Original Article

Biopsy proven renal diseases at PNS SHIFA, Karachi, Pakistan: Clinicopathological correlations

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Objective: To determine the clinicopathological correlations of biopsy proven renal disease (BPRD) from a tertiary care naval hospital in Karachi, Pakistan.

Methodology: All the adequate native renal biopsies (RBs) in adult patients (≥18 years) performed at our hospital from 2008 to 2012 were retrospectively analyzed. These were studied by light microscopy and immunofluorescence.

Results: A total 47 cases met the inclusion criteria. The mean age was 33.23±12.11 years. Nephrotic syndrome (NS) was the most frequent indication, followed by renal failure (RF). Focal segmental glomerulosclerosis (FSGS) was the most common cause of NS, followed by membranous GN (MN) while chronic sclerosing GN was the most common cause of RF. The mean total number of glomeruli included in all RBs was 14.43±7.06. The mean number of gobally sclerosed glomeruli was 3.66±6.23 (range: 0-39) and the mean of segmentally sclerosed glomeruli, 0.94±1.55 (range: 0-7). Overall, global glomerulosclerosis (GS) was found in 31(66%) biopsies, and segmental glomerulosclerosis (SS) in 19 (40.4%) biopsies. Arteriolosclerosis (AS) was present in 12 (25.5%) biopsies and hyaline arteriolosclerosis in 11(23.4%). Fibrointimal thickening of arteries was found in 13 (27.6%) cases. A variable degree of interstitial fibrosis and tubular atrophy (IFTA) was found in 41 (87.2%) cases and interstitial inflammation in 16 (34%) cases. Acute tubular necrosis (ATN) was found in 5 (10.6%) cases.

Conclusion: This study provides the clinicopathological correlates of RBs in patients with medical renal diseases. Our data are more or less similar to those recently reported from around the world. (Rawal Med J 2014;39: 154-158).

Key Words: Glomerulonephritis, nephrotic syndrome, renal biopsy, renal failure.

INTRODUCTION

The diagnostic renal pathology is an integrated process wherein the results of all pathological assessments are correlated with the clinical and the serological data to arrive at the correct diagnosis.[1-3] Recent advances in the serology and percutaneous renal biopsy (RB) study have proved invaluable for an accurate diagnosis of medical renal diseases, especially the glomerulopathies.[2] To harvest the most advantages from RB studies, many developed countries have established national or regional RB registries.[3-10] The data from RB registries has helped in understanding the pathoepidemiology of the renal diseases in different parts of the world.[5-10] The RB indications and the extent of its pathological assessment vary from country to country and even from center to center.[11-15]

It is well known that the prevalence of biopsy proven renal diseases (BPRD) varies widely depending on a number of factors including the race, age, demography geographic region, socioeconomic conditions, and indication of renal biopsies.[11,12-18] Unfortunately, there is no national or centralized RB registry in Pakistan,[1] however, a few single center studies have been published from this country.[19,20] The aim of this study was to determine the clinicopathological correlations of native RBs performed at our center.

METHODOLOGY

All the consecutive percutaneous RBs performed at PNS, Shifa Hospital from January 2008 to July 2012 were included in the study. The indications for RB were classified into the five standard clinical categories: nephrotic syndrome (NS), non-nephrotic proteinuria (NNP), proteinuria-hematuria (PH), renal failure (RF), and rapidly progressive glomerulonephritis (RPGN). In some cases, there was more than one indication, such as RF in a case of NS. In such cases, the primary indication was

included for analysis. Standard definitions were used for all these biopsy indications.[20] In cases of RF as a biopsy indication, RB was performed only if kidney sizes were within normal limits. Systemic hypertension was diagnosed when blood pressure was higher than 140/90 mm Hg. All the biopsies were obtained by percutaneous automated biopsy gun under ultrasonographic guidance. A written informed consent was obtained prior to the procedure. The research was conducted according to the tenets of Declaration of Helsinki.

The RBs were evaluated at the Histopathology Department of SIUT, Karachi, Pakistan. The specimens were studied by an experienced nephropathologist (MM). The study included light microscopy (LM) and immunofluorescence (IF). IF study was done by using polyclonal antibodies against human IgG, IgM, IgA, C3, and C1q (Dako, Glosstrup, Denmark). Electron microscopy (EM) was not performed on these cases. Standardized histological classification was used to diagnose the kidney pathological conditions.[20] The original RB request forms, admission records and biopsy reports were retrieved and the relevant data items noted in a spreadsheet. The data included age, gender, indication for RB, histopathological diagnosis and the relevant laboratory investigations such as serum creatinine, 24-hour urinary protein excretion, virology (HBsAg, anti HCV, HIV) and serology (ANA, anti-dsDNA antibody, C3, C4). The statistical analysis was carried out using SPSS version 13. The correlational analysis was done using Pearson's Chi- square test.

RESULTS

A total of 47 patients had adequate RB material and clinical data. However, the total number of biopsies performed over the study period was 60. Only one biopsy was inadequate and in 12, detailed clinicopathological data were not available to carry out correlational analysis and were excluded. No major biopsy-related complications were observed. The overall demographic, clinical and laboratory characteristics of all these patients are shown in Table 1. NS was the most common indication for RB, followed by RF (Table 2).

Table 1. Demographic, clinical and laboratory characteristics of study population (n=47).

Males, n (%)	35 (74.5%)
Females, n (%)	12 (25.5%)
Male to female ratio	2.9:1
Mean age (in years)	33.23±12.11
Age range (in years)	18 – 72
Hypertension, n (%)	18 (38.3%)
Hematuria, n (%)	8 (17%)

Table 2. Clinical indications for renal biopsy.

Indication	Number	Percentage
Nephrotic syndrome	26	55.31
Renal failure	13	27.65
Non-nephrotic proteinuria	6	12.76
Non-nephrotic proteinuria, hematuria	2	4.25
Total	**47**	**100.00**

Table 3. Histopathological diagnoses in 26 renal biopsies from adult nephrotic patients.

Renal Diseases	Number	Percentage
FSGS	11	42.3
Membranous GN	7	26.9
Chronic sclerosing GN	1	7.7
IgAN	1	3.8
Amyloidosis	1	3.8
MCD	1	3.8
MPGN	1	3.8
MesPGN	1	3.8
Lupus nephritis, class V	1	3.8
Total	1	100

FSGS, focal segmental glomerulosclerosis, IgAN, IgA nephropathy, MCD, minimal change disease, MesPGN, mesangial proliferative GN MPGN, membranoproliferative GN.

Table 4. Histopathological diagnoses in 13 renal biopsies from adult patients with renal failure.

Renal Diseases	Number	Percentage
Chronic sclerosing GN	4	30.8
FSGS	2	15.4
IgAN	2	15.4
Amyloidosis	1	7.7
Acute cortical necrosis	1	7.73.8
MesPGN	1	7.73.8
Tubulointerstitial nephritis	2	15.4
Total	**13**	**100**

FSGS, focal segmental glomerulosclerosis, IgAN, IgA nephropathy, MesPGN, mesangial proliferative GN.

Since NS and RF formed the main bulk of the study cohort, these cases were analyzed in further detail. The mean age of patients with NS was 32.04±14.04 years. The age range was 18 to 72 years. There were 20 (76.9%) males and 06 (23.1%) females, with a male to female ratio of 3.3:1. The mean 24-hour urinary protein excretion was 5.23±2.54 grams (range: 2-12). The mean serum albumin concentration was 1.88±1.5 gram/dl (range: 0-4). The mean serum creatinine was 0.94±1.17 mg/dl (range: 0-4). Renal diseases underlying NS in adult patients in the present study are shown in Table 3. As is seen in this table, FSGS is the most prevalent cause of NS in adults in our area. MN is the second most common cause in adults and MCD is distinctly rare in this age group.

The mean age of patients with RF was 29.92±8.48 years. The age range was 20 to 45 years. There were 9 (69.3%) males and 4 (30.7%) females, with a male to female ratio of 2.2:1. Both hypertension and hematuria were found in 4 (30.7%) patients with RF. The mean serum creatinine was 1.37±1.84 mg/dl (range: 0-7). The renal disorders underlying RF in adult patients in this study are shown in Table 4. As is seen in this table, chronic sclerosing GN is the most prevalent cause of RF in adults in this part of the world. This is most probably related to delayed presentation of the patients to the nephrologists.

When analyzing the clinical utility, it was found that the procedure of RB changed management of the patients in 40% of the cases and the biopsy diagnosis was different from the most likely clinical diagnosis in 60% of cases.

Pathological findings and the clinicopathological correlations

The mean of total number of glomeruli included in all the RBs was 14.43±7.06. The mean number of gobally sclerosed glomeruli was 3.66±6.23 (range: 0-39) and the mean number of segmentally sclerosed glomeruli, 0.94±1.55 (range: 0-7). Overall, global glomerulosclerosis (GS) was found in 31(66%) biopsies, and segmental glomerulosclerosis (SS) in 19 (40.4%) biopsies. Arteriolosclerosis (AS) was present in 12 (25.5%) of biopsies and hyaline arteriolosclerosis in 11(23.4%) cases. Fibrointimal thickening of arteries was found in 13 (27.6%) cases. A variable degree of interstitial fibrosis and tubular atrophy (IFTA) was found in 41 (87.2%) cases and interstitial inflammation in 16 (34%) cases. Acute tubular necrosis (ATN) was found in 5(10.6%) of cases.

On clinicopathological correlation of demographic, clinical, laboratory and histopathological features with the disease diagnosis in patients with NS, it was found that there was significant association with renal dysfunction at the time of biopsy (p=0.03), serum creatinine (p=0.005), fibrointimal thickening (p=0.02), IFTA (p=0.01), and interstitial inflammation (p=0.02). There was no correlation between disease diagnosis and age (p=0.38), sex (p=0.10), hypertension (p=0.61), proteinuria (p=0.34), serum albumin concentration (p=0.24), hematuria (p=0.22), GS (p=0.10), SS (p=0.15), AS (p=0.19), Ah (p=0.12) and ATN (p=0.92). The lack of correlation of most clinicopathological parameters may reflect small number of individual renal diseases in the present study.

On correlation analysis of the same clinicopathological features with the disease diagnosis in patients with RF, the only partially significant correlation was found with SS (p=0.054), while rest of all demographic, clinical, laboratory and histopathological features showed no significant correlation with the disease diagnosis. This may partly be due to true non-association but mostly due to the small size of the sample.

DISCUSSION

It is well known that the different renal diseases present with different clinical syndromes and this can help in the diagnosis of a particular disease, but, there is significant overlap in the presenting features, hence the need for clinicopathological correlation.[2,5,6] The situation in majority of the developing countries is far from optimal and RB registries are either non-existent or at a primitive stage.[1,3,13-18,21-25] More recently, we have published our experience on the pattern of BPRD in our country.[20] The findings of the present study also to some extent recapitulate the findings of our earlier studies. All the cases could be diagnosed in the study by correlation of the clinical, serological, LM and IF data.

Among the clinical syndrome, NS is the most

common indication for RB the world over. In our series, also NS was the most common indication. The distribution of underlying glomerulopathies is also concordant with other local and international studies during the recent past. In this regards, the primacy of FSGS is noteworthy. FSGS is a heterogenous lesions and its incidence is on the rise throughout the world, both in adults and children.[26]

MN was the second most common lesion in our adult nephrotic population. This is also concordant with the recent findings in the local and international literature.[26] This lesion was the predominant lesion in adult NS few decades back but now FSGS has superseded it as the most common lesion, especially in younger adults. Other causes of NS were rare and included both PGD and SGDs. Amyloidosis is also one of the common causes of NS in adults in this region and in the vast majority of cases, it is of secondary nature. This is due to endemicity of tuberculosis in our country.[20]

Renal failure was the second most common RB indication in our study. RB were only performed if there was no obvious cause for RF and the kidney size was normal or enlarged on ultrasonography. The causes of RF in this series were more or less similar to those reported from this region of the world.[20]

On correlational analysis, there was a poor correlation between the clinicopathological and demographic features and the disease diagnosis in both NS and RF cohorts. This may partly be due to the small number of patients with individual lesions. Large-scale and longitudinal studies may help determine the correlations among these parameters.

There are several limitations in this study. These include small sample size and its origin from a single center of defense personnel. However, some civilian personnel are in this study. We acknowledge that the study results are not truly representative of the general population given the above limitations. Moreover, EM was also not performed on these cases. However, there was no case of RB in the present series, where EM was indispensable.

CONCLUSION

This study provides important information on the clinicopathological correlation of RBs from southern region of Pakistan. There is an urgent need to establish a central RB registry to collect and analyze accurate data on BPRD in this part of the world.

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REFERENCES

1. Mubarak M. Toward establishing renal biopsy registry: a step in right direction. Ind J Nephrol 2013;23:159-60.
2. Mubarak M, Kazi JI. Role of immunoflourescence and electron microscopy in the evaluation of renal biopsies in nephrotic syndrome in a developing country. Ultrastruct Pathol 2009;33:260-4.
3. Al-Homrany M. Need for renal biopsy registry in Saudi Arabia. Saudi J Kidney Dis Transpl 2008;19:346-9.
4. Sugiyama H, Yokoyama H, Sato H, Saito T, Kohda Y, Nishi S, et al. Japan Renal Biopsy Registry: the first nationwide, web-based, and prospective registry system of renal biopsies in Japan. Clin Exp Nephrol 2011;15:493-503.
5. Rivera F, Lopez-Gomez JM, Perez-Garcia R. Clinicopathologic correlations of renal pathology in Spain. Kidney Int 2004;66:898-904.
6. Gesualdo L, Di Palma 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.
7. Simon P, Ramee MP, Boulahrouz R. Epidemiologic data of primary glomerular diseases in western France. Kidney Int 2004;66:905-8.
8. Covic A, Schiller A, Volovat C. Epidemiology of renal disease in Romania: a 10 year review of two regional renal biopsy databases. Nephrol Dial Transplant 2006; 21:419-24.
9. Naumovic R, Pavlovic S, Stojkovic D. Renal biopsy registry from a single centre in Serbia: 20 years of experience. Nephrol Dial Transplant 2009;24:877-85.
10. McQuarrie EP, Mackinnon B, Young B, Yeoman L, Stewart G, Fleming S, et al. Centre variation in incidence, indication and diagnosis of adult native renal biopsy in Scotland. Nephrol Dial Transplant 2009;24:1524-28.
11. 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;24:3050-4.
12. Braden GL, Mulhern JG, O'Shea MH, Nash SV, Ucci AA

Jr, Germain MJ. Changing incidence of glomerular disease in adults. Am J Kidney Dis 2000;35:878-83.
13. Li LS, Liu ZH. Epidemiologic data of renal diseases from a single unit in China: Analysis based on 13,519 renal biopsies. Kidney Int 2004;66:920-23.
14. Choi IJ, Jeong HJ, Han DS. An Analysis of 4,514 cases of renal biopsy in Korea. Yonsei Med J 2001;42:247-54.
15. 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.
16. Golay V, Trivedi M, Abraham A, Roychowdhary A, Pandey R. The spectrum of glomerular diseases in a single center: A clinicopathological correlation. Indian J Nephrol 2013;23:168-75.
17. 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.
18. Alkhunaizi AM. Pattern of renal pathology among renal biopsy specimens in Eastern Saudi Arabia. Saudi Med J 2007;28:1676-81.
19. Jamal Q, Jafarey NA, Naqvi AJ. A review of 1508 percutaneous renal biopsies. J Pak Med Assoc 1988;38:272-5.
20. Mubarak M, Kazi JI, Naqvi R, Ahmed E, Akhter F, Naqvi SA, et al. Pattern of renal diseases observed in native renal biopsies in adult in a single center in Pakistan. Nephrology 2011;16:87-92.
21. 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.
22. 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.
23. Yahya TM, Pingle A, Boobes Y. Analysis of 490 Kidney biopsies: data from the United Arab Emirates Renal Diseases Registry. J Nephrol 1998;11:148-50.
24. Huraib SO, Abu-Aisha H, Mitwalli A, Mahmood K, Memon NA, Sulimani F. The spectrum of renal disease found by kidney biopsies at King Khalid University Hospital. Saudi Kidney Dis Transpl Bulletin 1990;1:15-9.
25. Arrayed A, George SM, Malik AK. The spectrum of glomerular diseases in the Kingdom of Bahrain: An epidemiological study based on renal biopsy interpretation. Transplant Proc 2004;36:1792-95.
26. Haas M, Spargo BH, Conventry S. Increasing incidence of focal segmental glomerulosclerosis among adult nephropathies. Am. J Kidney Dis 1995;26:740-50.