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Original Article

Biopsy Proven Renal Morphology Cognizance into its Four-Year Evolving Pattern; A Pakistani Perspective

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ABSTRACT

Objective: To determine the pattern of Biopsy Proven Renal Diseases (BPRD) in a single tertiary care centre in Islamabad, Pakistan.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Nephrology, KRL Hospital, Islamabad Pakistan, from Mar 2016 to Nov 2020.

Methodology: The archival records of all native renal biopsies performed in adults (>18 years) were retrospectively analyzed. The biopsies were performed according to standard indications and evaluated by light microscopy and immunofluorescence.

Results: A total of 134 renal biopsies were studied. Among these, 85(61.1 %) were males, and 49(36.5 %) were females. The mean age was 44.70±14.63 years. Primary glomerulonephritis's were the predominant group of diseases found in 93(69.4%) cases. Membranous nephropathy (MN) was the most common lesion in 52(38.8%), followed by focal segmental Glomerulosclerosis (FSGS) in 22(16.4%) cases. Chronic tubulointerstitial nephritis (Ch. TIN) 12(9.0%) was the third most common lesion among all biopsies. Other diagnoses included lupus nephritis (LN) 10(7.5%) and IgA nephropathy (IgAN) 9(6.7%). One sample one-sided t-test was used to estimate the minimum proportion of occurrence of different biopsies in our concerned population. The estimated minimum proportion of membranous nephropathy (MN) was 0.31, with a *p*-value of 0.034.

Conclusion: We concluded that primary Glomerulonephritis (PGN) is the most common renal disease, and membranous nephropathy is the most common biopsy-proven Glomerulopathy in our concerned population.

Keywords: Biopsy, Glomerulonephritis, Kidney disease, Renal Disease.

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INTRODUCTION

The systematic analysis of the global burden of disease conducted in 2017 showed that the prevalence of Chronic kidney disease (CKD) was 9.1% (697.5 million cases).[1] The assessment of urine and renal function is used to detect renal diseases.[2] In China, the percentage of diabetes has exceeded other common causes like Glomerulonephritis (GN) as an aetiology of CKD patients.[3]

In developing countries, the rising incidence of low birth weight is an increasingly common cause of low nephron numbers, which may later result in renal diseases.[4] A local community-based study showed the prevalence of CKD to be 12.5% in the Pakistani population.[5] In another local study, hypertension is the most common cause of CKD (39%), followed by diabetic nephropathy (DN) (37.4%) and GN (9%).[6,7]

A projection analysis of End Stage Renal Disease (ESRD) concluded that in the United States, the proportion of ESRD will increase in 2030 due to population, clinical and lifestyle vicissitudes in the population.[8,9]

The researcher included 29 laboratories on four continents and 60340 cases in a multi-continent study. A total of 42603 glomerular diseases were found. Furthermore, they concluded that the frequencies of glomerular disease were different for the patient's race and ethnicity.[10] As the renal disease is associated with region, race and ethnicity, this study aimed to determine the pattern of biopsy-proven renal disease in Islamabad.

METHODOLOGY

The cross sectional study was conducted at the Department of Nephrology, KRL Hospital, Islamabad Pakistan. The research was approved by the Ethical Committee of KRL Hospital Islamabad (Letter No. KRL-HI-ERC/Dec20/31-C). The subjects were scrutinized for the last five years, from March 2016 to November 2020 came into the department for biopsy. Out of the total of 250 cases, 134 cases were matched with the inclusion criteria.

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Inclusion Criteria: All adult patients aged more or equal to 20 years of either gender who came in for native kidney biopsies were included in the study.

Exclusion Criteria: Patients having other comorbid, i.e. skin diseases (like complicated Acne, diabetic carbuncles, Eczema), heart diseases (CCF, Recent MI or CABG), blood diseases (like iron deficiency or vitamin B-12 deficient anaemias, aplastic anaemia, haematological malignancy) and pregnant women were excluded from this study.

The biopsy request forms, clinical records and biopsy reports were reviewed to collect relevant data components. Written informed consent was taken from all patients prior to biopsies. All biopsies were performed under ultrasound guidance using Monopty Gun (18G×20cm for native biopsies). The histopathological evaluation included Light Microscopy (LM), and Immunofluorescence (IF) was noted down. For LM, hematoxylin, Eosin (H & E), Periodic acid Schiff (PAS), and Masson's trichrome and silver stains were used. IF was performed using polyclonal antibodies against IgG, IgM, IgA, C3, and C1q according to manufacturers' instructions.

Statistical Package for Social Sciences (SPSS-version 23.00) was used to analyze the data. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to find out the association. One sample t-test was used to assess the maximum and minimum proportion of the biopsy in the concerned population. The *p*-value ≤0.05 was considered significant.

RESULTS

A total of 134 native renal biopsies were included in the study. The average age of male patients was 45.03±14.57 years which was slightly higher compared to the female patients having a mean age of 43.35± 13.66 years. The most common biopsy indication was nephrotic syndrome in 82(61.2%) cases. This was followed by acute kidney injury, which was indicated in 30 (22.4%) cases. The result showed that the patients' age was not associated with clinical indication and renal disease, with *p*-values of 0.763 and 0.541, respectively (Table-I).

Table-I: Association of Clinical Indication and Renal Disease with Patients' Age (n=134)

Parameters		Age Groups of Adults				*p*-value
		Young n(%)	Middle Age n(%)	Senior Middle Age n(%)	Elder n(%)	
Clinical Indication	Nephrotic Syndrome	16(19.5)	32(39)	22(26.8)	12(14.6)	0.763
	Acute kidney injury	7(23.3)	7(23.3)	10(33.3)	6(20.0)	
	Nephritic Syndrome	3(17.6)	6(35.3)	6(35.3)	2(11.8)	
	Non-Nephrotic Proteinuria	2(40.0)	1(20.0)	2(40.0)	0	
Renal Disease	Primary Glomerulonephritis	18(19.4)	33(35.5)	26(28.0)	16(17.2)	0.541
	Secondary Glomerulonephritis	5(22.7)	7(31.8)	8(36.4)	2(9.1)	
	Tubulo Interstitial Nephritis	5(33.3)	3(20.0)	5(33.3)	2(13.4)	
	Vascular Disease	0	3(75.0)	1(25.0)	0	

Among PGD, MN was dominant in 52(38.8%), while FSGS was the second most common finding, observed in 22(16.4%) biopsies. Among SGD (secondary Glomerulonephritis), Lupus Nephritis (LN) was the most common category of renal disease 10(7.5%). Among Tubulo-Interstitial Disease (TID), Tubulo-Interstitial Nephritis (TIN) was the most common finding, observed in 12(9%) biopsies. Finally, Hypertensive Vasculopathy (HV) was the most common biopsy 3(2.2%) found among vascular diseases (Table-II).

Table-II: Spectrum of Renal Diseases (n=134)

Biopsy	n(%)
Primary Glomerulo-Nephritis (PGN)	
Membranous Nephropathy	52(38.8)
Focal Segmental Glomerulosclerosis	22(16.4)
Immunoglobulin A Nephropathy	9(6.7)
Membranoproliferative glomerulonephritis (MPGN)	6(4.5)
Minimal change disease	4(3.0)
Secondary glomerulonephritis (SGN)	
Lupus Nephritis	10(7.5)
ANCA-associated glomerulonephritis	4(3.0)
C1q Nephropathy	2(1.5)
Chronic Sclerosing glomerulonephritis	2(1.5)
Amyloidosis	2(1.5)
Alport's Syndrome	1(0.7)
Crescentic glomerulonephritis	1(0.7)
Tubulo-Interstitial Disease (TID)	
Tubulo interstitial Nephritis	12(9.0)
Acute Tubular Necrosis	3(2.2)
Vascular Disease	
Hypertensive Vasculopathy	3(2.2)
Hemolytic Uremic Syndrome (HUS)	1(0.7)

Based on our study, the proportion of MN was at least 0.31 and not more than 0.46 in our concern population with *p*-values 0.034 and 0.046, respectively. The second most common biopsy in our population is FSGS which was at least 0.11 and not more than 0.22, with a *p*-value of 0.046 and 0.043, respectively. The maximum proportion of the most common biopsy in our concerned population was mentioned in Table-III.

Table-III: Estimated Proportions of the Most Common Biopsies (n=134)

Biopsy	Estimated Maximum Proportion in the Population	*p*-value
Membranous Nephropathy	0.46	0.046
Focal Segmental Glomerulosclerosis	0.22	0.043
Tubulo interstitial Nephritis	0.14	0.022
Lupus Nephritis	0.12	0.025
Immunoglobulin A Nephropathy	0.11	0.025

DISCUSSION

The important source of accurate epidemiological data and the clinical presentation of renal disease is biopsy registries. If not read correctly, some of them will mislead in identifying high-risk patients. On the other hand, if renal diseases are not treated properly will lead to chronic kidney disease.[11,12] Our study has provided a stimulus for comparing the evolving patterns of biopsy-proven renal diseases.

A Saudi study over two years included 405 cases that showed FSGS to be the most common real pathology identified, similar to the world over pattern noted.[13] In a large Indian study, the most common indication of renal biopsy was the Nephrotic syndrome .mirror image to the other international data, and they also found FSGS to be the most common pattern and MCD to be second. MCD is commonly a disease in children, and in our centre, we only deal with adult nephrology, which is why we did not find a high percentage of MCD.[14]

In the meta-analysis conducted in China, the researcher revealed that biopsy-proven Lupus Nephritis among systemic lupus erythematosus (SLE) patients cases have increased in Saudi Arabia. In contrast, it has decreased percentages in Asia/Latin America (63% as compared to Europe 34% with a *p*-value <0.05.)[15] our study shows a very low percentage of LN cases, maybe because this disease is not yet common in SLE patients.

Zhou *et al*. discussed the renal biopsy cases of the last 15 years in Eastern China. They found IgAN(50%) to be the most common renal biopsy pattern led by MN(16.8%) similar to our study, and they have noted MN cases are increasing, which shows that previously known glomerular diseases patterns are now changing.[16]

In another Chines study, the researcher included 969 patients from 2008 to 2017. They found that Although IgAN is still the most common renal pathological pattern seen, their frequency has decreased. On the other hand, similar to other Chinese studies, they also found that MN cases have increased from 6.8% to 16.2%.[17] In China, researchers discussed the pattern of biopsies through a large ten years of data from 2004-2014 and revealed the frequency of MCD and IgA nephropathy as 29% and 17%, respectively.[18] We rarely dealt with children in our centre, which is why we do not see a high frequency of MCD in our study.

In another study in China where the researchers assessed 176355 patients over the last 30 years from 15 different cities/provinces of China. The frequency of IgAN was 24.3%, whereas MN, MCD and FSGS were 12.6%, 9.8% and 4.6%, respectively. This shows the evolving pattern of renal Glomerulopathy.[19]

We routinely do not do renal biopsies of diabetic nephropathy patients in Pakistan; that is why we see a low frequency of biopsy-proven diabetic Glomerulosclerosis in Pakistani studies.

PGD was the most common renal disease in both male and female patients. There was no association between the sex of the patient and renal disease. The highest frequency of renal disease was MN. There was no association between renal disease and patients' age. Among PGD, MN was dominated by both males and females, whereas it was also most frequent in all age groups. This finding was surprising as the largest local study from Karachi highlighted FSGS as the most common lesion in PGD.[11]

CONCLUSION

We concluded that primary Glomerulonephritis (PGN) is the most common renal disease, and membranous nephropathy is the most common biopsy-proven Glomerulopathy in our concerned population.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

ZA & ZN: Conception, drafting the manuscript, approval of the final version to be published.

NA & FH: Study design, drafting the manuscript, critical review, approval of the final version to be published.

KM & MI: Data acquisition, data analysis, data interpretation, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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