materials and Methods:* A total of 75 cases were studied over a period between 31-07-2005 and 31-07-2008 which includes 1 year retrospective and 2 years prospective study. The renal biopsy was performed by 18 Gauge Bard's 'bioptic gun' under real time ultra sound guidance and a renal tissue ranging from 2-3cm was obtained. Sections were studied with Haematoxylin and Eosin, Special stains like Periodic Schiff Stain, Silver and Congo-red. Immunofluorescence was done where ever necessary. *Results:* The study showed that among 75 cases the majority of biopsies were of primary glomerular diseases in which focal segmental glomerulosclerosis was most common accounting for (25.00%) of cases followed by mesangioproliferative glomerulonephritis (22.03%) of cases. Among the secondary glomerular diseases renal amyloidosis (55.00%) was found to be more common in patients who presented with nephrotic syndrome and maximum cases were of secondary amyloidosis in which tuberculosis and chronic respiratory infections like bronchiectasis were common. *Conclusion:* Focal segmental glomerulosclerosis, mesangioproliferatve glomerulonephritis and amyloidosis of kidney were found to be common in the present study.

Keywords: Renal Biopsy; Focal Segmental Glomerulosclerosis; Amyloidosis.

Introduction

The present knowledge of the pathology of renal diseases has been derived to a large extent from the introduction of percutaneous needle biopsy of the kidney and the systematic study of these small samples of renal tissue by light microscopy, electron microscopy and immunofluorescence microscopy. The technique of percutaneous renal biopsy was introduced in to clinical usage in the early 1950s and till today it is one of the most common and widely accepted invasive procedures for the diagnosis of renal diseases [1].

The review of literature reveals that minimal change disease, membranoproliferative glomerulonephritis, membranous nephropathy, focal segmental glomerulosclerosis and crescentic glomerulonephritis can still be diagnosed by light microscopy with more reproducibility [2].

Although the role of diagnostic tools like immunofluorescence and electron microscopy in the study of renal pathology cannot be overemphasized, light microscopy also has its own advantages. It is a simple procedure and it provide the first insight about the renal pathology and in majority of cases it is also possible to come to a final conclusive diagnosis. A three year study was done on renal biopsies performed

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in our hospital. The biopsies selected were those which were performed by percutaneous route for suspected glomerular diseases.

The purpose of the study was to interpret and classify the renal biopsies according to the disease process and to correlate the pathological findings of glomerular diseases with clinical and laboratory parameters. In this study, most of the biopsies were studied by light microscopy and a few were subjected to immunofluorescence microscopy.

Material and Methods

Renal biopsy specimens for the present study were obtained from the department of Medicine (Nephrology Unit), B. L. D. E. A's Shri. B. M. Patil Medical College, Hospital and Research Centre, Bijapur. All the renal biopsies over a period from 1st July 2005 to 31st July 2008 were recorded which included 1 year retrospective and 2 years prospective study. A total of 75 renal biopsies were obtained during the 3 years.

A detailed clinical history, examination findings, laboratory findings of the patient were recorded from the patients of prospective group undergoing percutaneous renal biopsies for suspected glomerular diseases. Non glomerular and neoplastic diseases were excluded.

The biopsies were done by using 18 gauze Bard's bioptic gun under real-time ultrasound guidance and a renal tissues ranging from 1-2 cm was obtained. The specimens obtained were immediately fixed in 10% formalin for histopathological examination and in isopentane, snap frozen in liquid nitrogen and sent for immunofluorescence study where there was difficulty in diagnosis by light microscopy.

Thin sections of 3 to 4 microns thickness were taken and stained with haematoxylin and eosin, PAS and methenamine-silver. In selected cases of amyloidosis and interstitial fibrosis, Congo red and Massons Trichome were done respectively.

Results

During the three years study from August 2005 to July 2008 which included a 1 year retrospective and 2 years prospective study, a total of 75 renal biopsies were reviewed for suspected glomerular diseases and classified as glomerular diseases, other diseases and inadequate tissue sample.

Table 1: Classification of renal biopsies of suspected glomerular diseases

Diseases	No of cases	Percentage
Glomerular diseases	71	94.66%
Other diseases	2	2.66%
Inadequate tissue sample	2	2.66%
Total	75	100.00%

Table 2: Classification of glomerular diseases

Diseases	No of cases	Percentage
Primary glomerular diseases	59	78.66%
Secondary glomerular diseases	12	16.00%

Table 3: Classification of primary glomerular diseases

Glomerular diseases	No of cases	Percentage
FSGS	15	25.00%
MESPGN	13	22.03%
MPGN	9	15.00%
MN	9	15.00%
MCD	4	6.66%
DPGN	3	5.00%
CGN	2	3.33%
Cortical necrosis	2	3.33%
Chr. GN	2	3.33%
Total	**59**	**100.00%**

Table 4: Classification of secondary glomerular diseases

Secondary glomerular diseases	No of cases	Percentage
Amyloidosis of kidney	7	55.00%
Lupus nephritis	5	45.00%
Total	12	100.00%

Table 5: Clinical features of various glomerular diseases

Glom. Diseases	Facial puffiness	Pedal edema	Hematuria	Hypertension
FSGS	13	7	-	-
MesPGN	10	4	-	-
MPGN	7	3	-	-
MN	6	3	-	-
MCD	4	-	-	-
CGN	-	-	2	-
Chr.GN	-	-	1	1
DPGN	2	-	-	1
Amy	7	7	-	2
LN	4	1	-	1

Table 6: Laboratory findings in various glomerular diseases

Glom. Diseases	Proteinuria	Raised serum Creatinine	Raised blood Urea	Raised C3	ANA positivity
FSGS	15	8	5	6	-
MesPGN	6	2	-	-	-
MPGN	9	7	3	-	-
MN	9	6	4	-	-
MCD	4	-	-	-	-
DPGN	3	1	2	-	-
CGN	2	1	-	-	-
Chr.GN	1	2	1	-	-
Amy	7	7	7	-	-
LN	3	4	3	-	3

Table 7: Immunofluorescence studies of glomerular diseases

Serial No.	Diseases	IgG +ve	IgG-ve	IgA+ve	IgA-ve	C3 +ve	C3-ve	IgM+ve	IgM-ve
1.	FSGS	1	4	1	4	3	2	3	2
2.	MESPGN	0	9	0	9	0	9	4	5
3.	MPGN	2	3	0	5	5	0	0	5
4.	MN	4	0	0	4	1	3	0	4
5.	MCD	0	2	0	2	0	2	2	0
6.	LN IV	3	0	3	0	3	0	3	0
7	AMY	0	1	0	1	0	1	1	0
8.	Cresentic GN	1	1	0	2	1	1	0	2

The glomerular diseases accounted up to 94.66% of the all renal biopsies. Other diseases like tubulointerstitial nephritis and inadequate biopsies accounted up to 2.66% each, as shown in Table 1.

Among all the glomerular diseases, maximum were due to primary causes, which accounts for about 78.66% of the total biopsies, as shown in Table 2.

Out of 59 cases of primary glomerular diseases, the maximum cases were of focal segmental glomerulosclerosis (25.005%), while mesangio-proliferative GN accounted for second category of about 22.03% as shown in Table 3.

Among the twelve cases of glomerular diseases which occurred secondary to some systemic causes the highest were due to amyloidosis accounted for 55.00% followed by systemic lupus erythematosus accounted for 45.00% as shown in Table 4.

Out of 59 primary glomerular diseases 42 cases presented with facial puffiness, 17 cases with pedal edema, 3 cases with hematuria and 2 cases with hypertension. Out of 12 secondary glomerular diseases 11 cases presented with facial puffiness, 8 cases with pedal edema and 3 cases with hypertension. Rashes and joint pains were seen in 5 cases of lupus nephritis. As shown in Table 5.

Out of 59 primary glomerular diseases 39 cases presented with proteinuria, 23 cases with raised serum creatinine levels, 15 cases with raised blood urea levels and 6 cases with raised C3 levels. Out of 12 secondary glomerular diseases 10 cases presented with proteinuria, 11 cases with raised serum creatinine levels and 10 cases with raised blood urea levels. ANA / AntidsDNA positivity was seen in 3 cases of lupus nephritis. As shown in Table 6.

Immunofluorescence studies were done for 35 cases where there was difficulty in diagnosis by light microscopy. IgG, IgA, IgM and C3 were used and the pattern of deposition was studied. Systemic lupus erythematosus class IV showed full house positivity that is all the four IgG, IgA, IgM and C3 deposits were positive. As shown in Table 7.

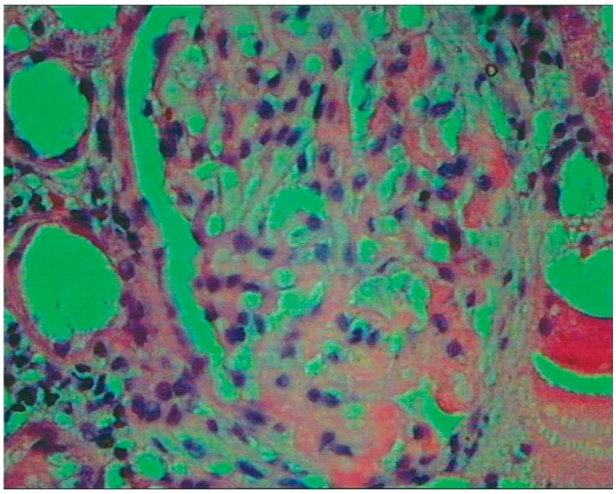

Fig. 1: Photomicrograph of glomerulus showing sclerosis-FSGS (H&E, 400X)

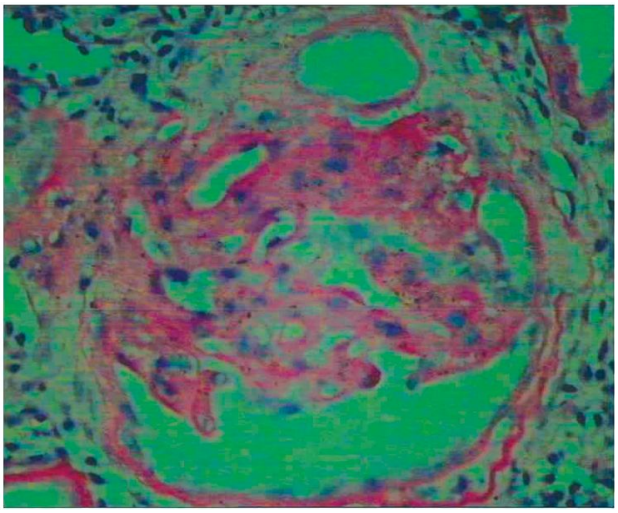

Fig. 2: Photomicrograph of glomerulus showing esinophilic deposits-FSGS (PAS, 400X)

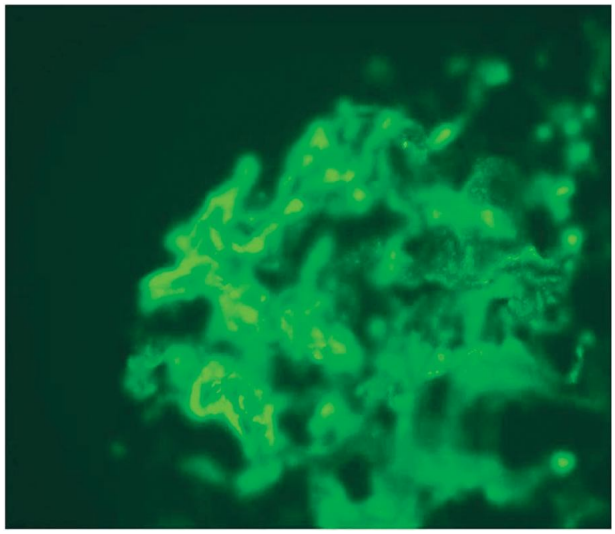

Fig. 3: Photomicrograph of immunofluorescence showing C3 deposits-FSGS

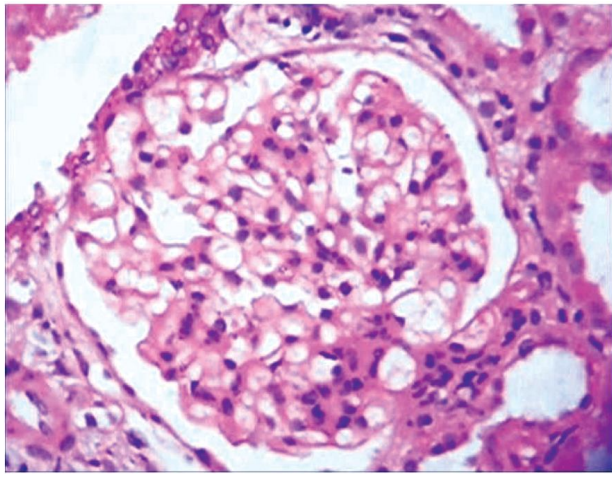

Fig. 4: Photomicrograph of glomerulus showing mesangial proliferation - MesPGN(H&E, 400X)

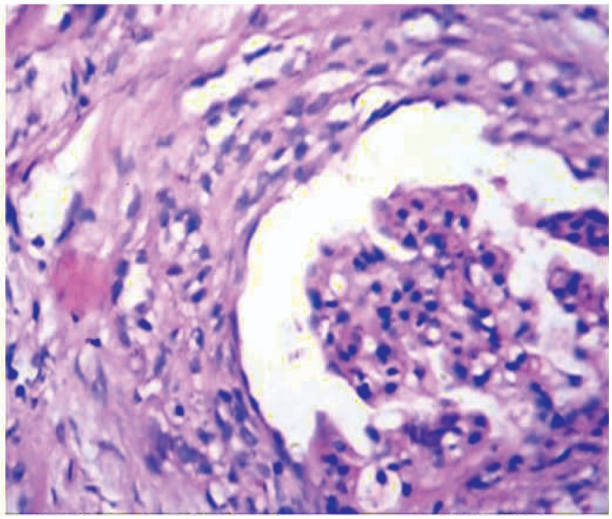

Fig. 5: Photomicrograph of glomerulus showing crescents-RPGN(H&E,400X)

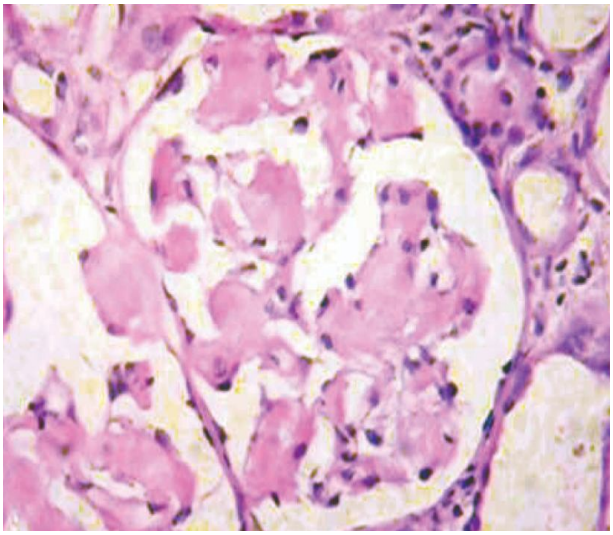

Fig. 6: Photomicrograph of glomerulus with acellular amorphous deposits-AMY(H&E,400X)

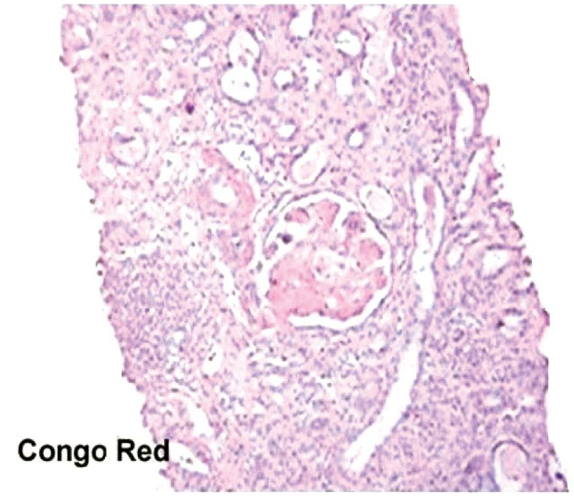

Fig. 7: Photomicrograph of glomerulus with pink-red deposits-AMY(100X)

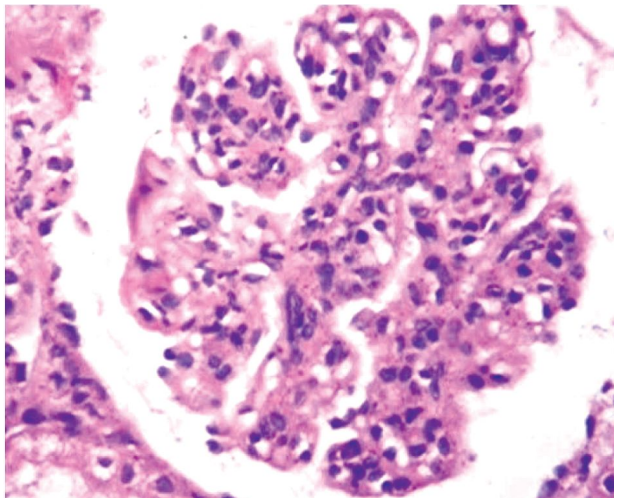

Fig. 8: Photomicrograph of glomerulus with mesangial proliferation-LNIV(H&E, 400X)

Discussion

Among seventy five cases 25% cases were of Focal Segmental Glomerulosclerosis, in the age group of 10 – 35 years, followed by Mesangioproliferative glomerulonephritis which contributed to 22.03%. These cases were predominantly seen in males and they presented with nephrotic range proteinuria and some patients with elevated Urea and Creatinine levels.

Winn and Nikki revealed FSGS is the most common cause of nephrotic syndrome in adults accounting for 35% of cases, as shown in Table 8. The clinical hallmark of these cases had nephrotic range proteinuria [3].

Hass have reviewed reports from all non-transplant adult renal biopsies from year 1974 to 1993 which comprised of 7,420 cases. The authors were of the opinion that among all biopsies there was increase in the incidence of focal segmental glomerulosclerosis over the 20 years during 1974 to 1993, which comprised 10% to 15% of idiopathic nephrotic syndrome cases in adults [4].

Table 8: Incidence of FSGS in various studies

Serial No.	Studies	FSGS %
1	Daskalakis and Winn[3]	35%
2	Haas et al[4]	35%
3	Abrantes MM et al[5]	32%
4	Rana K et al[6]	20%
5	Rennke and Klein et al[7]	20%
6	Chandrika KB[8]	18.84%
7	Present study	25%

Abrantes MM et al [5] studied 110 patients with biopsy proven FSGS and compared with clinical and laboratory data. The clinical data included nephrotic syndrome symptoms, height, weight, response to steroid therapy and laboratory data included urea, creatinine , 24- hour protein excretion and hematuria .

In the present study Nephrotic syndrome was the commonest presentation in primary glomerular diseases with FSGS accounting for 25% of cases.

Rana K et al revealed FSGS is the most common cause of nephrotic syndrome in adults [6]. Rennke et al [7] and Chandrika KB [8] revealed FSGS was the commonest occurrence in their studies.

Overall incidence of FSGS is increasing over the past two decades and the commonest cause of nephrotic syndrome in adults is Focal segmental glomerulosclerosis.

Minimal change disease is more common in boys than in girls. It is most common in young children less than six years. However MCD can occur at any age and is the commonest cause of nephrotic syndrome in adults. The incidence of minimal change disease is 2 to 16 / 100,000 per year in children younger than 16 years [9].

In the present study Minimal change disease seen commonly below 10 years of age with male predominance. In the present study out of 59 primary glomerular diseases, 52 cases showed clinical and laboratory finding correlation in arriving histopathological diagnosis.

Abrantes MM et al [10] studied 110 patients with biopsy proven FSGS and compared with clinical and laboratory data. The clinical data included nephrotic syndrome symptoms, height, weight, response to steroid therapy and laboratory data included urea, creatinine, 24- hour protein excretion and hematuria.

In the present study out of 12 secondary glomerular diseases 7 cases (55.00%) were of renal amyloidosis and clinically these cases were in the age group of 40-60 years. There was male predominance with high creatinine and urea levels with nephrotic range proteinuria > 3.5gm/kg and clinical features of nephrotic syndrome. All the cases were associated with chronic inflammatory states in which tuberculosis, bronchiectasis and rheumatoid arthritis were common.

There were totally five cases of Lupus nephritis which showed class IV and class V changes. Four showed diffuse proliferative glomerulonephritis (class IV) and one case showed membranous nephropathy (class V). All the cases were seen in adult females with features of nephrotic syndrome. Laboratory data of these patients showed ANA, Anti dsDNA positivity.

Agarwal revealed that among the secondary glomerular diseases diabetic nephropathy was the commonest cause of nephrotic syndrome (53%) followed by amyloidosis (16.4%) and Lupus nephritis (8.3%) [11]. Tuberculosis was the commonest cause of renal amyloidosis seen in 50% of cases [12].

Dikman and Thomas compared the clinical and morphological course of amyloid renal disease. They showed that the renal amyloidosis was common in adults and these patients presented with nephrotic syndrome symptoms with nephrotic range massive proteinuria with elevated blood urea nitrogen and creatinine levels. Progression to azotemia and renal failure was common in all forms of renal amyloidosis [13]. Primary amyloidosis is common in developed countries and secondary amyloidosis common in developing countries. AA amyloidosis affects patients of various ages with median age of 50 years. However in younger patients affected by AA amyloid a hereditary component must be considered. The conditions associated with secondary amyloidosis are inflammatory arthritis, chronic inflammatory states, chronic infections and malignancies. The overall incidence of renal amyloidosis is 3% and nephrotic syndrome was the commonest presentation [14].

Conclusion

Among 75 cases the majority of the biopsies were of primary glomerular diseases, and FSGS was the most common accounting for (25.00%) of cases followed by MESPGN (22.03%). Among the secondary glomerular diseases, renal amyloidosis was found to be more common in the patients who presented with nephrotic syndrome, and maximum cases were of secondary amyloidosis in which tuberculosis and chronic respiratory infections were common. Out of 75 cases which included both primary and secondary glomerular diseases, 64 cases showed correlation of pathological findings with clinical and laboratory parameters. The clinical examination, laboratory findings including biochemical tests were very much helpful in arriving the histopathological diagnosis. Immunofluorescence was done in selected cases where there was difficulty in diagnosis by light microscopy.

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