RENAL CAUSES OF SIGNIFICANT PROTEINURIA IN POPULATION ABOVE 40 YEARS OF AGE

Nisar Anwar, Ahmad Zeb Khan, Amer Azhar, Mian Ayaz ul Haq

Department of Nephrology,
Khyber Teaching Hospital, Peshawar
Rehman Medical Institute, Peshawar

ABSTRACT

Objective: The objective of this study is to highlight the importance of renal biopsy in adult population (above 40 years age) with significant proteinuria due to renal diseases, so that accurate diagnosis and treatment plan can be devised.

Material and Methods: This is a retrospective study carried out at the department of Nephrology, Khyber Teaching Hospital, Peshawar. The biopsies carried out between June 1999 and June 2002 were scrutinized. All these were ultrasound guided percutanous renal biopsies. Biopsies carried out in patients with the following findings were included in our study

1. Nephrotic range proteinuria in adults.
2. Non-nephrotic range proteinuria with evidence of hypertension / haematuria / deranged renal function or active sediments on urine microscopy.
3. Patients having age above 40 years.
4. Patients not suffering from Diabetes, Chronic Renal Failure, Adult Polycystic Kidney Disease, or any Congenital Renal Disease.

Results: A total of 260 renal biopsies were carried out in the above-mentioned period. Out of these only 56 patients fulfilled the above criteria. In these 46 (82.14%) were male patients and 10 (17.86%) were females. In the adult population having age above 40 years, the most frequent entity was membranoproliferative GN 11(19.64%) cases followed by membranous GN 9(16.07%) cases and tubulointerstial nephritis 8(14.28%) cases. It is noted that nephrotic range proteinuria is most prevalent in membranous GN followed by focal segmental glomerulosclerosis. While non-nephrotic range proteinuria is mostly seen in membranoproliferative GN. It is also noticed that crescentic GN (100%) is invariably associated with deranged renal function followed in frequency by renal amyloidosis (60%) and acute tubular necrosis (40%).

Conclusion: We conclude that in the adult population membranoproliferative GN is the leading histopathological entity in middle aged population followed by membranous GN in our population. Percutanous renal biopsy is a safe procedure. It helps us to determine the underlying histopathology for accurate diagnosis and guiding physicians in the management of such cases.

Key words: Nephrotic Syndrome, Renal Biopsy, Proteinuria, Glomerulopathy

INTRODUCTION

Injury to glomeruli results in a variety of signs and symptoms of disease, including proteinuria, haematuria, azotemia, oligouria, edema and hypertension. Specific glomerular diseases tends to produce particular syndromes of renal dysfunction, although multiple glomerular diseases can produce the same syndrome.

Evaluation of pathogenic features identified in a renal biopsy specimen may be required for definitive diagnosis. In patients with renal disease, renal biopsy provides tissue that can be used to determine the cause, predict the prognosis, and direct the treatment. Renal tissue obtained by biopsy has contributed enormously to the field of Nephrology. In 1934 it was Ball who performed the first closed needle biopsy with an aspiration device.[1,2] In 1954 Kark and

Muchrecke performed percutanous renal biopsy using intravenous pyelography[3]. Because of exposure to radiation in pyelography, many modifications in technique for localization of kidney have been described, including ultrasound marking prior to biopsy, continuous ultrasound guidance with the help of transducer and use of C.T scan in massive obese patients.

Similarly modification of percutanous biopsy needle from Menghini needle, Vim Silvermann and its Franklin modification (Tru-cut), to automated spring loaded gun have increased the yield of successful biopsies from 60% to 90% with associated minimal complications. Recently there has been a major shift towards utilization of spring-loaded disposable gun devices. In addition to percutanous and open renal biopsy, transjugular and even laproscopic renal biopsies are being carried, where indicated.

A close correlation has been established in diseases affecting kidney diffusely, such as glomerulopathies, and percutanous renal biopsy. Renal biopsy is indicated in a patient with renal disease when all the three following conditions are met;

1) The cause cannot be determined or adequately predicted by less invasive diagnostic procedures.
2) The signs and symptoms suggest paranchymal disease that can be diagnosed by pathological evaluation and
3) The differential diagnosis includes diseases that have different treatments, and different prognosis.

Contraindication to renal biopsy include an uncooperative patient, solitary kidney, hemorrhagic diathesis, severe hypertension, severe anemia, cystic disease, hydronephrosis, acute pyelonephritis / perinephric abscess, renal neoplasm and ESRD.

It is a safe procedure in experience hands but still complications do occur; including gross haematuria in < 10% of patients, arteriovenous fistula < 1%, hemorrhage that require surgery in < 1% and mortality in 0.1%.[4]

The objective of this study was to find out the frequency of different glomerulopathies in the adult population of this region. We also wanted to determine the safety profile of this invasive procedure.

MATERIAL AND METHODS

This retrospective study was carried out in the department of Nephrology at Khyber Teaching Hospital Peshawar, over a period of 3 years (June 1999 till June 2002). A total of 260 renal biopsies were performed during this period. To determine the frequency of different glomerulopathies in middle age population having significant proteinuria due to renal diseases, we used strict inclusion and exclusion criteria, as per following details.

Inclusion criteria;

1. Nephrotic range proteinuria in adults.
2. Non-nephrotic range proteinuria with evidence of hypertension / haematuria / deranged renal function or active sediments on urine microscopy.
3. Patients having age equal to or above 40 years.

Exclusion criteria;

1. Age less than 40 yrs.
2. Long standing diabetics with proteinuria (>7 years for IDDM and >5 years for NIDDM).
3. Bilateral small echogenic or scared kidneys and chronic renal failure.
4. Adult Polycystic Kidney Disease and congenital nephritis.

All patients who met the above mentioned criteria were included in this study. Blood pressure, PT / APTT, Platelets count, 24 hrs urinary protein estimation, HBs antigen, Anti HCV antibodies and abdominal ultrasound were scrutinized of all the included cases.

Real time ultrasound guided renal biopsies were done. Spring-loaded disposable percutanous biopsy needle was used in all the patients (16G for adults).

Biopsy material was fixed in 10% buffered formaline and was sent for histopathology to Agha Khan Clinical Laboratory with relevant information. Biopsy containing only tubules, interstitium and less then 5 glomeruli were considered inadequate for reporting purpose and excluded from the study.

RESULTS

A total of 260 renal biopsies were performed in our department during these 3 yrs. Out of these 56 cases fulfilled the inclusion criteria and hence selected for this study. In these 46 (82.14%) were male patients while only 10 (17.86%) were females. When gender related renal impairment causes were excluded, males significantly out numbered females in this series.

The mean age of the patients in our study was 47.03 ± 8.60 years (SD) with a range of 40 years to 75 years. The average duration of illness in this series was 9.4 months (ranging from 15 days to 10 years).

In the adult population having age above 40 yrs, the most frequent entity was membranoproliferative GN 11 (19.64%) cases followed by membranous GN 9 (16.07%) cases and tubulointerstial nephritis 8 (14.28%) cases. The next entities in frequency were focal segmental glomerulosclerosis and renal amyloidosis, each having 7 (12.5%) cases. (Table I)

Regarding the indications for renal biopsy in this series, the commonest cause was proteinuria alone accounting for 26 (46.4%) cases. The next commonest cause was proteinuria with deranged renal function 18 (32.1%) cases, and finally proteinuria with haematuria 12 (21.4%) cases.

The associated conditions that were encountered with different glomerulopathies in this series are summarized in table 2.

Also the presence of nephrotic range proteinuria versus non-nephrotic range proteinuria in different glomerulopathies are summarized in table 3.

Similarly in table 4, the association of impaired renal function with different entities are highlighted.

Pattern of Glomerulopathies in above 40 years old patients

No.	Type of Glomerulopathy	No. of patients	Percentage
1	Membranoproliferative GN	11	19.64%
2	Membranous GN	9	16.07%
3	Tubulointerstial Nephritis	8	14.28%
4	F.S.G.S *	7	12.50%
5	Amyloidosis	7	12.50%
6	Chronic interstitial Nephritis	4	7.14%
7	Crescentic GN	4	7.14%
8	Acute Tubular Nephritis	2	3.57%
9	Benign Nephrosclerosis	2	3.57%
10	Post Infective GN	2	3.57%
	Total	56	100%

* Focal Segmental glomerulosclerosis

Table -1

Associated conditions with different Glomerulopathies

Type of G.N	HBs	HCV	SLE	T.B.	COPD	URTI	TOTAL
Memb.Pro.GN* (n=11)			1				1
Membranous GN (n=9)	3	1	1				5
Amyloidosis (n=7)				2	3		5
FSGS** (n=7)			1				1
Post. Inf. GN*** (n=2)			1			1	2
TOTAL	3	1	4	2	3	1	14

Table -2

* Membranoproliferative glomerulonephritis
** Focal Segmental glomerulosclerosis
*** Post infective glomerulonephritis

DISCUSSION

Renal biopsy helps nephrologists in establishing accurate diagnosis, identifying any reversible pathology, helps in devising appropriate management plan for the patients and is very useful in understanding the histological nature of the disease. Currently renal biopsy is recommended and routinely done by the nephrologist to identify various types of renal lesions specially the glomerular diseases[5].

In the adult population (age >40 years) this series showed that the most frequently occurring glomerulopathy in our region is membranoproliferative GN, accounting for 11 (19.64%) cases closely followed by membranous GN 9 (16.07%) cases and tubulointerstial nephritis 8 (14.28%) cases. This is very similar to the pattern of glomerulopathy reported from PIMS Islamabad.[6] Muzaffar et al[7] has also reported that membranoproliferative GN is the leading cause of glomerulopathy followed by focal segmental glomerulosclerosis, which is quite in agreement with the finding of this series.

The audit report of renal biopsies at JPMC, Karachi, has shown that focal

Deranged renal function in different glomerulopathies

Glomerulopathy	Patients with deranged renal functions.	Percentage
Crescentic GN (n=4)	4	100%
Amyloidosis (n=7)	6	85.7%
* MPGN (n=11)	9	81.8%
** A.T.N (n=2)	1	50%
Chronic Interstitial Nephritis (n=4)	2	50%
Benign Nephrosclerosis (n=2)	1	50%
Tubulointerstitial Nephritis (n=8)	2	25%
Membranous GN (n=9)	2	22.2%
*** F.S.G.S (n=7)	1	14.2%
Post. Infective GN (n=2)	0	0%

Table -3

* Membranoproliferative glomerulonephritis
** Acute Tubular Necrosis
*** Focal Segmental glomerulosclerosis

Proteinuria as predictor of Glomerulopahy

Glomerulopathy	Proteinuria
	Patients with > 3gms / day
* Memb. GN (n=9)	9 (100%)
Amyloidosis (n=7)	6 (85.7%)
** F.S.G.S (n=7)	5 (71.4%)
*** A.T.N (n=2)	1 (50%)
**** Tubulointer Neph (n=8)	4 (50%)
Crescentic GN (n=4)	2 (50%)
***** M.P.G.N (n=11)	4 (36.3%)

Table -4

* Membranous glomerulonephritis
** Focal Segmental glomerulosclerosis
*** Acute Tubular Necrosis
**** Tubulointerstitial Nephritis
***** Membranoproliferative glomerulonephritis

segmental glomerulosclerosis is the most frequently occurring entity followed by membranous GN and minimal change disease.[8] While from Al Amiri Renal Center of Kuwait, it was reported that focal segmental glomerulosclerosis is the leading histopathological entity followed by minimal change disease and Ig A nephropathy in that region.[9] The reason for this might be that in both these studies the population sample included both young and elderly patients.

The association of different glomerulopathies with nephrotic versus non-nephrotic range proteinuria, the earlier finding by Yaqoob et al[10] from Rawalpindi, were also validated by similar findings in our study. They showed that membranoproliferative GN was the leading cause of non-nephrotic range proteinuria while membranous GN was mostly associated with nephrotic range proteinuria. We found that membranous GN is the commonest entity with proteinuria of more then 3 gm/day, followed by focal segmental glomerulosclerosis and renal amyloidosis. (Table 3).

More importantly the finding of deranged renal function in different entities, we found that almost all patients of crescentic GN and renal amyloidosis were associated with some degree of impaired renal functions (Table IV). The next commonest entity was membranoproliferative GN with more then two third of cases presenting with impaired renal function. In this series, as shown in the table IV, the tubulointerstitial nephritis, F.S.G.S, and membranous GN are rarely associated with significant renal dysfunction.

We could not find any significant number of mesangioprolifirative GN in this series (cases that were suspected of having post-infective GN were excluded from this study). Similarly we could not have any IgA nephropathy due to the lack of Immunofluorescence studies on the biopsy samples.

The associated conditions which we encountered in our study did show the already established fact that HBs antigen positive patients were more likely to have membranous GN but the new finding was a case of HCV positive patient with membranous GN. This might be chance finding and only a large population study can establish any firm association. The association of chronic obstructive pulmonary disease and pulmonary TB with renal amyloidosis implies that this is the most important cause of secondary amyloidosis in our country.

As different studies have shown, the risk of complications significantly reduces when biopsy is carried out by an expert person[4]. In the recent past spring loaded biopsy needle has been used to obtain renal tissue[11] because the technique have several advantages[12,13] including smaller size of needle, increased speed at which samples can be obtained with less bleeding complications, simple and easy to learn technique. This was also confirmed in this series, as our team encountered no major complications during the study period.

We conclude that in our adult population membranoproliferative GN is the leading histopathological entity followed by membranous GN. We also found percutanous renal biopsy to be a safe procedure, with adequate yield and providing histological diagnosis in most of the cases.

REFERENCES

1. Gwyn N B. Biopsies and the completion of certain surgical procedures. Med Assoc J 1923; 13:820.
2. Ball R P. Needle (aspiration) biopsy. J Tenn Med Assoc 1934; 27:203.
3. Pirani C R. Renal Biopsy: a historical perspective. In: Silva F D, Agati V, Nadasy T, editors. Renal Biopsy interpretation. New York : Churchill Livingstone, 1996:1-19.
4. Ori Y, Neuman H, Chagnac A, et al. Using automated biopsy gun with real-time ultrasound for native renal biopsy. Isr Med Assoc J 2002; 4: 698-701.
5. Reisman L, Dikman S, Churg J, et al. Renal Biopsy: why and when. Mt Sinai J Med 1996; 63 : 178-90.
6. Lakhnana N K, Khalid F, Khan H, et al. morphology of nephrotic syndrome in adults, An experience at PIMS, Islamabad. J Rawal Med Coll 2001; 5(2): 84-8.
7. Muzaffar M, Mushtaq S, Khadim M et al. morphologist pattern of glomerular diseases in patients with nephrotic syndrome in Northern Pakistan. Pak

Armed Forces Med J 1997; 47(1): 3-6.

8. Osmani M H, Farooqi S. An audit of Renal Biopsies. J Surg Pak 2001; 6(4): 28-30.
9. El-Reshaid W, El-Reshaid K, Kapoor M M, et al. Glomerulopathy in Kuwait: The spectrum over the past 7 years. Renal Failure 2003; 25 : 619-30.
10. Yaqoob N, Malik J M, Latif N, et al. An audit of renal biopsies. Rawal Med J 2000; 3:13-5.
11. Kovalik EC, Schwab SJ, Gunnells JC, et al. No change in complication rate using spring loaded gun compared to traditional percutaneous renal allograft biopsy techniques. Clin Nephrol 1996; 45 : 383-5.
12. Wiseman DA, Hawkins R, Numerow LM, et al. Percutaneous renal biopsy utilizing real time, ultrasonic guidance and a semi automated biopsy device. Kidney Int 1990; 38 :347-9.
13. Dowd PE, Mata JA, Crow A, et al. Ultrasound guided percutaneous renal biopsy using an automatic core biopsy system. J Urol 1991; 146 : 1216-7.

Address of correspondence:
Dr Nisar Anwar
Associate Professor and Head
Department of Nephrology, Khyber Teaching Hospital,
Main Jamrud road, Peshawar. NWFP