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Pattern of Biopsy-Proven Renal Disease in Pakistan: A Single Center Experience

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ABSTRACT

Background: This study was conducted to determine pattern (spectrum) of renal diseases on basis of renal biopsy in a tertiary care hospital in Islamabad.

Methodology: This retrospective observational study was conducted at Nephrology department of Pakistan Institute of Medical Sciences Islamabad from February 2012 to April 2020. Results of all biopsies done during this period were analyzed to determine the prevalence of different renal diseases on basis of histopathology and immunofluorescence.

Results: There were 254 kidney biopsy samples studied during the course of study. Out of total 254 patients 133 (52.4%) were male and 121 (47.6%) were female. Mean age of participants was 34.47±7.67 years (Range:15-60 years). Primary glomerulonephritis and secondary glomerulonephritis was found in 169 (66.5%) and 48 (18.9%) respectively, while tubulo-interstitial disease was reported in 37 (14.6%) of the total biopsies. Among 169 biopsies that showed primary GN, IgA Nephropathy (IgAN) was the most common in 16% of the biopsies, followed by membranous GN in 15.4% while membranoproliferative GN (MPGN) was seen in 13.6%, and focal and segmental glomerulosclerosis (FSGS) was seen in 13% of primary GN. Among 48 biopsies with secondary GN, lupus nephritis (LN) was found to be most common in 83.3% followed by amyloidosis in 6.3%. Among 37 biopsies having tubulo-interstitial disease, acute tubular nephritis (ATN) and renal cortical necrosis was seen in 29.7% each followed by tubulo-interstitial nephritis in 18.9% and acute interstitial nephritis (AIN) was seen in 16.2%.

Conclusion: This study shows that primary GN is the most common finding on renal biopsy. Among them IgA Nephropathy is the commonest lesion followed by membranous nephropathy, MPGN and FSGS. Among secondary GN, Lupus Nephritis is the commonest lesion.

Key words: Glomerulonephritis, Renal Biopsy, Renal Disease, Renal histopathology

Authors' Contribution:
[1,2]Conception; Literature research; manuscript design and drafting; [2,3] Critical analysis and manuscript review; [5,6] Data analysis; Manuscript Editing.

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Introduction

Renal biopsy is considered to be the investigation of choice to diagnose renal diseases especially

glomerulopathies. Its safety has been repeatedly assessed and it was proven to be a safe and effective tool.[1] It plays a vital role in the diagnosis of vascular, glomerular, tubulointerstitial, and genetic diseases. It provides important information regarding stage of the disease and also helps in management as well. The indications for renal biopsy are divergent and vary from center to center.[2] Various familial renal diseases are among the common clinical conditions where a biopsy is required.[3] In a developing country, the exact prevalence of renal diseases is difficult to determine since medical facilities are limited and unevenly distributed between urban and rural areas. In the absence of a central registry, the only data available is center based.[4] In order to understand the regional epidemiology of glomerular disease in a specific geographic area, it is crucial to study the prevalence of biopsy-proven renal disease (BPRD) and its variation and distribution as per geographic areas, socioeconomic conditions, race, age, and indication for renal biopsy.[5] Data from numerous international journal publications suggests that the course of glomerular disease has changed during the past few decades.[6-9]

The study of epidemiology of renal pathologies on biopsy not only helps us to understand the incidence and prevalence of different kidney diseases but also aids to understand the specific pattern of disease in a specific region and change of disease pattern as well. This change and variation of disease pattern has been observed within a country[10,11] and internationally.[12-14] The most frequent diagnosis found on renal biopsy is glomerulonephritis (GN). Glomerulonephritis is characterized by inflammation of the glomerular compartment of the kidney and is caused by the different immune mediated mechanisms.[15] Glomerulonephritis (GN) can be divided into primary and secondary GN. If no associated cause is found it is said to be primary GN. If it is associated with any other disease like systemic lupus erythematosus (SLE) or polyarteritis nodosa, Rheumatoid arthritis, Hepatitis or malignancy it is called as secondary GN. Glomerulonephritis is also classified on the basis of their clinical presentation and histopathological findings.[16] It became clear that patients with immunological complex GN displayed a diversity of histologic characteristics once renal biopsy was implemented into clinical practice. The first pathologic classification of lupus nephritis was developed in 1974 under by World Health Organization in an effort to standardize definitions and improve communication. This classification has been revised multiple times, most recently in 2003 and 2018 by the International Society of Nephrology/Renal Pathology Society (ISN/RPS). These amendments' specifics, which are covered elsewhere, are outside the purview of this review.[17]

If we look at the international data[18,] it is difficult to predict that which diseases are more prevalent in local population. Second, has variation of disease pattern been also observed with the passage of time or not. However, the literature on the entire spectrum of glomerular diseases of renal biopsy, especially from Pakistan, is scanty; hence, the present study was undertaken. To explore an updated and local data showing different histopathological lesions on renal biopsy in a single center tertiary kidney hospital, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

Methodology

This observational study was conducted at Nephrology department of Pakistan institute of medical sciences Islamabad Pakistan from February 2012 to April 2020 after approval from institutional ethical review board. Every procedure was carried out in accordance with the Helsinki Declaration. Nephrotic syndrome, nephritic syndrome, asymptomatic hematuria with proteinuria, acute renal failure, and chronic renal failure with a kidney of relatively normal size were the reasons for renal

biopsy. All patients who were above the age of 18 years and underwent renal biopsy during the study period were included in the study. Cases with graft biopsies or inadequate biopsies were excluded from the study. All biopsies were done with patient's consent according to hospital protocol. Two samples were taken through percutaneous approach under ultrasound visualization and sent to the laboratory. The samples of biopsies were processed in the laboratory according to the standard protocols. Light microscopy and immunofluorescence were done on each biopsy specimen; however, electron microscopy could not be performed due to its non-availability in our setup. Results of biopsies were analyzed. Experienced nephropathologists made all of the diagnoses based on histology and clinical research. The date of the kidney biopsy, the patient's age, gender, and pathological diagnosis were all recorded. The baseline demographics and clinical data/ biochemical parameters like serum creatinine, serum urea and 24-hour urinary protein were also analyzed.

SPSS version 21.0 was used to analyze the data. All categorical variables were characterised using frequency and percentage, and all continuous variables were reported using mean and standard deviation.

Results

In total 254 kidney biopsy samples studied during the course of study from February 2012 to April 2020. Out of 254 patients, 133 (52.4%) were male while 121 (47.6%) were female. Mean age of participants was 34.47±7.67 years with a range of 15-60 years. (Table I). Regarding glomerulonephritis (GN) type, Primary GN was found in 169 (66.5%), secondary GN was found in 48 (18.9%) and tubule-interstitial disease was reported in 37 (14.6%) of the total 254 biopsies (Table I).

Among 169 biopsies that showed primary GN, immunoglobulin A nephropathy (IgAN) was the most common in 27 (16%) biopsies, 19 males and 8 females, followed by membranous GN in 26 (15.4%), 16 males and 10 females followed by membranoproliferative GN (MPGN) lesion in 23 (13.6%), 12 males and 11 females and focal and segmental glomerulosclerosis (FSGS) was seen in 22 (13%), 13 males and 9 females while MCD and crescentic GN has equal number i.e. (15) 8.9% each. However 14 out of 15 Patients were males in Minimal Change Disease (Table II).

With regards to different histopathological lesions of IgA Nephropathy, among total 27 biopsies with IgAN subclass III (Mesangial expansion with hypercellularity) was found to be most prevalent in 10 (37%) biopsies followed by subclass V (sclerosis of glomeruli) in 7 biopsies (26%). 5 biopsies (18.5%) fall in subclass IV (diffuse proliferation) while 3 (11%) in subclass II (focal and segmental sclerosis). Only 2 biopsies (7.4%) were classified as subclass I (minimal changes without hypercellularity). Among biopsies with secondary GN, lupus nephritis (LN) was seen in 83.3% of the biopsies followed by amyloidosis among 6.3% of the 48 biopsies (Table III).

Distribution of lupus nephritis types with LN V was most abundant with 25%, followed by LN IV was 18%, LN II was present among 17%, LN IV was present among 15% of the lupus nephritis types. Among 37 biopsies having tubulo-interstitial disease, acute tubular nephritis (ATN) and renal cortical necrosis was seen in 11 (29.7%) each followed by tubulo-interstitial nephritis among 7 (18.9%) and acute interstitial nephritis (AIN) was seen in 6% (16.2%) biopsies (Table IV).

The frequencies of kidney diseases, gender ratio, mean age (years), mean 24 hours urinary protein, mean creatinine and mean urea among primary GN, secondary GN and tubulo-interstitial disease (Table I to IV).

Table I: Frequency of Renal Diseases (n=254)						
Variables	Frequency	Male/Female	Age (Years)	Serum Creatinine (µmol/L)	Blood Urea (mmol/L)	Proteinuria (g/24-h)
Primary Glomerulonephritis	169 (66.5%)	112/57	33.34±7.71 (15-50)	1.98±1.64 (0.6-7.8)	50.16±26.36 (20-149)	3.21±2.94 (0.2-22.8)
Secondary Glomerulonephritis	48 (18.9%)	10/38	37.91±7.53 (23-60)	1.24±0.81 (0.6-5.5)	39.39±16.92 (23-134)	2.62±1.41 (0.3-5.8)
Tubulo-Interstitial nephritis	37 (14.6%)	11/26	35.16±6.34 (25-55)	5.29±1.68 (0.7-8.7)	99.16±37.84 (28-222)	0.94±0.74 (0.3-4.4)
Total	254 (100%)	133/121	34.47±7.67 (15-60)	2.33±1.98 (0.6-8.7)	55.27±32.64 (20-222)	2.77±2.61 (0.2-22.8)

Table II: Frequency of types of primary glomerulonephritis in the kidney biopsies studied (n=169/254)						
Variables	Frequency	Male/Female	Age (Years)	Serum Creatinine (µmol/L)	Blood Urea (mmol/L)	Proteinuria (g/24-h)
Immunoglobulin A nephropathy (IgAN)	27 (16%)	19/8	28.63±5.86 (18-37)	1.07±0.21 (0.7-1.5)	38.85±9.41 (25-65)	3.14±3.95 (1.3-22.8)
Membranous Glomerulonephritis (MGN)	26 (15.4%)	16/10	34.69±6.47 (22-47)	0.81±0.15 (0.6-1.1)	31.77±4.61 (23-38)	7.60±2.44 (2.5-14.1)
Membranous Proliferative Glomerulonephritis (MPGN)	23 (13.6%)	12/11	33.22±4.78 (23-40)	1.30±1.15 (0.8-6.5)	43.56±12.14 (29-76)	2.86±0.55 (1.7-3.8)
Focal & segmental glumerosclerosis (FSGS)	22 (13%)	13/9	35.54±6.60 (22-44)	1.10±0.26 (0.6-1.7)	41.27±11.57 (23-60)	3.6±0.44 (2.8-4.6)
Minimal Change diseases	15 (8.9%)	14/1	38.67±3.31 (33-45)	2.62±0.59 (1.8-3.6)	51.53±11.51 (35-70)	0.84±0.24 (0.5-1.2)
Crescentic GN	15 (8.9%)	9/6	27.2±3.69 (23-36)	5.95±0.98 (4.6-7.8)	115.93±24.59 (70-149)	1.78±0.42 (1.3-2.9)

Table III: Frequency of Secondary Glomerulonephritis in the kidney biopsies studied (n=48/254)						
Variables	Frequency	Male/Female	Age (Years)	Serum Creatinine (µmol/L)	Blood Urea (mmol/L)	Proteinuria (g/24-h)
Lupus Nephritis (LN)	40 (83.3%)	5/35	36.85±4.41 (27-45)	1.09±0.5 (0.6-3.6)	36.45±9.49 (23-60)	2.74±1.38 (0.7-5.8)
Amyloidosis	06 (6.3%)	3/3	32.5±4.64 (26-38)	4.55±1.79 (1.1-6.1)	82.67±27.74 (34-112)	1.2±0.65 (0.6-2.3)
Secondary Membranous Glomerulonephritis (Secondary MGN)	02 (4.2%)	2/0	57.67±2.52 (55-60)	1.07±0.06 (1.0-1.1)	35.67±1.53 (34-37)	3.6±0.36 (3.3-4.0)

Table IV: Frequency of tubulo-interstitial in the kidney biopsies studied (n=37/254)						
Variables	Frequency	Male/ Female	Age (Years)	Serum Creatinine (µmol/L)	Blood Urea (mmol/L)	Proteinuria (g/24-h)
Acute Tubular Nephritis	11 (29.7%)	4/7	38.0±8.61 (25-55)	5.4±1.06 (2.8-6.8)	107.18±28.26 (51-145)	0.59±0.13 (0.3-0.7)
Renal Cortical Necrosis	11 (29.7%)	00/11	31.81±3.19 (27-36)	6.58±1.21 (4.4-8.7)	121.91±42.59 (76-222)	0.62±0.07 (0.5-0.7)
Tubular interstitial Nephritis	07 (18.9%)	02/05	38.43±5.19 (28-43)	4.54±1.43 (2.9-7.2)	78.57±28.67 (55-134)	1.3±0.53 (0.6-2.2)
Acute Interstitial Nephritis	06 (16.2%)	03/03	32.5±4.64 (26-38)	4.55±1.79 (1.1-6.1)	82.67±27.74 (34-112)	1.20±0.65 (0.6-2.30)

Discussion

This study showed that mean age of kidney disease is 34 years. It was almost the same as found in the study reported from India.[19] Gender distribution showed male predominance. These findings are comparable to other studies except one reported from Oman where females patients were higher than the males.[20,21] Regarding glomerular diseases, a great variation in prevalence of different lesions has been reported worldwide. For example, North America FSGS has been found to be the most common lesion in all ethnic groups.[22]

On the other hand, if we look at the data available from the studies conducted in Europe population, IgA Nephropathy is a common lesion while FSGS is a very uncommon.[23]

A study conducted in Japan reported that the most common cause of proteinuria is MCD[7,] while data from northern India showed MN is most common lesion.[11] A study conducted in Brazil reported FSGS as the most prevalent lesion.[24]

In our study GN (85.4%) was the most common diagnosis. Primary GN was seen in 66.5% and secondary GN was found in 18.9% followed by tubulointerstitial disease 14.6%. Among primary GN IgA nephropathy (IgAN) was the most commonly seen in 16% of the biopsies, followed by membranous GN in 15.4%, followed by membranoproliferative GN (MPGN) in 13.6%, and focal and segmental glomerulosclerosis (FSGS) were seen in 13% among 169 biopsies. Among biopsies with secondary GN, lupus nephritis (LN) was seen in 83.3% of the biopsies followed by amyloidosis among 6.3% of the 48 biopsies.

Khalid et al. and others reported that FSGS was the commonest lesion followed by membranous nephropathy and IgA nephropathy in proteinuria patients.[15,25,26]

All these studies reported that FSGS was the commonest lesion, and third commonest lesion was IgA nephropathy. In contrast to these studies, in our study IgA Nephropathy is the most common lesion followed by membranous nephropathy, MPGN and then FSGS. Why is there difference? it is difficult to answer!

It may be due to different sociodemographic characteristics change of pattern. It is thus required to conduct further studies locally.

A recent article by Al Yousef et al published from Kuwait showed that IgA Nephropathy was the most common cause of glomerular disease on renal biopsy.[27] Secondary GN is another common finding seen on renal biopsy. Lupus nephritis was the most common diagnosis on biopsy followed by amyloidosis. .Lupus is high in Middle East, Oman.[18]

Conclusion

Primary GN is the most common finding on renal biopsy. Among them IgA Nephropathy is the commonest lesion followed by membranous nephropathy, MPGN and FSGS. However, almost across the world, the most common secondary glomerular disease is Lupus Nephritis, the commonest lesion.

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