# MORPHOLOGICAL PATTERNS OF GLOMERULONEPHRITIS IN MALES: A MULTICENTRE STUDY

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## ABSTRACT

Background: Glomerulopathies present in a variety of clinical signs and symptoms. This study was designed to determine the histological pattern of glomerulopathy in male patient presenting with proteinuria, haematuria and deranged renal functions.

Materials and Methods: A total of 111 consecutive male patients of nephritic and nephrotic syndrome (both children and adults) were included in the study. After clinical evaluation, baseline investigations and taking into consideration the inclusion criteria of male gender only these cases were selected for this particular study. They were taken from Sheikh Zayed Hospital, Children Hospital, Services, Fatima Memorial and Jinnah Hospitals Lahore.

Results: Among the selected renal biopsies, 111 (100%) were males. The minimum age at biopsy was 02 years and maximum was 73 years. Among the 111 patients microscopical haematuria was present in 51 (45.9%) and macroscopical haematuria in 19 (17.1%) patients. Duration for haematuria was 01 – 24 months. Proteinuria was present in 107 patients, among them 45 (40.5%) had < 2 g / day while 62 (55.9%) had > 2 g / day. Duration for proteinuria was 1 – 24 months. Diabetes mellitus and documented in 15 (13.51%) patients. Out of 111 patients 48 (43.2%) had hypertension. Predominant histomorphological patterns were mesangial proliferative nephritis (focal mesangial proliferative nephritis 14 (12.6%) and diffuse mesangial proliferative nephritis 13 (11.7%), End Stage renal disease, focal segmental glomerulosclerosis, minimal change disease followed by amyloidosis, membranoproliferative glomerulone-phritis, membranous glomerulopathy, chronic transplant rejection, diabetic nephropathy and rapidly progressive glomerulonephritis found on renal biopsy.

Conclusion: In adult population mesangial proliferative glomerulonephritis is the leading histopathological entity in our set up followed by end stage renal disease. In children mesangial proliferative glomerulonephritis is the most commonly encountered glomerulopathy followed by minimal change disease and diffuse proliferative glomerulonephritis. Renal biopsy helps the nephrologists to find out the original histopathology for accurate diagnosis leading to enhanced management plan.

Keywords: Glomerulonephritis, mesangial proliferative glomerulonephritis, amyloidosis.

## INTRODUCTION

Glomerulonephritis is a group of diseases that damages the glomeruli. When the kidney is injured, it cannot get rid of wastes and extra fluid in the body. If the illness continues, the kidneys may stop working completely, resulting in renal failure.<sup>1</sup> Glomerular diseases present in variable manners ranging from asymptomatic proteinuria and haematuria, acute nephritis, acute renal failure, nephrotic or nephritic syndrome, rapidly progressive nephritis which ultimately progresses to chronic renal failure.<sup>2</sup> The incidence of glomerulonephritis varies according to the population, genetic and demographic characteristics, environmental factors like climatology, socio-economics, prevalence of infectious diseases and time period. In addition, the incidence varies according to the detection level of urinary

findings, the biopsy resources of the community and the biopsy policy which are reflected as the biopsy rate.<sup>3</sup> The introduction of renal biopsy transformed the study of renal diseases, particularly glomerular diseases, by providing the histological information that helps in the classification of renal diseases and insight into pathogenesis. Renal biopsy is a safe and informative technique that has played a key role in the evolution of nephrology as a specialty. The most common pathological problems encountered in biopsy samples from native kidney specimen are of glomerular diseases.<sup>4</sup> Glomerulonephritis is usually divided into primary and secondary according to whether the causes are known or unknown. Primary glomerular diseases are more frequent in males (55.1%) than in females; on the other hand, secondary glomerular diseases are more

frequent in females (71.8%) and are associated with different diseases.  $\!\!^5$ 

## MATERIALS AND METHODS

This study was conducted in the Department of Morbid Anatomy and Histopathology, at University of Health Sciences, Lahore. A detailed history, socio-demographic information physical and systemic examinations were performed. Serum, creatinine, urinalysis results, ASO titre, ANF, anti-DNA, serum complement levels ( $C_3$  and  $C_4$ ), serum IgA level, creatinine clearance were carried out wherever it was possible. One hundred and eleven consecutive male patients of nephritic and nephritic syndrome, both children and adult, were included in the study.

Renal biopsies were taken by well trained nephrologists after consent from the patients and / or parents of the patient (under 18 years of age). Samples were collected from the department of Nephrology Institute of Child Health and Children Hospital, Services Institute of Medical Sciences, Fatima Memorial Hospital, Jinnah Hospital and Sheikh Zayed Hospital, Lahore. Cores of renal biopsies were obtained from each patient under real - time ultrasound guidance to localize the kidney, using a needle biopsy gun. The core for light microscopy was preserved in 10% formol saline. The biopsies were stained with H&E, JMS, and Masson trichrome, whenever there was a disagreement between the two persons viewing the slides were reviewed by another senior person until the consensus was reached.

## RESULTS

Among these 111 renal biopsies, all (100%) were males. They were selected from different hospitals of Lahore.

The minimum age at biopsy was 02 years and maximum was 73 years, mean  $\pm$  S.D of age was 28.92  $\pm$  17.16. The age distribution showed that patients



Fig. 1: Photomicrograph of Diffuse mesangial proliferative glomerulonephritis showing two glomeruli.



Fig. 2: Photomicrograph of Membranous nephropathy shows a glomerulus with diffuse thickening of the glomerular capillary basement membrane (H&E).



Fig. 3: Photomicrograph of amyloidosis shows glomeruli stained with congo red and examined by light microscopy, showing characteristic salmon-colored deposits of amyloid (Congo red).

below 12 years were 22 (19.81%) showing mean ± S.D of 6.55 ± 2.93 and above 12 years of age were 89 (80.18%) with mean ± S.D of 34.45 ± 14.50. Among 111 patients microscopical haematuria was present in 51 (45.9%) and macroscopical haematuria in 19 (17.1%) patients. Duration for haematuria was 01 - 24 months with mean  $\pm$  S.D of 5.93  $\pm$  4.68. Proteinuria was present in 107 patients, among them 45 (40.5%) had < 2 g/day while 62 (55.9%) had > 2 g/day proteinuria. Duration for proteinuria was 1 – 24 months with mean  $\pm$  S.D of 5.41  $\pm$  4.05. Diabetes mellitus was documented in 15 (13.51%) patients. Among 111 patients 48 (43.2%) were detected to have hypertension. Four patients had underwent kidney transplant. Ten (9%) of 111 patients gave history of blood transfusion. Serum IgA level was raised in 14 (12.61%) patients, serum ANA and Anti dsDNA were raised in 7 (6.30%) pati-

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Fig. 4: Photomicrograph of ESRD in a glomerulus showing chronic inflammatory cells in the stroma and thickened blood vessels H&E.

ents. Eighteen (16.21%) patients were anti-hcv positive and 8 (7.20%) were HBs antigen positive. Four patients (3%) gave a history of blood transfusion while 1 (0.8%) had a shrunken liver. Jaundice was not documented in any patient. Among 111 renal biopsy cases, 11 (9.9%) were diagnosed as minimal change disease, 8 (7.2%) were diagnosed as membranoproliferative glomerulonephritis, 27 (24.3%) were mesangial proliferative nephritis (focal mesangial proliferative nephritis 14 (12.6%) and diffuse mesangial proliferative nephritis 13 (11.7%), focal segmental glomerulosclerosis 13 (11.7%), membranous glomerulopathy 7 (6.3%), amyloidosis 10 (9.0%), diabetic nephropathy 3 (2.7%), chronic transplant rejection 4 (3.6%), diffuse proliferative glomerulonephritis 8 (7.2%), end stage renal disease 18 (16.2%) and rapidly Progressive Glomerulonephritis 2 (1.8%).

In all the 111 patients, the minimum serum creatinine was 0.30 mg/dl and maximum serum creatinine was 205 mg/dl with a mean  $\pm$  S.D of serum creatinine was 5.20  $\pm$  19.41 mg/dl. The minimum serum bilirubin in the 111 renal biosies was 0.17 mg/dl and maximum serum bilirubin was 0.48 mg/dl with a mean  $\pm$  S.D of serum bilirubin was 0.380  $\pm$  0.12 mg/dl.

The minimum serum albumin was 1.80 g/dl and maximum was 6.10 g/dl with a mean  $\pm$  S.D of 3.62  $\pm$  1.59 g/dl. The normal value for serum albumin was 3.4 - 5.4 g/dl. The minimum serum transaminase value was 0.40 U/L and maximum serum transaminase was 55.0 U/L with a mean  $\pm$  S.D of serum transaminase being 27.74  $\pm$  15.61 U/L.

All the biopsies, in addition to the Haematoxylin – eosin stain with Periodic acid Schiff's reaction (PAS) to view the mesangial matrix, potential expansion in matrix, mesangial cells, alterations in basement membrane and vessels, Congo red to visualize amyloid deposits, Masson's trichrome to see the extent of fibrosis and Jones Methenamine silver stain for the detection of change of GBM. The results were as follows:

Diagnosis on Renal Biopsy	Patients	%
Minimal Change Disease	11	9.9
Mesangial Proliferative Nephritis	27	24.3
Focal Segmental Glomerulosclerosis	13	11.7
Membranoproliferative glomerulonephritis	8	7.2
Membranous Glomerulopathy	7	6.3
Amyloidosis	10	9.0
Diabetic Nephropathy	3	2.7
Chronic Transplant Rejection	4	3.6
Diffuse Proliferative Glomerulonephritis	8	7.2
End Stage Renal Disease	18	16.2
Rapidly Progressive Glomerulonephritis	2	1.8

	Frequency	Percent	Valid Percent	Cumulative Percent
Minimal Change Disease	3	13.6	13.6	13.6
Mesangial Proliferative Nephritis (both local and diffuse pattern)	11	50.0	50.0	63.6
Focal Segmental Glomerulosclerosis	1	4.5	4.5	68.2
Membranoproliferative Glomerulonephritis	2	9.1	9.1	77.3
Diffuse Proliferative Glomerulonephritis	3	13.6	13.6	90.9
End Stage Renal Disease	1	4.5	4.5	95.5
Rapidly Progressive Glomerulonephritis	1	4.5	4.5	100.0
Total	22	100.0	100.0	

*Histopathological Diagnosis of Patients under 12 Years of Age* 

Biopsies of patients under 12 years of age showed the following morphological patterns on light microscopy.

# DISCUSSION

Renal biopsy helps nephrologists in establishing accurate diagnosis, identifying any reversible pathology, helps in practicing appropriate management plan for the patient and is very practical in understanding the morphological nature of the disease.

The most common histopathological lesion in pediatric population (age < 12 years) in our series is mesangial proliferative glomerulonephritis (50%). This is in contrast to study conducted by Moorani and Sherali<sup>6</sup> in Karachi.<sup>6</sup> According to them Overall, minimal change disease and focal segmental glomerulosclerosis are the two most common in primary glomerular disease and both dominated in primary nephrotic syndrome whereas mesangioproliferative glomerulonephritis accounted for 7.62% of all biopsies and 8.13% among primary nephrotic syndrome. According to Hafeez and Rasool, mesangioproliferative GN is the leading entity followed by membranoproliferative GN is the leading entity followed by membranoproliferative GN and minimal change disease.<sup>7</sup>

In this study minimal change disease and diffuse proliferative glomerulonephritis constitute 13.6% biopsies from patients less than 12 years of age. This is also not comparable to that reported by Farida and Azhar.<sup>8</sup>

In the adult population this series showed that the most frequently occurring glomerulopathy in our region is ESRD (19%). Chronic kidney disease (CKD) and end - stage renal disease place an immense strain on the health - care system in any society. Poor control of hypertension and diabetes mellitus also contribute in early glomerulopathy. In our study 48 (43.2%) had hypertension and 3.4% patients were diagnosed as suffering from diabetic nephropathy. Treatment of ESRD is a low priority for the cash – strapped public hospitals and in the absence of health insurance plans. Patients are generally younger at the time of detection of ESRD and two - thirds first see nephrologists after they have reached end stage. The vast majority of patients starting hemodialysis dies or stop treatment because of cost limitation within the first three months. The incidence of ESRD is likely to be higher than that reported from the developed world, with chronic glomerulonephritis being the most common cause, accounting for more than one third of patients, while diabetic nephropathy accounts for about one fourth of all patients in India. Although renal transplantation is the cheapest option, only about 5% of all patients with ES-RD end up having a transplant. However increasing awareness of renal disease amongst the population and general practitioners could result in early diagnosis of chronic renal failure and give opportunity for preventive strategies to delay the onset of ESRD.9

In adults second most common cause is mesangial proliferative glomerulonephritis followed by focal segmental glomerulosclerosis. Audit of renal biopsies at JPMC, Karachi has shown that focal segmental glomerulosclerosis is the most frequently occurring entity followed by membranous glomerulonephritis and minimal change disease.<sup>10</sup> Muzaffar et al, has reported that membranoproliferative GN is the leading cause of glomerulopathy followed by minimal change disease and focal segmental glomerulosclerosis, which is moderately in agreement with the finding of this series.<sup>11</sup>

Our study revealed high occurrence of biopsy proven renal amyloidosis. In this study amyloidosis was confirmed in 11.2% biopsies microscopically, and all the glomeruli showed widening of mesangial matrix and a diffusely thickened glomerular basement membrane (GBM) with amorphous hyaline deposits. There was no remarkable glomerular hypercellularity. The walls of some arterioles were also thickened with bulky hyaline deposits. The deposits found in the mesangium and arterioles were positively stained after Congo red, and showed apple - green birefringence with polarized light. However, United Arab Emirates and Italy also reported a high incidence of amyloidosis.12 High incidence of renal amyloidosis in Pakistan is probably due to the high prevalence of tuberculosis and other infectious diseases.13-17 However; we had performed renal biopsy only on unsuspected cases of amyloidosis.

Significant differences in morphological patterns have been observed in our study.

Glomerulonephritis constitutes a burden on the already over wrought health services in the developing countries. Early diagnosis and treatment can prevent long – term complications. Renal biopsy is a safe and informative technique that has played a key role in the evolution of nephrology as a specialty. The study had limitations in terms of sample size, since glomerulonephritis is not a very common disease. However a total of 111 male were found valuable enough for our study.

#### Conflict of Interest: None.

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