

## HISTOPATHOLOGICAL PATTERN OF GLOMERULAR LESIONS ON PER-CUTANEOUS RENAL BIOPSY IN PROTEINURIC PATIENTS

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### ABSTRACT

**Objective:** To determine the histopathological pattern of glomerular lesions on per-cutaneous renal biopsy in patients presenting with proteinuria.

**Study Design:** Cross-sectional descriptive study.

**Place and Duration of Study:** Department of Medicine, Combined Military Hospital Peshawar, from Aug 2012 to May 2015.

**Material and Methods:** From the adult patients undergoing renal biopsy for various indications in our department, we selected a cohort of 200 patients who had proteinuria of  $\geq 1$  gram/24 hours on presentation. A percutaneous renal biopsy was performed in these patients and the specimens were subjected to histopathology and immunofluorescence studies. The results of biopsy findings were considered along with other clinical and laboratory data to reach conclusive clinico-histopathological diagnoses of various glomerular diseases.

**Results:** Most patients with proteinuria (91%, n=182) have glomerular disease. Among glomerular diseases, primary ones are more common (69.8%) than secondary disorders (26.9%). In our study cohort, focal segmental glomerulosclerosis is the most common diagnosis (23%), while lupus nephritis the most common secondary glomerular disorder (7%). Other common glomerular disorders are membranous nephropathy (12%), IgA nephropathy (9%), and post-infectious glomerulonephritis (6%).

**Conclusion:** Glomerular disease is common in patients presenting with proteinuria. Its histopathological pattern appears similar to that mentioned in many other studies of the region.

**Keywords:** Glomerulonephritis, Kidney disease, Proteinuria, Renal biopsy, Renal pathology, Urinalysis.

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### INTRODUCTION

Glomerular diseases (GD) are common in our as well as other countries of the world. They are associated with heavy burden of renal morbidity and mortality, and happen to be the leading cause of end stage renal disease (ESRD). In the absence of a national or regional renal biopsy registry, we lack the essential epidemiological data to formulate a comprehensive plan to manage the glomerular diseases and their long-term sequelae. In our healthcare system of meagre resources and limited nephrology services, there is a dire need for ways and protocols whereby these diseases can be detected and managed early. Proteinuria being the hallmark of glomerular disease can be

utilized as one basic laboratory parameter that is readily detectable on a urine dipstick test and can prompt a further investigation into the diagnosis of a possible glomerular disease<sup>1</sup>.

Importance of timely urinalysis in managing glomerular disease cannot be over emphasized<sup>2</sup>. Similar is the utility and cost-effectiveness of proteinuria screening in an emerging country like ours. Proteinuria is a marker of kidney disease, and it plays a role in screening, diagnosis, and monitoring. It is also an independent risk factor for cardiovascular events and progressive kidney disease<sup>3</sup>.

Nephrotic-range proteinuria is absolutely characteristic of glomerular disease. Asymptomatic proteinuria (<3.5 g/24 hrs) is much less specific and may occur with a wide range of renal and urinary tract conditions that must be excluded by clinical evaluation and investigation. As physiologic proteinuria does

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not exceed 150 mg/24 hrs for adults and 140 mg/m<sup>2</sup> for children, the fact remains that significant proteinuria will most commonly be seen in association with glomerular disease<sup>4</sup>.

Glomerular diseases generally present with variable degree of proteinuria, hematuria, hypertension, impaired renal function or ESRD. It can present as nephrotic syndrome (NS), nephritic syndrome, rapidly progressive renal failure (RPRF), acute kidney injury (AKI), chronic kidney disease (CKD), macroscopic hematuria (MH), as well as isolated proteinuria or hematuria. Clinical presentation of glomerular disease may not essentially conform to a given morphological GD<sup>5</sup>. That is why the diagnosis of glomerulopathies requires a close cooperation between clinicians and pathologists.

Renal biopsy has a fundamental role in the evaluation of proteinuric patients, their treatment and to assess prognosis. Since its introduction into clinical usage in the early 1950's, percutaneous renal biopsy is one of the most common and widely accepted invasive procedures for the diagnosis of renal diseases. It is safe, easy and convenient to perform, and has a high diagnostic yield with few complications. Although immunofluorescence and electron microscopy have important role in the study of renal pathology, most of the glomerulonephritides can still be diagnosed by light microscopy with reproducibility<sup>6</sup>.

The incidence of glomerulonephritis varies according to the population characteristics, environmental factors, socioeconomics and prevalence of infectious diseases. In addition, the incidence varies according to the detection level of urinary findings, the biopsy resources of the community and the biopsy policy whether liberal or strict. As not all patients with renal disease are biopsied, the rate of biopsy-proven renal diseases underestimates their true prevalence. The incidence rates vary in different countries. Changing incidence of glomerular diseases over time has been noted in different communities

possibly due to genetic and environmental factors<sup>7</sup>.

Since renal biopsy has a pivotal role in the assessment and management of proteinuric patients therefore we aim to determine the histopathological pattern of glomerular lesion by percutaneous renal biopsy in proteinuric patients.

## **MATERIAL AND METHODS**

This descriptive cross-sectional study was performed at the Department of Medicine, Combined Military Hospital Peshawar from August 2012 to May 2015. Our sample comprised a cohort of 200 patients having proteinuria of  $\geq 1$  gm/24 hours on presentation, selected with simple random sampling technique from all the patients undergoing renal biopsy for various indications in our department during the study period. Essential inclusion criterion was the presence of proteinuria of  $\geq 1$  gm/24 hours on presentation; this being our cut-off value as lesser degrees of proteinuria can occur due to non-glomerular causes. Exclusion criteria comprised a bleeding diathesis, a single functioning kidney, small kidneys, multiple cysts, urinary tract infection, non-compliance to advice, longstanding diabetes or hypertension, evident myelomatosis and renal transplant.

Data collection procedure started after the study protocol was approved by the medical ethics committee of the hospital. A written informed consent was obtained from the eligible patients for inclusion in this study and to undergo a per-cutaneous renal biopsy. Both male and female patients aged 13 years and above were included. Their demographic data, detailed medical history and findings of physical examination and laboratory data were recorded. Clinical features in various subjects included hematuria, renal failure, nephrotic and nephritic syndromes, systemic disease with evidence of renal involvement, edema and presence of urinary abnormalities. Investigations relevant to their clinical conditions were performed that generally included basic hematology, biochemistry and urinary parameters,

complement levels, auto-immune profile, anti-neutrophil cytoplasmic antibodies (ANCA), anti-nuclear antibodies (ANA), ASO titers and virology tests for hepatitis B and C. The 24 hour urine for protein excretion was the method used for quantification of proteinuria; this being the gold standard method for this purpose.

Renal biopsy samples were obtained by a percutaneous method using a spring-loaded Trucut® biopsy needle under real time ultrasound guidance. Two renal biopsy samples were taken from each patient, which were processed for light microscopy and immunofluorescence studies. Electron microscopy was not performed in any case because of its non-availability. All specimens were analyzed at a single center by expert pathologists. The number of glomeruli, a

histopathological diagnosis was given in almost all cases.

Data analysis were carried out using SPSS® Statistics for Windows version 20. Descriptive statistics were used to find out results. Categorical variables were expressed as frequencies and percentages. Mean and SD, were calculated for quantitative variables.

**RESULTS**

Over the period of study we analyzed the renal biopsies of a cohort of 200 adult patients having proteinuria of ≥1 gram/24 hours on presentation. There were 114 male (57%) and 86 female subjects (43%) with a male to female ratio of 1.325. Mean age of the patients was 37.45 ± 15.16 years ranging from 13 to 73 years.

Glomerular histopathological changes were

**Table: The Histopathologic diagnoses, abbreviations, their frequency and percentages for total number of biopsies as well as gender-wise pattern.**

Histopathological Diagnosis	Total n (%)	Male n (%)	Female n (%)
Focal segmental glomerulosclerosis (FSGS)	46 (23)	26 (23)	20 (23)
Normal histology (Normal)	18 (9)	11 (10)	7 (8)
Minimal change disease (MCD)	9 (4.5)	5 (4)	4 (5)
Membranous nephropathy (MGN)	24 (12)	15 (13)	9 (10)
Iga Nephropathy (IgAN)	18 (9)	13 (11)	5 (6)
Membranoproliferative glomerulonephritis (MPGN)	14 (7)	8 (7)	6 (7)
Lupus nephritis (LN)	14 (7)	0 (0)	14 (16)
Post-infectious Glomerulonephritis (PIGN)	12 (6)	9 (8)	3 (3)
Amyloidosis (Amy)	12 (6)	6 (5)	6 (7)
Crescentic glomerulonephritis (CresGN)	8 (4)	5 (4)	3 (3)
Mesangial proliferative glomerulonephritis (MesPGN)	8 (4)	6 (5)	2 (2)
Vascular nephropathy (VN)	8 (4)	3 (2)	5 (6)
Chronic glomerulosclerosis (CGS)	6 (3)	4 (4)	2 (2)
Light chain deposition disease (LCDD)	2 (1)	2 (2)	0 (0)
Total	200 (100)	114 (57)	86 (43)

description of the main findings and a morphological diagnosis was given by the pathologist. The renal biopsy findings were considered along with other clinical data with the aim to clinically define certain typical glomerular disease patterns. Thus a unified clinico-

found in most renal biopsies (86.5%, n=173). Twenty seven (13.5%) biopsies were reported normal on light and IF microscopy. From this sub-group of normal looking biopsies, 33.33% (n=9) were associated with nephrotic range proteinuria and were thus labelled as minimal

change disease (MCD). Rest showed sub-nephrotic proteinuria from treatment naïve patients and also did not reveal a particular cause of proteinuria on usual evaluation. These biopsies were considered to be normal (66.66%, n=18). Number of patients suffering from GD, thus, was 182 (91% of all biopsy patients).

Among the 182 cases with GD, 69.8% (n=127) cases were due to primary causes, which accounted for 63.5% of the total biopsies in our cohort of proteinuric patients. Focal segmental glomerulosclerosis (FSGS) was the leading histopathological diagnosis, found in 23% (n=46) of all biopsies, followed by membranous glomerulonephritis (12%, n=24). There were six cases of chronic glomerulosclerosis (CGS) (3.3%) which could not definitely be attributed to a primary or secondary etiology.

Secondary glomerular disease (n=49) accounted for 24.5% of the total biopsies or 26.9% of all glomerular diseases. Here, lupus nephritis was the commonest secondary GN (28.6%, n=14) followed by amyloidosis (24.5%, n=12). Among the total 14 cases of LN, 64.3% (n=9) showed diffuse proliferative glomerulonephritis (class IV) and 35.7% (n=5) cases showed MN (class-V) changes. All the cases were seen in adult females with features of NS in 12 (85.7%).

Vascular nephropathy (VN) was found in 4.4% (n=8), whereas post-infectious GN was present in 6.6% (n=12) of all GD.

Various types of glomerular diseases determined in our study, their frequency and percentages, both total and gender-wise are shown in table.

## DISCUSSION

This study highlights a high incidence of glomerular diseases as well as a diverse histopathological pattern in patients having proteinuria on presentation. This cohort of proteinuric patients was selected from all our patients undergoing renal biopsy for various indications. The study population is a heterogeneous one in terms of demographic data

as our hospital receives patients from all over the province as well as other parts of the country. There exist several biases including socioeconomic, geographical, climatic and racial characteristics. However the strengths of our study were our liberal biopsy policy, and the uniform protocols for biopsy indications, analysis of clinical syndromes and the histopathological evaluation of biopsy. Results of this report cannot be generalized and it cannot by any means be representative of a national epidemiological study of the biopsy-proven renal diseases.

Male predominance was obvious in our study except in the case of LN that was seen exclusively in females, and VN with a female-to-male ratio of 1.6. This reflects the increased prevalence of LN in the female population. All recently published studies worldwide show a similar pattern<sup>8</sup>.

FSGS was the commonest of all GD as well as the most common cause of NS in our study. This is in agreement with many studies reported from our region<sup>9</sup> and other countries<sup>8,10</sup>. A worldwide increase has been noted in the incidence of FSGS despite racial variations<sup>11</sup>.

The vascular and hereditary diseases were less frequent in our and almost all other studies<sup>8</sup>. We could not find a case of thin basement membrane disease (TBMD) or Alport syndrome obviously due to lack of requisite diagnostic facilities.

There were 12 cases of renal amyloidosis, all in the age group of 40-60 years with equal number of males and females. These cases were associated with chronic inflammatory conditions like tuberculosis, bronchiectasis and rheumatoid arthritis as reported by another study from Pakistan and other countries<sup>9</sup>.

There are not data available on true incidence of glomerular diseases in Pakistan and there have been conflicting reports from Pakistani studies whether our data of various GN incidences coincides with that from other countries<sup>9,12</sup>. Reason for this discrepancy may be the fact that some centers have strict biopsy

criteria and obtain a biopsy only when the pathology would alter the therapy while other centers have liberal biopsy policy and try to establish an early specific diagnosis, whenever there is evidence of kidney disease on urinalysis<sup>13</sup>.

Although our data may not be a true reflection of the histopathological pattern of renal diseases in our region, this study fulfils the purpose of our objective as well as highlights usefulness of proteinuria screening for diagnosing glomerular diseases. A proactive approach is required for identification of glomerular diseases especially in patients harboring a risk factor like proteinuria. Provision of optimum diagnostic facilities at hospitals, and establishment of a national renal biopsy registry are recommended to know the true incidence of glomerular diseases. Collection of data relating to renal biopsies in a national registry is a useful tool for nephrologists in that it will allow epidemiologic studies for both prevention and treatment of renal diseases<sup>14,15</sup>.

## CONCLUSION

Glomerular disease is common in patients presenting with proteinuria. Its histopathological pattern appears similar to that mentioned in many other studies of the region.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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