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Original Research Paper

Nephrology

HISTOPATHOLOGICAL OBSERVATIONS FROM RENAL BIOPSY: A SINGLE CENTRE EXPERIENCE FROM MAHARASHTRA, INDIA

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ABSTRACT

INTRODUCTION: Incidence of glomerular disease varies worldwide depending upon age, gender, and geographical region. Understanding the aetiology is very important for management of these diseases. Biopsy based technique helps in precise diagnosis and improved treatment outcomes.

AIM: This study aimed to classify glomerular diseases based on histopathological findings of renal biopsies in patients below 20 years to above 60 years.

MATERIALS AND METHODS: This cross-sectional study was conducted at Department of Nephrology, Grant Medical College and Sir JJ Group of Hospitals, Mumbai between October 2017 and August 2019 among patients who underwent renal biopsy. Histological diagnosis was performed using light microscopy, electron microscopy and immunohistochemistry staining. Histological findings were divided into primary glomeruli disease (PGD), secondary glomeruli disease (SGD), tubulointerstitial disease (TID) and others. Statistical analysis was done using one sample t-test to determine the differences in disease frequencies.

RESULTS: Total of 189 patients (102 men and 87 women) included were from age of 3-90 years. The mean (SD) age was 31.11 (16.05) years. The most common histological disease was PGD (48.67%) followed by SGD (33.33%) and TID (6.34%). Incidence of SGD was more common in elderly patients (>60 years). Among total population, incidence of focal segmental glomerulosclerosis (FSGS) (14.81%) and lupus nephritis (LN) (11.11%) were highest in PGD and SGD observed, respectively. Incidence of diabetic nephropathy (DN) was highest (33.33%) in elderly population (>60 years). In PGD, incidence of membranous glomerulonephritis (MGN) was significantly higher in men (87.5%) compared to women (12.5%) (p=0.001); however, in SGD, incidence of LN was significantly common in women (85.71%) compared to men (14.29%) (p=0.015).

CONCLUSION: FSGS and LN were prevalent PGD and SGD, respectively. Incidence of MGN was most common in men while, LN was prevalent in women who underwent renal biopsy.

KEYWORDS : Diabetic Nephropathy, Elderly Population, Focal Segmental Glomerulosclerosis, Lupus Nephritis

INTRODUCTION:

Renal biopsy is a widely used diagnostic tool all over the world which helps in correct evaluation of renal diseases and their prognosis which benefits in identifying treatment strategies. Renal biopsy observations from previous studies differ greatly and common factors which contribute to this variation are ethnicity, age characteristics of the population and the geographic location. Advances in technology over time also impact this variation [1-4].

Although several country specific renal biopsy registries available, there is no renal biopsy registry in India which might give information regarding overall spectrum of glomerular diseases. Few Indian studies have attempted to evaluate and report a wide range of glomerular diseases after renal biopsy; however, most of the studies include paediatric patients or adolescents [1, 5-7]. Studies which include geriatric population are scanty [8].

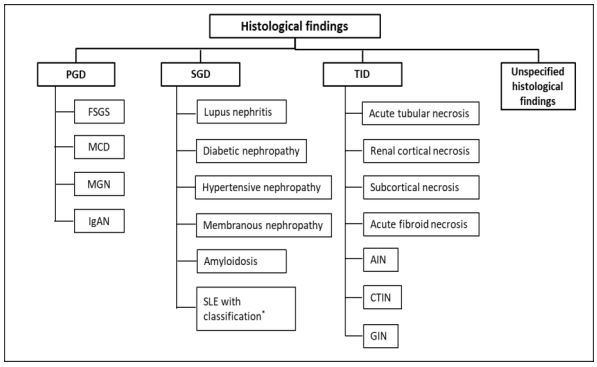
There are limited Indian studies demonstrating spectrum of glomerular diseases (GDs) based on renal biopsy and most of them are from southern part. There is a paucity of data from western India. We believe that this will contribute to the literature. The present study aimed to assess spectrum of GDs with the help of histopathological findings in patients below 20 years to above 60 years. The objective of this study was to evaluate trend of GDs in different age groups and to analyse the difference in pattern of GDs based on gender.

MATERIALS AND METHODS:

This cross-sectional study was conducted at Grant Medical College and Sir JJ Group of Hospitals, Mumbai between October 2017 and August 2019. The present study included data of 189 patients who underwent renal biopsy. Hematoxylin and eosin (H and E), periodic acid Schiff, Masson trichrome, were used to stain the specimen, and Congo-Red stain whenever necessary. All the biopsies were analysed through light microscopy and immunohistochemistry staining was performed using IgG, IgM, IgA, C3, C4, and fibrinogen, and electron microscopy was used.

As shown in flow chart histological findings were divided into 4 categories after histopathological evaluation **(Figure 1).**

Figure 1. Flow chart of classification of histological findings



*Crescentic GN / anti-neutrophil cytoplasmic antibody GN / anti- glomerular basement membrane disease/deposition diseases. AIN, acute interstitial nephritis; CTIN, chronic tubulo interstitial nephritis; FSGS, focal segmental glomerul o scle rosis; GIN, granulomatous interstitial nephritis; GN, glomerul onephritis; IgAN, IgA nephropathy; MCD, mini mal changed disease; MGN, membranous glomeru lonephritis; PGD, primary glomeruli disease; SGD, secondary glomeruli disease; SLE, systemic lupus erythematosus; TID, tubulointerstitial disease.

STATISTICAL ANALYSIS

The data were analysed using online statistics calculator. The frequencies of patients were expressed as percentages. One sample t-test was used to determine the differences in disease frequencies according to age group and gender in which biopsy was performed. A $p < 0.05$ was considered statistically significant.

RESULTS

A total of 189 patients were included in this study, of which 102 were men and 87 were women. The mean (SD) age was 31.11 (16.05) years with 47 patients (24.87%) below 20 years of age, 90 patients (47.62%) between 21-40 years of age, 40 patients (21.16%) between 41-60 years of age, and 12 patients (6.34%) above 60 years of age.

The distributions of histopathological diagnoses are summ arized in **(Table 1)** PGD (n=92, 48.67%) were the most common followed by SGD (n=63, 33.33%) and TID (n=12, 6.34%). Till the age of 60, incidence of PGD and SGD were comparable. However, incidence of SGD was found to be more common in elderly patients (>60 years) **(Figure 2)**. Incidence of PGD was in the range of 41.66% - 50%.

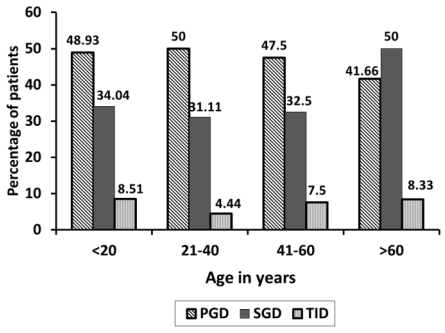
Table 1. Histopathological findings

	<20 years (n=47)	21-40 years (n=90)	41-60 years (n=40)	>60 years (n=12)	Total (N=189)
Primary glomeruli disease					
FSGS	3 (6.38)	16 (17.78)	8 (20)	1 (8.33)	28 (14.81)
MCD	12 (25.53)	5 (5.56)	0 (0)	0 (0)	17 (8.99)
Membranous GN	1 (2.13)	2 (2.22)	5 (12.5)	0 (0)	8 (4.23)
MPGN	1 (2.13)	5 (5.56)	1 (2.5)	1 (8.33)	8 (4.23)
IgA Nephropathy	1 (2.13)	6 (6.67)	1 (2.5)	0 (0)	8 (4.23)
Diffuse proliferative GN	2 (4.25)	4 (4.44)	0 (0)	0 (0)	6 (3.17)
Acute glomerulonephritis	1 (2.13)	1 (1.11)	3 (7.5)	0 (0)	5 (2.64)
ANCA/Anti GBM	0 (0)	2 (2.22)	0 (0)	1 (8.33)	3 (1.59)
Atypical haemolytic uraemia syndrome	1 (2.13)	1 (1.11)	0 (0)	0 (0)	2 (1.06)
Pauci-immune crescentic GN	0 (0)	1 (1.11)	1 (2.5)	0 (0)	2 (1.06)
RPGN	1 (2.13)	0 (0)	0 (0)	1 (8.33)	2 (1.06)
Differential proliferative GN	0 (0)	1 (1.11)	0 (0)	0 (0)	1 (0.53)
Minimal mesangial GN	0 (0)	1 (1.11)	0 (0)	0 (0)	1 (0.53)
Crescentic MPGN	0 (0)	0 (0)	0 (0)	1 (8.33)	1 (0.53)
Secondary glomeruli disease					
LN	5 (10.64)	13 (14.44)	2 (5)	1 (8.33)	21 (11.11)
DN	1 (2.13)	5 (5.56)	4 (10)	4 (33.33)	14 (7.41)
SLE	4 (8.51)	5 (5.56)	0 (0)	0 (0)	9 (4.76)
Focal proliferative Lupus Nephritis	2 (4.25)	1 (1.11)	0 (0)	0 (0)	3 (1.59)
Amyloidosis	0 (0)	0 (0)	2 (5)	1 (8.33)	3 (1.59)
Crescentic GN	0 (0)	1 (1.11)	1 (2.5)	0 (0)	2 (1.06)
Focal endocapillary proliferative GN	0 (0)	2 (2.22)	0 (0)	0 (0)	2 (1.06)
PIGN	1 (2.13)	0 (0)	1 (2.5)	0 (0)	2 (1.06)
Hypertensive nephropathy	0 (0)	1 (1.11)	1 (2.5)	0 (0)	2 (1.06)
Membranous nephropathy	1 (2.13)	0 (0)	1 (2.5)	0 (0)	2 (1.06)
PSGN	1 (2.13)	0 (0)	0 (0)	0 (0)	1 (0.53)
Fibroid necrosis	1 (2.13)	0 (0)	0 (0)	0 (0)	1 (0.53)
HIV/HBsAg/HCV	0 (0)	0 (0)	1 (2.5)	0 (0)	1 (0.53)
Tubulointerstitial disease					
Acute tubular necrosis	0 (0)	1 (1.11)	1 (2.5)	1 (8.33)	3 (1.59)
Focal necrosis	3 (6.38)	0 (0)	0 (0)	0 (0)	3 (1.59)
Renal cortical necrosis	0 (0)	1 (1.11)	2 (5)	0 (0)	3 (1.59)

Cortical necrosis	0 (0)	2 (2.22)	0 (0)	0 (0)	2 (1.06)
Subcortical necrosis	1 (2.13)	0 (0)	0 (0)	0 (0)	1 (0.53)
Others	4 (8.51)	13 (14.44)	5 (12.5)	0 (0)	22 (11.64)

Data shown as n (%).
ANCA, antineutrophil cytoplasmic antibodies; DN, diabetic nephropathy; FSGS, focal segmental glomerulosclerosis; GBM, glomerular basement membrane; GN, glomerulonephritis; HIV, human immunodeficiency virus; HCV, hepatitis C virus; LN, lupus nephritis; MCD, minimal changed disease; MPGN, membranoproliferative glomerulonephritis; PIGN, post-infectious glomerulonephritis; RPGN, rapidly progressive glomerulonephritis; PSGN, poststreptococcal glomerulonephritis; SLE, systemic lupus erythematosus.

Figure 2. Distribution of histopathological findings accor ding to age group



Data represented as percentage of patients in each age group. PGD, primary glomerular disease; SGD, secondary glomerular disease; TID, tubulointerstitial disease.

Table 2. Distribution of pathological findings of renal biopsy based on sex

Histopathology	Men (n=102)	Women (n=87)	P value
Primary glomeruli disease			
FSGS	19 (67.85)	9 (32.14)	0.053
MCD	10 (58.82)	7 (41.17)	0.470
Membranous GN	7 (87.5)	1 (12.5)	0.015
MPGN	4 (50)	4 (50)	>0.05
IgA Nephropathy	5 (62.5)	3 (37.5)	0.489
Diffuse proliferative GN	2 (33.33)	4 (66.67)	0.426
ANCA/Anti GBM	3 (100)	0 (0)	-
Atypical haemolytic uraemia syndrome	2 (100)	0 (0)	-
Pauci-immune crescentic GN	1 (50)	1 (50)	>0.05
RPGN	1 (50)	1 (50)	>0.05
Differential proliferative GN	0 (0)	1 (100)	-
Minimal mesangial GN	0 (0)	1 (100)	-
Crescentic MPGN	0 (0)	1 (100)	-
Acute glomerulonephritis	1 (20)	4 (80)	>0.05
Secondary glomeruli disease			
LN	3 (14.29)	18 (85.71)	0.001
DN	10 (71.43)	4 (28.57)	0.099
SLE	2 (22.22)	7 (77.78)	0.079
PSGN	1 (100)	0 (0)	-
Focal proliferative Lupus Nephritis	3 (100)	0 (0)	-
Crescentic GN	0 (0)	2 (100)	-
Fibroid necrosis	1 (100)	0 (0)	-
Focal endocapillary proliferative GN	1 (50)	1 (50)	>0.05
PIGN	0 (0)	2 (100)	-
Amyloidosis	1 (33.33)	2 (66.67)	0.603
Hypertensive nephropathy	2 (100)	0 (0)	-
Membranous nephropathy	1 (50)	1 (50)	>0.05
HIV/HBsAg/HCV	1 (100)	0 (0)	-
Tubulointerstitial disease			
Acute tubular necrosis	3 (100)	0 (0)	-
Focal necrosis	0 (0)	3 (100)	-
Renal cortical necrosis	1 (33.33)	2 (66.67)	0.603
Subcortical necrosis	1 (100)	0 (0)	-
Cortical necrosis	0 (0)	2 (100)	-
Others	16 (72.72)	6 (27.27)	-

Data shown as n (%).
ANCA, antineutrophil cytoplasmic antibodies; DN, diabetic nephropathy; FSGS, focal segmental glomerulosclerosis; GBM, glomerular basement membrane; GN, glomerul onephritis; HIV, human immunodeficiency virus; HCV, hepatitis C virus; LN, lupus nephritis; MCD, minimal changed disease; MPGN, membranoproliferative glome rulonephritis; PIGN, post-infectious glomerulonephritis; RPGN, rapidly progressive glomerulonephritis; PSGN, poststreptococcal glomerul onephritis; SLE, systemic lupus erythematosus.

Table 3. Histological findings of renal biopsies in this study and comparison with other published registries

Country	India, present study	India [1]	India [5]	India [6]	India [7]	India [9]	India [10]	Korea [11]	China [12]
Study site	Maharashtra	West Bengal	Chandigarh	Vellore	Tirupati	Tamil Nadu	Kerala	-	Northeast china
Study period	2017-2019	2010-2012	2009-2012	1996-2015	2010-2012	2010-2016	2009-2016	1987-2014	2007-2016
Number of patients	189	666	177	1740	137	231	271	345	2725
Age group, years	3-90	5-48	13–19	≤18	15-74	>60	11-80	5-18	≥14
Age in years, mean (SD)	31.11 (16.05)	28 (14.62)	16.2 (1.9)	12.8 (4.9)	37.99 (14.74)	64.2 (6.03)	41.98 (14.96)	9.7 (3.6)	41.24 (15.18)
PGD	92 (48.67)	527 (79.13)	150 (84.75)	1321 (75.9)	137 (75.6)	-	210 (77.78)	266 (77.10)	2156 (79.12)

FSGS	28 (14.81)	150 (22.58)	45 (25.42)	191(10.9)	9 (6.57)	16 (6.78)	37 (13.70)	11 (3.4)	73 (2.68)
MCD	17 (8.99)	134 (20)	38 (21.46)	369 (21.2)	23 (16.79)	-	16 (5.92)	68 (21.3)	346 (12.69)
SGD	63 (33.33)	139 (20.87)	27 (15.25)	323 (18.5)	41 (22.6)	-	33 (12.22)	46 (13.33)	417 (15.30)
LN	21 (11.11)	102 (15.31)	19 (10.7)	282 (16.2)	-	43 (18.5)	14 (5.18)	5 (1.5)	115 (4.22)
DN	14 (7.41)	1 (0.15)	-	1 (0.05)	-	33 (14.3)	16 (5.92)	-	42 (1.54)

Data shown as n (%), unless otherwise specified.
DN, diabetic nephropathy; FSGS,focal-segmental glomerulosclerosis; LN, lupus nephritis; MCD, minimal change disease; PGD, primary glomeruli disease; SGD, secondary glomeruli disease.

Majority of patients had FSGS in all the age groups. MCD was found in 12 patients below age of 20 years and in 5 patients between 21-40 years of age. MGN, MPGN, and IgAN was observed in eight patients each, while diffuse proliferative GN and acute GN were found in six and five patients, respectively. In SGD, majority of patients had LN (11.11%), followed by DN (7.41%) and SLE (4.76). Focal proliferative LN and amyloidosis was observed in three patients each. TID, classified into acute tubular necrosis, ANCA/Anti GBM, focal necrosis, renal cortical necrosis, were found in three patients each.

Male patients comprised the majority of the overall population **(Table 2)**. PGD was similar in men (50.98%) and women (49.02%). SGD observed were comparatively more in women (42.52%) than men (25.49%). Incidence of FSGS was comparable between men (67.85%) and women (32.14%). Incidence of MGN was significantly higher in men (87.5%) than women (12.5%) (p=0.015). Incidence of FSGS, MCD, IgAN, diffuse proliferative GN and acute GN were comparable between men and women.

In SGD, LN was significantly higher in women (85.71%) than men (14.28%) (p=0.001). DN and SLE were found in 71.43% and 22.22% men and 28.57% and 77.78% women, respectively. However, there were no significant difference observed in incidence of DN and SLE between men and women. Incidence of amyloidosis was comparable between men (33.33%) and women (66.67%). Three male patients found with acute tubular necrosis and three female patients were found with focal necrosis.

DISCUSSION:

Management and prognosis of glomerular diseases vary with patient age. Early interventions help to reduce the prevalence and mortality associated with glomerular disease in these patients. The most common PGDs that can cause end-stage renal disease are MCD and FSGS. Renal biopsy is a safe and efficient procedure that aids in better understanding of histological pattern of glomerular disease, its prognosis and management.

The present study was an attempt to add an evidence of a wide range of GD on the basis of histopathological observations post renal biopsy to the existing literature. This study included patients from a wide age range of 3-90 years and no previous study from India had evaluated patients from such a wide age group [1, 5-7, 9, 10]. Generally previous similar studies included either paediatric, adult or elderly patient population alone, thereby providing age specific spectrum of histopathological diagnosis in patients undergoing renal biopsy **(Table 3)** [1, 5-7, 9-12].

In the present study, the most common histological diagnosis was PGD (n=92, 48.67%) followed by SGD (n=63, 33.33%) and TID (n=12, 6.34%). These observations are in conco rdance with previously published literature [1, 5, 6]. Present study observed comparable incidence of PGD across all age groups with decreasing trend according to increasing age. However, incidence of SGD was similar in age groups below 60 years and was more common in elderly patients (>60 years). These observations are suggestive of the fact that as age increases, there is an increased risk of SGD diagnosis. Previous studies have established the relationship between increasing age and increased incidence of SGD [8,9,13].

Incidence of FSGS (14.81%) and LN (11.11%) were highest in PGD and SGD observed, respectively, among total study population. These observations indicate FSGS and LN as the most prevalent GDs in the present study. Similar observations have been reported in several previously published literatures. A retrospective analysis of a large single centre paediatric renal biopsy cohort from South Asia highlights important differences in the spectrum and trends of kidney disease compared to data from other regions. Authors reported incidence of minimal change disease (21.2%) and LN (16.2%) was prevalent in primary and secondary GNs, respectively. They further observed decrease in frequency of MCD and increase in frequency of FSGS and LN during the last 20 years [6]. A recently published Indian study by Gopaliah LR, et al. included 271 consecutive percutaneous kidney biopsies and evaluated the histopathologic pattern of renal biopsies from a tertiary care centre in south India. They reported the distribution of biopsy proven renal diseases among patients which highlighted PGD as the most common (77.78%) renal disease, followed by SGD (12.22%) and TID (10 %). The IgAN (23.33%) was the most common PGD followed by FSGS (13.70%) and DN (5.92%) and LN (5.18%) were the two most common biopsy-proven SGDs [10]. These observations corroborate the present study findings. A Pakistani study published in 2010 reported that the FSGS was the leading histopathological diagnosis, found in 29% of PGD, followed by membranous GN (23.5%). In SGD, LN was most prevalent (44.1%), followed by amyloidosis (42.1%) and DN (8.1%) [14].
Present study reported the incidence of DN was highest (33.33%) in elderly population (>60 years). A recently published study by Su S, et al. reported slightly similar observations showing incidence of DN was highest in patients of age group 40-64 (64.3%) years and ≥65 years (16.7%) [12].
A previous study conducted over the period of 27 years comparing the pathological results of renal biopsy with clinical features in paediatric patients demonstrated PGD as the most common renal biopsy finding and IgA nephropathy as the most common histopathological lesion [9]. Another study by Su et al. demonstrated MN as the most frequent pathological finding, however, IgAN was most commonly reported in other past literature [4, 12, 15, 16]. An Indian study by Golay et al. retrospectively analysed 666 patients of biopsy proven GD and reported MCD (20.12%) as the most common GD followed by FSGS (18.02%), LN (15.32%), membranous nephropathy (12.01%), and IgAN (8.11%). They further reported FSGS was the most common PGD in adults, MCD in children, and MN in the elderly patients and concluded that the spectrum of GD varies according to the area of study and changes over time [1].

A previously published study reported a significant difference in incidence of membranous nephropathy and MCD between men and women. They observed significantly higher male patients with diagnosis of membranous nephropathy and MCD as compared to female patients (p<0.001 and p=0.001,

respectively). In SGD, LN was diagnosed in significantly higher number of female patients as compared to male patients ($p<0.001$) [12]. These observations are in parallel with the present study.

The present study had a limitation of shorter study duration of only two years. Therefore, a longer duration study is required to evaluate the optimal pattern of renal diseases.

CONCLUSION:

In overall patient population, FSGS and LN were the most common PGD and SGD, respectively, diagnosed based on histopathological observations. Incidence of DN was highest in elderly population; whereas MGN was more common in men and LN was more common in women.

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